PPRS: The Study into the Extent of Competition in the Supply of Branded Medicines to the NHS

Department of Health and
the Association of the British Pharmaceutical Industry

December 2002

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Executive Summary

Background

An integral part of the current Pharmaceutical Price Regulation Scheme (PPRS) agreement that took effect on 1 October 1999 is a joint assessment by the Department of Health (DH) and the Association of the British Pharmaceutical Industry (ABPI) of the scope, pace of change and practical impact of competition in the supply and use of branded medicines for the NHS. The results of this study will be available to both the Government and the pharmaceutical industry in considering the future direction of policy on the PPRS.

The study comprised seven components and work on each of the components was undertaken jointly by DH and the ABPI. It covered the period up to 2000. Some elements of the analysis were contracted out to third parties. The study allowed an unprecedented level of shared data collection and analysis between DH and the branded pharmaceutical industry in the UK.

The full terms of reference for the study are set out at Appendix 1 of this report. In summary, these are as follows:

- *Establishment of key indicators*: required to monitor the conditions for an efficient and competitive pharmaceuticals market.

- *In-patent sector*: a study of some aspects of competition over the last five years in products on the market in the in-patent sector including a degree of substitutability between products, price differences between competing products, and the impact of new products entering the market.

- *Out-of-patent sector*: speed and availability and penetration of generics for products that have recently come off patent.

- *Demand-side effectiveness*: the effectiveness of the demand-side and the price sensitivity of prescribers.

- *International perspective*: prices in the UK, including new products compared to those in comparable countries.

- *The hospital sector:* assessment of the hospital market and the relationship between pricing in that market and the community.

- *Less regulated markets*: the experience in less regulated markets in the period under analysis such as the United States and Germany.

The results of the work undertaken for each of the components are set out in this report and are summarised below.

Competition in the branded pharmaceuticals market depends on:

- Supply-side factors – a range of actual or potential suppliers of any product, or range of alternative products from independent suppliers, so that prescribers and patients have a choice;

- Demand-side factors – information available to prescribers on the qualities and prices of products on offer and the operation of incentives and controls that influence prescribing decisions.

Overall the branded market in the UK is influenced by two significant factors that typically are absent in almost all other markets:

- The PPRS limits companies' ability to increase the prices of branded medicines. Companies are free to price individual products at the level they choose when they are introduced to the market. Thereafter companies may only obtain an increase in the overall level of their prices if their profitability falls below the target set out in the agreement. One of the historic effects of the PPRS, therefore, is the infrequency of price changes – many medicine prices remain fixed in nominal terms for many years, regardless of the rate of inflation or prices of competing products etc. More flexibility was introduced under the 1999 PPRS agreement but it is too early to assess this as it was only available for the last 15 months of the period studied. In addition as a global industry, pharmaceutical pricing strategies are developed with multiple markets in mind. Thus, UK pricing decisions cannot be divorced from the context of other international regulations and the impact on export market prices.

- The decision on the medicines required by the patient is made by the prescriber on the basis of an assessment of a patient's clinical need. Neither the prescriber nor the patient personally pays the cost of the medicine and the amount paid as a prescription charge where applicable is not related to the cost of the medicine received.

Over the years, the Government has introduced measures to increase prescribers' awareness of the cost of different medicines, but the costs of medicines dispensed are paid for by the Government.

Summary of principal findings

Analysis conducted as part of the study considered, in particular the extent of price competition across a wide range of medicines used by the NHS. Companies also compete to innovate and bring new medicines to the NHS and on other factors such as product efficacy and ease of use, but these were not included in the study.

Supply-side

The supply of branded medicines to the NHS comprises a significant number of therapeutic categories or sub-markets made up of individual medicines for the treatment of different conditions.

On the supply-side the principal findings of the study are that:

- Overall, the industry is not highly concentrated. The company with the largest aggregate share of the UK market has only 13% of the total community market for medicines, and the top 10 companies have less than 60% (Component 1, Section 2.1);

- 5 of the top 10 and 10 of the top 20 therapeutic categories (by sales value) in 2000 have one firm that supplies more than 40% of the sub- market (Component 1, Section 2.2) - the benchmark level of concentration below which the Office of Fair Trading (OFT) considers it unlikely that a company will have a dominant position. In total 61% of sub-markets had one firm supplying more than 40% of the sub-market, accounting for 56% of community sales (Component 1, Section 2.2). This is slightly lower than in 1995 when 64% of sub-markets had one supplier accounting for more than 40% of sales;

- Of the 11 'new' sub-markets studied the average time lag between the originator entering a new market and the second product appearing is 3 years, (varying between 0 and 9 years), with a third likely to appear within the year (Component 1, Section 2.3);

- Prices of later entries into a sub-market are usually lower than that of the incumbent, and their market shares generally increase over time while that of the originator declines. This suggests subsequent entries are seeking to compete on price. However, the fact that the first entrant seems to account for the majority of the sub-market even by the end of the sample period in most of the sub-markets studied suggests there is a first mover advantage. Component 2 found that in most sub-markets studied, the incumbent does not usually reduce its list price in response to subsequent entrants (Component 2, Section 4.5).

Demand-side

Research undertaken as part of the study indicates that doctors choose the drugs they prescribe primarily on the basis of their clinical efficacy, safety, tolerability and convenience to the patient, in that order. Although NICE guidance and other guidelines were found to influence prescribing decisions, it seems that only after all these considerations have been taken into account is the cost of the drug, and of alternatives, considered explicitly by the prescribers. Further, whereas the prescribers consider themselves to be reasonably well aware of comparative drug costs, they did not perform well in ranking the relative prices of many commonly used drugs (Component 1, Section 3.1 and Component 4, Section 3.2.2). There is little evidence that the various demand-side initiatives that have been implemented so far have established a significant response by prescribers to the relative prices of competing drugs (Component 2, Section 3.2).

The study was unable to find a well-defined relationship between price and volume. From the initial work undertaken as part of Component 2, it is unclear whether this was the result of data limitations (non-separation of new and repeat prescriptions), the lack of price changes which may have resulted from the perceived constraints of the PPRS or that no changes in prescribing behaviour are made in response to price changes. Subsequent analysis looked only at newly instigated prescriptions in nine therapy areas, but found a statistically significant negative relationship between price and volume in two therapeutic areas only.

For some drugs, when patent protection is lost, competition from generics develops. This is most likely to occur where the market is sizeable, the manufacturing process and product form are straightforward and there are no barriers to entry such as possible legal disputes (Component 3, Section 5). Community pharmacy reimbursement arrangements provide pharmacies with incentives to buy at the best price available and this can result in strong price

competition between generic medicine manufacturers. These incentives have encouraged discounting of both generics and brands in the post patent expiry market in the community sector (Component 3 Section1, Component 1 Section 5.8, Component 2 Section 3.2). Dispensing doctors also respond to incentives, for example in their use of branded generics. However, the brand headline price seldom reduces in response to competition from cheaper generic products (Component 2, Section 4.6), although some companies compete on the basis of discount allowed to wholesalers and community pharmacies.

Hospital sector

The hospital sector is responsible for 19% of total UK sales of branded pharmaceuticals. It is a little less concentrated than the community sector, with fewer categories having one company providing more than 40% of the category – for example, only three of the top ten markets have one firm supplying more than 40% of the market (Component 6, Section 2.2). It also makes greater use of generics than the community sector. Nearly half of sales to hospitals are in categories where hospital sales predominate. Hospitals are able to negotiate discounts on the prices charged in the community through tendering. The magnitude of discount varies across products and across trusts. The data suggest that discounts are larger where competing products, including generics, are available (Component 6). This suggests that price competition is a feature of parts of this market.

International comparisons

Comparing UK prices with those in other countries (Component 5) has some methodological difficulties – past exchange rates changes and the expected future exchange rate path affect the prices charged, as do variations in volumes of sales and presentation of the product, alternative institutional factors and differing regulatory regimes. A further factor is the difficulty of collecting "true" price data that reflect discounts that are key features of some markets. The results of the exercise show that:

- The 2000 weighted index, based on bilateral comparisons, and based on 2000 market exchange rates showed prices in the UK to be:
    - Significantly lower than those in the USA
    - Higher than those in the other European comparator countries

- However, if a longer-term five-year average exchange rate is used, prices in the UK are broadly comparable with Germany, Finland, Ireland and France and higher than the other European Union countries.

In the USA where there is a minimal level of medicine price regulation compared to Europe, medicine list prices increase by 3.5% to 5.5% per annum.

Conclusions

The supply of branded medicines to the NHS is not a conventional market. The role of the prescriber, the clinical needs of the patient and the responsibility of the Government to fund the cost of medicines as well as the operation of the PPRS are key factors in the operation of the market and of price competition. At the same time competition between branded pharmaceutical companies is not limited to price as they also compete on the basis of efficacy and ease of use. Companies also compete to bring new products to the market as quickly as they can in the patent life. This study looks at the extent of price competition only.

The definition of a 'market' within the context of branded medicines is not straightforward. It is clear that the supply of branded medicines to the NHS does not comprise a single market. Accordingly it is necessary to define markets for branded medicines as those that comprise medicines for the treatment of a specific condition. Within this definition companies with the first entrant may sometimes retain exclusivity in that market for a limited period of time only but this period varies considerably.

Overall the industry is not highly concentrated although some 60% of the therapeutic sub-markets examined by the study have a player with more than 40% market share - the benchmark level of concentration below which the Office of Fair Trading (OFT) considers it unlikely that a company will have a dominant position. This is despite the presence of more than one product in most markets. There is evidence that first entrants retain market share despite the entry later of cheaper products. Equally second entrants out-perform cheaper third entrants. On the demand-side prescribers rate cost below efficacy when making prescribing decisions and it is a matter of debate as whether the awareness of relative prices is high enough to stimulate price competition. It is too early to assess the impact of primary care trusts on prescribing behaviour. Generic prescribing is taking an increasing share of the market and there is some evidence of price competition in parts of the hospital sector.

As acknowledged above the operation of this market has been affected by the PPRS. However, where price changes have occurred, the study was unable to find consistent volume responses to such changes. Over half of price changes triggered no response from competitors. In the majority of cases, the launch of new products provoked no price response from competitor products.

The results of this study will be available to both the Government and the pharmaceutical industry in considering the future direction of policy on the supply and distribution of medicines to the NHS. Both the Government and the pharmaceutical industry remain committed to using competition where possible to obtain value for money from NHS medicines expenditure.

Component 1:

Performance Management Framework

December 2002

Component 1

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Component 1

Performance Management Framework

1. Executive Summary

Supply side indicators

The top ten firms in 2000 accounted for 58.8% of the branded pharmaceutical market, up from 48.1% in 1995 – recent mergers accounting for about seven percentage points of this increase. At the therapy class level there are 175 markets (61% of all markets), where one firm accounts for more than 40% of sales - the benchmark level of concentration below which the Office of Fair Trading (OFT) considers it unlikely that a company will have a dominant position. These markets account for 55.6% of Net Ingredient Cost (NIC). This is lower than in 1995 when 64% of markets had one supplier accounting for more than 40% of sales – these markets accounted for 57.6% of NIC.

The speed of entry of second and subsequent entrants into a particular class (or market) has a bearing on the scope for potential competition. An analysis of the time lags of subsequent entry of products for 11 new therapy classes that appeared between 1987 and 1999 found that the average time lag between the originator entering the new market and the second product appearing is 11 quarters, the values varying between 0 (for Leukotriene Receptor Antagonists) and 9 years (for Somatostatin Analogues).

Most subsequent entrants come into the market with a price discount relative to the incumbent. When prices are compared on the basis of modal strengths, based on weighted average prices, the discount offered by the second entrant relative to the incumbent is 11%. But when prices are compared on the basis of Defined Daily Dose (DDD), based on weighted average prices, the second entrant comes in at a price premium of 4%. DDD strengths are based on World Health Organisation estimates of prescribing practice across many countries and they do not necessarily coincide with prescribing patterns in the UK.

The originators' shares decline from their original dominant position, but only down to an average of 56% in quarter 40. The 11-market sample suggests that there is some degree of first-mover advantage although subsequent entrants will tend to be more numerous and have greater market shares in markets with higher NIC.

Price changes were constrained by the rules of the Pharmaceutical Price Regulation Scheme (PPRS) for much of the period under analysis but both price increases and decreases can and do take place. An analysis of the number of price changes as recorded by PCA data over the period 1991 Quarter 3 to 2001 Quarter 2 across a total sample of just over 500 products shows that the average number of price increases is 16.4 per quarter, 6.7 for high NIC products and 9.7 for low NIC products. The average number of price decreases is 18.1 per quarter, 8.8 for high NIC products and 9.3 for low NIC products. However, these price falls are disproportionately concentrated in quarter 4 of 1993 and quarter 4 of 1999, the time when the PPRS price reductions were implemented. Removing these two periods from the sample brings down the average number of price decreases over the period to 7.0 per quarter. There is a statistically significant downward trend in the number of price rises per quarter for high NIC products overall. The net cash impact over the period is negative at -£38 million, however, this is dominated by the 1993 and 1999 price reductions required under the PPRS. When these are excluded the net impact is positive, but small at about £5 million.

Demand side indicators

An analysis of GP knowledge of relative prices of products within five drug therapy classes based on face-to–face interviews with 200 GPs found that there is considerable variation in awareness across therapy groups. The overall average was for GPs to get 63% of pairwise choices between the prices of products in the same therapy class correct. However, in one market (SSRIs), the percentage of correct rankings is only marginally above 50%, which is what would be expected if GPs had no knowledge of price and simply guessed. It is, therefore, open to debate whether the overall average, at 63% is sufficiently high to allow us to conclude that there is sufficient price awareness to stimulate price competition. This analysis was highly sensitive to the inclusion or exclusion of one product (Dutonin – a product closely related to SSRIs). If Dutonin is included in the analysis the overall average correct response falls to 56% (44% for SSRIs).

Prescribing incentive schemes were first introduced into the NHS in 1995 and are intended to improve the quality and cost-effectiveness of prescribing. A survey conducted among 91 Primary Care Organizations (PCOs) showed that schemes had a number of different objectives. These included achieving cost savings through underspends on budget targets, meeting generic prescribing targets, reducing prescribing in specific therapy areas, e.g. anti-bacterial agents and achieving quality targets. It is too early to know what impact these schemes are having on GP prescribing behaviour.

Contextual Indicators

Over the period 1992 to 2000 the growth in expenditure (NIC) in the community sector averaged 8.7% per annum. The largest component of the growth in NIC was the product mix residual, which rose at an average rate of 5.4% per year. This takes account of both the shift from prescribing older, cheaper medicines to newer more effective but higher-priced ones, and countervailing effects of increased generic prescribing. The increase in the number of prescriptions and the quantity per prescription also made large contributions to the increase in NIC – taken together as an overall measure of volume, this grew by an average of 4.9% per year over the period. Prices fell over the period by an average of 1.8% per year reflecting price decreases for both branded medicines and generics.

There has been a significant increase in the proportion of prescriptions written and dispensed generically. Between 1991 and 2000 the proportion of prescriptions written generically has increased from 41% (27% by value) to 71% (62% by value) and the proportion dispensed generically has risen from 35% (14% by value) to 52% (22% by value).

The Department undertakes an annual price comparison of the best-selling branded medicines in the NHS with prices elsewhere in Europe and in the USA. The results published in the Fifth PPRS Report to Parliament showed that 'UK prices were in the middle range of the countries in this study over the period 1992 to 1996 but the UK's position has changed since 1996, largely as a result of sterling appreciation. For the countries for which we have 2000 data, the average sterling appreciation was 26% since 1996.

The 2000 weighted index, based on bilateral comparisons, and based on 2000 market exchange rates showed prices in the UK to be:

- Significantly lower than those in the USA;
- Higher than those in the other European comparator countries.

However, if a longer-term five-year average exchange rate is used, prices in the UK are broadly comparable with Germany, Finland, Ireland and France and higher than the other European Union countries.'

2. Introduction

2.1 Terms of Reference

The scope of Component 1 was defined as:

'To establish a set of key indicators aimed at monitoring the conditions for an efficient and competitive pharmaceuticals market. This will focus on demand-side measures, but will also include indicators for the areas covered by other components. The list of indicators will be developed in consultation, but will need to cover where relevant Primary Care Groups, NICE[1] and CHIMP[2]. Full use will be made of information already being collected by the Department. These indicators will provide a 'baseline' for assessing progress over the period of the new PPRS[3]. The Department will be mainly responsible for the completion of this work.'

2.2 The Rationale for Identifying Indicators

Competition in the branded pharmaceuticals market at any time depends on:

- Supply-side factors – a range of actual or potential suppliers of any product, or a range of substitute products from independent suppliers, so that prescribers and patients have an effective choice.

- Demand-side factors – prescribers who are well informed, knowledgeable about the qualities, profiles and prices of the products on offer, and have incentives to take account of differences in quality and price.

This indicator set is focused on the amount of competition, which may exist within the existing set of products, looking at both supply-side and demand-side factors. This is a separate issue to the competitive pressures that drive innovation and new product development. These pressures depend on intellectual property rights and the uptake of new medicines in the international pharmaceuticals market, of which the UK is only a small part. These major issues are being addressed separately and are outside the scope of the proposed indicator list.

1 National Institute for Clinical Excellence
2 Commission for Health Improvement
3 Pharmaceutical Price Regulation Scheme

The supply-side factors may be broken down into:

- Concentration of supply – where there are several rival suppliers of the same, similar or other substitute products, a market may be more competitive if it is not dominated by one or two large players.

- Ease of entry and exit for potential new suppliers. The rate of growth of the market is a relevant factor here: it may be easier to enter a rapidly growing market than a stagnating one. Also the speed with which first entrants into a new therapeutic area are followed by second and subsequent entrants can indicate the potential to challenge the first entrant by providing choice to prescribers. Whether these later entrants are successful in terms of achieving market share is also of importance.

- Extent of price changes, both on the entry of new products, looking at their pricing behaviour relative to the incumbent and more generally in terms of the degree of price changes within the market.

The demand-side factors covered by the proposed competition indicators have the following components:

- Ease or difficulty (cost) of acquiring information about products, and their substitutes, qualities and prices. In particular, GP knowledge of relative prices of products.

- Incentives to acquire and act on that information, e.g. budgets for prescribing and rewards/penalties for keeping to or breaking those budgets and the evidence to date on the nature of prescribing incentive schemes.

In addition to indicators of demand and supply-side factors determining whether the conditions for an efficient and competitive branded pharmaceuticals market are present in the UK, some contextual indicators are provided. To a certain extent some of these indicators can be viewed as indicators of the outcomes of those conditions i.e. indicators of the extent to which competition exists in practice. The contextual indicators are:

- the extent of the use of generics and the potential for use of generics in terms of rates of generic prescribing and dispensing.

- the drivers of growth in medicines expenditure.
- how UK pharmaceutical prices compare with those elsewhere in the world.

The indicators have, therefore, been divided into three sections:

1. Supply-side conditions.
2. Demand-side conditions.
3. Contextual indicators.

This mirrors the three-part structure that is being used for the Pharmaceutical Industry Competitiveness Task Force (PICTF) competitiveness and performance indicators, which are presented under the headings 'demand and regulatory conditions', 'supply conditions' and 'industry outputs'.

2.3 Data Sources

The indicators included in this report were either calculated from existing sources e.g. IMS data for UK community retail pharmacy purchases or Prescription Cost Analysis (PCA) data for prescriptions dispensed in the community in England or were created from the analysis or research conducted as part of components 2-7. No specific indicators were commissioned for this study.

3. Supply Side Indicators

3.1 Aggregate Company Concentration[4]

Concentration is a measure of the market[5] shares held by the top companies in a given market and has implications for the potential competitiveness of the market. In general terms, the greater the level of concentration the greater the potential for market dominance by one or two suppliers.

[4] This analysis excludes hospital sales.

[5] Defining a market is not a straightforward task. For ease of analysis a working definition at BNF sub-chapter level (or the next level up if sub-chapter is not available) has been assumed when defining a market. That is not to say that all products in each category will be substitutable and part of the same market, nor that products in different categories need never be substitutes and part of the same market.

Table 1 – Market Shares of Top Ten Companies, 2000

	Company	NIC (£m)	Market Share (%)	Cumulative Market Share (%)
1	GlaxoSmithkline	550	13.3	13.3
2	AstraZeneca	475	11.4	24.7
3	Pfizer	376	9.1	33.8
4	Merck Sharp & Dohme	250	6.0	39.8
5	Wyeth	237	5.7	45.5
6	Novartis	152	3.7	49.2
7	Pharmacia & Upjohn	106	2.6	51.8
8	Eli Lilly	100	2.4	54.2
9	Janssen-Cilag	100	2.4	56.6
10	Schering	91	2.2	58.8

The top ten companies in 2000 accounted for 58.8% of the branded pharmaceutical market, up from 48.1% in 1995 – recent mergers accounting for about seven percentage points of this increase. Mergers would not have been allowed to happen if there were competitive issues at the sub-market level.

3.2 Concentration Index at Market Level

In 2000, 5 of the top 10 and 10 of the top 20 markets (by sales value) have one firm that supplies more than 40% of the market. This is an increase on 1995 when the figures were 3 and 6 respectively. However, the overall position is more complex, there are 175 markets (61% of all markets), where one firm accounts for more than 40% of sales (see Table 2 below). These markets account for 55.6% of NIC. This is a little lower than in 1995 when 64% of markets had one supplier accounting for more than 40% of sales – these markets accounted for 57.6% of NIC - resulting in sub-markets that are less concentrated in 2000 compared to 1995. This suggests that companies may be competing with each other in a broader range of sub-markets in 2000 compared to 1995, although more than half of the market remains concentrated.

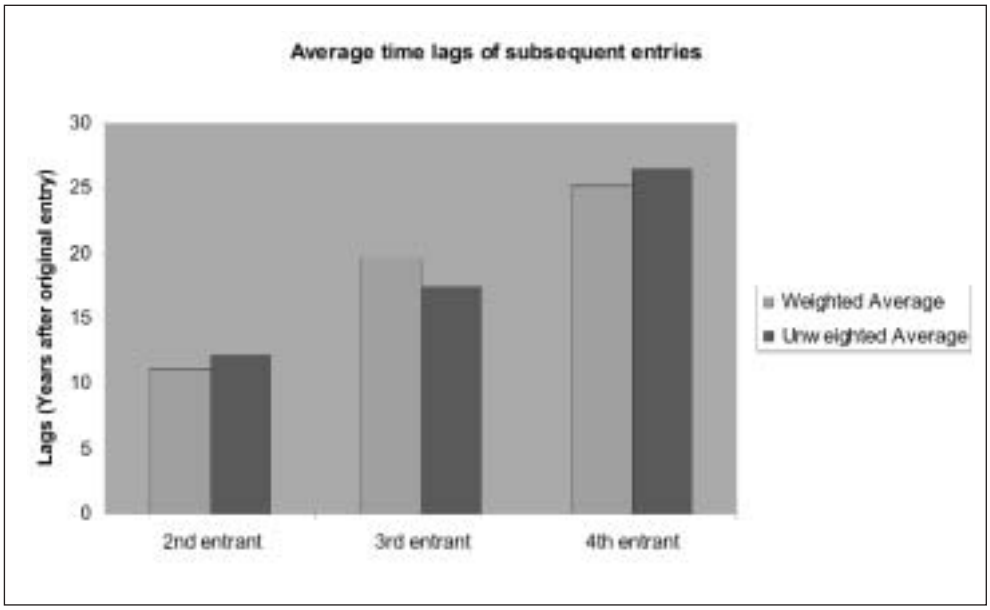
Table 2 – Value and Share of Sales by Concentration of Market, 2000

CR1	NIC (£m)	NIC Share	Number of Markets	% of Markets
1	24.0	0.5%	30	10%
>0.9	90.3	1.7%	47	16%
>0.8	416.5	7.9%	77	27%
>0.7	662.3	12.5%	96	33%
>0.6	1,040.0	19.7%	123	43%
>0.5	1,733.4	32.8%	151	53%
>0.4	**2,939.7**	**55.6%**	**175**	**61%**
>0.3	3,582.5	67.8%	192	67%
>0.2	4,091.7	77.4%	200	70%
>0.1	4,101.0	77.6%	201	70%
>0	5,283.5	100.0%	287	100%

3.3 Time Lag between First and Second Entry

The first product launched in a particular drug class will have a monopoly position and there will be little scope for competition. Competition can only really occur when further products come on the market although there maybe a degree of cross category competition. Therefore the speed of entry of second and subsequent entrants into a particular class (or market) clearly has a bearing on the scope for competition.

The time lags of subsequent entry of products into a market have been measured for 11 new markets (drug classes) that appeared between 1987 and 1999. See Appendix 6.3 and Table 8 for details of the 11 markets.



The average time lag between the originator entering the new market and the second product appearing is 11 quarters , the values varying between 0 (Leukotriene Receptor Antagonists) and 9 years (Somatostatin Analogues).

Third entry can be expected to occur with a time lag with respect to the originator of 20 quarters, the values varying between 8 (SSRIs) to 30 quarters (PPIs). Three out of the 11 markets do not register a third entry.

The time lag for the fourth entry is 25 quarters on average, the values varying between 11 (Angiotensin-II Receptor Antagonists) and 37 (Proton-Pump Inhibitors). Six out of the 11 markets did not register a fourth entry.

3.4 Market Share of Subsequent Entries

In general terms, the greater the market share that subsequent entrants take up, the more we can be confident that there is competition taking place.

This chart shows market shares for the originators and the 2nd, 3rd and 4th entrants. The series for each originator product are made to start at the same point in time (t=0), with the intent of capturing all markets at equivalent points in their life cycles[6]. Even after allowing for different launch dates in this way, the different length of the data series inevitably produces quirks and kinks, as certain markets drop out of the series[7]. The products launched at earlier dates will dominate the values towards the end of the time-series, as other markets progressively drop out. For that reason we only look at the evolution of the market in the first 40 quarters after launch, when most of the products are still included. The evolution of the curve after that point is not a good representation of the market share of each group of subsequent entrants.

The originators' shares decline from their original dominant position, down to 56% in quarter 40. Second entrants have a market share of 4% four quarters after entry, rising to 7% four years after entry. The average shares of third and fourth entrants change from 5% to 9% and 1% to

[6] This is the reason why the figures below are not completely consistent to the weighted averages that appear at table 8 in Appendix 6.3

[7] At launch the sample includes all markets. However some markets are relatively new, so they will not feature towards the end of the series – they have simply not been around long enough. For instance, the sharp change in the market share of originators and second entrants in quarter 10 coincides with the ending of the Cox II inhibitors series - this is simply because Cox II inhibitors had only been around for 10 quarters. Likewise, the kink experienced by the originators' market shares in quarter 26 is a consequence of the dropping out of the Angiotensin-II receptor antagonists market.

0.2% respectively. The share of third entrants appears to follow an upward trend until quarter 18, then it experiences a fall and a slight decline up to quarter 26. From then onwards it follows a moderate growth path. Fourth entrants experience a fall in quarter 24 but sustained growth afterwards, and by the end of the sample they have a higher market share than third entrants do. However, this difference could be biased upwards by the very high share (35% four years after launch) attained by one of the fourth entrants (Lipitor) in the sample.

By the end of the sample, each of the originator products remained the biggest seller in its market. Most of them (particularly the lower NIC ones) maintained a market share of more than 50%, and none of them had a market share of less than 40%.

The 11-market sample seems, therefore, to suggest that there is some degree of first-mover advantage and that subsequent entrants will tend to be more numerous and have greater market shares in markets with higher NIC. See Appendix 6.4 for charts tracing the market shares and relative prices of the products in each of the 11 markets.

3.5 Price of Subsequent Entries

Most subsequent entrants come into the market with a price discount relative to the incumbent. Based on weighted average price changes, the discount offered by the second entrant relative to the incumbent is 11%. This percentage increases to 28% when the average is unweighted. (Appendix 6.4 of this chapter gives examples of drug classes).

The price of the third entrant is on average, 12% lower than the incumbent when weighted. This percentage increases further to –19% when the average unweighted price change is used. The price of the fourth entrant is on average, 18% and 24% lower, in weighted and unweighted terms respectively. See Appendix 6.4 for charts tracing the market shares and relative prices of the products in each of the 11 markets.

3.6 Number of Price Changes

This indicator examines the number of price changes occurring over time. The rationale being that, the greater the amount of competition the more price changes there will be, reflecting companies reactions to competition from other products. However, the branded pharmaceuticals market is influenced by two significant factors that typically are not present in almost all other markets:

- The PPRS limits companies' ability to increase the prices of branded medicines. Companies are free to price individual products at the level they choose when they are introduced to the market. Thereafter, a company may only obtain an increase in the overall level of their prices if its profitability falls below the target set out in the agreement.

- The decision on the medicines required by the patient is made by the prescriber on the basis of an assessment of a patient's clinical need. Neither the prescriber nor the patient personally pays the cost of the medicine and the amount paid as a prescription charge where applicable is not directly related to the cost of the medicine received. Over the years, the Government has introduced measures to increase prescribers' awareness of the cost of different medicines, but the costs of medicines dispensed are paid for by the Government.

The analysis examines the number of price changes as recorded by PCA data over the period 1991 quarter 3 to 2001 quarter 2. Please note there are a number of caveats to this analysis. (See Appendix 6.5 for details)

The average number of price increases is 16.4 per quarter, 6.7 for high NIC products and 9.7 for low NIC products, across a total sample of just over 500 products. The average number of price decreases is 18.1 per quarter, 8.8 for high NIC products and 9.3 for low NIC products. However, these price falls are disproportionately concentrated in quarter 4 of 1993 and quarter 4 of 1999, the time when the PPRS price reductions were implemented. Removing these two periods from the sample (as they were, in the main, non-discretionary) brings down the average number of price decreases over the period to 7.0 per quarter, 3.1 for high NIC products and 3.9 for low NIC products.

There is no significant trend in most of the number of price increases or price decreases. However, there is a statistically significant downward trend in the number of price rises per quarter for high NIC products overall, though small (declining at a rate of 0.1 per quarter).

The net cash impact over the period is negative at -£38 million[8], however, this is dominated by the 1993 and 1999 price reductions. When these are excluded the net impact is positive, but small at about £5 million[8]. Again, there is no clear trend in the net impact of price changes (after allowing for the 1993 and 1999 price cuts).

[8] Note that the net impact figure is simply the percentage change in price times the sales value (NIC) in the **quarter** when the price change took place, summed across all products which were found to have price changes. As such they do not represent an annual figure.

4. Demand Side Indicators

4.1 GP Knowledge of Relative Prices of Products within Drug Classes

This analysis is based on a study sponsored by the ABPI, which comprised face-to–face interviews with 200 GPs. The study focused on five drug classes:

- lipid lowering statins (LLS)
- proton pump inhibitors (PPI)
- hormone replacement therapies (HRT)
- calcium antagonists (CIA)
- antidepressants (Selective serotonin re-uptake inhibitors (SSRI)

For each of the five drug classes GPs were asked to 'show their perception of the price of each product in relation to the cost of other products within its drug class, in terms of the cost of 28 days treatment.' Responses were analysed to identify the numbers of errors that GPs made in the ranking of products. This is summarized in Table 3 below.

Table 3 - Percentage of correct pairwise comparisons by drug class treating equal rank and non-responses as errors

Drug Class	SSRI excluding Dutonin	PPI	CIA	HRT	LLS	All Drug Areas
% Correct Stating a Price	62%*	61%	64%	70%	53%	63%**

(*When Dutonin is included % correct = 44%).
(**When Dutonin is included % correct = 56%).

Whilst a benchmark figure for correct rankings (whereby we could be confident that there was sufficient awareness of price to allow price competition to take place) is a matter of judgement, it is clear that there is considerable variation across drug classes. In one market, the percentage of correct rankings is only marginally above 50%, which is what would be expected if GPs had no knowledge of price and simply

guessed. In the SSRI market the results are highly sensitive to the inclusion or exclusion of Dutonin, a related antidepressant which inhibits re-uptake of serotonin. It is, therefore, open to debate whether the overall average, at 63% (which falls to 56% if Dutonin is included) is sufficiently high to allow us to conclude that there is sufficient price awareness to stimulate price competition.

4.2 Prescribing Incentive Schemes

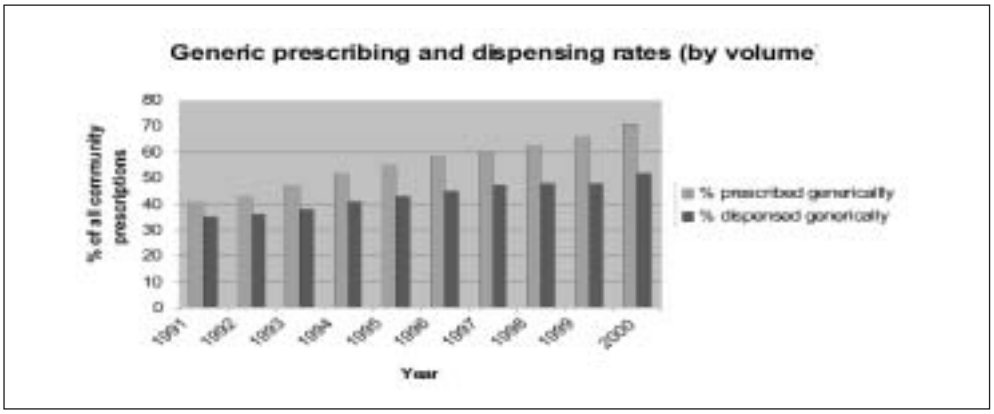
Prescribing incentive schemes were first introduced into the NHS in 1995. Family Health Service Authorities (FHSAs) were given a statutory duty to establish, operate and make payments to practices under a prescribing incentive scheme.

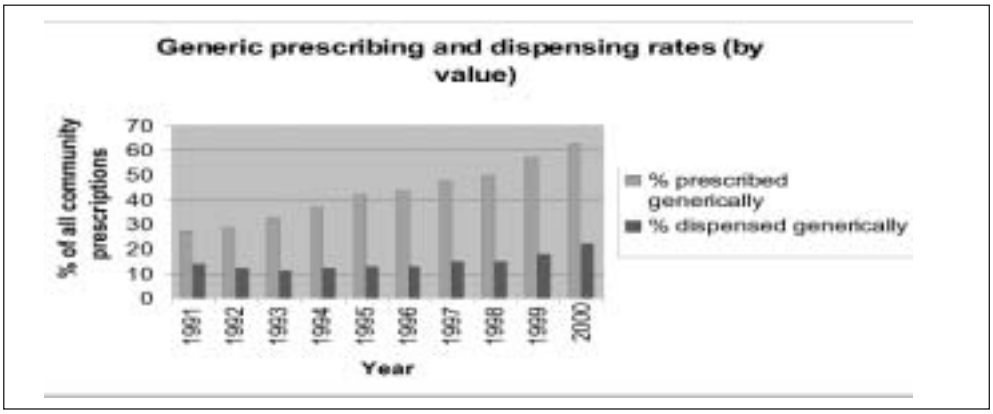
A survey conducted among 91 Primary Care Organisations (PCOs) showed schemes fall into the following categories:

- Underspends on budgeting targets.
- Meeting or exceeding generic prescribing targets.
- Reduced prescribing in specific therapy areas, e.g. anti-bacterial agents.
- Achieving quality targets.

4.3 Generic Prescribing Rates

There has been a significant increase in the proportion of prescriptions written and dispensed generically. Between 1991 and 2000 the proportion of prescriptions written generically has increased from 41% (27% by value) to 71% (62% by value), the proportion dispensed generically has risen from 35% (14% by value) to 52% (22% by value).





5. Contextual Indicators

5.1 Growth in Medicines Expenditure

Between 1991/2 and 2000/1 total expenditure on medicines grew at an average rate of 9.7% per year[9], though there are fluctuations over the period. The average growth rate is a little lower for the community sector (9.3%), and higher for the hospital sector (11.2%).

It is possible to estimate the contribution made to the growth in expenditure (in Net Ingredient terms) by various factors including volume, product mix, price movements etc[10]. Over the period 1992 to 2000 total NIC grew by 8.7%. The largest component of the growth (NIC) was the product mix residual, which takes account of both the shift from prescribing older, cheaper medicines to newer more expensive ones and countervailing effects of increased generic prescribing. This rose at an average rate of 5.4% per year over the period. Next at an average growth of 4.8% per year during the period was volume growth. This comprises the increase in the number of prescriptions and the increase in the quantity per prescription. Prices fell over the period by an average of 1.8% per year reflecting price decreases for branded medicines and generics over the period.

5.2 International Price Comparisons

The Department undertakes an annual price comparison of the best selling branded medicines in the NHS with prices elsewhere in Europe and in the USA using IMS data on prices and NHS volume weights from PCA data. The results of the latest exercise were published in the

[9] Arithmetic mean.
[10] See Appendix 6.9 for a fuller explanation.

Pharmaceutical Price Regulation Scheme (PPRS) Fifth Report to Parliament. In 2000 it compared the prices of all preparations for the top 150 branded medicines in the UK with those in Austria, Belgium, Finland, France, Germany, Ireland, Italy, Netherlands, Spain and the USA.

The study concluded:

'Previous reports showed that UK prices were in the middle range of the countries in this study over the period 1992 to 1996 but the UK's position has changed since 1996, largely as a result of sterling appreciation. For the countries for which we have 2000 data, the average sterling appreciation was 26%.

The 2000 weighted index, based on bilateral comparisons, and based on 2000 market exchange rates showed prices in the UK to be:

- Significantly lower than those in the USA;
- Higher than those in the other European comparator countries.

However, if a longer-term five-year average exchange rate is used, prices in the UK are broadly comparable with Germany, Finland, Ireland and France and higher than the other European Union countries.'

6. Appendices

6.1 Aggregate Company Concentration

The analysis for this indicator used annual PCA data for 1995 and 2000. A link code was used to identify the manufacturers of each product. This link code was not perfect, however, and the manufacturers for some products could not be identified. Where this happened, a value of '#N/A' was returned for the manufacturer. The entry for '#N/A' – clearly not a single manufacturer, but largely a sum of very small products – was removed from the tables.

Also excluded from these tables was the entry for 'Generics' – 'Generic' was inserted as the manufacturer name for all products of preparation class 1[11], and again, the entry for generics is clearly not one single manufacturer, but rather the sum of all generics in the market. It is in any case irrelevant as this indicator looks at the branded market.

The analysis below shows various measures of market concentration. Note that this analysis is based on community sales (for England) only.

Table 1 – Market Shares of Top 10 Companies – 2000

	Company	NIC (£m)	Market Share (%)	Cumulative Market Share (%)
1	GlaxoSmithkline	550	13.3	13.3
2	AstraZeneca	475	11.4	24.7
3	Pfizer	376	9.1	33.8
4	Merck Sharp & Dohme	250	6.0	39.8
5	Wyeth	237	5.7	45.5
6	Novartis	152	3.7	49.2
7	Pharmacia & Upjohn	106	2.6	51.8
8	Eli Lilly	100	2.4	54.2
9	Janssen-Cilag	100	2.4	56.6
10	Schering	91	2.2	58.8

[11] Class of preparation within the PCA system is classified in four ways, as follows:
- Class 1 – Drugs prescribed and available generically
- Class 2 – Drugs prescribed generically but because a generic is not available (e.g. proprietary is still under patent) a proprietary product or parallel import has been dispensed
- Class 3 – Drugs prescribed and dispensed by proprietary brand name
- Class 4 – Dressings and appliances

By comparison, the equivalent table for 1995 is as follows:

Table 2 – Market Shares of Top 10 Companies – 1995

	Company	NIC (£m)	Market Share (%)	Cumulative Market Share (%)
1	Glaxo	467	13.5	13.5
2	Astra	284	8.2	21.7
3	Novartis	156	4.5	26.2
4	Smithkline Beecham	146	4.2	30.5
5	Merck Sharp & Dohme	130	3.7	34.2
6	Bayer	109	3.1	37.3
7	Pfizer	100	2.9	40.2
8	Wyeth	99	2.9	43.1
9	Zeneca	96	2.8	45.9
10	Bristol-Myers Squibb	78	2.3	48.1

In other words, the 10-firm concentration ratio has increased from 48.1% to 58.8% over five years. It should be noted that the analysis used a link code to identify the manufacturer of each product. This link code was not perfect, however, and one of the faults was the fact it was not quite up to date, with the mergers of Glaxo Wellcome and SmithKline Beecham, Astra and Zeneca, and Pfizer and Warner not yet registered. As a result, it is possible to see what impact these mergers have made on the table. Table 3 shows the figures for 2000 *before* the figures for the merged companies were added up.

Table 3

	Company	NIC (£m)	Market Share (%)	Cumulative Market Share (%)
1	Glaxo Wellcome	379	9.1	9.1
2	Astra	295	7.1	16.3
3	Merck Sharp & Dohme	250	6.0	22.3
4	Pfizer	243	5.9	28.2
5	Wyeth	237	5.7	33.9
6	Zeneca	180	4.3	38.2
7	Smithkline Beecham	171	4.1	42.3
8	Novartis	152	3.7	46.0
9	Warner-Parke-Davis	133	3.2	59.2
10	Pharmacia & Upjohn	106	2.6	51.8
11	Eli Lilly	100	2.4	54.2
12	Janssen-Cilag	100	2.4	56.6
13	Schering	91	2.2	58.8

Had it not been for the mergers, then the 10-firm concentration ratio would have risen to 51.8%. In other words, concentration has been increasing, with mergers accounting for 7 percentage points out of the 10.7% increase.

6.2 Concentration Index at Market Level

Value and % of sales in markets supplied by only one manufacturer/where one manufacturer has 40% or more of sales

The source of data for these indicators was the same as for the previous set (see Appendix 6.1) – annual PCA data for 1995 and 2000. A link code was again used to identify the manufacturers (again resulting in '#N/A' and 'Generic' entries). For each market (defined as a BNF sub-chapter where available, or the next level of aggregation if not available) the company with the largest NIC was then identified, allowing the CR1 to be calculated.

Two caveats should be mentioned here. As a methodological necessity, all drugs of preparation class 1 (generic drugs) have 'generic' as the manufacturer name. Clearly this does not necessarily mean that all sales of that generic compound are down to one single generic manufacturer. When the largest company in a given market was 'generic', therefore, the CR1 was set to zero, on the assumption that this figure for 'generic' represents several manufacturers. This is likely to *under*-estimate the degree of concentration, as it assumes all markets where most sales are generic are in effect *perfectly* competitive. This is likely to exaggerate the effect of generics. It is also entirely possible that a single manufacturer *does* indeed supply the generics in any given market in at least some of the smaller markets. Indeed a closer look at the figures indicates that markets with a CR1 of zero tend to be disproportionately small. The bottom 100 markets, for instance (accounting for just 0.2% of total NIC), *all* have a CR1 of well over 40%, or zero[12]. This suggests these markets are so small they may be able to accommodate only one producer, and it is very much possible that all generics in any such markets are produced by the one manufacturer.

The second caveat is that where the top manufacturer was '#N/A', it *was* assumed it is a single manufacturer, and the CR1 was therefore left as was.

Table 4 below summaries the data for the next four indicators in this section.

Table 4 – Value and Share of Sales by Concentration of Market, 2000

CR1	NIC (£m)	NIC Share	Number of Markets	% of Markets
1	24.0	0.5%	30	10%
>0.9	90.3	1.7%	47	16%
>0.8	416.5	7.9%	77	27%
>0.7	662.3	12.5%	96	33%
>0.6	1,040.0	19.7%	123	43%
>0.5	1,733.4	32.8%	151	53%
>0.4	**2,939.7**	**55.6%**	**175**	**61%**
>0.3	3,582.5	67.8%	192	67%
>0.2	4,091.7	77.4%	200	70%
>0.1	4,101.0	77.6%	201	70%
>0	5,283.5	100.0%	287	100%

[12] The lowest market where CR1 is less than 0.4 but non-zero is some 137 markets off the bottom.

This table shows the number of markets where concentration is above a certain threshold. The table also shows the proportion of NIC that these markets account for.

CR1 refers to the 1-firm concentration ratio – in other words the market share held by the top firm in that market (a market is defined here as a BNF sub-chapter, or the next level of aggregation if not available at sub-chapter level).

The top row therefore refers to 100% concentrated markets (i.e. with only one manufacturer), and a look at the table will show there are 30 such markets (10% of all markets). However, these markets account for a mere 0.5% of total pharmaceutical sales (i.e. markets with only one producer are disproportionately small in terms of value).

The row for CR1>0.4 indicates figures for markets where (at least) one firm has 40% or more of the market. There are 175 such markets (61% of the total), accounting for 55.6% of total NIC. A market share of 40% or more for the top firm is one of the indications used by the OFT as a standard benchmark for market dominance.

Table 5 below shows another summary of these figures.

Table 5 – Concentration by Size of Market, 2000

Top	Proportion of NIC	Number of markets With CR1>0.4	Ave. CR1
5	26.7%	4	45.3%
10	42.1%	5	40.8%
20	58.1%	10	38.4%
50	81.5%	24	38.6%
100	94.9%	50	39.3%
287	100.0%	175	39.7%

This table shows the proportion of total NIC accounted for by the top 5, 10, 20, 50 and 100 markets (by market NIC), as well as the number of markets with a CR1 higher than the benchmark of 0.4 and a weighted average of the CR1 for each category. So for instance, five of the ten largest markets have a CR1>0.4 and the weighted average of the CR1 of the ten is 40.8%.

For comparison, the equivalent tables for 1995 are shown in Tables 6 and 7 below.

Table 6 - Value and Share of Sales by Concentration of Market, 1995

CR1	NIC (£m)	NIC Share	Number of Markets	% of Markets
1	8.45	0.2%	24	8%
>0.9	318.55	9.2%	65	20%
>0.8	420.15	12.1%	89	28%
>0.7	888.55	25.7%	119	37%
>0.6	1,137.48	32.9%	148	47%
>0.5	1,592.61	46.0%	180	57%
>0.4	**1,991.58**	**57.6%**	**205**	**64%**
>0.3	2,793.15	80.8%	229	72%
>0.2	3,104.41	89.8%	242	76%
>0.1	3,104.41	89.8%	242	76%
>0	3,458.65	100.0%	318	100%

Table 7 - Concentration by Size of Market, 1995

Top	Proportion of NIC	Number of markets With CR1>0.4	Ave. CR1
5	27.7%	3	62.7%
10	44.0%	6	56.2%
20	59.3%	11	51.0%
50	83.0%	26	49.5%
100	94.8%	57	49.8%
318	100.0%	205	49.6%

The comparison between 1995 and 2000 suggests markets have been getting *less* concentrated[13]. 61% of the markets, accounting for 55.6% of NIC, had a CR1>0.4 in 2000 – down from 64% of markets accounting for 57.6% of NIC.

In conjunction with the figures in Tables 1-3, this shows that the top ten companies account for an increasing share of the total market, but are – perhaps – competing with each other in a broader range of sub-markets, resulting in sub-markets that are actually less concentrated.

6.3 Time Lags between First and Second Products in the Market, Impact on Market Share and Relative Prices of Subsequent Entrants

The analysis for this set of indicators used PCA data from 1985 onwards (annual data for 1985-1990, quarterly for Quarter 1 1991 to Quarter 2 2001[14]). BNF classification has been used, with a drug class defined as a BNF sub-chapter (the most disaggregated/narrow level in this classification) where available[15].

The PCA data identifies over 300 markets. However, only 44 were identified which had no brands at the start of the period. Seventeen of these had no brands by the end of the period – either because the only entry/entries were generic, or because any product had a tiny and erratic NIC. The latter group often had very sporadic sales, with long periods with no sales – in other words the lack of sales at the start of the period does *not* mean the market did not exist. Such markets were excluded from this analysis.

Of the remaining markets, 19 had just the one entry over the period examined. These markets are disproportionately small, between them accounting for 0.3% of NIC (in 2001 Quarter 2, the last observation in the sample).

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[13] Despite the emergence of several new sub-chapters between 1995 and 2000, the number of markets has fallen by over 30 over the period, due to the disappearance of some 35 markets. All the disappearing markets are tiny, with a NIC of under £90,000 during 1995 – with the exception of 9.3, intravenous nutrition, with a NIC of £1.7million. This market, along with many of the disappearing markets, comprises hospital-only treatments that should not be appearing on PCA data at all (it is unclear why they appeared in 1995). Others are clearly mis-recordings by PPA – for instance chapter 9.6.2.1 does not actually exist (9.6.2 – vitamin B preparations – does not have any sub-chapters listed in the BNF).

[14] The pre-1991 annual data is not necessarily consistent with later quarterly data, because of changes in methodology. For the products included in this sample there appeared to be a reasonable degree of consistency between the two sets of data. Also, additional information on dates of entries was extracted from IMS data for some of the markets.

[15] Some chapters do not have sub-chapters, for instance, in which case the chapter was treated as the market.

This leaves eight new markets, in which a first entry was followed by subsequent entry/entries, and it is these plus three additional markets not classified as such by BNF[16] for which Tables 8a and 8b below provide a detailed summary. The markets are in order of NIC and the date and name of the first entrant is given for each. For each of the subsequent three entries, the entry lag, market share gained and relative price are provided, with the definitions as detailed below:

- **Lags** are defined as the period of time between *first* entry and the entry in question[17], and measured in quarters;

- **Market shares** are measured by value, with figures showing the market share gained one year after the relevant entry and – in brackets – four years after entry (unless otherwise stated);

- **Prices** are at the time of launch, relative to the incumbent in the quarter before the second entrant arrives on the market. Where any impact was made on the incumbent price since the start of the market, this is indicated in footnotes in the tables. Relative prices are calculated on i) modal strengths (table 8a) and ii) on a cost per Daily Defined Dose basis (using DDDs calculated by the World Health Organisation) across all strengths (table 8b).

- **Average** price relativities (relative to the first entrant) across the sample for second, third and fourth entrants respectively are also provided, both unweighted and weighted by NIC[18].

One notable finding is that this analysis could only identify 11 new markets appearing during the 15-year period examined. From this limited sample it is possible, however, to make some observations. For instance, there is a lag of some three years on average between the originator entering the new market and the second product appearing. The second entrant can expect to obtain, on average, some 12% market share within one year of entry, rising to 22% after 4 years. Where they occur, third and fourth entries can expect to gain a smaller share of the market (on average fourth entrants seem to obtain a bigger market share than third entrants, but this may be biased upwards by fourth entrant

[16] Those markets are Statins (Simvastatin, Pravastatin, Fluvastatin Sodium and Atorvastatin), Triptans (Sumatriptan Succinate, Zolmitriptan, Naratriptan, and Rizatriptan) and Cox inhibitors (Rofecoxib and Celecoxib).

[17] As recorded by the PCA data.

[18] The weight used is the total NIC for the market concerned at the end of the sample period – i.e. 2001 Q2. Note that the same weighting method has been used for the weighted average lags and market shares. For the latter (weighted average market shares) this method produces different results to those shown in section 3.4.

Lipitor which has a share of 35%). This suggests there is some degree of first-mover advantage – a conclusion supported by the fact that incumbent products seem to account for the majority of the market even by the end of the sample period in most of the markets studied here.

The study looked at the price discount of subsequent entrants relative to the incumbent based on relative prices of modal strengths (table 8a). Most subsequent entrants come into the market with a price discount relative to the incumbent. Based on weighted average price relativities, the discount offered by the second entrant relative to the incumbent is 11%. This percentage increases to 28% when the average is unweighted. The price of the third entrant is on average, 12% lower than the incumbent when weighted. This percentage increases further to 19% when the average unweighted price relativity is used. The price of the fourth entrant is on average, 18% and 24% lower, in weighted and unweighted terms respectively.

The study also examined the price discount of subsequent entrants relative to the incumbent based on relative prices calculated on the basis of Daily Defined Dose (table 8b). In this case, just over half of subsequent entrants come into the market with a price discount relative to the incumbent. However, based on weighted average price relativities, the second entrant comes in at a price premium of 4%[19], 6% when unweighted. The price of the third entrant is on average 9% lower than the first entrant when weighted, though the unweighted average is 4% higher than the first entrant. The price of the fourth entrant is, on average, 26% and 13% lower, in weighted and unweighted terms respectively.

Appendix 6.4 provides more detailed findings, market-by-market, in the form of charts tracing the market shares and relative prices of the products in each market. The price charts show price relativities of modal strengths and on a DDD basis across all strengths. Note that the price charts showing relative prices in terms of cost per DDD are subject to fluctuations due to strength mix effects where prices are not pro rata to strength.

[19] This average is highly skewed by one product, Lipostat, which comes in priced 28% higher than Zocor on a cost per DDD basis. As Statins is the biggest market, this has a large impact on the average. Excluding Lipostat gives an average price 6% less than the incumbent.

Table 8a – Impacts of subsequent entries into new markets (Using Modal Strength for relative prices)

BNF sub-paragraph	1st entry	2nd entry			3rd entry			4th entry			NIC (£000s) in 2001 Q2 (Share of originator at end of sample (%))
		Lag	Share (%)	Price	Lag	Share (%)	Price	Lag	Share (%)	Price	
Statins	1989 Q2	5	18 (18)	-12	19	2 (4)	-19	31	14(35)	3	100,484 (43%)
	Zocor		Lipostat			Lescol			Lipitor		
Proton-Pump Inhibitors	1989 Q2	20	6 (29)	-7[20]	30	3 (3)	-18	37	2 (7[21])	-34	89,144 (49%)
	Losec		Zoton						Protium		Pariet
SSRI Antidepressants	1989 Q1[22]	8	9 (19)	-3	8	22 (28)	15	25	2 (9)	-22	56,131 (40%)
	Prozac		Lustral			Seroxat			Cipramil		
Angiotensin-II Receptor Antagonists	1995 Q1	7	12 (17)	-9	10	11 (16)	0	11	2 (3)	-22	22,925 (45%)
	Cozaar		Diovan			Approvel			Amias		
Triptans	1991 Q3	23	7(13)	-50	23	9 (14)	-50	28	3 (6[23])	-44	13,115 (67%)
	Imigran		Zomig			Naramig			Maxalt		
Cox II inhibitors	1999 Q2	4	28[24]	-21	-	-	-	-	-	-	11,213 (72%)
	Vioxx		Celebrex								
Leukotriene Receptor Antagonists	1998 Q1	0	10 (12[25])	-50	-	-	-	-	-	-	2992.4 (88%
	Singulair		Accolate								
Somatostatin Analogues	1989	37	17 (18[26])	N/A	-	-	-	-	-	-	2,540 (82%)
	Sandostatin		Somatuline								
Drugs for dementia	1997 Q2	4	8 (9[9])	-54	14	6[27]	-60	-	-	-	2,446 (81%)
	Aricept		Exelon			Reminyl					
Drugs used in neutropenia	1991 Q2	6	2 (4)	-50	15	10 (26)	-2	-	-		79 (67%)
	Neupogen		Leucomax			Granocyte					
Bowel-cleansing[28] solutions	1986	16	6 (17)	N/A	20	1 (2)	N/A	-	-	-	39 (65%)
	Picolax		Klean-Prep			Citramag					
Average weighted		**11**	**12(22)**	**-11**	**20**	**7(10)**	**-12**	**25**	**6(18)**	**-18**	**27,373 (48%)**
Average unweighted		**12**	**11(16)**	**-28**	**17**	**8(12)**	**-19**	**26**	**5(15)**	**-24**	**27,373 (64%)**

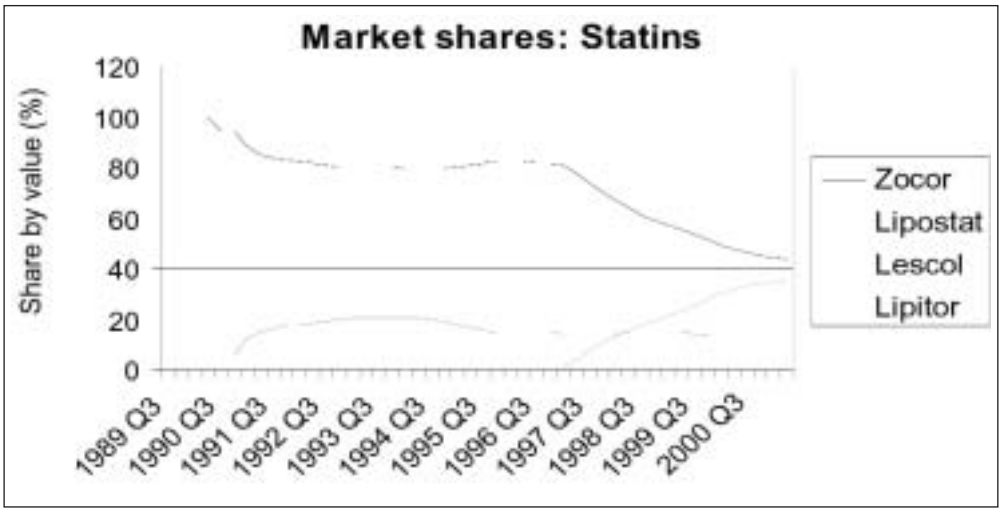
[20] The price of Losec dropped some 20% by the sample end, with Zoton and Protium also seeing prices fall below their launch levels.
[21] After 11 quarters (sample end).
[22] The sample for SSRIs finishes on the first quarter of 2000, when generic Fluoxetine is introduced.
[23] After 11 quarters (sample end)
[24] After 4 quarters (sample end)
[25] After 13 quarters (sample end).
[26] After three years (sample end).
[27] After 6 months (sample end).
[28] The prices calculated from PCA data for this group seem to move erratically and so are not taken into account.

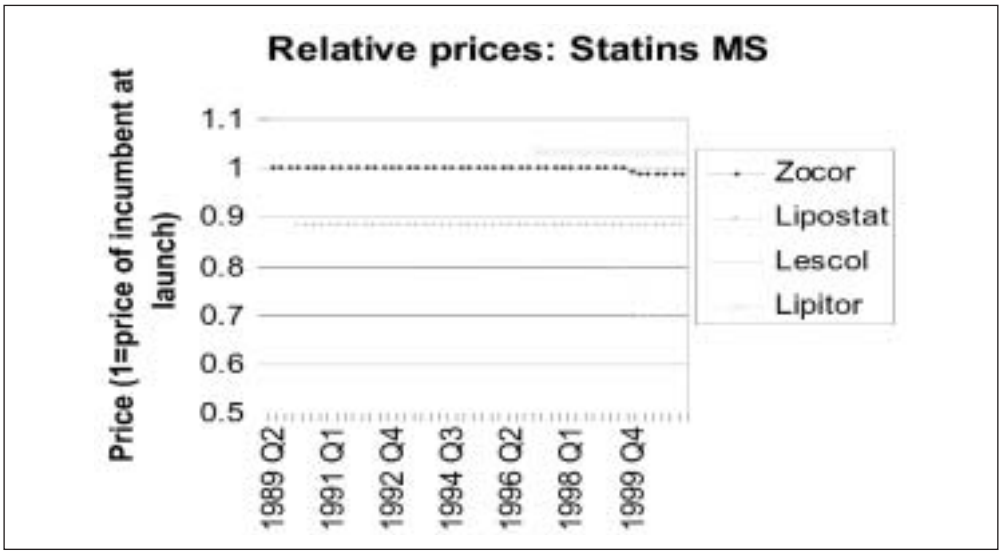
Table 8b – Impacts of subsequent entries into new markets (Using DDDs for relative prices)

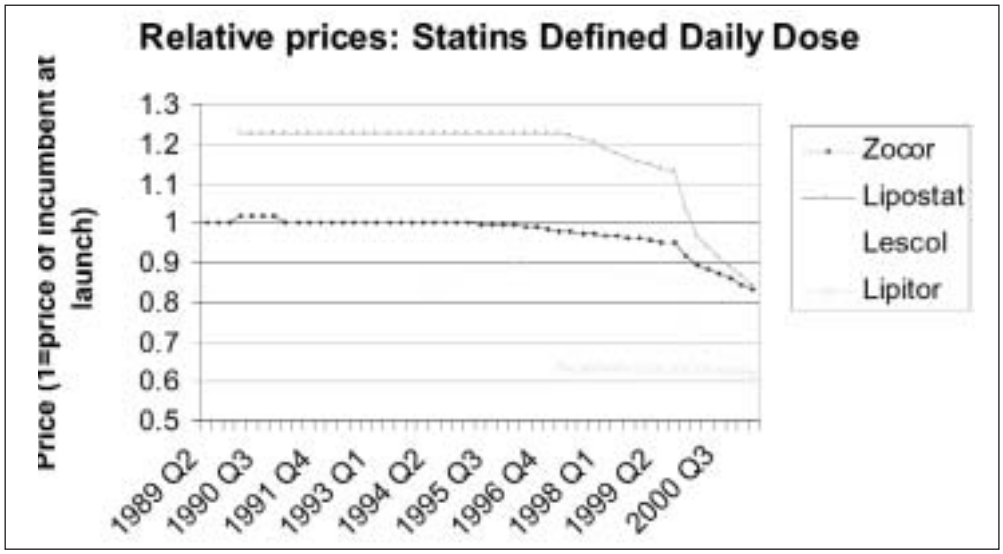
BNF sub-paragraph	1st entry	2nd entry			3rd entry			4th entry			NIC (£000s) in 2001 Q2 (Share of originator at end of sample (%))
		Lag	Share (%)	Price	Lag	Share (%)	Price	Lag	Share (%)	Price	
Statins	1989 Q2	5	18 (18)	23	19	2 (4)	-18	31	14(35)	-36	100,484 (43%)
	Zocor		Lipostat			Lescol			Lipitor		
Proton-Pump Inhibitors	1989 Q2	20	6 (29)	-7	30	3 (3)	-18	37	2 (7)	-31	89,144 (49%)
	Losec		Zoton			Protium			Pariet		
SSRI Antidepressants	1989 Q1	8	9 (19)	-7	8	22 (28)	15	25	2 (9)	-22	56,131 (40%)
	Prozac		Lustral			Seroxat			Cipramil		
Angiotensin-II Receptor Antagonists	1995 Q1	7	12 (17)	-13	10	11 (16)	-6	11	2 (3)	16	22,925 (45%)
	Cozaar		Diovan			Approvel			Amias		
Triptans	1991 Q3	23	7(13)	-5	23	9 (14)	-5	28	3 (6)	11	13,115 (67%)
	Imigran		Zomig			Naramig			Maxalt		
Cox II inhibitors	1999 Q2	4	28	2	-	-	-	-	-	-	11,213 (72%)
	Vioxx		Celebrex								
Leukotriene Receptor Antagonists	1998 Q1	0	10 (12)	-5	-	-	-	-	-	-	2,992 (88%)
	Singulair		Accolate								
Somatostatin Analogues	1989	37	17 (18)	N/A	-	-	-	-	-	-	2,540 (82%)
	Sandostatin		Somatuline								
Drugs for dementia	1997 Q2	4	8 (9)	63	14	6	47	-	-	-	2,446 (81%)
	Aricept		Exelon			Reminyl					
Drugs used in neutropenia	1991 Q2	6	2 (4)	0	15	10 (26)	12	-	-	-	79 (67%)
	Neupogen		Leucomax			Granocyte					
Bowel-cleansing solutions	1986	16	6 (17)	N/A	20	1 (2)	N/A	-	-	-	39 (65%)
	Picolax		Klean-Prep			Citramag					
Average weighted		**11**	**12(22)**	**4**	**20**	**7(10)**	**-9**	**25**	**6(18)**	**-26**	**27,373 (48%)**
Average unweighted		**12**	**11(16)**	**-28**	**17**	**8(12)**	**-19**	**26**	**5(15)**	**-24**	**27,373 (64%)**

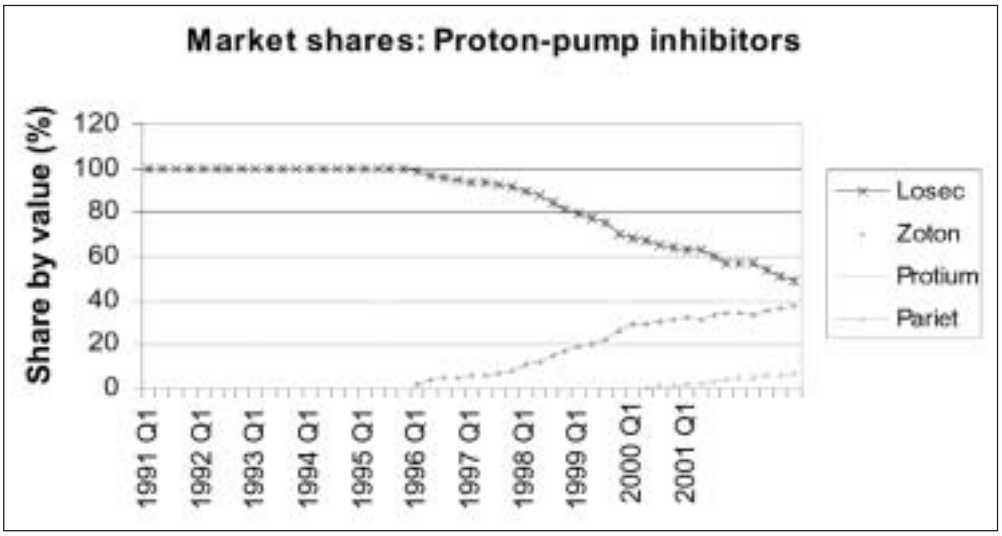
[29] The price of Losec dropped some 20% by the sample end, with Zoton and Protium also seeing prices fall below their launch levels.
[30] After 11 quarters (sample end).
[31] The sample for SSRIs finishes on the first quarter of 2000, when generic Fluoxetine is introduced.
[32] After 11 quarters (sample end)
[33] The injectable presentations of Imigran are not taken into account in the calculation of the relative prices.
[34] After 4 quarters (sample end)
[35] After 13 quarters (sample end).
[36] After three years (sample end).
[37] After 6 months (sample end).
[38] The prices calculated from PCA data for this group seem to move erratically and so are not taken into account.

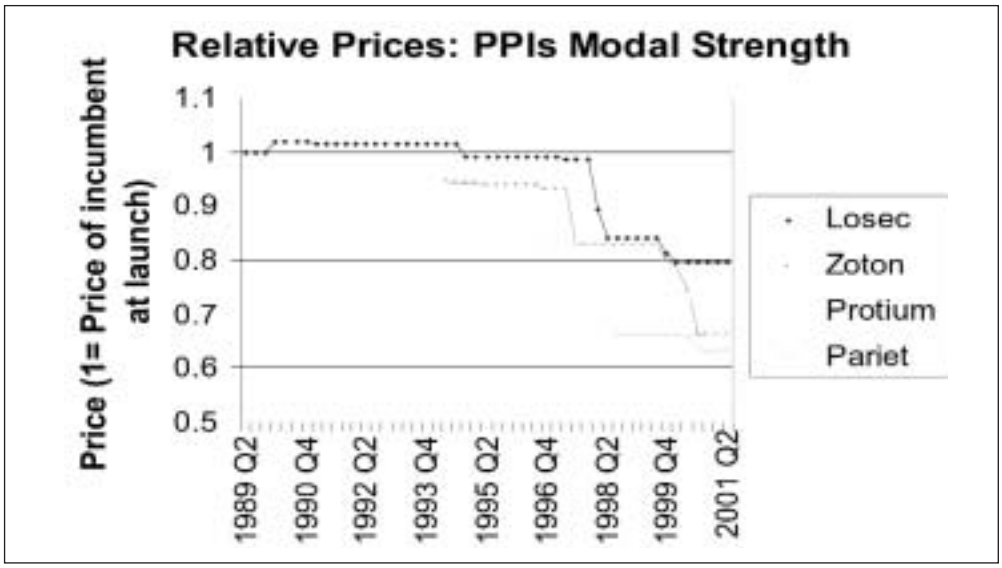
6.4 Drug Classes - Examples of Market Share and Relative Prices of Subsequent Entries

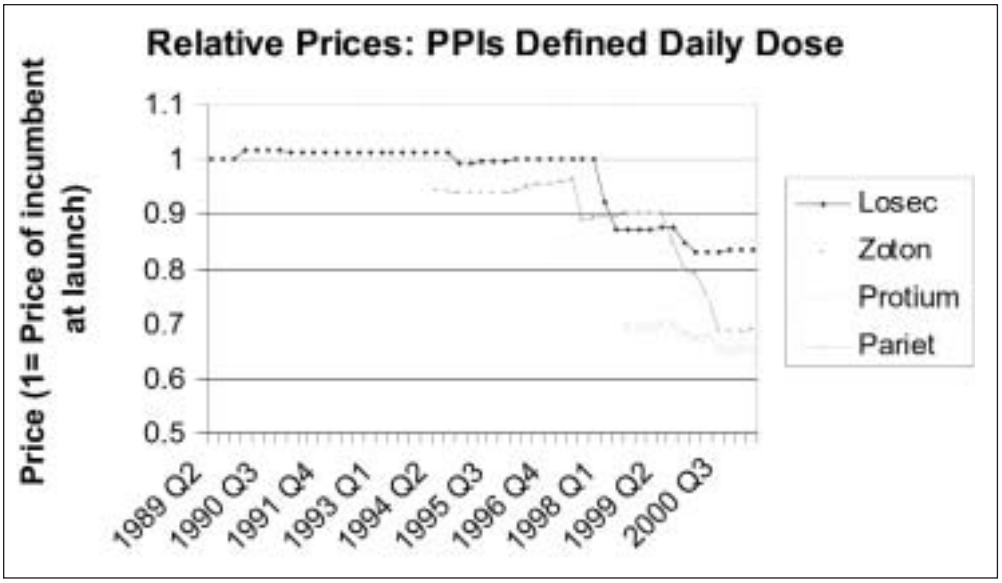


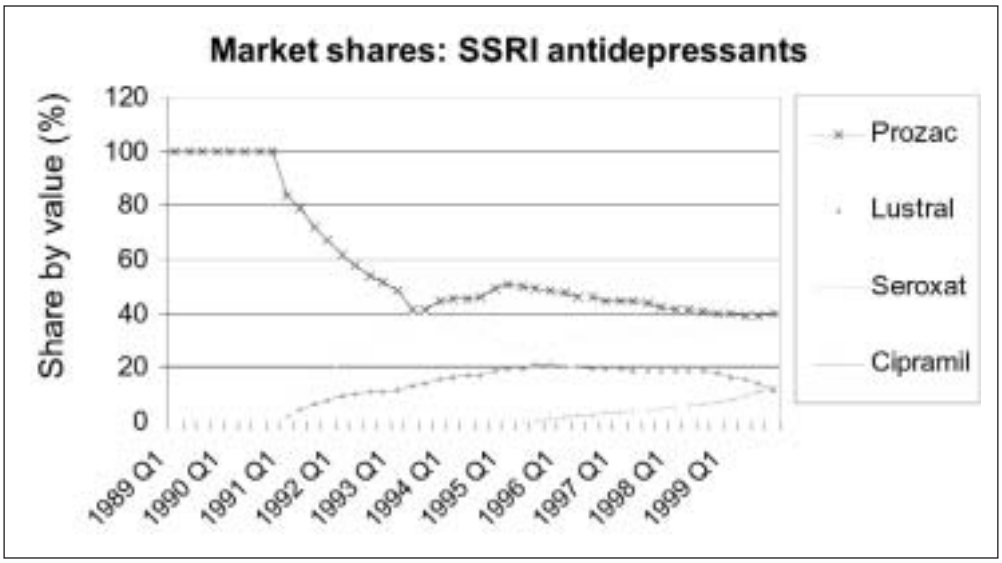


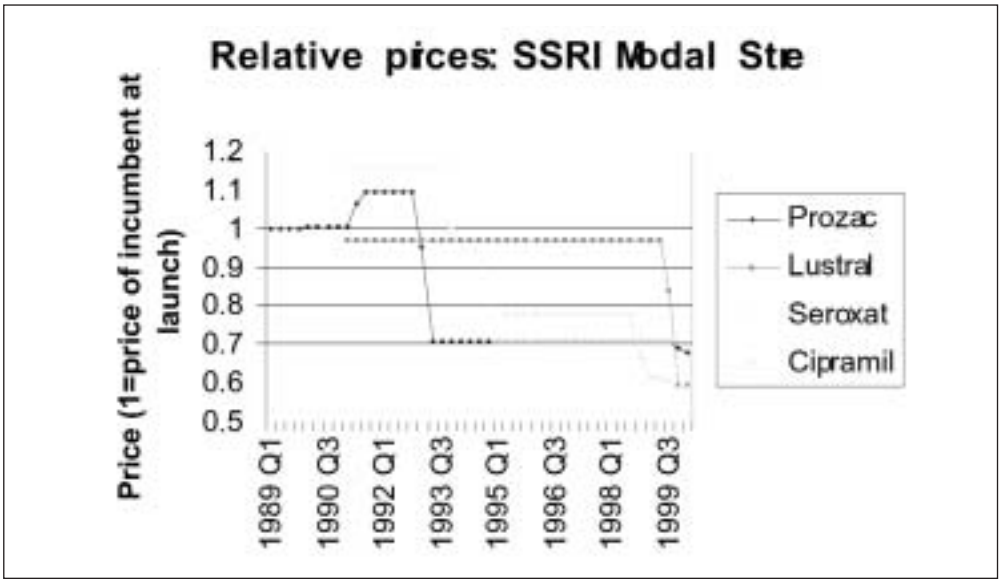


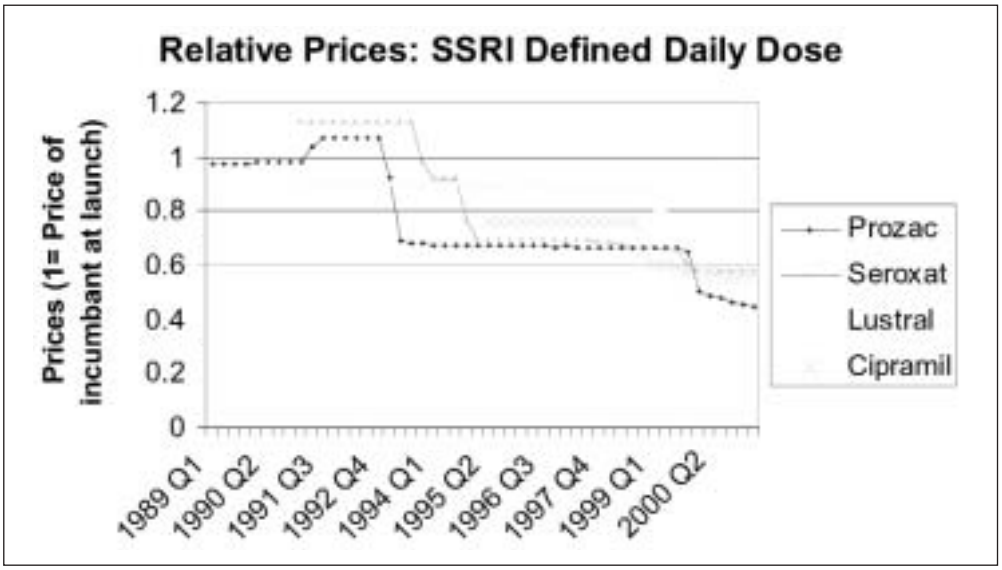

Market shares: Proton-pump inhibitors
Share by value (%)
120
100
80
60
40
20
0
1991 Q1
1992 Q1
1993 Q1
1994 Q1
1995 Q1
1996 Q1
1997 Q1
1998 Q1
1999 Q1
2000 Q1
2001 Q1
Losec
Zoton
Protium
Pariet

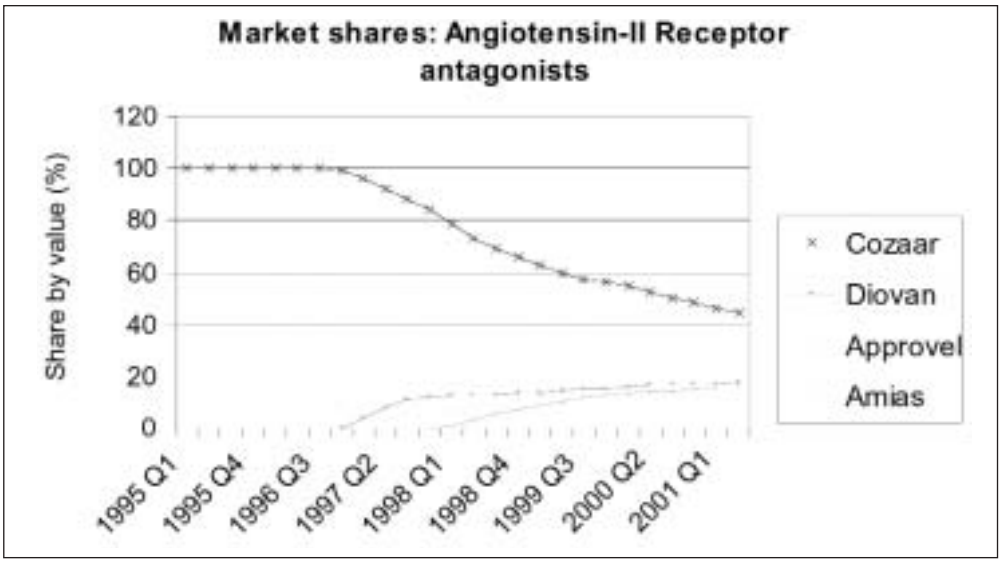

Relative Prices: PPIs Modal Strength
Price (1= Price of incumbent at launch)
1.1
1
0.9
0.8
0.7
0.6
0.5
1989 Q2
1990 Q4
1992 Q2
1993 Q4
1995 Q2
1996 Q4
1998 Q2
1999 Q4
2001 Q2
Losec
Zoton
Protium
Pariet

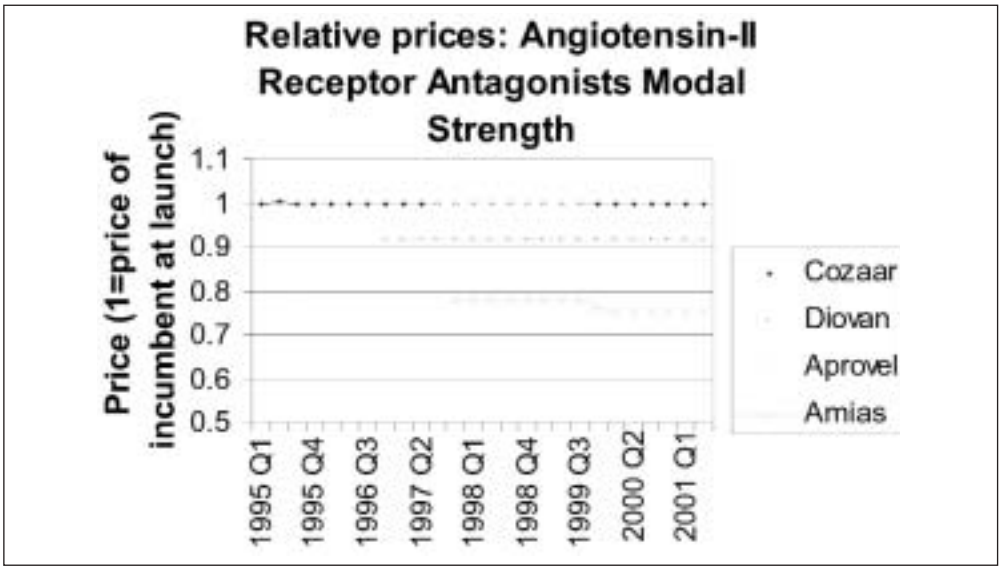

Relative Prices: PPIs Defined Daily Dose
Price (1= Price of incumbent at launch)
1.1
1
0.9
0.8
0.7
0.6
0.5
1989 Q2
1990 Q3
1991 Q4
1993 Q1
1994 Q2
1995 Q3
1996 Q4
1998 Q1
1999 Q2
2000 Q3
Losec
Zoton
Protium
Pariet

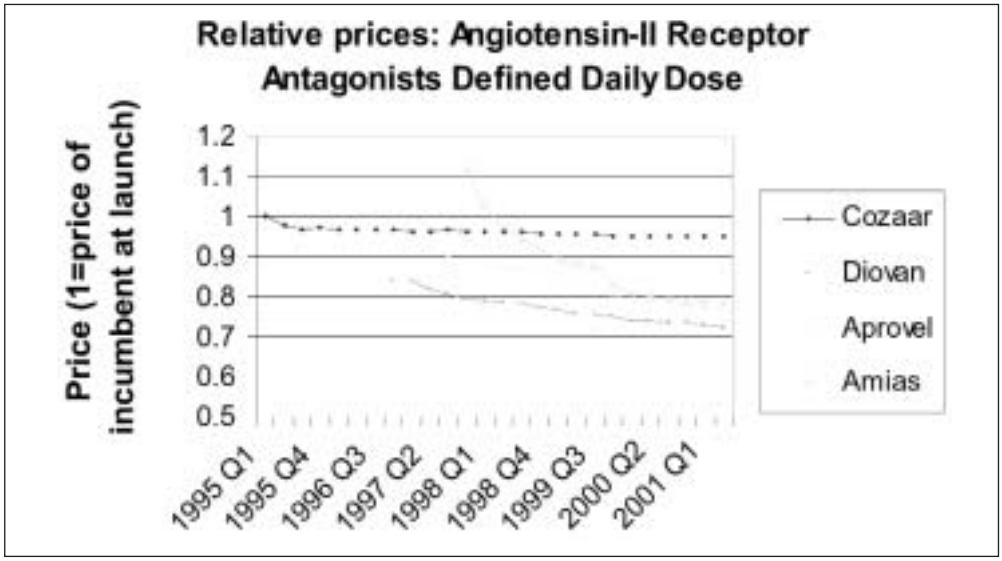

Market shares: SSRI antidepressants
Share by value (%)
120
100
80
60
40
20
0
1989 Q1
1990 Q1
1991 Q1
1992 Q1
1993 Q1
1994 Q1
1995 Q1
1996 Q1
1997 Q1
1998 Q1
1999 Q1
Prozac
Lustral
Seroxat
Cipramil

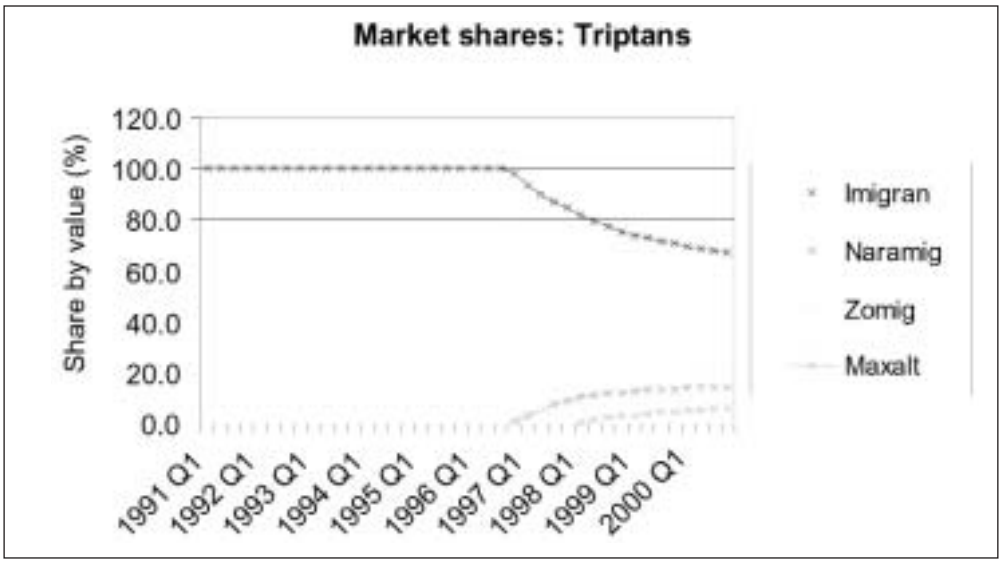

Relative prices: SSRI Modal Ste
Price (1=price of incumbent at launch)
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
1989 Q1
1990 Q3
1992 Q1
1993 Q3
1995 Q1
1996 Q3
1998 Q1
1999 Q3
Prozac
Lustral
Seroxat
Cipramil

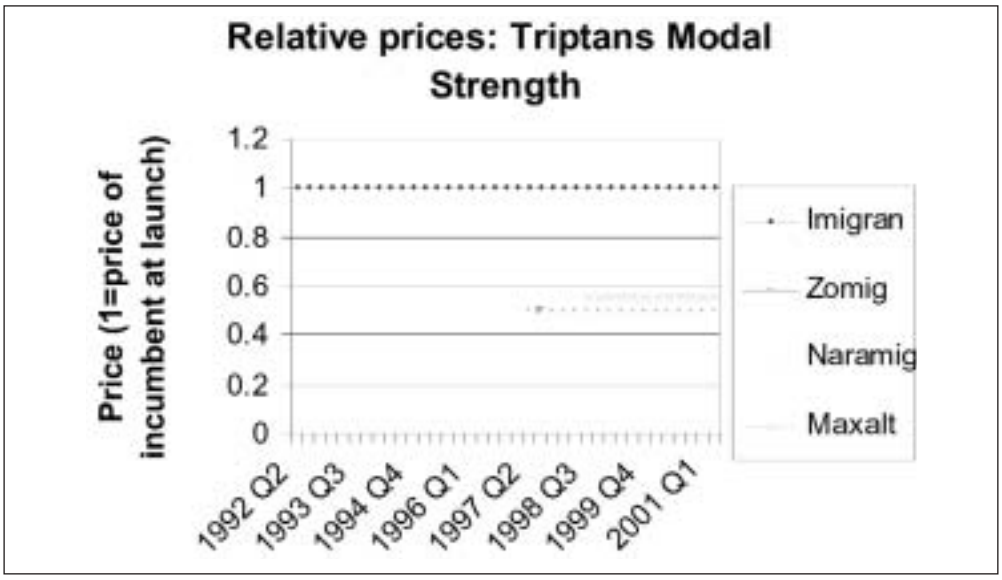

Relative Prices: SSRI Defined Daily Dose
Prices (1= Price of incumbant at launch)
1.2
1
0.8
0.6
0.4
0.2
0
1989 Q1
1990 Q2
1991 Q3
1992 Q4
1994 Q1
1995 Q2
1996 Q3
1997 Q4
1999 Q1
2000 Q2
Prozac
Seroxat
Lustral
Cipramil

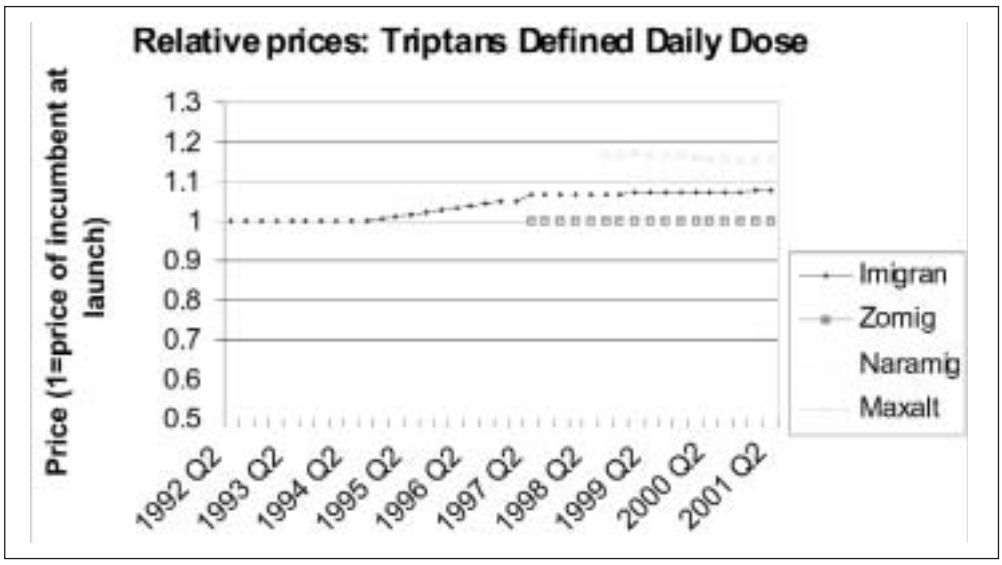

Market shares: Angiotensin-II Receptor antagonists
Share by value (%)
120
100
80
60
40
20
0
1995 Q1
1995 Q4
1996 Q3
1997 Q2
1998 Q1
1998 Q4
1999 Q3
2000 Q2
2001 Q1
Cozaar
Diovan
Approvel
Amias

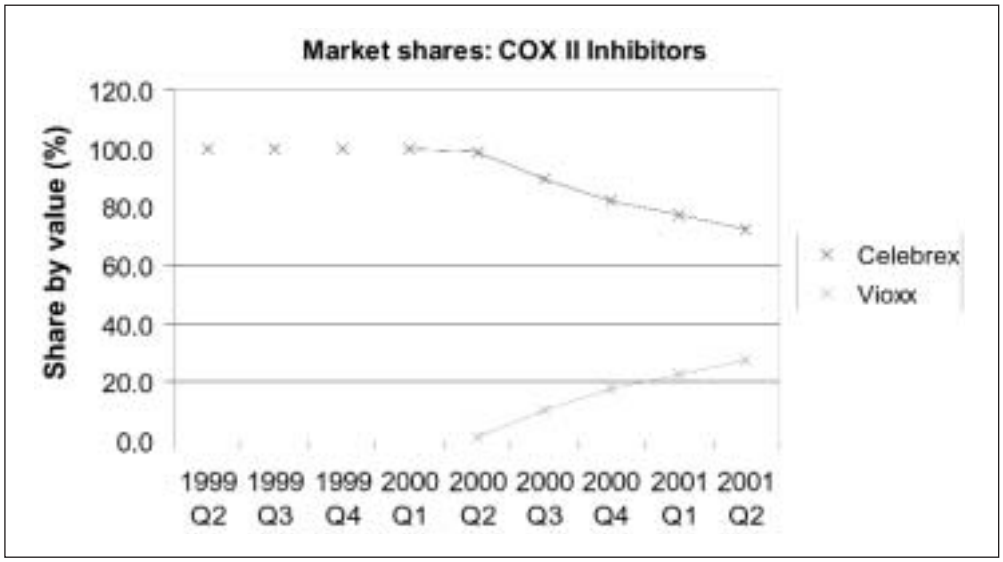

Relative prices: Angiotensin-II Receptor Antagonists Modal Strength
Price (1=price of incumbent at launch)
1.1
1
0.9
0.8
0.7
0.6
0.5
1995 Q1
1995 Q4
1996 Q3
1997 Q2
1998 Q1
1998 Q4
1999 Q3
2000 Q2
2001 Q1
Cozaar
Diovan
Aprovel
Amias

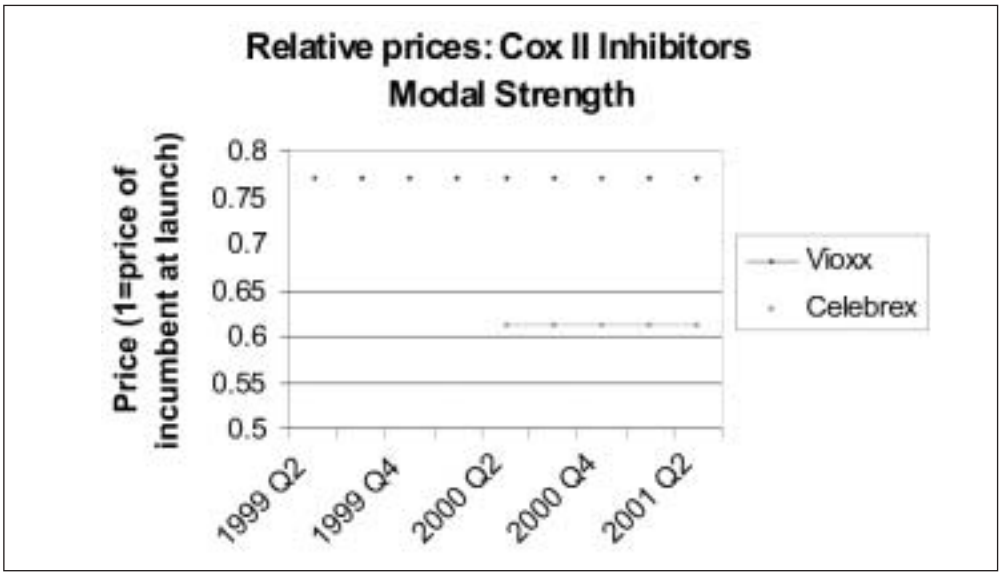

Relative prices: Angiotensin-II Receptor Antagonists Defined Daily Dose
Price (1=price of incumbent at launch)
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
1995 Q1
1995 Q4
1996 Q3
1997 Q2
1998 Q1
1998 Q4
1999 Q3
2000 Q2
2001 Q1
Cozaar
Diovan
Aprovel
Amias

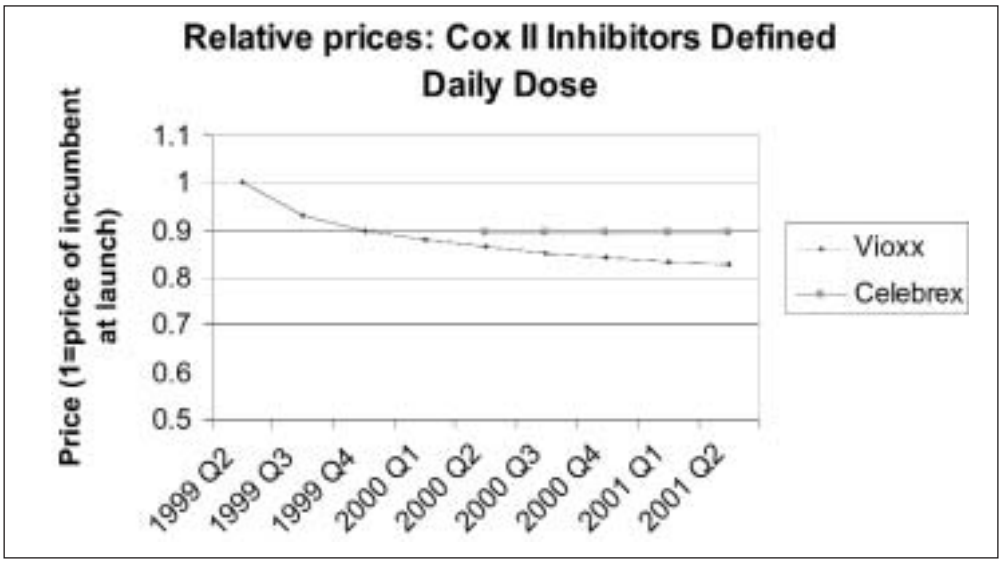

Market shares: Triptans
Share by value (%)
120.0
100.0
80.0
60.0
40.0
20.0
0.0
1991 Q1
1992 Q1
1993 Q1
1994 Q1
1995 Q1
1996 Q1
1997 Q1
1998 Q1
1999 Q1
2000 Q1
Imigran
Naramig
Zomig
Maxalt

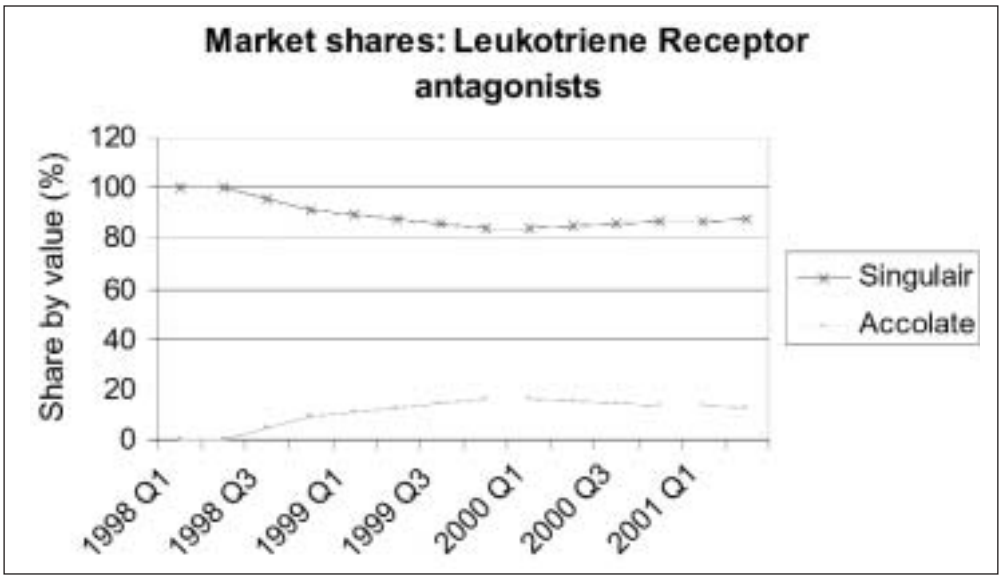

Relative prices: Triptans Modal Strength
Price (1=price of incumbent at launch)
1.2
1
0.8
0.6
0.4
0.2
0
1992 Q2
1993 Q3
1994 Q4
1996 Q1
1997 Q2
1998 Q3
1999 Q4
2001 Q1
Imigran
Zomig
Naramig
Maxalt

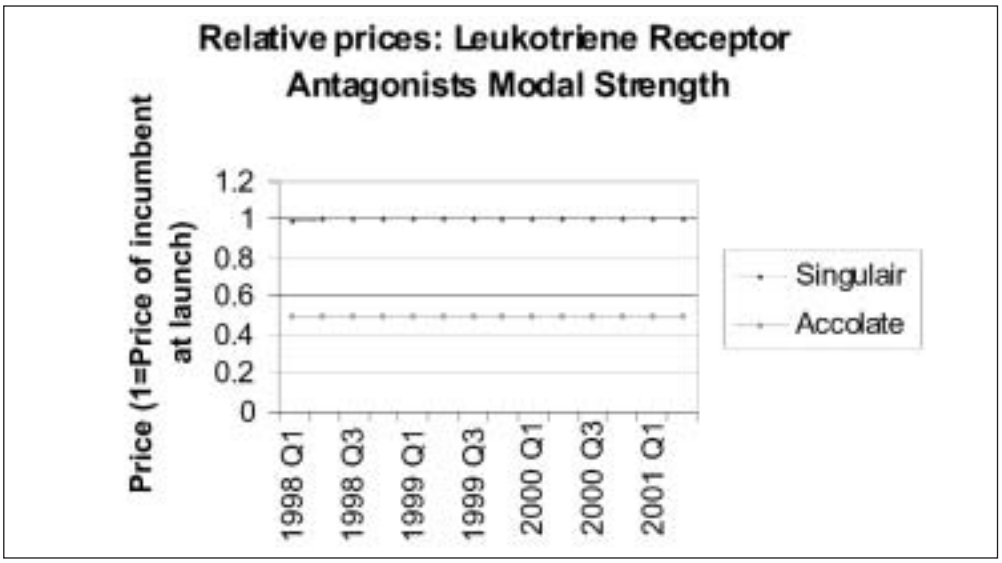

Relative prices: Triptans Defined Daily Dose
Price (1=price of incumbent at launch)
1.3
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
1992 Q2
1993 Q2
1994 Q2
1995 Q2
1996 Q2
1997 Q2
1998 Q2
1999 Q2
2000 Q2
2001 Q2
Imigran
Zomig
Naramig
Maxalt

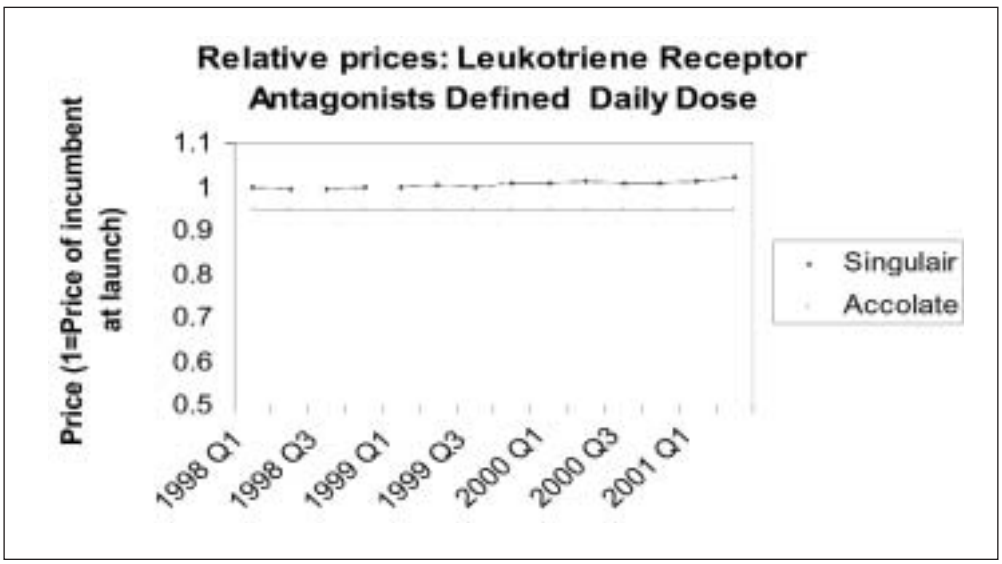

Market shares: COX II Inhibitors
Share by value (%)
120.0
100.0
80.0
60.0
40.0
20.0
0.0
1999 Q2
1999 Q3
1999 Q4
2000 Q1
2000 Q2
2000 Q3
2000 Q4
2001 Q1
2001 Q2
Celebrex
Vioxx

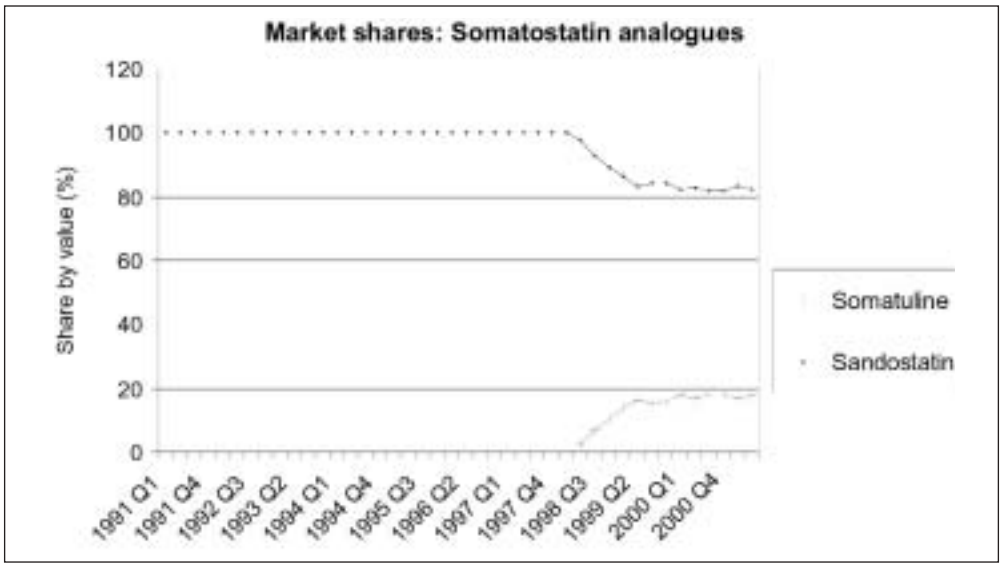

Relative prices: Cox II Inhibitors
Modal Strength
Price (1=price of incumbent at launch)
0.8
0.75
0.7
0.65
0.6
0.55
0.5
1999 Q2
1999 Q4
2000 Q2
2000 Q4
2001 Q2
Vioxx
Celebrex

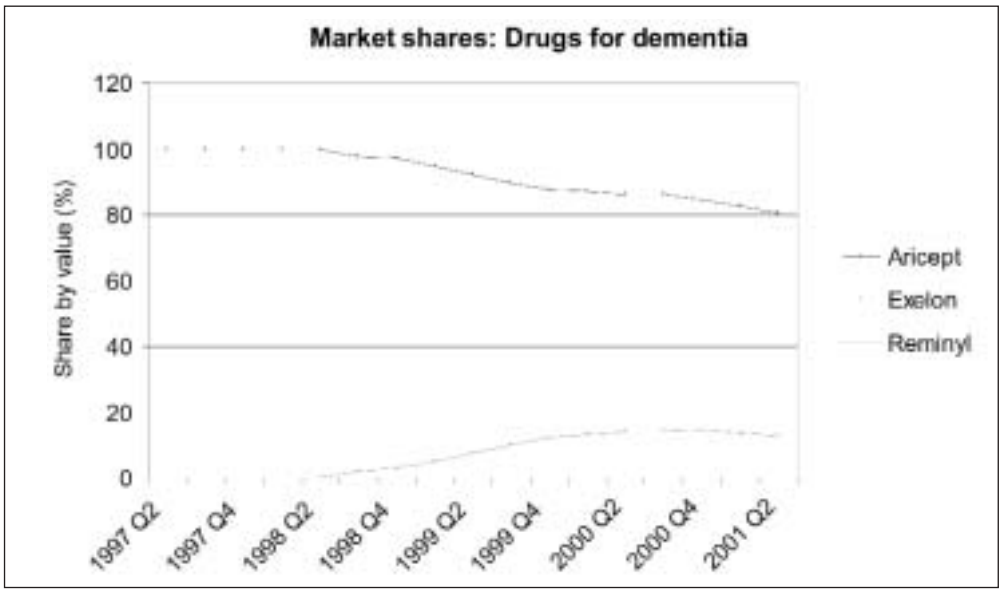

Relative prices: Cox II Inhibitors Defined Daily Dose
Price (1=price of incumbent at launch)
1.1
1
0.9
0.8
0.7
0.6
0.5
1999 Q2
1999 Q3
1999 Q4
2000 Q1
2000 Q2
2000 Q3
2000 Q4
2001 Q1
2001 Q2
Vioxx
Celebrex

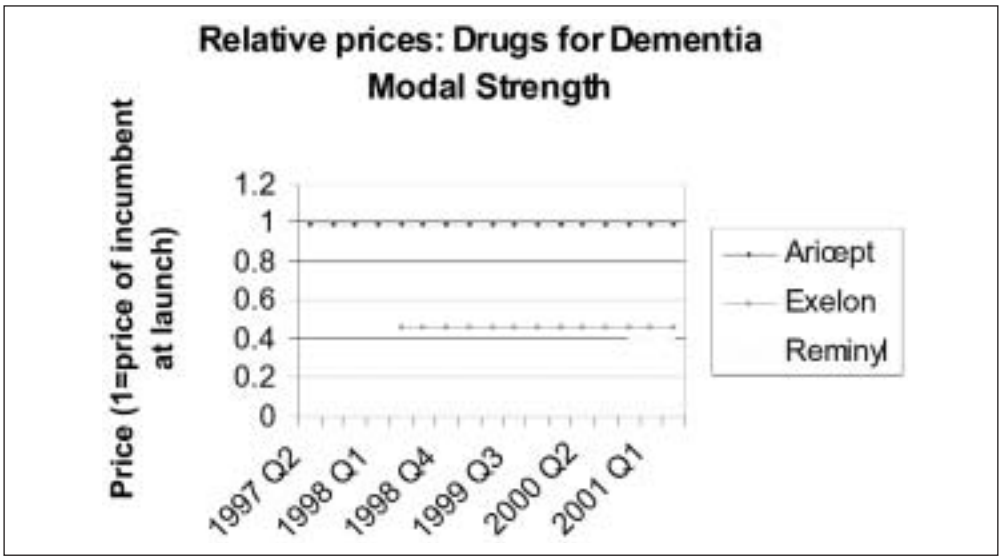

Market shares: Leukotriene Receptor antagonists
Share by value (%)
120
100
80
60
40
20
0
1998 Q1
1998 Q3
1999 Q1
1999 Q3
2000 Q1
2000 Q3
2001 Q1
Singulair
Accolate

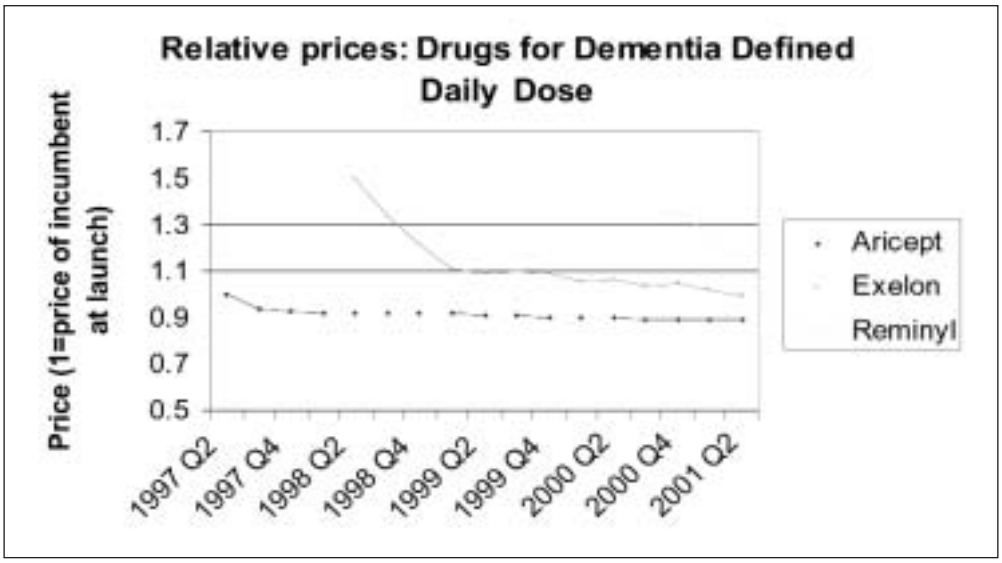

Relative prices: Leukotriene Receptor Antagonists Modal Strength
Price (1=Price of incumbent at launch)
1.2
1
0.8
0.6
0.4
0.2
0
1998 Q1
1998 Q3
1999 Q1
1999 Q3
2000 Q1
2000 Q3
2001 Q1
Singulair
Accolate

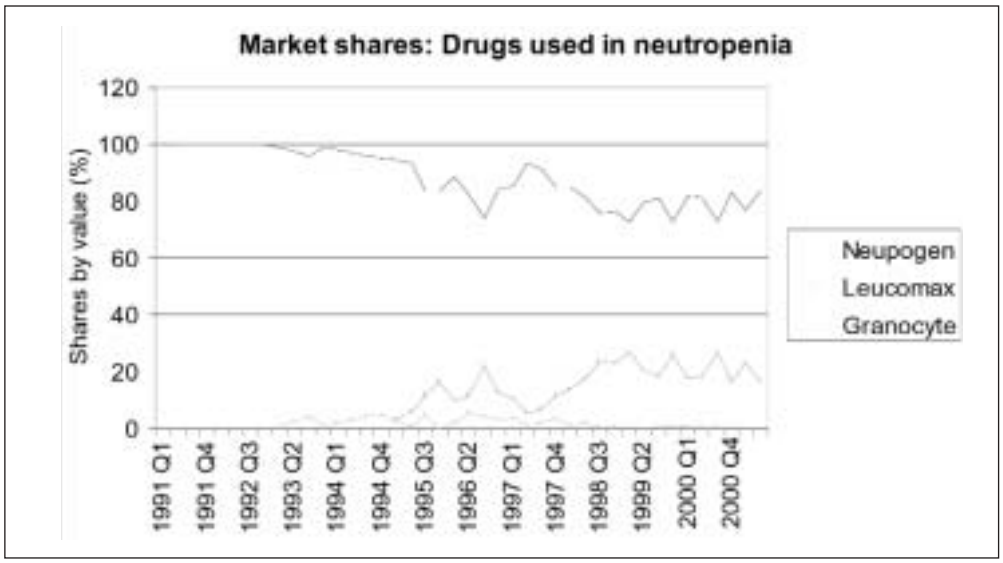

Relative prices: Leukotriene Receptor Antagonists Defined Daily Dose
Price (1=Price of incumbent at launch)
1.1
1
0.9
0.8
0.7
0.6
0.5
1998 Q1
1998 Q3
1999 Q1
1999 Q3
2000 Q1
2000 Q3
2001 Q1
Singulair
Accolate

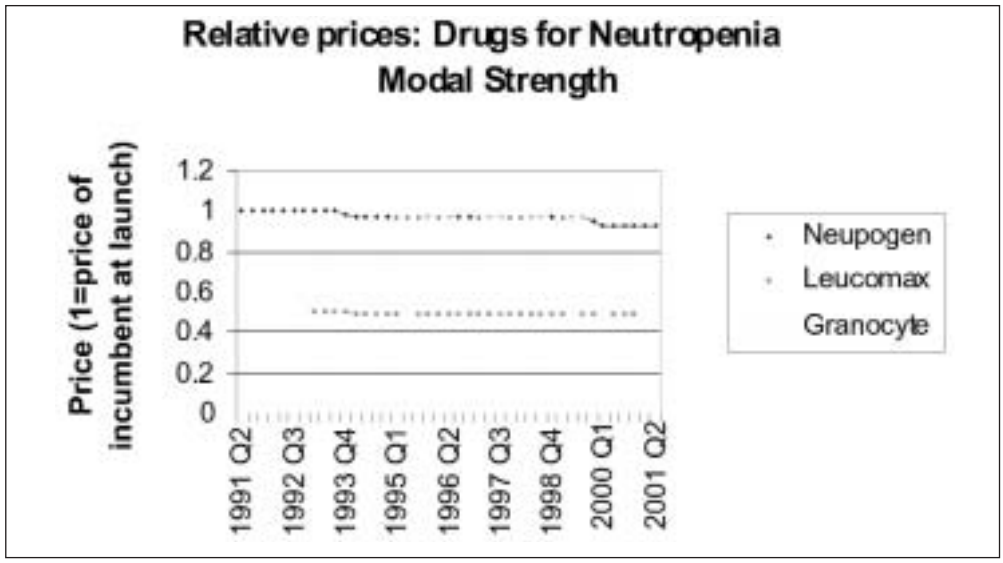

Market shares: Somatostatin analogues
Share by value (%)
120
100
80
60
40
20
0
1991 Q1
1991 Q4
1992 Q3
1993 Q2
1994 Q1
1994 Q4
1995 Q3
1996 Q2
1997 Q1
1997 Q4
1998 Q3
1999 Q2
2000 Q1
2000 Q4
Somatuline
Sandostatin

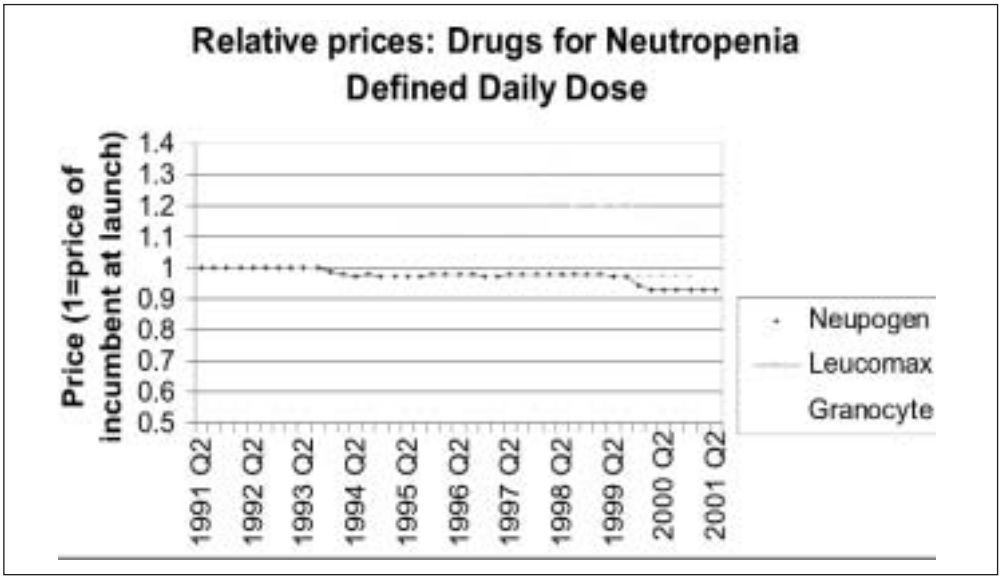

Market shares: Drugs for dementia
Share by value (%)
120
100
80
60
40
20
0
1997 Q2
1997 Q4
1998 Q2
1998 Q4
1999 Q2
1999 Q4
2000 Q2
2000 Q4
2001 Q2
Aricept
Exelon
Reminyl

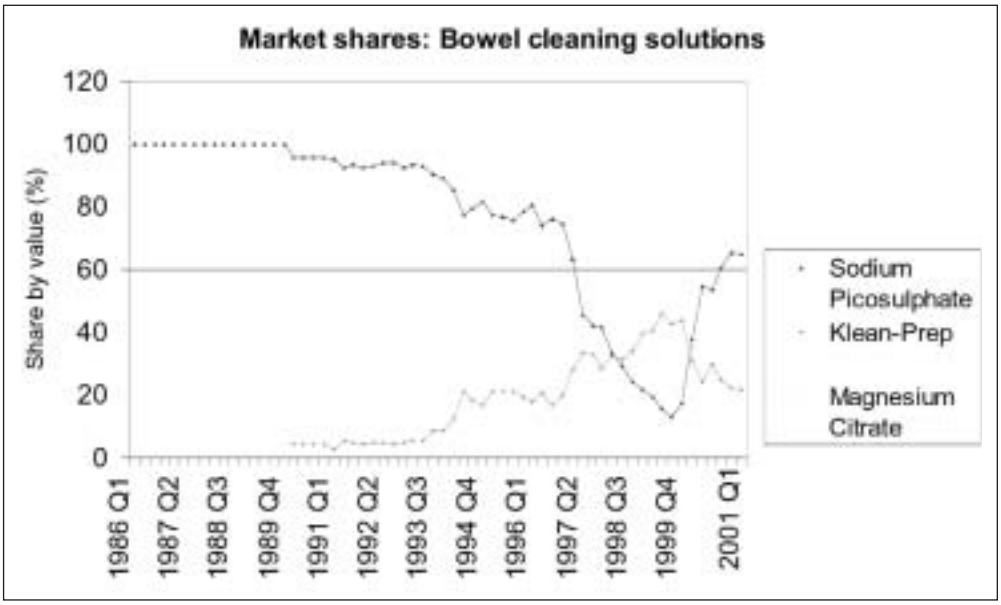

Relative prices: Drugs for Dementia
Modal Strength
Price (1=price of incumbent at launch)
1.2
1
0.8
0.6
0.4
0.2
0
1997 Q2
1998 Q1
1998 Q4
1999 Q3
2000 Q2
2001 Q1
Aricept
Exelon
Reminyl


Relative prices: Drugs for Dementia Defined Daily Dose
Price (1=price of incumbent at launch)
1.7
1.5
1.3
1.1
0.9
0.7
0.5
1997 Q2
1997 Q4
1998 Q2
1998 Q4
1999 Q2
1999 Q4
2000 Q2
2000 Q4
2001 Q2
Aricept
Exelon
Reminyl


Market shares: Drugs used in neutropenia
Shares by value (%)
120
100
80
60
40
20
0
1991 Q1
1991 Q4
1992 Q3
1993 Q2
1994 Q1
1994 Q4
1995 Q3
1996 Q2
1997 Q1
1997 Q4
1998 Q3
1999 Q2
2000 Q1
2000 Q4
Neupogen
Leucomax
Granocyte


Relative prices: Drugs for Neutropenia
Modal Strength
Price (1=price of incumbent at launch)
1.2
1
0.8
0.6
0.4
0.2
0
1991 Q2
1992 Q3
1993 Q4
1995 Q1
1996 Q2
1997 Q3
1998 Q4
2000 Q1
2001 Q2
Neupogen
Leucomax
Granocyte


Relative prices: Drugs for Neutropenia
Defined Daily Dose
Price (1=price of incumbent at launch)
1.4
1.3
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
1991 Q2
1992 Q2
1993 Q2
1994 Q2
1995 Q2
1996 Q2
1997 Q2
1998 Q2
1999 Q2
2000 Q2
2001 Q2
Neupogen
Leucomax
Granocyte


Market shares: Bowel cleaning solutions
Share by value (%)
120
100
80
60
40
20
0
1986 Q1
1987 Q2
1988 Q3
1989 Q4
1991 Q1
1992 Q2
1993 Q3
1994 Q4
1996 Q1
1997 Q2
1998 Q3
1999 Q4
2001 Q1
Sodium Picosulphate
Klean-Prep
Magnesium Citrate

6.5 Number of Price Changes 1991 to 2001

Introduction

This indicator examines the number of price changes occurring over time. The rationale being that, the greater the amount of competition the more price changes there will be, reflecting companies reactions to competition from other products.

The Method

In brief, the method takes all branded medicines and strips out low cost products (those which had a Net Ingredient Cost (NIC) of less than £1 million in any one full year over the period 1990 to 2001). The analysis uses PCA data for NIC and quantity to construct prices at preparation level for each quarter over the period. Price changes are based on the change in average cost of each preparation quarter on quarter (price changes of less than 1% are ignored). Price changes for each preparation were then aggregated up to product level to give a total average price change for each brand.

There are a number of important caveats to bear in mind. The nature of the data is such that a given price change, unless it occurs on the first day of the first month in a given quarter, will affect average NIC in two subsequent quarters. An element of judgement is, therefore, required in order to measure the size and timing of the price change. Also, average NIC can be affected by changes in pack mix for a given preparation if the price structure is not linear to pack size. Finally, and most importantly, many of the observed price falls will have been due to price cuts imposed by the 1993 and 1999 PPRS agreements (and subsequent readjustments if the target price cut was not achieved). Also, some price falls were in lieu of repayment of excess profits under the PPRS.

Results

The results are presented in the Tables 9 to 13 below. These show the total number of price changes over the period 1991 quarter 3 and 2001 quarter 2, split by size of price change and by high and low NIC products. High NIC products are defined as those with a NIC greater than the median NIC in the sample (in the region of £0.5 million for any given quarter). The table also shows whether or not there is a trend increase or decrease over the period[39], and whether or not this is

[39] This is based on a simple OLS regression on time.

statistically significant (at the 95% confidence level). For price falls an allowance has been made to strip out the effect of the 1993 and 1999 price reductions resulting from the respective PPRS agreements[40].

Table 13 shows the results in terms of the net price change over the whole period expressed in terms of the net cash impact of price movements[41] (£000s) and the average change in price over all products (%) over the period covered. Figures are shown for the whole period and excluding the two quarters where modulations took place (1993 Quarter 4 and 1999 Quarter 4).

The average number of price increases is 16.4 per quarter (6.7 for high NIC products and 9.7 for low NIC products) across a total sample of just over 500 products. The average number of price decreases is 18.1 per quarter (8.8 for high NIC products and 9.3 for low NIC products). However, these price falls are disproportionately concentrated in quarter 4 of 1993 and quarter 4 of 1999 when the PPRS price reductions were implemented. Excluding these two quarters reduces the average number of price decreases over the period to 7.0 (3.1 for high NIC products and 3.9 for low NIC products).

In the main, these results seem to suggest there is no clear trend of an increase or decrease in the number of price changes over time excluding the price cuts agreed as part of the 1993 and 1999 PPRS agreements. However, there is a statistically significant downward trend in the number of price rises per quarter for high NIC products overall, although small (declining at a rate of 0.1 per quarter).

The net cash impact over the period is negative at -£38 million[42] however this is dominated by the 1993 and 1999 price reductions. When these are excluded the net impact is positive, but small at about £5 million[42]. Again, there is no clear trend in the net impact of price changes (after allowing for the 1993 and 1999 price cuts).

[40] Dummy variables have been used for 1993 Quarter 4 and 1999 Quarter 4.

[41] Note that the net impact figure is simply the percentage change in price times the sales value (NIC) in the **quarter** when the price change took place, summed across all products which were found to have price changes. As such they do not represent an annual figure.

[42] Note that the net impact figure is simply the percentage change in price times the sales value (NIC) in the quarter when the price change took place, summed across all products which were found to have price changes. As such they do not represent an annual figure.

Price Changes 1991 Quarter 2 to 2001 Quarter 3: Results

Table 9 - Price Rises – High NIC Products

	1% - 5%	5% - 10%	10%-20%	>20%	Total
Total	117	84	45	20	266
Average per quarter	2.9	2.1	1.1	0.5	6.7
Trend	Downward	Downward	Downward	Downward	Downward
Significant?	No	No	No	No	Yes

Table 10- Price Rises – Low NIC Products

	1% - 5%	5% - 10%	10%-20%	>20%	Total
Total	162	107	59	59	387
Average per quarter	4.1	2.7	1.5	1.5	9.7
Trend	Upward	Downward	Downward	Downward	Downward
Significant?	No	No	Yes	No	No

Table 11 - Price Falls – High NIC Products

	1% - 5%	5% - 10%	10%-20%	>20%	Total
Total	224	42	46	38	350
Average per quarter	5.6	1.1	1.2	1.0	8.8
Excluding Q4 1993 and Q4 1999 (PPRS price cuts)					
Total	64	15	19	19	117
Average per quarter	1.7	0.4	0.5	0.5	3.1
Trend	Upward	Upward	Upward	Downward	Upward
Significant?	No	No	No	No	No

Table 12 - Price Falls –Low NIC Products

	1% - 5%	5% - 10%	10%-20%	>20%	Total
Total	266	31	34	42	373
Average per quarter	6.7	0.8	0.9	1.1	9.3
Excluding Q4 1993 and Q4 1999 (PPRS price cuts)					
Total	65	17	23	22	147
Average per quarter	2.2	0.4	0.6	0.6	3.9
Trend	Upward	Upward	Downward	Downward	Upward
Significant?	No	No	No	No	No

Table 13 - Net Impact of Price Changes

	Cash Impact[43] (£000)	%
Total	-37,839	-0.12
Excluding Q4 1993 and Q4 1999 (PPRS price cuts)		
Total	5,344	0.02
Trend	Downward	
Significant?	No	

6.6 GP Knowledge of Relative Prices of Products within Drug Classes

This analysis is based on a study sponsored by the ABPI which comprised face-to–face interviews with 200 GPs. The sample was generally representative on geographic location of GPs, list sizes, and the mix of drugs they prescribe, though not representative in respect to sex, single handed practitioners, fundholders and dispensing doctors.

Face to face interviews were undertaken so problems of self-selection should be lower than with a postal survey, and should also lead to better responses from interviewees than postal surveys - in particular, it eliminates any possibility of a GP looking up prices before responding to the relative price questions.

[43] See footnote 42.

The study focused on five drug classes - chosen because there are at least three products in each of these classes, and they are, for most GP practices, areas of significant prescribing expenditure:

- lipid lowering statins (LLS)
- proton pump inhibitors (PPI)
- hormone replacement therapies (HRT)
- calcium antagonists (CIA)
- antidepressants (Selective serotonin re-uptake inhibitors (SSRI)

For each of the five drug classes GPs were asked to "show their perception of the price of each product in relation to the cost of other products within its drug class, in terms of the cost of 28 days treatment." The results are measured on a 100-point scale in terms of prices of 28 days of treatment.

Responses were analysed to identify the numbers of errors that GPs made in the ranking of products. The question addressed is - using pairwise comparisons of products, how many errors did individual GPs make in ranking product prices? The results are presented with equal rankings being treated as errors (unless prices were identical) and as non-responses for a particular pairwise comparison also being treated as errors. Where GPs did not respond to *any* of the price comparison section of the questionnaire for a particular drug class they were excluded. This ranged from 5 out of 200 GPs for PPIs to 13 out of 200 for HRT and CIA. The results are summarised in Table 14.

Table 14 - Error rates

Drug Class	Number of Products	Number of pair-wise comparisons	Cumulative % of errors				
			0	1 or less	2 or less	3 or less	4 or less
LLS	5	10	5	14	23	41	59
PPI	3	3	25	72	85	100	-
HRT	6	15	3	7	18	27	53
CIA	4	6	8	35	41	62	67
SSRI *	6	15	0	1	4	8	14

* Excluding Dutonin, a related antidepressant

Table 14 shows that few GPs were able to rank all products in a class in the correct order of price - ranging from none (SSRIs) to 25% (PPIs). In all classes except PPIs, less than 10% of GPs were able to rank all products in the correct order.

It is important, however, when looking at the rankings to assess what proportion of pairwise comparisons GPs are getting right. We can measure this by the proportion of pairwise comparisons that GPs on average get right in each drug class – as opposed to the error rates presented above. These results are set out in Table 15.

Table 15: Percentage of correct pairwise comparisons by drug class, based on GPs with complete responses across products in each area

Drug Class	SSRI excluding Dutonin	PPI	CIA	HRT	LLS	All Drug Classes
Total	2850	585	1112	2805	1910	9262
Correct	1775	359	715	1950	1016	5815
% correct stating a price	62*	61	64	70	53	63%**

*When Dutonin is included % correct = 44%
**When Dutonin is included % correct = 56%

One interpretation of these results is that whilst the average results do conceal error rates amongst individual GPs, most GPs are getting most comparisons correct, in that none of the percentages ranked correctly are less than 50. However, it is important to remember that if GPs had absolutely no knowledge of prices, and simply guessed the prices of all the drugs, on average we would expect 50% of pairwise rankings to be guessed correctly. Also, the analysis excludes one product in the SSRI class – Dutonin, a related antidepressant which inhibits re-uptake of serotonin, as there was poor knowledge of the relative price and a high level of "don't knows" amongst respondents. Had this product been included the percentage of respondents stating correct pair wise comparisons for SSRIs would have been 44%, reducing the overall total of correct responses for all drug areas to 56%.

Whilst a benchmark figure for correct rankings (whereby we could be confident that there was sufficient awareness of price to allow price competition to take place) is a matter of judgement, it is clear that there is considerable variation across drug classes. In one market, the percentage of correct rankings were only marginally above what would be expected if GPs had no knowledge of price and simply guessed. In the SSRI market the results are highly sensitive to the treatment of Dutonin – if it is included in the analysis the "per cent" correct falls to below 50%. It is open to debate, therefore, whether the overall average, at 63% (56% if Dutonin is included) is sufficiently high to allow us to conclude that there is sufficient price awareness for price competition to occur.

6.7 Prescribing Incentive Schemes

Background

Prescribing incentive schemes were first introduced into the NHS in 1995. The regulations defined the schemes as follows:

Regulation 1(2): "prescribing incentive scheme" means a scheme under which a [Family Health Service Authority] is required to make a payment to a practice, which, in any financial year, has contained its prescribing costs as specified in directions.

On 25th March 1999, Directions were issued by the Secretary of State for Health, listing the operation of the national Prescribing Incentive Scheme arrangements as one of six functions that could be delegated by Health Authorities to Primary Care Groups (PCGs). In April 2000, amendment regulations came into force enabling PCGs to exercise this statutory duty. A Department of Health circular stated that 'incentives for Primary Care Groups are at the heart of the system' and outlined the scope that schemes should cover (paragraphs 78 – 89). Paragraph 83 states:

A national scheme will apply whereby all PCGs must have a prescribing incentive scheme and each practice will participate.

The essence of the Directions is that PCGs *must* reward practices that meet two criteria:

- PCGs must reward practices that *either* contain their costs within the target budget *or* exceed the target budget with 'good cause' *or* that exceed the target budget by a reduced amount compared with the previous year.

- Secondly, the PCG may specify 'additional conditions' that practices must, or may, meet to qualify for an incentive payment.

The Directions repeat HSC1998/228, both in the guidance on how incentive payments relate to savings (which indicate a suggested maximum annual payment of £45,000 per practice) and also in the purposes to which payments may and may not be put. No money can go directly as income to practices. The maximum recommended reward would be available only to practices achieving an underspend on their prescribing budget of at least £70,000. The objective is to improve the value for money obtained from prescribing by seeking to reduce cost and increase quality.

Prescribing Incentive Schemes: Survey Findings

The Management of Medicines survey conducted by the University of York in 2001 included a number of questions relating to prescribing incentive schemes. Ninety-one Primary Care Organisations (PCOs) participated in the survey for 2001/02, covering almost one-quarter of the PCOs in England.

The budgetary targets in the schemes were relatively straight forward. Most of these schemes (94%) required practices to achieve an underspend (or remain within prescribing allocation) in relation to the target budget. Most schemes (81%) including budgetary targets offered practices multiple targets, reflecting the DH directive that practices reducing their overspend should also qualify for a reward.

However, there was a great deal of diversity in the rewards given, quality targets and the indicators used.

In respect of the rewards given, about one-quarter of schemes cited the maximum payment allowable as £45,000 per practice, in line with ceiling given by the DH directive. Small numbers of schemes scaled the payment according to the number of whole time equivalent (WTE) GPs with per-practice maximums ranged from £6,000 to £15,000. Others used a per-patient basis, with an average of about £200/1000 ASTRO-PUs[44], or about £2.40/patient. 30% of the schemes did not specify, or give enough information to estimate, the maximum reward payable.

[44] Age, sex and temporary resident originated prescribing units (units of prescribing adjusted for the age, sex and other characteristics of the population)

The prescribing targets used covered a wide range of therapeutic areas. In some cases the objective was to reduce use and in other cases to increase it.

- Over three-quarters of schemes included a target for generics and about 86% of schemes included antibacterial targets, with almost one fifth including a target specifically on quinolones;

- Oral NSAID targets were slightly less popular, appearing in 78% of schemes. Twelve schemes included a specific target on topical NSAIDs and eight focussed specifically on modified release NSAIDs. Seven schemes addressed Cox 2 inhibitors specifically and three of these addressed no other type of NSAID. Excluding targets on topical NSAIDs, 20 schemes had a target for drugs of limited clinical value;

- Coronary Heart Disease (CHD) medications were frequently targeted: among the categories of drug included in the schemes were antihypertensives (4 schemes), antiplatelets (4), aspirin (24), ACE inhibitors (11), beta-blockers (8), diuretics (20), nitrates (13), warfarin (4), and lipid-lowering drugs in general (6);

- Targets particularly associated with lipid status were included in ten schemes and 10 of the 13 references to nitrates were aimed at reducing the use of modified release isosorbide mononitrate. Schemes employed a variety of indicators to achieve this target, mostly volume- rather than cost-based.

A wide range of indicators was used to measure the prescribing targets including the following:

- Volume measures, such as a specified level of items (19% of all indicators) for a particular patient denominator or the proportion of patients within a particular group who had been prescribed a certain drug (5%);

- Ratios of items of two drugs, or class of drugs, were also used, especially for PPIs (treatment-dose ratio was used in 56 of the 75 PPI indicators and there were three instances of PPI /H2 antagonists ratios);

- Approved lists formed 11% of indicators, most commonly applied to antibacterials (46 schemes) and to NSAIDs (30 schemes), although they were also, but less frequently, used for beta-blockers (5), diuretics (5) and generics (4).

These prescribing incentive schemes have significant potential to influence the choice of therapy and of drug within therapy class. It is too early however for the impact of these schemes to be assessed. Literature on the impact of incentive schemes is included in Component 4.

6.8 Generic Prescribing and Dispensing Rates

Table 16 – Generic prescribing and dispensing rates by volum

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
% prescribed generically	41	43	47	52	55	58	60	63	66	71
% dispensed generically	35	36	38	41	43	45	47	48	48	52

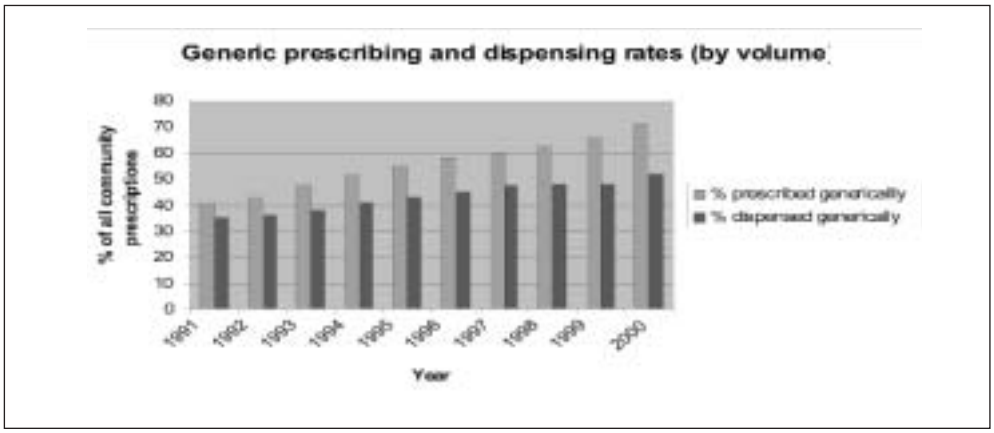
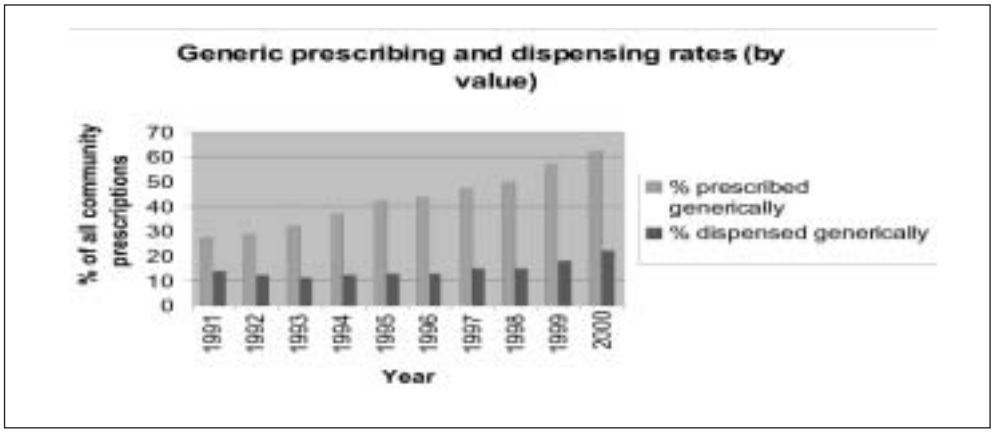


Table 17 – Generic prescribing and dispensing rates by value

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
% prescribed generically	27	29	32	37	42	44	47	50	57	62
% dispensed generically	14	12	11	12	13	13	15	15	18	22



The data for both tables was obtained from PCA data for all prescriptions dispensed in the community, England only.

6.9 Annual Growth in Medicines Expenditure

Table 18 – Growth in NHS Spending on Drugs

Year	NHS Spending on Drugs			Growth in NHS Spending on Drugs (Cash terms)		
	Community (£m)	Hospitals (£m)	Total (£m)	Community (%)	Hospitals (%)	Total (%)
1991/2	2,317	591	2,908	-	-	-
1992/3	2,641	643	3,284	14.0	8.8	12.9
1993/4	2,951	710	3,661	11.7	10.4	11.5
1994/5	3,230	764	3,994	9.5	7.6	9.1
1995/6	3,498	874	4,372	8.3	14.4	9.5
1996/7	3,774	961	4,735	7.9	10.0	8.3
1997/8	4,085	1,088	5,173	8.2	13.2	9.3
1998/9	4,339	1,211	5,550	6.2	11.3	7.3
1999/00	4,833	1,369	6,202	11.4	13.0	11.7
2000/01	5,161	1,530	6,691	6.8	11.8	7.9

Source: DH Finance

Note that the figures in this table comprise NIC plus container cost plus VAT minus discount. Therefore, they are not directly comparable with the tables showing the component elements of the growth in NIC shown below.

Table 19 – Breakdown of NIC Growth, 1992-2000, all Prescriptions

	Average annual % change								
	1992-2000	92-93	93-94	94-95	95-96	96-97	97-98	98-99	99-00
Total NIC	8.7	10.5	7.8	8.1	8.9	9.0	7.6	12.5	5.5
Total volume	3.3	4.8	2.4	3.8	2.4	3.1	2.6	3.2	4.2
Pure demography	0.4	0.3	0.4	0.4	0.4	0.4	0.4	0.5	0.5
Items per head	2.9	4.4	2.0	3.4	2.1	2.7	2.2	2.7	3.7
Average NIC (all)	5.2	5.5	5.3	4.1	6.3	5.7	4.9	9.0	1.3
Average NIC (existing)	5.1	4.0	5.0	3.0	6.1	4.3	4.3	8.9	0.1
Paasche	-1.8	-3.2	-1.7	-1.3	0.0	-0.4	-2.6	2.7	-5.7
QPP	1.5	2.3	0.5	1.2	0.8	1.4	1.4	0.1	2.9
Product mix residual	5.4	5.0	6.3	3.2	5.3	3.3	5.5	5.9	3.2
Entry and exit effect	0.8	1.4	0.3	1.1	0.1	1.3	0.6	0.1	1.2
Exit effect	-0.1	0.0	-0.9	0.0	-0.3	0.0	0.1	0.0	0.3
Entry effect	0.9	1.4	1.2	1.1	0.5	1.3	0.6	0.2	0.9

[1] The data are from the PCA data based on items dispensed in England.
[2] The data cover prescriptions dispensed by community pharmacists and appliance contractors, dispensing doctors and personal administration.
[3] All data in this table is in cash terms

The table divides total NIC as follows:

1. Increase in **total volume**

    a) **Pure demography** (i.e. effect of increase of total population – no account is taken here of changing age distributions)
    b) Increase in the **number of prescriptions per head**

2. Increase in **average NIC per prescription item**

    a) Change in **average NIC per item for existing products** (i.e. products dispensed in both base and review year)
        i) **Pure price effect** (Paasche index; the effect of changes in actual prices of individual products)
        ii) Change in **quantity per prescription** (QPP index)
        iii) **Product mix effect** (the effect of a switch from older, cheaper drugs to newer, more expensive ones)
    b) **Entry effect** (effect on average NIC of new products)
    c) **Exit effect** (effect on average NIC of products being discontinued)

Table 20 shows a similar breakdown, for branded prescriptions only:

	Average annual % change								
	1992-2000	92-93	93-94	94-95	95-96	96-97	97-98	98-99	99-00
Total NIC	7.3	11.2	7.1	7.1	8.6	6.9	7.5	9.0	1.2
Total volume	-0.4	0.2	-2.0	-0.4	-0.1	-0.5	0.7	2.3	-2.9
Pure demography	0.4	0.3	0.4	0.4	0.4	0.4	0.4	0.5	0.5
Items per head	-0.8	-0.1	-2.3	-0.8	-0.5	-0.9	0.2	1.7	-3.3
Average NIC (all)	7.7	11.0	9.3	7.5	8.7	7.5	6.8	6.6	4.1
Average NIC (existing)	7.2	9.9	9.1	6.6	8.7	7.3	6.2	6.7	3.3
Paasche	-1.9	-1.8	-1.6	-1.1	0.3	0.4	-2.3	-0.6	-7.9
QPP	1.5	2.7	0.6	1.3	0.9	0.4	1.8	0.1	3.8
Product mix residual	7.7	8.9	10.2	6.4	7.4	6.5	6.7	7.2	8.1
Entry and exit effect	0.4	1.0	0.2	0.8	0.0	0.2	0.5	-0.1	0.8
Exit effect	0.0	0.2	-0.7	0.0	-0.1	0.0	0.2	0.0	0.6
Entry effect	0.4	0.8	0.9	0.8	0.1	0.2	0.3	-0.1	0.2

6.10 International Price Comparisons

The Department undertakes an annual price comparison of the best selling branded medicines in the NHS with prices elsewhere in Europe and in the USA using IMS data on prices and NHS volume weights from PPA data. The results of the latest exercise were published in the Fifth PPRS Report to Parliament. In 2000 it compared the prices of all preparations for the top 150 branded medicines in the UK with those in Austria, Belgium, Finland, France, Germany, Ireland, Italy, Netherlands, Spain and the USA.

The tables below (taken from the report) set out the price comparisons.

We see that the position of the UK has changed quite significantly between 1996 and 2000, largely due to the appreciation of Sterling. If a five year (1996-2000) exchange rate is used, UK prices are slightly lower than those in Germany, roughly the same as Finland and Ireland and higher than in other EU countries (though much less so than if the 2000 exchange rate is used).

Table 21 – Bilateral Comparisons of Ex-Manufacturer Prices

At that year's market exchange rate						
Country	**1996**	**1997**	**1998**	**1999**	**2000**	**2000***
France	112	86	85	84	80	96
Germany	124	108	108	97	91	103
Italy	91	82	81	83	79	90
Netherlands	112	93	N/A	N/A	81	93
Spain	88	71	71	67	64	74
UK	100	100	100	100	100	100
US	183	175	174	184	209	189
Austria			81	83	77	88
Belgium			86	84	78	89
Finland			86	85	83	95
Ireland			90	88	83	96

Table 22 – Multilateral Comparisons of Ex-Manufacturer Prices

At that year's market exchange rate						
Country	**1996**	**1997**	**1998**	**1999**	**2000**	**2000***
France	105	85	85	86	83	94
Germany	125	101	109	103	94	108
Italy	93	86	88	82	82	93
Netherlands	108	93	N/A	N/A	N/A	N/A
Spain	89	74	77	72	70	80
US	191	184	188	213	243	220

The study concluded:

'Previous reports showed that UK prices were in the middle range of the countries in this study over the period 1992 to 1996 but the UK's position has changed since 1996, largely as a result of sterling appreciation. For the countries for which we have 2000 data, the average sterling appreciation was 26%.

* At five-year average exchange rate.

The 2000 weighted index, based on bilateral comparisons, and based on 2000 market exchange rates showed prices in the UK to be:

- Significantly lower than those in the USA;
- Higher than those in the other European comparator countries.

However, if a longer-term five-year average exchange rate is used, prices in the UK are broadly comparable with Germany, Finland, Ireland and France and higher than the other European Union countries.'

Component 2:

Competition in the In-Patent Sector

December 2002

Component 2

Contents

6.6.23	Tricyclic Antidepressants
6.6.24	B_2-Stimulant Inhalants (Short-acting): Manual MDI Devices
6.6.25	B_2-Stimulant Inhalants (Long-acting): Manual MDI Devices
6.6.26	Corticosteriods Inhalants: Manual MDI
6.6.27	Corticosteriods – BAI Dry Powder requiring minimal dexterity

Component 2

Competition in the in-patent sector

1. Executive Summary

This component is concerned with the extent of competition in the in-patent sector. The study was conducted by an independent economics consultancy, Europe Economics Research (EER).

For the pilot phase, EER analysed monthly IMS Health data for the five-year period May 1995 to April 2000 for quantities sold to pharmacies and revenues from those pharmacy sales for each presentation of each product within the four broad categories of antidepressants; diabetes treatments; stomach acid and ulcer treatments; and asthma treatments. The data covered UK pharmacy sales and excluded hospitals. EER's report concluded 'For none of the four therapeutic classes did the econometric investigation consistently find well-behaved demand functions with well-established and plausible answers on substitution.' However it is unclear whether this was the result of data limitations (in particular, the inability to separate newly instigated from repeat prescriptions), the lack of price changes which may have resulted from the perceived constraints imposed by the Pharmaceutical Price Regulation Scheme (PPRS), or there being no switching behaviour in response to price changes.

The report also notes important points relating to incentives for doctors and pharmacists under the NHS that impact responsiveness to price changes.

The main study involved an analysis of 27 therapeutic areas or 'markets'. EER analysed monthly IMS Health list price and quantity series for each presentation for the period October 1995 to September 2000. The data were for sales to pharmacies only, so exclude sales to hospitals. The markets chosen accounted for some 60% of total expenditure (Net Ingredient Cost) on branded pharmaceuticals in primary care in England in the year to September 2000.

The main findings from the cross-market analysis are:

Price Changes for Branded Medicines

- There were 24 price increases of more than 10% of major branded medicines in the 27 markets and 20 price reductions of more than 10% over the five-year period. The majority of the price falls resulted from price reductions required under the PPRS.

- Five of the 27 markets accounted for more than half of all the price changes. Nine of the markets had no price changes of more than 10%.

- The prior trend in sales value did not seem to affect the sign or magnitude of price changes.

- The availability of generics did not impact on headline price changes in one particular direction.

Volume Responses to Price Changes

- Over the five-year period, only a third of price changes led to a discernible effect on sales volume.

- For seven of the 24 price increases, the price increase was followed by a discernible reduction in sales volume compared to the volume trend before the price increase.

- For seven of the 20 price reductions, the price reduction was followed by a discernible increase in the trend of sales volume.

Competitor Price Responses to Price Changes

- Over half of price changes triggered no response from competitors.

- Following the 24 price increases, there were nine increases for other products that were possibly competitive responses (two within three months and seven within 12 months).

- Following the 20 price decreases, there were 11 decreases for other products that were possibly competitive responses (three within three months and eight within 12 months)

New Products (New Molecules)

- There were 43 new molecule entries across the 27 markets in the five-year period. 30 were in the seven markets with three or more new entries. Ten of the 27 markets saw no new molecule entry.

- New products were as likely to enter the market at a higher price to existing products in the same market as at a lower price. Using prices per Defined Daily Dose (DDD) of the modal strength of the new entrant, entry price was below that of the incumbent in 20 cases and above it in 18.

- In the majority of cases, the launch of new products provoked no price response from competitor products. In only two of the 43 entries is there a price reduction by the incumbent that may be associated with entry.

Generic Entry and Generic Competition

- There were 18 first entries of branded generic products across the 27 markets, and 14 first entries of unbranded generics.

- In most cases, there was no reduction in the headline price of the branded product in response to generic entry. Some branded companies compete with generics on the basis of discount allowed to wholesalers and community pharmacies.

- Generics are as likely to enter at a headline price (per DDD at modal strength) above that of the original branded product as at a price below that of the branded product.

- In many cases generic versions of major branded products took substantial shares, often equalling those of the original brands after two or three years despite, in some cases, being priced (before discount) at or above the original brand.

- Overall the number of market sectors dominated by generics (over 80% sales) rose from three to six (out of the 27 markets studied) during the study period but the number of markets with small generic share (less than 20%) hardly changed by the end of the period when there were nine markets with small generic share.

2. Introduction

Component 2 of the Competition Study is concerned with the extent of competition in the in-patent sector. The main output of component 2 is an analysis of 27 drug classes, the results of which are described at section 4 below. The study followed a scoping exercise and a Peer Review Workshop in November 1999, which considered the available evidence and made recommendations for a more detailed analysis of the extent of competition.

Following an open tendering exercise, an independent economics consultancy, Europe Economics Research (EER), was commissioned to carry out the work in two stages (a pilot study and main study). The specification required them to:

- use the approaches set out in Office of Fair Trading (OFT) guidelines to divide the market into relevant sub-groups for assessing market power, identifying close substitutes and links between product classes, and presenting estimates of cross-price demand elasticities between products in each market;

- analyse five years' monthly data from the IMS British Pharmaceutical Index monitor of retail purchases. This analyses pharmacy purchases and reflects total prescribing including repeat prescriptions and not just recent new patient and switch decisions.

- provide evidence relevant to an assessment of market power in each market.

Four therapeutic areas were specified for the pilot phase of the study - antidepressants; diabetes treatments; asthma corticosteroids; and proton pump inhibitors. The results of the pilot were used to agree an approach for the main study covering 27 markets. In addition to the market definition and market power elements in the pilot study, the full study required a comparison with other non-pharmaceutical product markets and consideration of possible synergies with other components of the Competition Study e.g. generic supply changes and demand side prescribing patterns. The full terms of reference are at Appendix 6.1.

In order to understand the significance of the findings of the study it is important to recognise the framework that impacts upon competition in the supply of branded medicines to the NHS.

- On the supply side, prices are controlled by the Pharmaceutical Price Regulation Scheme (PPRS). Companies have freedom of pricing for new active substances but in other circumstances whereas companies are allowed to reduce prices, increases may only be made with the agreement of the Department. There are two circumstances in which companies are allowed to increase prices:

    - as part of the modulation provisions of the agreement where prices can change (within limits) provided that this is at nil cost to the NHS;

    - where overall profitability falls below a threshold expressed as return on capital or return on sales specified in the agreement. It is generally acknowledged that this created a disincentive for companies to reduce prices because this provision severely limited or in many cases ruled out price increases in the future. To remove this restriction, from October 1999 companies may make price reductions outside the modulation and overall profitability provisions and increase the price subsequently to its previous level without the agreement of the Department;

- On the demand side, which has gained momentum over the last few years, the pharmaceutical market is influenced by a number of factors which include:

    - financial incentives for doctors (via Primary Care Group (PCG) prescribing incentive schemes) and pharmacists;

    - limitations on promotion expenditure allowed under the PPRS (although many companies spend significantly more than this limit);

    - a strong emphasis on generic prescribing which results in some 70% of prescriptions being written generically and some 50% dispensed generically;

    - the introduction of formularies by many PCGs and greater co-operation between the hospital and community sectors in the development of these formularies (most of which provide advice and are not compulsory). These formularies tend to promulgate best practice and the extent to which cost factors influence the formulary development varies.

The National Institute for Clinical Excellence (NICE) was not relevant to the study, as the first guidance on medicines was not issued until the very end of the period covered by the study. The influence of the demand side measures has been looked at in some depth in component 4 of this study.

3. Pilot Study

EER analysed monthly IMS Health data for the five-year period May 1995 to April 2000 for quantities sold to pharmacies and revenues from those pharmacy sales for each presentation of each product within the four broad categories of antidepressants; diabetes treatments; stomach acid and ulcer treatments; and asthma treatments. The data covered pharmacy sales in England, Scotland, Wales and Northern Ireland and excluded hospitals. EER submitted their report in September 2000 and their conclusions are summarised below. Their findings on the four therapeutic areas are summarised at Appendix 6.2.

EER noted that 'The most striking feature of the data is that for many products and molecules, the price remained constant for much of the five year period. This stability in prices is not surprising given the strict limits on price increases under the PPRS and the consequent irreversibility of any decision to reduce prices. However, it reduces the likelihood of econometric analysis providing clear and robust evidence on substitution.'

EER's report concluded 'For none of the four therapeutic classes did the econometric investigation consistently find well-behaved demand functions with well-established and plausible answers on substitution. Hence the judgement on market definition had to give considerable weight to the medical advice and the assessment of market behaviour to what could be observed from entry and price changes.'

'It is not possible to say at this stage how far the inconclusive econometric results on doctors' substitution of medicines in response to price changes within any one class were due to:

- the limitations of the data set, in particular the inability to separate prescriptions written for new and existing patients;
- the effects of the constraints on price increases imposed by the PPRS; or
- there being no such switching behaviour for those molecules.'

EER reported that their limited analysis of advertising showed some interesting results on the effects of variables other than price:

- 'for the two major therapeutic classes studied where most or all of the medicines are still in patent (SSRIs and PPIs), higher advertising expenditures (measured as a stock subject to depreciation) were found to lead to increased sales volumes and market shares.

- for these two categories, the age and entry order of drugs were both found to affect market shares.

In addition, a survey of advertisements in the British Medical Journal showed that advertising in each of the four therapeutic areas studied emphasised efficacy, with price being mentioned in only a minority of cases.'

EER concluded that 'competitive behaviour in these markets cannot be understood by concentrating solely on the companies' pricing decisions. There are elements of non-price competition and, of course, competition in innovation, that will need to be taken into account in a fuller analysis than attempted so far.'

4. Main Study

4.1 Analysis Background

Exhaustive econometric analysis had failed to produce estimates of demand elasticities in the pilot study since the numbers of changes in price were not sufficient to be able to derive robust, meaningful results. It was, therefore, decided to devote the rest of the project instead to providing more descriptive, less technical analyses of price changes and new entry events and market reactions to them.

The EER analysis covered 27 therapeutic areas or "markets". The markets chosen were those with the highest or most rapidly growing expenditure within the 18 broad (ATC2) therapeutic categories specified by the DH and ABPI. The 27 markets covered 17 of the original 18 ATC2 categories giving a broad coverage of the major areas of NHS expenditure on pharmaceuticals. It was agreed to drop a small number of markets comprising older products or where many products were available OTC and/or were delisted as analysis was unlikely to shed much light on the competition between patented medicines.

Market Number	Name of Market
1	H_2 Antagonists
2	Proton Pump Inhibitors
3	Sulphonylureas
4	Biphasic Insulins
5	Loop Diuretics
6	Thiazides and Analogues (Plain)
7	Beta-blockers
8	Calcium Antagonists (Plain)
9	ACE Inhibitors (Plain)
10	Angiotensin-II Antagonists (Plain)
11	HMG-CoA Reductase Inhibitors
12	Topical Corticosteroids
13	Penicillins and Cephalosporins (Oral)
14	Antifungals
15	Treatments for Herpes and Varicella Zoster
16	Antirheumatics
17	Narcotic Analgesics
18	Migraine Treatments
19	Anti-Epileptics
20	Antipsychotics
21	Non-Barbiturate Hypnotics
22	SSRI Antidepressants
23	Tricyclic Antidepressants
24	B_2-Stimulant Inhalants (Short-Acting): Manual MDI
25	B_2-Stimulant Inhalants (Long-Acting)
26	Corticosteroid Inhalants: Manual MDI
27	Corticosteroid Inhalants: Breath Activated Inhaler (BAI) dry powder requiring minimal dexterity

Products in the 27 markets analysed accounted for £3.4 billion of NHS expenditure in the year to September 2000, up from £2.4 billion in the year to September 1996. In the year to September 2000, they accounted for 77% of the total NHS expenditure on products within the 18 broad therapeutic categories identified for the study and some 60% of total expenditure (net ingredient cost) on branded pharmaceuticals in primary care.

The data analysed were monthly IMS Health list price and quantity series for each presentation for the period October 1995 to September 2000. The data were for sales to pharmacies only, so that all the volume and expenditure figures exclude sales to hospitals. Markets were defined at the ATC4 level except where medical advice on the degree of therapeutic substitutability, or DH and ABPI advice on the workings of particular markets, suggested that a broader or narrower definition was appropriate. This does not mean that all products in each of the markets, as defined, are close therapeutic substitutes for all patients and all indications. The degree of therapeutic substitutability of products within the markets varies.

For the analysis of the five-year period from October 1995 to September 2000, the relevant competition is between:

- different patented medicines;
- out-of-patent products and their generics; and
- generics in the determination of generics prices: this is not studied here, and generic prices are treated as exogenous.

For this project, EER were directed to focus principally on price competition, with other forms of competition e.g. the relative therapeutic value of products considered only insofar as they are relevant to establishing the nature and extent of price competition.

The factors used to assess the level of price competition in a given market can be grouped into demand-side factors and supply-side factors. Demand-side factors are concerned with whether customers are sufficiently well informed about the choice of alternative suppliers and with how expensive or disruptive is it for them to exercise this choice. Supply-side considerations look at the number and strength of existing competitors and at the ability of other firms to enter the market.

4.2 Demand-side – Incentives under the NHS

Important points relating to incentives for doctors and pharmacists under the NHS include:

- The separation of the decision to purchase a prescription medicine, typically made by the prescriber, from the responsibility for paying for it, which in the UK lies with the NHS. This means that demand may not respond to price signals, especially if prescribers' incentives to reduce prescribing costs are weak.

- Doctors do not yet face truly "hard" prescribing budgets, and their responsiveness to relative prices is undermined by this. Quantitative GP incentive scheme targets may well have contributed to the dramatic increase in the extent of generic prescribing – now over 70% of the total - but are not equivalent to establishing responsiveness to relative prices.

- GPs' awareness of new products or price reductions is very dependent on whether they read "new information" in monthly publications such as MIMS (Monthly Index of Medical Specialities). If not, they may not learn of the change until advice comes from the PCG pharmacist or from the company.

- Non-price influences on prescribing can, depending on their nature, either dampen or invigorate price competition. Manufacturers seek to establish their brands in the minds of prescribing doctors using marketing activities such as publications, conferences, symposia, doctors' meetings and seminars at which research on new treatments is presented.

- Pharmacists and dispensing doctors have a direct influence over what product is dispensed against generic prescriptions. As they are reimbursed at a fixed Drug Tariff price for generics, it is in their interest to dispense the product, which provides them with the best profit margin. For some categories they may have a variety of generics including parallel imports to choose from. Although they are unable to substitute different products for a medicine prescribed by brand name, pharmacists are able to dispense a parallel imported product provided the brand name is identical. Again they will have an incentive to do this if sourcing the product from overseas offers a better margin.

- Once a patient is established on a particular drug therapy, there can be expected to be significant medical reasons why it is disadvantageous to alter their medication. Added to this, are the costs in GP time in effecting a switch, and associated patient confusion and/or unwillingness to change. Switching costs vary between classes. For example, in diabetes, or for many psychiatric products the difficulties associated with changes in medication are particularly high in terms of the negative clinical effects that can result, with patients' tolerance of, and reaction to, new products or different formulations having to be carefully monitored.

4.3 Supply-Side: Pharmaceutical Price Regulation Scheme (PPRS)

The pharmaceutical market is not a free market in economic terms. Various regulations govern the conduct of companies operating in the sector. Pricing is moderated by the PPRS and this distorts pricing behaviour and the effect of price changes.

The PPRS sets limits on the profits that can be earned by individual companies on reimbursable sales to UK pharmacies, including NHS hospital pharmacies. Within those limits and with consideration of existing competitive products companies are free to set the entry price of major new licensed products (new active substances) and that price, which includes a wholesaler's margin, will be reimbursed by the NHS. However prices cannot normally be increased above their launch level and prices of other products may have to be reduced to accommodate the profits from new products.

The PPRS is likely to influence pricing and competitive behaviour in the following ways:

- The design of the PPRS is likely to distort price competition between rival patented products. As explained above over the years the scheme has laid down firm rules for circumstances in which prices may be changed subsequent to the entry into the market of a new active substance (NAS)/new chemical entity (NCE).

- The PPRS virtually ensures that a new medicine will be launched with a (modified) skimming price strategy, regardless of its degree of innovation.[1] This is because penetration pricing presupposes the ability to raise selling prices later, if the product is notably successful. This launch price strategy is here described as a 'modified' skimming strategy because it is influenced by the existence of price controls as well as normal market constraints on a high initial selling price such as existing competition.

It can therefore be expected (and is apparent in the study findings) that pharmaceutical prices will be static for longer periods than would otherwise be the case:

- The number of price increases observed will be limited since companies cannot raise the price of a product unless their returns are below their lower limit or they reduce the price of another product;

- The number of price reductions will be constrained, since such reductions become more risky as companies considering reducing the price of a product face the prospect of not being subsequently able to raise it again.

- As demonstrated below the overall price of a day's drug treatment as reported across all categories increased by 2.5% per year. This was largely driven by product mix changes rather than product price increases. The average rate of inflation (RPI) over the five-year period of study was 2.7%.

- With the introduction of the new PPRS scheme in October 1999, companies were required to reduce the prices of their branded medicines by an average of 4.5%, but had a substantial degree of freedom as to where these reductions were made (this rebalancing is known as 'modulation'). As you would expect companies decided to make the reductions in areas which they estimated would give them maximum advantage in the market.

[1] The economic literature on pricing indicates that companies launching new products can choose between a "skimming" price policy and "penetration pricing". A skimming price policy involves setting a high initial price and then lowering it over time. Penetration pricing is the strategy of setting a low initial price, with the intention of obtaining a rapid growth of market share, and then perhaps raising the price over time if the product proved successful enough to sustain this.

4.4 Supply-Side – Market Power

Competition can be said to be effective when the incumbent is constrained from raising prices or lowering quality standards, relative to the competitive level, by the possibility that customers will switch to alternative suppliers. Where competition is not effective, the incumbent operator may, unless otherwise constrained, possess sufficient market power to enable it to act against the interests of customers and competitors.

Market power can arise from:

- the existence of a single dominant firm;
- collective dominance, involving some form of collusion (explicit or tacit) between any number of firms (although this is likely to be easier to maintain the fewer companies that are involved).

The concept of effective competition thus goes beyond the issue of whether a single firm is dominant or not and takes into account how firms compete with each other and whether competition is efficient and sustainable.

It is convenient to divide supply-side factors affecting pharmaceuticals competition into two groups: those relating to the existing structure of the market and conduct of its participants; and those relating to the ability of new firms to enter the market.

4.5 Potential Competitors – Market Entry

In order to assess the prospective level of competition in the relevant market, it is also important to understand the potential for new firms to enter the market. Where entry is relatively easy, an incumbent may be constrained by firms not yet operating in the market. Time lags between first, second and subsequent entrants and strategic interaction between incumbents and new entrants are therefore important. One of the most crucial determinants of the propensity for firms to enter markets is the existence of barriers to entry.

Pharmaceuticals markets are characterised by high barriers to entry as a result of regulation such as product licensing and intellectual property laws. Other firms cannot respond to a high price with entry within a short period of time except where:

- they have developed a new medicine through extensive R&D efforts and can obtain a licence for it; or

- one or more of the main products in the market is out-of-patent.

Patent protection and the high investment and long timelines for R&D mean that entry into most pharmaceutical markets is unlikely in the short to medium term. It follows that, even though the EER analysis covered a five-year period, you would not expect to find many new entrants, irrespective of market developments, such as large price rises or high profit margins. This would only be possible if companies had products already nearing the market.

While in economic terms intellectual property laws (such as patents) and marketing authorisation regulations will be considered high barriers to entry, it is important to note that these provisions are required for a successful industry and to ensure safety and efficacy of medicines.

Other potential barriers to entry into drug markets are less absolute in nature but are still capable of influencing entry decisions and may therefore be relevant to some of the observed market behaviour. These include the existence of sunk costs and any exclusionary conduct by incumbents.[2]

[2] A potential entrant's expectations about the reaction of firms already in the market can also deter entry. If existing firms are expected to retaliate forcefully then entry may not be attempted. Conditions that suggest the likelihood of strong retaliation to entry may include: an incumbent's reputation for successful retaliation; the ability of the incumbent to finance losses incurred; the incumbent's degree of commitment to the industry; and excess capacity. The threat of retaliation may deter entry if retaliation is seen as a rational strategy for the incumbent. This will be the case if, once competition has been eliminated, the incumbent can raise prices without attracting other new entrants. This in turn will depend on the strength of barriers to entry.

5. Main Findings from the Cross Market Analysis

5.1 Introduction

In addition to its analysis of 27 individual markets, EER provided a cross-market analysis working paper in April 2001 with its evidence on the workings of competition between branded products. Their main points are shown at sections 5.2 to 5.7 below.

The supporting data provided by EER is reproduced at Appendices 6.3 to 6.5. Appendix 6.3 provides market summary data; Appendix 6.4 lists significant price changes; and Appendix 6.5 lists entry events. A summary of the main points for each of the 27 individual market analyses is at Appendix 6.6. For each market, a table highlights the number of new entrants; relative entry price; whether the product gained significant market share and whether there was a price response. It also shows the number of significant price changes and whether there was a price response, impact on prescriber usage or impact on volume.

5.2 Initial overview

- The total value of sales fell in only three of the 27 markets between October 1995 and September 2000, and the volume (measured in terms of the Defined Daily Dose (DDD) specified by the World Health Organisation) fell in only four markets.

- Looking across all the markets, the implicit average price of a day's treatment – total value divided by total number of DDDs – rose by over 10% in 11 markets and fell by more than 10% in seven markets. Aggregating across all of the markets, the average implicit price of a day's treatment rose by 13% over the period studied, equivalent to 2.5% on an annual basis. However, it is important to note that this increase is not primarily driven by price changes. The 'product mix effect', with patients being changed to newer, more effective and more expensive treatments over time, will have a larger impact.

- The volume share of generics rose markedly in eight markets and fell markedly in two markets. The number of markets dominated by generics, with 80% or higher generic share, increased from three to six but the number of markets with small generic share (less than 20%) hardly changed by the end of the period when there were nine.

- In 18 markets the Herfindahl concentration indexes fell, while seven markets became more concentrated. At the end of the period ten of the markets had levels of concentration with a market share in excess of 40%, which would imply dominance under OFT rules. There may be some selection bias as several markets were selected on the basis of being fast-growing and it may be the case that these saw significant new entry and subsequently experienced a decrease in concentration.

5.3 Price Competition between Established Branded Products

- Over the five-year period, there were 24 price increases of more than 10% of major branded products in the 27 markets, and 20 price reductions of more than 10%. Over half of the reductions took place in or around October 1999, when companies were required to reduce prices by an average of 4.5% on the introduction of the new PPRS. A further 12 price changes were due to subsequent adjustments (price remodulations) to ensure delivery of the price reduction. In total 23 out of the 44 price changes resulted from price reductions required under the 1993 and 1999 PPRS. Of the other price changes, half of the price increases, which were mainly to older low volume products, were not authorised by the Department and two major price decreases were in lieu of repayments of excess profits under the PPRS. Only five price changes were agreed rather than required under the PPRS.

- The PPRS Reports to Parliament record the value of all price increases agreed through the proper operation of the PPRS and the value of savings to the NHS from the price reductions required under the 1993 and 1999 schemes rather than the 27 markets analysed by EER.

    - Between 1995 and 2000, 41 companies were allowed to increase prices under the PPRS at an estimated cost to the NHS of £154 million. In addition, in 1998, 24 small companies increased product prices without the Department's agreement at an estimated cost to the NHS of £30 million a year.

- Savings to the NHS from the 2.5% price reduction between 1995 and 1998 are estimated as £370 million. During the 15 months ending 31 December 2000, the 4.5% price reduction produced an estimated saving to the NHS of £200 million. There may also have been some price decreases apart from those required by the 2.5% and 4.5% price reductions, which were not required to be notified to the Department.

- Five of the 27 markets accounted for more than half of all the significant price changes amongst major branded products over the five years. In nine of the 27 markets, there were no price increases or decreases of more than 10%.

- Other than for the compulsory price reductions of October 1999, the prior trend in sales value did not seem to affect the sign or magnitude of significant price changes. The sales values of products had been in decline prior to 11 of the 24 significant price rises observed amongst major branded products.

- All four of the products for which prices were reduced by more than 25% in October 1999 - and five of the 10 products for which prices were reduced by more than 10% - had been on a declining sales trend before that price reduction.

- The availability of generics did not impact on price changes in one particular direction. Of the 24 significant price increases of major products, 14 had generic versions available. Of the 20 significant price decreases, generic versions of the molecule were available in 10.

5.4 Volume Responses to Price Changes

- For seven of the 24 observed significant price increases amongst major products, the price increase was followed by a discernible reduction in sales volume compared to the volume trend before the price increase. For seven of the 20 significant price reductions, the price reduction was followed by a discernible increase in the trend of sales volume.

- Of 10 large price increases (over 50%), there is an apparent reduction in sales volume trend in five cases, but in none of these five does the volume response appear sufficient to potentially bring the sales value below its trend before the price increase within a

few years. Of five large price decreases (over 25%), there is an apparent increase in sales volume trend in three cases. In one of these three, the volume response appears sufficient to potentially bring the sales value above its trend before the price reduction within a few years.

5.5 Competitor Price Responses to Price Changes

- Of the 24 significant price increases of major products, price increases that may possibly be competitive responses can be seen as follows: two responses within three months; seven within 12 months.

- Of the 20 significant price decreases of major products, price decreases that may possibly be competitive responses included three decreases within three months; eight within 12 months.

- The patterns of these responses are symmetric: there is no evidence that price cuts were followed by price cuts by competitors more often than price rises were followed by price rises.

5.6 New Molecule Entry

- There were 43 new molecule entries across the 27 markets in the five-year period. 30 were in the seven markets with three or more new entries. Ten of the 27 markets saw no new molecule entry.

- Using prices per DDD of the modal strength of the new entrant, entry price was below that of the incumbent in 25 cases and above it in 10. There was no obvious change in this pattern within the time period.

- A tabulation of the relative price of entrants against the growth in sales value in the market suggested that while entry prices in high-growth markets were evenly distributed around those of the incumbents, entry-price in low-growth markets (0-50% value growth from Year 1 to Year 5) were above those of the incumbents (all 11 observations).

- A tabulation of the relative price of entrants against their value market shares after one year suggested that lower relative prices helped gain volume share.

- With two of the 43 entries there is a price reduction by the incumbent that may be associated with entry. Overall however there does not appear to be evidence to support the view that incumbents respond to entry by lowering their own price (either prior or subsequent to entry).

5.7 Generic Entry and Generic Competition

- There were 18 first entries of branded generic products across the 27 markets, and 14 first entries of unbranded generics.

- Of the 29 initial generic entries for which the comparison could be made, generics entered at a price (per DDD at modal strength) above that of the original branded product in 12 cases, at a price below that of the branded product in 11, and at the same price in six.

- In four of 30 examples of generic entry for which the comparison could be made, there was a price reduction of the branded product shortly before or shortly after generic entry. In the other 26 cases there was no discernible response.

- In many cases generic versions of major branded products took substantial shares, often equalling those of the original brands after two or three years. In some cases, this was despite the generics being priced at or above the original brand.

6. Appendices

6.1 Terms of Reference

'A scoping exercise has been undertaken providing an initial overview of competition in the pharmaceuticals market. This examined:

- the size and growth of different sub-markets concentrating on the top 40 or so classes, which account for around 80% of sales, and others considered relevant to understanding the full picture;

- numbers of competitor companies and products, market shares, and changes in market shares over time (including entry/exit) for each of the leading classes;

- price dynamics between products.

This material was presented to a Peer Review Workshop in November 1999, which considered the available evidence and made recommendations for a more detailed analysis of the extent of competition.

Taking these recommendations into account, the Department and the ABPI will jointly agree a methodology for selecting and analysing sub-markets for closer investigation, covering a range of market conditions. This analysis, based on the agreed approach, will be contracted out to one or more independent consultants.

The specification for the work will be developed through the initial stages of Component 2, but is likely to cover:

- an overview of each market, identifying close substitutes and 'grey areas' (where there are links between product classes, even though they may not be direct substitutes);

- substitutability between products in each market, in particular, whether changes in relative prices lead to (or would be expected to lead to) significant changes in demand for these products;

- price differences between competing products and whether these reflect prescribers' perceptions of relative price differences;

- timing and impact of new products entering these markets, including whether originator products appear to hold a significant first mover advantage (e.g. because of inertia created by repeat prescribing of a product);

- an understanding of whether prices are at competitive levels, taking account of the need for companies to achieve a return on investment in R&D over the life cycle of a product portfolio.

The Department and the ABPI will agree a specification for a project that will be contracted out to a third party. The contractor will have relevant experience, for example, in competition economics. The arrangement will provide objectivity while still allowing judgement to be exercised by the Department and ABPI on the meaning of the findings.'

6.2 Pilot Study – Summary of Conclusions

Antidepressants

Based on medical advice, four groups of products were identified (SSRIs[3] (70% of market by value), tricyclics, MAOIs[4] and other antidepressant drugs). Doctors were reluctant to switch existing patients because of the complexity and potential severity of side effects from switching to a new molecule. For new patients, SSRIs were generally considered as close substitutes.

"The econometric analysis was inconclusive on substitution, both between the four groups of products identified and within the SSRI class, as it failed to identify demand equations with satisfactory properties."

Competitive behaviour in prices was suggested by the sharp fall in prices of Prozac and the other branded SSRIs when generic versions of the market leader fluoxetine (Prozac) entered the market. However, "the evidence from the econometric analysis is that sales of products within the SSRI group are not sensitive to changes in the prices of other products in the group. On the face of it, this would suggest that the producers of these products enjoyed a considerable degree of market power. However, given the failure to obtain satisfactory demand equations from the data available, it would be safer to conclude that the evidence on substitutability and on market power for this product group is inconclusive."

[3] Serotonin re-uptake inhibitor antidepressants
[4] Monoamine-oxidase inhibitors

Diabetes

Medicines for non-insulin-dependent diabetes were classified into three categories (sulphonylureas (the largest class with two molecules accounting for 90% of revenue), biguanides; and other antidiabetics).

"The econometric results at the group level suggested that for each group of medicines the quantity sold would fall if its price increased. However, the results were less clear-cut when substitutability between groups was analysed. In only one case did sales prove to be sensitive to changes in the price of that group relative to other group's prices. The econometric analysis suggested that only a very limited degree of substitution takes place between sulphonylurea molecules in response to changes in relative prices."

The two main sulphonylurea molecules are off-patent, and generics took increasing shares over the period studied. The branded products do not seem to possess any degree of market power.

Asthma

There are three molecules within the class of asthma corticosteroids (beclomethasone (off patent), budesonide and fluticasone). Medical advice was that they are close substitutes therapeutically but that the delivery device can be more important for certain patients.

As the prices of individual presentations hardly moved over the five-year period, "it was no surprise that the econometric evidence was inconclusive on substitution in response to changes in relative prices, both between molecules *within* each of these three groups of devices, and *between* the three groups."

Proton Pump Inhibitors and other Treatments for Stomach Acid and Stomach Ulcer

There are four molecules in the PPI class all in patent (Losec (the market leader), Zoton, Protium and Pariet) and medical advice was that they are close substitutes therapeutically. H_2 antagonists also control stomach acid and are substitutable with PPIs to a lesser degree.

Econometric analysis of demand 'did not generate equations with satisfactory economic and statistical properties. This evidence was therefore inconclusive on substitution in response to price changes between PPIs. There was some evidence of a limited degree of substitution between the PPI class and the H_2 antagonist class in response to relative price changes.'

'Analysis of own-price elasticities for molecules within the PPI class provided inconclusive results on market power. However, the price series suggest a high degree of price awareness and price responsiveness within the PPI category:

- new entrants Protium (1996) and Pariet (1998) entered at prices below those of the PPIs already on the market; and

- in each case within a year or so of entry the prices of the other PPIs had all fallen.

Other forms of analysis suggested that the limitations of the data set, particularly the inability to separate new and existing patients, could be obscuring an underlying degree of responsiveness of demand to price within the PPI class.'

6.3 Data

Market Name		Value of Market (£ millions)				Volume of Market (million DDDs)		Growth - (Oct 1995 Sep 2000)		Generic share of volume		Herfindahl Concentration Index	
		Oct-95	Sep-00	Year 1	Year 5	Oct-95	Sep-00	Value	Volume	Oct-95	Sep-00	Oct-95	Sep-00
1	H_2 Antagonists	21	9	245	146	26	19	-55%	-28%	17%	56%	0.60	0.23
2	Proton Pump Inhibitors	23	35	303	406	18	36	56%	104%	0%	0%	0.86	0.44
3	Sulphonylureas	2	3	23	43	12	17	98%	41%	48%	86%	0.50	0.45
4	Biphasic Insulins	2	5	30	61	6	10	120%	83%	100%	94%	0.63	0.54
5	Loop Diuretics	1	3	9	37	32	40	263%	25%	75%	91%	0.45	0.55
6	Thiazides & Analogues	1	3	7	32	43	62	382%	42%	87%	94%	0.24	0.68
7	Beta-blockers	7	11	86	123	40	55	47%	38%	45%	54%	0.28	0.24
8	Calcium Antagonists	19	26	237	303	52	73	37%	41%	24%	20%	0.21	0.25
9	ACE Inhibitors	17	22	212	265	41	79	34%	90%	0%	25%	0.27	0.17
10	Angiotensin-II Antagonists	0	7	4	72	0	12	4079%	4696%	0%	0%	1.00	0.32
11	HMG-CoA Reductase Inhibitors	5	33	75	348	5	47	607%	869%	0%	0%	0.68	0.33
12	Topical Corticosteroids	2	2	27	27	N/A	N/A	7%	N/A	(19%)	(20%)	0.47	0.38
13	Penicillins & Cephalosporins	11	7	122	96	13	9	-35%	-36%	45%	50%	0.20	0.17
14	Antifungals	2	3	25	34	1	2	60%	57%	0%	0%	0.56	0.57
15	Treatments for Herpes	2	2	25	23	0	0	-7%	25%	3%	36%	0.53	0.38
16	Antirheumatics	17	19	204	224	86	73	12%	-15%	32%	44%	0.12	0.09
17	Narcotic Analgesics	3	5	35	52	3	6	63%	80%	43%	41%	0.24	0.24
18	Migraine Treatments	3	5	39	59	1	1	64%	30%	1%	1%	0.76	0.40
19	Anti-Epileptics	5	10	67	112	10	13	91%	25%	26%	18%	0.18	0.21
20	Antipsychotics	2	10	28	104	5	6	374%	28%	31%	25%	0.21	0.32
21	Non-Barbiturate Hypnotics	2	3	23	35	31	28	61%	-7%	87%	83%	0.32	0.16
22	SSRI Antidepressants	12	27	175	342	16	46	125%	180%	0%	21%	0.32	0.19
23	Tricyclic Antidepressants	4	4	46	54	19	19	13%	0%	52%	83%	0.15	0.17
24	B_2-Stimulant Inhalants (Short-Acting)	4	4	46	49	45	47	6%	3%	31%	38%	0.47	0.43
25	B_2-Stimulant Inhalants (Long-Acting)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
26	Corticosteroid Inhalants: Manual MDI	13	16	166	194	33	36	18%	10%	23%	31%	0.61	0.53
27	Corticosteroid Inhalants: BAI	3	4	44	55	5	6	36%	16%	0%	4%	0.89	0.55

6.4 List of Significant Price Changes

Market	Market Name	Date of Change	Product Name	Product Type	Price Change
1	H_2 Antagonists	Dec-98	Axid (nizatidine)	Original	-19%
1	H_2 Antagonists	Oct-99	Zantac (ranitidine)	Original	-28%
2	Proton Pump Inhibitors	Jun-97	Zoton (lansoprazole)	Original	-10%
2	Proton Pump Inhibitors	Feb-98	Losec(omeprazole)	Original	-14%
2	Proton Pump Inhibitors	Oct-99	Protium (pantoprazole)	Original	-11%
2	Proton Pump Inhibitors	May-00	Zoton (lansoprazole)	Original	-14%
2	Proton Pump Inhibitors	Jul-00	Protium (pantoprazole)	Original	-11%
4	Biphasic Insulins	Jan-97	Human Mixtard 30/70	Branded Generic	25%
4	Biphasic Insulins	Apr-97	Humulin 30/70	Branded Generic	10%
4	Biphasic Insulins	Jan-98	Humaject 30/70	Branded Generic	11%
4	Biphasic Insulins	Oct-99	Human Mixtard 30/70 (vial)	Branded Generic	-29%
4	Biphasic Insulins	Mar-00	Humaject 30/70	Branded Generic	-14%
5	Loop Diuretics	Feb-98	Lasix (furosemide)	Original	100%
5	Loop Diuretics	Feb-98	Lasikal (furosemide+K)	(minor) Original	200%
6	Thiazides & Analogues	Jan-97	Aprinox K3L	Original	25%
6	Thiazides & Analogues	Feb-98	Metenix (metolazone)	Original	150%
6	Thiazides & Analogues	Jul-98	Hygroton (chlotalidone)	Original	23%
6	Thiazides & Analogues	Jun-99	Aprinox (bendro'thiazide)	Original	290%
7	Beta-blockers	Oct-98	Celectol (celiprolol)	Original	100%
8	Calcium Antagonists	Oct-99	Tildiem (diltiazem)	Original	-11%
9	ACE Inhibitors	Oct-99	Lisinopril (original)	Original	-18%
11	HMG-CoA Reductase Inhibitors	Oct-99	Lescol (fluvastatin)	Original	-20%
13	Penicillins & Cephalosporins	Jul-96	Augmentin (co-amoxiclav)	Original	10%
13	Penicillins & Cephalosporins	Aug-97	Augmentin (co-amoxiclav)	Original	10%
15	Treatments for Herpes	Aug-97	Famvir (famciclovir)	Original	10%
15	Treatments for Herpes	Oct-99	Zovirax (aciclovir)	Original	-36%
16	Antirheumatics	Oct-99	Voltarol (diclofenac)	Original	-54%
16	Antirheumatics	Oct-99	Arthrotec	Original	-11%
18	Migraine Treatments	Feb-97	Paramax	Original	50%
18	Migraine Treatments	Jul-98	Cafergot	(minor) Original	180%
18	Migraine Treatments	Oct-98	Paramax	Original	11%
20	Antipsychotics	Jul-96	Stelazine (trifluoperazine)	Original	10%
20	Antipsychotics	Aug-97	Stelazine (trifluoperazine)	Original	10%
20	Antipsychotics	Nov-97	Neulactil (periciazine)	(minor) Original	250%
20	Antipsychotics	Oct-98	Dolmatil (sulpiride)	Original	-17%
20	Antipsychotics	Oct-98	Fluanxol (flupentixol)	Original	10%
20	Antipsychotics	Oct-98	Largactil (chlorpromazine)	(minor) Original	90%
20	Antipsychotics	Jan-99	Stelazine (trifluoperazine)	Original	10%
22	SSRI Antidepressants	Oct-98	Cipramil (citalopram)	Original	-24%
22	SSRI Antidepressants	Aug-99	Lustral (sertraline)	Original	-49%
22	SSRI Antidepressants	Oct-99	Seroxat (paroxetine)	Original	-16%
23	Tricyclic Antidepressants	Jun-97	Surmontil (trimipramine)	Original	27%
23	Tricyclic Antidepressants	Jan-98	Surmontil (trimipramine)	Original	56%
24	B_2-Stimulant Inhalants (Short)	Jul-96	Airomir (salbutamol)	Branded Generic	-10%

6.5 List of Entry Events

Market	Market Name	Date of Change	Product	Type	Relative Entry Price
17	Narcotic Analgesics	Dec-95	Methex	Branded generics	29
25	B_2-Stimulant Inhalants (Long)	Dec-95	Foradil	Original	81
9	ACE Inhibitors	Jan-96	Moexipril	Original	150
3	Sulphonylureas	Feb-96	Gliclazide	Unbranded generics	107
16	Antirheumatics	Mar-96	Preservex	Original	195
14	Antifungals	Apr-96	Sporanox Pulse	Original	100
17	Narcotic Analgesics	May-96	MXL	Branded generics	87
24	B_2-Stimulant Inhalants (Short)	May-96	Asmasal	Branded generics	236
26	Cortic'oid Inhalants: Manual MDI	May-96	Asmabec	Branded generics	90
20	Antipsychotics	Jun-96	Serdolect	Original	150
15	Treatments for Herpes	Jul-96	Aciclovir	Branded generics	90
16	Antirheumatics	Aug-96	Mobic	Original	265
2	Proton Pump Inhibitors	Oct-96	Protium	Original	84
7	Beta-Blockers	Oct-96	Sotalol	Unbranded generics	140
10	Angiotensin-II Antagonists	Oct-96	Valsartan	Original	91
18	Migraine Treatments	Oct-96	Clotam	Original	130
20	Antipsychotics	Oct-96	Zyprexa	Original	116
8	Calcium Antagonists	Nov-96	Syscor	Original	220
1	H_2 Antagonists	Jan-97	Ranitidine	Unbranded generics	100
11	HMG-CoA Reductase Inhibitors	Jan-97	Lipitor	Original	80
5	Loop Diuretics	Feb-97	Bumetanide	Unbranded generics	99
9	ACE Inhibitors	Feb-97	Captopril	Unbranded generics	102
12	Topical Corticosteroids	Feb-97	Betamethasone	Unbranded generics	n/a
13	Penicillins & Cephalosporins	Feb-97	Cefaclor	Branded generics	59
18	Migraine Treatments	Mar-97	Zomig	Original	50
11	HMG-CoA Reductase Inhibitors	Apr-97	Lipobay	Original	75
21	Non-Barbiturate Hypnotics	Apr-97	Halcion	Original	43
18	Migraine Treatments	May-97	Naramig	Original	50
17	Narcotic Analgesics	Jul-97	Palladone	Original	39
22	SSRI Antidepressants	Jul-97	Edronax	Original	95
10	Angiotensin-II Antagonists	Sep-97	Irbesartan	Original	100
20	Antipsychotics	Sep-97	Seroquel	Original	116
22	SSRI Antidepressants	Sep-97	Zispin	Original	124
8	Calcium Antagonists	Oct-97	Posicor	Original	190
25	B_2-Stimulant Inhalants (Long)	Oct-97	Oxis	Original	83
20	Antipsychotics	Nov-97	Solain	Original	92
10	Angiotensin-II Antagonists	Dec-97	Cilexetil	Original	91
8	Calcium Antagonists	Jan-98	Zanidip	Original	115
18	Migraine Treatments	Jan-98	Domperamol	Original	225
21	Non-Barbiturate Hypnotics	Feb-98	Zilese	Branded generics	90
21	Non-Barbiturate Hypnotics	Feb-98	Zopiclone	Unbranded generics	100
3	Sulphonylureas	May-98	Amaryl	Original	115
12	Topical Corticosteroids	Jul-98	Beclometh Mx	Branded generics	n/a
18	Migraine Treatments	Jul-98	Maxalt	Original	56

6.5 List of Entry Events *Continued*

Market	Market Name	Date of Change	Product	Type	Relative Entry Price
13	Penicillins & Cephalosporins	Aug-98	Cefzil	Original	79
19	Anti-Epileptics	Aug-98	Gabitril	Original	90
2	Proton Pump Inhibitors	Sep-98	Pariet	Original	80
13	Penicillins & Cephalosporins	Sep-98	Nicef	Branded generics	99
16	Antirheumatics	Sep-98	Condrotec	Original	255
5	Loop Diuretics	Oct-98	Frusol	Branded generics	n/a
13	Penicillins & Cephalosporins	Oct-98	Cerfadine	Unbranded generics	99
19	Anti-Epileptics	Oct-98	Carbamazapine	Branded generics	130
27	Corticosteroid Inhalants: BAI	Nov-98	Asmabec	Branded generics	57
20	Antipsychotics	Dec-98	Zoleptil	Original	82
4	Biphasic Insulins	Jan-99	Humalog Mix 25/75 Cartridges	Branded generics	127
4	Biphasic Insulins	Jan-99	Humalog Mix 25/75 Pre-fill pen	Branded generics	112.5
13	Penicillins & Cephalosporins	Jan-99	Co-amoxiclav	Unbranded generics	100
18	Migraine Treatments	Jan-99	Dihydroergotamine	Original	n/a
7	Beta-blockers	Mar-99	Nebilet	Original	190
19	Anti-Epileptics	Mar-99	Pro Epantutin	Original	n/a
22	SSRI Antidepressants	Mar-99	Fluvoxamine	Unbranded generics	132
16	Antirheumatics	May-99	Piroxicam	Original	345
16	Antirheumatics	Jun-99	Vioxx	Original	620
7	Beta-blockers	Jul-99	Celiprolol	Unbranded generics	100
22	SSRI Antidepressants	Oct-99	Fluoxetine	Unbranded generics	100
16	Antirheumatics	Nov-99	Nabumetone	Unbranded generics	425
9	ACE Inhibitors	Dec-99	Enalapril	Unbranded generics	100
10	Angiotensin-II Antagonists	Dec-99	Telmisartan	Original	73
17	Narcotic Analgesics	Jan-00	Oxycontin	Branded generics	115
17	Narcotic Analgesics	Jan-00	Oxynorm	Branded generics	114
22	SSRI Antidepressants	Jan-00	Fluoxetine	Branded generics	90
19	Anti-Epileptics	Mar-00	Trileptal	Original	45
18	Migraine Treatments	Apr-00	Migravess	Branded generics	333
16	Antirheumatics	May-00	Celebrex	Original	385
2	Proton Pump Inhibitors	Aug-00	Nexium	Original	64

6.6 Summary of Market Analyses

6.6.1 H_2 Antagonists

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
1	No	Yes	No	2	No	Some	Some

- Market halved in value to some £10 million a month and fell by 28% in volume terms. Shift from H_2 Antagonists to PPIs.
- Significant reduction in prices of Zantac and Axid, former as price modulation to deliver 4.5% PPRS price cut.
- Ranitidine was the most prescribed molecule with average market share by value of 72%. Zantac lost market share to new entrant generic ranitidine.
- Prices of generics fluctuated considerably and for different molecules in opposite directions.
- Within a molecule some evidence of GP responsiveness to price changes.

6.6.2 Proton Pump Inhibitors (PPIs)

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
3	Yes	No	Yes	5	Some	No	Some

[5] New entrants include new molecules, branded generics and unbranded generics (Appendix 6.5). Generic entries refer in most cases only to the entry of the first branded or unbranded generic for a molecule.

[6] In most cases, the price of the entrant was compared to the price of the product with the largest market share of value at the beginning of the period. In some cases it was considered more suitable to make the comparison to a different product. The convention was to base the comparison on WHO's Defined Daily Dose (DDD).

[7] Price changes of +10% and above and –10% and below for "major" branded products – defined as those with 10% market share or above at any stage during the 5 year period plus smaller products where large rises and falls. See list at Appendix 6.4.

- Value of the market increased from £22 million to £35 million a month with cost of treatment falling with new entrants and price reductions.
- 5 molecules in the class (with high degree of therapeutic substitutability).
- 3 new entrants launched at prices below the 2 incumbents Losec and Zoton but gained only small market shares.
- Evidence of some competitive price reductions and volume responses to new entrants/price reductions.
- Market concentration as measured by the Herfindahl index[8] fell from 0.86 to 0.44.

6.6.3 Sulphonylureas

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
2	No	1	No	0	N/a	N/a	N/a

- Market doubled in value (to £3.5 million a month) and 41% growth in volume terms.
- Gliclazide remained the most prescribed molecule with an average market share by value of 80% but Diamicron rapidly lost market share to new entrant generic.
- One new molecule, Amaryl (glimepride) launched at higher price than other products and gained 6% market share.
- Prices of brands remained virtually unchanged but considerable increases in generic prices in 1999.
- No conclusions on GP responsiveness to price can be drawn.

[8] The Herfindahl concentration index is a sum of the squares of the firms' shares of value. The index ranges from one, which indicates a monopoly, to zero. A lower value indicates a less concentrated market. If there are n firms each with an identical market share, the Herfindahl index value will be . See market summary data at Appendix 6.3.

6.6.4 Biphasic Insulins

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
2	No	No	No	5	Yes	No	No

- Market doubled by value to £6 million a month and increased by around 80% in volume terms. Difference due to increase in the general price level of the main products.
- 2 companies, Lilly and Novo Nordisk account for 99% of the market. Herfindahl index very high at average of 0.585.
- Significant move from vial to more expensive cartridge form.
- Price of market leader, cartridge form of Human Mixtard 30/70 increased over the period.
- Humalog Mix 25/75 entered at premium price with some success (8% of market by volume).
- Price of competing products increased and reduced closely together.
- No discernible evidence of change in trend of sales following price changes.

6.6.5 Loop Diuretics

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
2	Yes	No	No	2	No	No	No

- Value of market increased by over 250% mainly as a result of large increase in price of generic furosemide in 1999[9]. Volume increased by 25%.

[9] The closure of a major generic manufacturer in 1999 along with other factors caused shortages and large price increases across the sector. This is likely to be the reason behind the very large increases in generic prices described at various points in the analysis.

- Large price increases of branded products (Lasix and Lasikal) despite falling sales volumes and with small effect on volume of sales.
- No price decreases among brands apart from 1999 PPRS price reductions.
- No entry of new molecules.
- Sales of Burinex fell substantially after entry of generic bumetanide despite generic being more expensive. No action by incumbent.
- Herfindahl index increased from 0.45 to 0.55.

6.6.6 Thiazides and Analogues (Plain)

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
0	N/a	N/a	N/a	4	No	No	No

- Value of sales increased sharply in 1999 whereas volume increased slowly throughout the period.
- Main product generic bendroflumethiazide increased ten-fold in price (although still among cheapest) and increased market share.
- Large increases in price of 2 brands (Aprinox and Metenix) without any obvious fall in volumes.
- Herfindahl index increased from 0.25% to 0.70%.

6.6.7 Beta-blockers

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
3	No	No	No	1	No	No	No

- Value (and volume) grew by over 40% to £11 million a month.
- 7 products (5 brands and 2 generics) accounted for 86% of value throughout.

- In terms of value, market leader was Tenormin but generic version maintained largest share of volume.
- One new molecule entered but did not gain significant market share.
- Generics share of volume over 50% for most of the period.
- The price of one product, Celectol, doubled. Although volume of sales declined slowly, revenue significantly increased.

6.6.8 Calcium Antagonists (Plain)

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
3	No	No	No	1	No	No	No

- Value (and volume) increased by around 40% to £26 million a month.
- None of 3 new molecule entrants achieved significant market share.
- Market share concentrated on Istin and Adalat with no other product (12 brands plus generics) having more than 10% share.
- Limited price changes amongst branded products but some evidence of price competition between off-patent products and generics.
- Adalat's market share fell but no response by reducing price.

6.6.9 ACE Inhibitors (Plain)

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
3	No	1	No	1	No	No	No

- Sales grew steadily from £17 million to £22 million a month while volume doubled possibly due to entry of cheaper generics.
- Generic versions of enalapril and captopril entered the market at prices similar to market leaders, who lost market share.

- 1 new molecule entered the market but gained minimal market share.
- No price changes of existing branded products other than October 1999.
- Total market share (volume and value) of generics increased.

6.6.10 Angiotensin-II Antagonists (Plain)

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
5	Yes	3	No	0	N/a	N/a	N/a

- Sales value of this new market increased 7-fold to £7 million a month.
- 5 new entrants launched (at prices lower than incumbent) of which 3 achieved significant market shares (15-20%)
- No price changes of incumbent (Cozaar) in response.
- Herfindahl index fell from 1 to 0.32 with new product entries.

6.6.11 HMG-CoA Reductase Inhibitors (Statins)

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
2	Yes	1	No	1	No	No	No

- Value of market grew rapidly – over 6 fold (to £30 million a month) and volume by 8 fold.
- 2 new entrants of which, Lipitor attained 33% market share.
- 3 incumbents did not react by changing prices – despite Zocor's market share falling from 80% to 45%.
- No price changes other than 1999 4.5% price reduction requirement.

6.6.12 Topical Corticosteroids

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
2	No	No	No	0	N/a	N/a	N/a

- Sales remained fairly stable at £2-2.5 million a month.
- Market leader was Betnovate (betamethasone) although share fell from 39% to 32%.
- 2 entries (branded generic of beclometasone and generic betamethasone) but neither gained significant market share.
- Herfindahl concentration index fell from 0.47 to 0.38 due to market share of Glaxo – supplier of 3 main products falling from 67% to 58%.

6.6.13 Broad-Spectrum Penicillins and Cephalosporins

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
5	4/5	1	No	2	No	Some	No

- Value and volume fell by around 35% to monthly sales of below £7 million.
- Generic co-amoxiclav gained market share of 10% but 4 other entrants including 1 new molecule failed to gain significant market share.
- Generic co-amoxiclav priced the same as Augmentin but no subsequent price competition between products despite substitution away from brand, which had increased twice before entry of generic.
- Following large price increase in generic amoxicillin, evidence of substitution to off-patent Amoxil.

- No evidence of competitive price reductions amongst 3 major branded products.
- Generics share of volume and value increased with launch of co-amoxiclav.
- Herfindahl index fell slightly from 0.20 to 0.17 but combined market share of top 3 products was 60-70% throughout.

6.6.14 Antifungals

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
1	No	1	No	0	N/a	N/a	N/a

- Volume and value of market almost doubled to sales of £3.6 million a month.
- Market leader was Lamisil (terbinafine) with 65-75% market share.
- One new product entry Sporanox Pulse (itraconazole) achieved 7% market share.
- Prices unchanged apart from 4.5% PPRS reduction on 2 products in October 1999.
- Herfindahl index remained in the range 0.48 to 0.58 over the period – 3 companies Novartis, Janssen-Cilag and Pfizer accounted for 95-99% of the market.

6.6.15 Treatments for Herpes and Varicella Zoster

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
1	Yes	No	No	2	No	Yes?	No

- Size of the market measured by value fell marginally (£2 million a month) while volume grew slowly.

- Move from Zovirax to generic versions of aciclovir and growth of Famvir.
- No entry of new molecules - one branded generic gained minimal market share.
- 2 leading brands Famvir and Zovirax each had one price change. Sales volume trends following price changes are consistent with some GP responsiveness to changes in relative price.
- Total market share of generics (by volume and value) increased.

6.6.16 Anti-rheumatics

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
7	No	1	1?	2	Yes?	No	No

- Sales value fluctuated around £17.5 million a month while volume gradually decreased.
- Generics form a significant part of the market with volume share increasing to 45%.
- 2 significant new entries (Mobic and Vioxx) at prices substantially above market leader. Vioxx, the more successful had a much higher price suggesting superior product or lack of pressure on prices.
- Some evidence of price responses to falling market share of 2 major products (Voltarol and Arthrotec). Otherwise little price movement in brands.
- Price of generic ibuprofen increased 3 fold in 1999 but decline in sales insufficient to prevent value of sales being much higher after price rise.

6.6.17 Narcotic Analgesics

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
5	3/5	No	No	0	N/a	N/a	N/a

- Value and volume doubled with sales reaching £4.7 million a month.
- Market dominated by generics.
- None of new entrants including one new molecule gained more than 2% market share.
- All products except Durogesic had roughly constant sales value and volume.
- Durogesic took over as market leader by value from MST Continus despite being 2nd highest price product, possibly due to superior therapeutic value.

6.6.18 Migraine Treatments

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
7	Yes	1	No	3	No	No	No

- Value grew by 64% to around £5 million a month and volume by 30% - move to more expensive products including new entrants.
- Market dominated by Imigran, market leader in terms of sales (85% falling to 60%).
- 3 of the new entrants established significant market share having entered market at some 50% the price of market leader by value.
- No price responses to entry events and no other price decreases amongst major products (apart from October 1999 PPRS price cut).

- Substantial price increases in older products (Paramax and Cafergot) without a major decrease in volume.
- Herfindahl index fell from 0.76 to 0.40 as a result of new entrants and decline in sales of Imigran.

6.6.19 Anti-epileptics

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
4	_	No	No	0	No	No	No

- Sales value almost doubled (to £10 million a month) but volume increased by only 25% - difference due to rising relative importance of newer more expensive drugs.
- 3 new molecules entered but won only small market shares.
- Top 3 products dominated with over 60% of the value of market throughout.
- No price changes of existing branded products.
- Total market share of generics (by volume and value) fell.
- Low competitive pressures may be due to medical differences between drugs reducing substitutability.

6.6.20 Anti-psychotics

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
5	2/5	1	No	7	No	No	No

- Value increased by a factor of 5 to sales of £10 million a month. Volume increased by 28% - difference due to entry of more expensive atypical antipsychotics, which gained 90% market share at expense of conventional antipsychotics.

- Several new entrants established significant market share with Zyprexa (olanzapine) becoming market leader in terms of value and volume.
- Risperdal (risperidone) lost substantial market share but no price response to new entries.
- Relative entry price did not seem the most important factor in determining a product' success and no subsequent price adjustments amongst new entrants.
- Some price reductions as well as increases amongst older drugs but no evidence to suggest competitive pressures on products' prices were high.
- The prices of 2 minor products increased greatly – volume response far too small to prevent sales values from increasing substantially.
- Herfindahl index increased from 0.21 to 0.32 despite rise in number of products due to dominance of 2 products Risperdal and Zyprexa with 75% of value.

6.6.21 Non-Barbiturate Hypnotics

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
3	1	1	No	2	No	No	No

- Sales value rose from £1.8 million to almost £3 million a month despite some falling off in volume: hypnotics becoming on average more expensive.
- Generics dominated the market accounting for over 80% by volume throughout.
- 1 new generic entrant (zopiclone) took some 50% of sales of molecule in 2.5 years; 1 new molecule entry took minimal share.
- Prices of branded medicines hardly changed. In one case a sharp increase in a generic (8 times its earlier level) led to a limited decline in sales.

6.6.22 SSRI Antidepressants

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
5	2/5	1	1?	3	No	No	No

- Market almost tripled in volume while sales increased from £12 to £27 million a month.
- Market leader Prozac (fluoxetine) overtaken by Seroxat (paroxetine).
- 5 new entrants, of which 2 new molecules. Generic fluoxetine gained significant market share and had significant effect on volume of sales of Prozac.
- Price of Cipramil cut by 24% followed by substantial and steady increase in volume of sales.

6.6.23 Tricyclic Antidepressants

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
0	N/a	N/a	N/a	2	No	No	No

- Value (and volume) remained stable at some £4 million until large increases in generic amitriptyline in 1999 led to an increase to £5 million a month.
- In terms of volume, the market leader was generic amitriptyline and the largest share by value was branded generic of dosulepin.
- No new products entered the market but 5 brands with minimal market share exited.
- Some significant price changes (Surmontil and generic amitriptyline).

- Generic market share (including branded generics) increased from 52% to 83%.

- Herfindahl concentration index remained in the range 0.14 to 0.18 with 4 manufacturers with significant market shares.

6.6.24 B_2-Stimulant Inhalants (Short-acting): Manual MDI Devices

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
1	N/a	No	No	1	No	No	No

- Value and volume steady with sales of around £4 million a month.

- Market dominated by one molecule salbutamol with Ventolin having 60% market share (despite being the most expensive salbutamol product).

- Price of Airomir reduced twice but no discernible effect on sales volume and no price reductions from other branded products.

- Generic salbutamol fluctuated in price and was 20% more expensive by end of period but changes in volume share did not seem to follow price movements.

- One new entry, a branded generic of salbutamol but only available as a space-inhaler and unsurprisingly gained only small market share.

- Main development was release of CFC-free versions – at higher prices than non-CFC free versions.

6.6.25 B_2-Stimulant Inhalants (Long-acting): Manual MDI Devices

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
2	Yes	Yes	No	0	N/a	N/a	N/a

- Value (and volume) increased by over 110% to £9 million a month.
- 3 markets within this category – manual MDI market has largest value of sales and Serevent (salmeterol) enjoys a monopoly position; BAI dry powder (easy to use) and (harder to use) smaller markets consist of Serevent and formoterol, sold as Oxis and Foradil respectively under a co-marketing arrangement.
- Serevent dominated markets despite new entrants Oxis and Foradil being priced at 80% of incumbent.
- No price changes apart from one in October 1999.

6.6.26 Corticosteroids Inhalants: Manual MDI

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
1	Yes	No	No	0	N/a	N/a	N/a

- Value grown by 18% and volume by 10%.
- Two main producers, Glaxo Wellcome and Baker Norton with average market share of 73% and 13% respectively. Herfindahl index very high – average 0.55.
- By end of the period, Glaxo Wellcome held 2 largest products Becotide (beclomethasone) and Flixotide (fluticasone).
- Beclomethasone was the most prescribed molecule with average market share by volume of 82% although declining with increasing sales of Flixotide.
- Virtually no price changes.
- Switch from non-CFC free version of Flixotide to CFC-free version.

6.6.27 Corticosteroids – Breath Activated Inhaler (BAI) Dry powder requiring minimal dexterity

No of new entrants	Lower entry price	Market share (10%+)	Price response	No of Price Changes (10%+)	Price response	Impact on prescriber usage	Impact on volume
1 Yes	No	No	0	N/a	N/a	N/a	

- Volume increased by 16% and value by 36% to sales of £5 million a month.
- 2 products - market leader Pulmicort's share fell from 94% to 67% as Flixotide's increased to 30%.
- One new entry – branded generic of beclometasone gained only 2% market share.
- Prices remained unchanged except Flixotide reduced in October 1999.

Component 3:

Competition in the Out-of-Patent Sector

December 2002

Component 3

Contents

Component 3

Competition in the Out-of-Patent Sector

1. Executive Summary

This paper sets out the work analysing the impact of generic entry on branded products that come off patent. The study, carried out mainly by the Department of Health, was discussed with the Association of the British Pharmaceutical Industry (ABPI) and incorporates their comments and additional analysis.

The study analysed 137 chemical entities, which lost patent protection in the UK between 1990 and 2000. The Department's analysis was based on data from the Prescription Pricing Authority (PPA) of all prescriptions dispensed in the community in England. It excludes expenditure on items dispensed in hospitals, although few of the top products are likely to have significant hospital sales, items dispensed in Scotland, Wales and N. Ireland and on private prescription. The Department used data on prices – the NHS list price for branded medicines and the Drug Tariff price for prescriptions written by their generic name. It did not have access to actual prices after discount. [1].

The ABPI's view is that the analysis presented in this component understates the extent of generic competition and the levels at which it occurs because of the mechanisms of pharmacy reimbursement.[1] Additionally, patent expiry and the entry or threat of entry of branded generics creates further competition for research-based manufacturers and greater loss of revenue than is shown as savings in the analysis.

[1] The reimbursement system is designed to secure cost-effective purchasing and value for money for the NHS by encouraging pharmacists to buy lower than the reimbursement price. The reimbursement price is the Drug Tariff price for prescriptions written by their generic name. The Drug Tariff price for the most commonly used medicines is based on a weighted average of the list prices of a basket of five suppliers consisting of two full line wholesalers and three generic manufacturers. Pharmacists are reimbursed the Drug Tariff price of the item dispensed less an assumed level of discount. Recovery of the estimated discount, by means of a scale of deductions using the results of a Discount Inquiry, aims to determine the difference between the actual cost of the products purchased by pharmacies and the amount they are reimbursed. This is not included in the analysis of the savings.

The main conclusions of the study are that:

- several conditions seem to be necessary to ensure effective generic competition once a product comes off patent: the market needs to be very large (an annual turn-over of at least £10 million), the product needs to have a certain level of generic prescribing, the manufacturing process must be relatively straightforward, and there must not be other major inhibiting factors;

- most significant products (with an annual net ingredient cost (NIC) of £3 million or more at the time of patent expiry) face some generic competition but the extent of generic entry is variable. In total, only 47 out of 137 products showed any generic entry by the end of 2000. 21 products had been discontinued and two products had recent patent expiry.;

- the impact of generic entry has been variable; of the 28 significant products, four experienced generic erosion of 40% or more (by value as opposed to volume), six between 20% and 30% and 14 products experienced no generic erosion or of less than 20%. The remaining four products were excluded either because the patent has only just expired, or because the product was withdrawn or because the market was substantially affected by decisions made by the Advisory Committee on Drugs;

- of the 109 smaller products with an annual NIC of less than £3 million, in only three cases (domperidone, dobutamine hydrochloride and mecillinam) has there been a significant impact on prices (25% or more);

- even where generic entry has occurred, it has often been slow to make an impression on drug tariff prices although actual prices may have fallen more quickly than shown by this analysis. The top five products on the list are now showing substantial savings for the NHS from generic competition, but the price of four of the five only fell significantly at least one or two years after their respective patents expired. Ten other significant products have faced generic entry, but without a significant fall in price (less than 10%). It appears that large-scale generic entry is needed to generate genuine price competition;

- overall expenditure on those products that came off patent between 1990 and 2000 is estimated to have been around a quarter lower than it would have been in the absence of generic competition;

- analysis of individual products has identified some of the reasons why generic competition may be less effective in some markets than others, including the size of the market (generic companies are not interested in small markets), complexity/cost of manufacturing process, existence of additional manufacture/process patents, the significance of modified release forms, licensing procedures/requirements, nature of the product, variable generic prescribing rates, uncertainties created by court cases and availability of parallel imports/OTCs.

2. Introduction

2.1 The terms of reference were:

"'To chart the speed of availability and penetration of generics for products that have recently come off patent or which come off patent during the new scheme. It will look at:

- information on those products due to expire during the new scheme;
- whether/ or how long before generics enter the market, particularly for the more significant products;
- fall in market share and/or price of branded products, including calculation of a sales-weighted post-patent price index;
- assessment of 'barriers to entry' where generic entry does not occur or is slow."'

2.2 Explanation

Once the patent for a product expires, it should be possible for generic versions of the chemical to enter the market and compete directly with the branded product. If the market is operating effectively, competition from generic suppliers should lead to lower prices for out-of-patent products or increased levels of discounting to pharmacy.

From the Department's perspective, a market that is operating efficiently would have the following characteristics:

- timely entry of generic suppliers into a market once a patent expires: the larger the market, the more generic "'interest"' and hence competition, as generic suppliers try to "'steal a march"' on other potential entrants;

- evidence of willingness by generic suppliers and proprietary companies to engage in price competition: the original supplier has the advantage of a marketed brand name. Generic suppliers are less likely to use this route and more likely to gain market share through price competition. This is encouraged by the reimbursement system, which provides pharmacists with an incentive to purchase the cheapest generic version and ensures that at least part of the savings are clawed back by the Department;

- where price competition is evident, generic versions would be expected to gain market share at the expense of the branded product and/or the original patent-holder would protect its market share by cutting the price of the branded product. In practice, companies tend to offer pharmacy discounts rather than cut the original branded price.

The aim of this analysis is to test whether these characteristics are borne out in practice, based on the experience of those products that came off patent between 1990 and 2000.

2.3 The Key Questions Addressed:

- Overall, what was the scale of generic entry in product markets where the patent expired? What were the actual and potential savings for the NHS? involved?

- Why did generic entry occur in some cases and not in others? Were there significant barriers to entry in certain cases?

- How fast was generic entry? Why was it faster in some cases than others?

- What happened to prices when generics entered the market?

3. Overall Impact of Generic Entry

The database covers 137 chemical entities, which were identified as having lost patent protection in the UK between 1990 and 2000 (Appendix 8.1). It shows the overwhelming importance of a relatively small number of drugs. Our analysis focuses on the "more significant" products, which had a NIC of at least £3 million in the year in which their patent expired, since the major generic companies have said they are unlikely to be interested in smaller markets. These 28 products accounted for 82% of total expenditure in 2000 on all products that have come off patent since 1990.

Out of these top 28 products, 22 are listed as having generic suppliers according to Chemist & Druggist's Generic List April – September 2001 (additional information from BNF September 2001). Additionally one only came off patent at the end of 2000; one is available only on a named patient basis and one has been withdrawn from the market. Thus, most significant products face some generic competition. By contrast, only 25 out of the 109 "minor" products are listed as having generic suppliers. In total, 47 out of 137 (some 34%) of products are listed as having generic alternatives. 21 products were discontinued.

IMS Retail data suggests that this is an under-estimate as it shows 42% of products more than 10 years old have a generic alternative. The proportion decreases with total size of sales but is still 32% for products with annual sales of less than £100,000.

The extent to which the NHS benefits from generic competition depends on the speed of generic entry, how quickly generic suppliers are able to secure a significant market share, and how the prices of branded and generic products are affected by competition between suppliers.

An estimate of savings to the NHS can be made by comparing actual expenditure on these products since patent expiry with the amount that would have been spent if all sales had been made at the price of the branded product (at the time its patent expired) (Appendix 8.2)[2]. For example, £69 million has been spent on captopril since its patent expired in the first quarter of 1997. If the same quantities had been purchased at the price of the branded product (Capoten) the total cost would have been £127 million. Thus, cumulative savings on captopril were around £58 million over this period (46%).

[2] The methodology used is a variant of a sales-weighted post-patent price index mentioned in the terms of reference and produces very similar results.

Overall, around £5.4 billion has been spent on these products since their respective patents expired, compared with an estimated expenditure of £7.4 billion in the absence of generic competition – a saving of nearly £2 billion or 27%.

The greatest savings were on atenolol (60%), captopril (46%), and cimetidine (44%) but many products showed no savings. Even for products that faced generic entry, savings were often small or non-existent including co-amoxiclav (0%), bezafibrate (3%), and nabumetone (0%). Note that the figures for savings exclude triazolam, which was withdrawn from the UK market in 1991; zopiclone and piroxicam (gel), because both these markets were substantially affected by rulings by the Advisory Committee on Drugs; and gabapentin, a recent patent expiry.

Not all these savings for the NHS can necessarily be attributed to the impact of generic competition. There are several products e.g. Distaclor, where significant reductions in the price of the branded product may not be linked to generic competition. Furthermore, the Department's estimates include some savings that are due to competition from parallel imports, as opposed to generics. (This is because PPA data does not distinguish between true generics and parallel imports that are dispensed under the generic name).

Table 1 provides a breakdown of savings between different categories of products. This shows that savings were concentrated on "high" NIC products (with annual expenditure of over £10 million); savings were greater for tablets than for capsules or other delivery forms; and savings were greater for products with three or more suppliers.

Table 1 - Savings from Generic Competition by Category

CategoryCumulative Savings (%)1,2	
Size of Market	
• High NIC: >£10m a year	25%
• Medium NIC: £3-10m a year	2%
• Low NIC:<£3m a year	0.3%
Delivery Form	
• Tablets	34%
• Capsules	12%
• Other	1%
Date of Patent Expiry	
• Early 1990s (1990-1994)	23%
• Late 1990s (1995-2000)	29%
Extent of Generic Entry	
• Three or more listed suppliers	38%
• One or two listed suppliers	1%
• No listed suppliers	1%

[1] Based on comparing actual expenditure (in terms of NIC) with what would have been spent if the same quantities had been purchased at the price of the branded product (at the time its patent expired).

[2] Excluding zopiclone, piroxicam (gel), triazolam and gabapentin.

Perhaps not surprisingly, savings increase in the period following patent expiry as generic suppliers take a greater market share and/or prices are driven down by competition between suppliers. Savings in the first complete year after patent expiry averaged around 17%, around 15% in the second year, rising to around 23% in the third and fourth year, and 22% in the fifth year (see Appendix 8.2). Thus, the impact of generic competition on drug tariff prices appears to be quite gradual. This would explain why total (cumulative) savings have so far been greater for those products, such as atenolol, whose patent expired in the early 1990s compare to those whose patent expired in the late 1990s.

In principle, the threat of generic competition could be sufficient to generate savings, if proprietary companies cut their prices to deter generic companies from entering particular markets. However, there is little evidence that "potential" competition is effective in practice. In markets where there are no generic suppliers or just one or two suppliers, prices have actually risen slightly, on average, since patent expiry. Thus, it would appear that large-scale generic entry is needed to generate genuine price competition.

An analysis by the ABPI of products that came off patent between 1990 and 1999 calculated the savings to the NHS on a different basis. This calculated that using IMS data for generic volumes in the year to July 2001 and current average generic prices, the savings were some £85 million a year higher than using the Department's methodology of the difference between the brand and Drug Tariff price (£261 million compared to £176 million). This analysis suggests savings to the NHS were greater at 30% rather than the 25% estimated by the Department. [3]

4. Analysis of Individual Products

As already noted, the impact of generic competition varies enormously between individual products. These products can be grouped into four broad categories:

(i) fairly rapid and large-scale entry with significant reduction in prices (e.g. captopril, cimetidine, enalapril maleate, fluoxetine hydrochloride);

(ii) slow generic entry, but substantial savings achieved relatively quickly thereafter (e.g. atenolol, ranitidine);

(iii) very slow generic entry and/or fairly modest impact on expenditure (e.g. aciclovir, terfenadine, fenbufen, cephalexin, metoprolol tartrate);

(iv) no or very little impact of generic competition even in the long term, either because there is no generic entry (e.g. budesonide, ciclosporin) or because competition does not appear to be effective (e.g. co-amoxiclav).

The first group is the "classic" model of what ought to happen if the generics market were operating efficiently. Although there are only really four products in this group, they are four of the most significant products to have come off patent during this period. Captopril is the one that is most often quoted as an example of the effectiveness, and benefits, of generic competition. The day after the patent expired, 13 players entered the market and prices dropped to 40-50% of the brand price. Within a week, captopril was available at 20% of the brand price. Generic volume share increased from 39% in February 1997 to more

[3] This reflects the fact that pharmacists are able to purchase generics for less than the Drug Tariff price. The Discount Inquiry and discount clawback is designed to secure this extra saving.

than 50% within six months. Brand volume share maintained by price equalisation deals. This was an attractive market for generic companies, because of its size and the relatively straightforward nature of the manufacturing process.

The experience of cimetidine was similar, though less dramatic. It is a slightly special case, because it was affected by the 1977 Patent Act. The UK product patent on cimetidine had an original term of 16 years. Under the Act, this patent was extended by four years subject to compulsory licences being available for this period. When the patent expired in 1992, there were already generic companies producing cimetidine, which probably explains why the impact of generic competition was more immediate.

The launch of generic fluoxetine hydrochloride had a significant effect on sales of Prozac. Generic volume share increased from 57% in January 2000 to more than 70% within six months. The price of the generic fell to 33% of the original brand within nine months. The price of the brand remained unchanged.

Following patent expiry of enalapril maleate in December 1999, generic volume share increased from 45% to more than 90% within 10 months. The generic Drug Tariff price fell to 50% of Innovace (the ABPI quoted the market place price falling to 13% of the original brand price) within 11 months.

The second group includes the largest product, ranitidine, and another large product, atenolol. In both cases, generic competition has been effective in bringing down prices, but took longer to come about. In the case of ranitidine, the patent situation is complex with two separate product patents for different forms of the molecule – Form 1 and Form 2. The patent of Form 1 expired in 1997, while that of Form 2 expired in 2001. One of the complications was said to be that it was difficult to manufacture Form 1 without infringing the Form 2 patent. Glaxo Wellcome are thought to have entered an agreement with a generics manufacturer to allow it (and sub-licensees) to manufacture Form 2. It is also thought that although the list prices remain relatively high, large discounts are being given on generic ranitidine. This is reflected in the Discount Inquiry.

Atenolol, like cimetidine, was subject to a designated "license of right" for the last four years of its patent, so there were generic versions of the product prior to the patent expiry date. This would explain why the generic market share was high even before the product's patent expired. However, the Drug Tariff price of atenolol did not drop significantly for

at least two years following patent expiry. The reasons for this are unclear, but this delayed the benefits of generic competition.

The third group includes a few smaller, but significant, products, where generic competition appears to have had only a relatively small impact. For some of these products, generic entry has been very slow. For example, a generic version of aciclovir cream did not appear for two years, possibly because most generic manufacturers are geared up to making tablets, rather than less standard presentations such as creams or syrups. As far as licensing is concerned, it is much more difficult to demonstrate essential similarity to the originator product for topical preparations. Generic versions of the tablets started to appear after a year or so, but only after four years is there evidence that they are making a significant breakthrough.

Terfenadine and fenbufen were also slow to attract generic entry. There were legal proceedings with terfenadine over an additional patent, which may have affected generic entry. In addition, there were some concerns about the side-effects of these products and this uncertainty may have been enough to deter greater potential suppliers. Both these markets were declining, so generic entry needed to be fast to secure significant savings from generic competition.

For other products, such as cephalexin and metoprolol tartrate, there were small price reductions in the Drug Tariff soon after generic entry occurred, but there has been no "dynamic" price-cutting even though both products have quite a few listed suppliers.

The fourth group includes the other products, where generic competition has been largely ineffective. Small market size or lack of potential is clearly a factor in restricting generic entry, given the significant fixed costs involved in entering a new market e.g. the costs involved in licensing new products, of sourcing raw materials and any adaptations that might need to be made to their manufacturing plant. This would rule out most "minor" products that come off patent.

But this group also includes quite a few very significant products, such as budesonide, ciclosporin, and co-amoxiclav, where the potential benefits from greater competition are substantial, but where generic entry has been impeded by various other factors.

In the case of budesonide, the proprietary company applied for Supplementary Protection Certificate (SPC) extension to its patent and then appealed against the rejection of its application. The legal

proceedings, which eventually went against the proprietary company, were only finalised in 1998, nearly five years after the original patent expired. However, the delivery method used is an inhaler device (turbohaler) which is still patented protected. This is the main reason for the lack of generic competition.

Ciclosporin is a specialised product for transplant patients. The proprietary manufacturer introduced a modified form of the drug, Neoral, shortly before the patent on the chemical expired at the end of 1994. The company sought to discontinue the original product, Sandimmun, and actively encouraged doctors to transfer their patients on to the new product. Sandimmun is now only available on a special order basis to patients who are unable to take Neoral. A branded generic version of ciclosporin oral solution was introduced but was withdrawn due to interaction/bioavailability problems in relation to Neoral.

A similar example is cefaclor, where the proprietary manufacturer introduced a modified release (MR) version of the main dosage form before the patent expired. The modified release (MR) version now dominates the market. The MCA requires that MR versions are branded, as the release profiles of different versions may differ. Although they could in principle introduce their own MR product(s), (subject to patent restraints) the mainstream generic manufacturers are likely to be put off by the additional complexity of licensing and manufacturing MR versions.

Co-amoxiclav was subject to complex legal proceedings concerning the patent. A generic version of the main dosage form (375mg) did not appear for nearly four years after the patent expired and was introduced at the same price as the branded product (which had risen twice prior to generic entry). The basic product patents on the two active ingredients expired in the late 1980s and mid 1990s, but the company had additional patents, including two strong process patents on the production of one of the ingredients, clavulanic acid.

Non-standard formulations could also explain why other sizeable products, such as ketoconazole shampoo and felbinac gel were slow to/or have not attracted generic entry, since their patents expired in 1997 and 1998 respectively. Not only are these presentations more difficult to manufacture, but it is also more difficult to demonstrate bioequivalence to the originator product, both of which increase the cost of entering a new market.

SPC expiry date for acarbose was September 1999 but a composition patent until 2006 covers highly purified form of acarbose.

5. Barriers to Entry

The analysis of specific products has identified a number of reasons why generic entry often does not occur or is slow in some markets. These include:

- Size of market: in most cases, generic companies are not interested in small and/or rapidly declining markets;

- Nature of product: apart from a few companies, which specialise in the manufacture of oral liquids, generic companies concentrate on oral solid dosage forms, in particular tablets and generally avoid other presentations;

- Complexity of the manufacturing process: some products, for example creams, ointments, gels etc and delivery systems for asthma inhalation products are difficult and more costly to manufacture and to demonstrate bioequivalence;

- Modified-release versions: it is the MCA's policy that all MR versions should be prescribed by brand name, so there are no true generics. Prescribers often favour MR versions, but most generic companies do not make their own (branded) MR versions, because they are more complex to license and manufacture;

- Existence of additional manufacture or process patents;

- Licensing procedures: in the UK, generic companies are not allowed to experiment with patented products before their patent expires, which may delay generic entry. In practice, the larger companies get around this by carrying out these activities outside the EU, but smaller generic companies may take longer to get a product licensed due to the patent restrictions. The legal protection provided by "data exclusivity" is based on when the branded product is launched rather than when the molecule is patented; in some cases, this can effectively prevent generic entry for a period following the expiry of a patent;

- Availability of raw material: there may be some cases where the supply of the raw material is controlled by the originator company, either by use of patents or by other means;

- Generic prescribing: whilst overall 72% of prescriptions are now written generically, there are still wide variations in the rate of generic prescribing between individual products. In the list of recent patent expiries, for example, the rates vary from as low as 20% of total NIC for felbinac to nearly 90% for captopril. Generic prescribing is often low for compound products, such as Gaviscon, because it is much simpler for prescribers to write and pharmacists to recognise the branded name. Modified release versions might also explain low rates of generic prescribing for the reasons already discussed. But, some of the variations are not well understood. Low rates of generic prescribing prior to patent expiry may deter generic companies, because it reduces the size of the market they are able to compete for;

- The availability of cheaper parallel imports and OTC products: also products with low margins which have not had a price increase for a long time are not attractive to generic companies;

- Uncertainty: on-going court cases or warnings about possible side-effects may deter potential suppliers, who do not want to face the additional risk involved in entering these markets.

6. Impact on Prices and Market Shares

Even where generic entry does occur, this does not automatically mean that effective price competition will result. Several generic versions may be required before the Drug Tariff price will begin to fall. Those products that have experienced significant price reductions have many – usually 10 or more – potential suppliers. It is also possible that the reimbursement system is less than effective in capturing the full benefits of generic competition or that the benefits are picked up elsewhere through the Discount Inquiry.

Another feature of the generics market is the general avoidance of price cuts on the originator brands, even following generic entry. Some companies compete on the basis of discount allowed to wholesalers and community pharmacies. Only some of this discount maybe recovered by the NHS through the Discount Inquiry. In the case of captopril and cimetidine, both of which have faced strong price competition from generics, the branded price has remained stable or has gone up. Presumably, the proprietary companies have decided it is more profitable to make their money on branded prescriptions than to attempt to compete for market share with the generic companies. Whilst generic

prescribing has been rising over time, a significant minority of prescriptions continue to be written for branded products even for products like captopril.

7. Products due to Expire during the 1999 Scheme

Appendix 8.3 lists 89 products identified as having patents expiring up to 2004 during the current PPRS. 31 of these products have sales exceeding £3 million in 2000 (based on Prescription Cost Analysis (PCA) data). Three major products with patent expiry in this period are Losec (omeprazole), Zestril (lisinopril) and Zocor (simvastatin), which all have 94% or more generic prescribing.

8. Appendices

8.1 List of Products that came Off-Patent between 1990-2000

	Chemical Name	Brand	Patent Expiry	NIC in year that patent expired (£m)	NIC in 2000 (£m)	Generic entry up to end of 2000?	No. of generic suppliers [1]	Main dosage form
1	Ranitidine Hydrochloride	Zantac	97-3	131.496	52.952	Yes	16	Tablet
2	Enalapril Maleate	Innovace	99-4	71.780	49.566	Yes	16	Tablet
3	Fluoxetine Hydrochloride	Prozac	00-1	61.056	61.056	Yes	14	Capsule
4	Atenolol	Tenormin	90-1	57.676	29.136	Yes	10	Tablet
5	Cimetidine	Tagamet	92-1	45.861	18.048	Yes	11	Tablet
6	Budesonide	Pulmicort	93-2	38.069	54.757	No	0	Inhaler
7	Ciclosporin	Sandimmun	94-4	27.121	33.102	No	0	Capsule
8	Co-Amoxiclav (Amoxycillin/ Clavulanic Acid)	Augmentin	95-2	26.422	17.503	Yes	6	Tablet
9	Captopril	Capsuleoten	97-1	26.257	11.910	Yes	12	Tablet
10	Aciclovir	Zovirax	95-3	19.011	8.507	Yes	9	Tablet
11	Terfenadine	Triludan	92-4	15.755	0.163	Yes	2	Tablet
12	Piroxicam	Feldene	90-2	15.453	4.643	Yes	11	Gel
13	Gabapentin	Neurontin	00-4	14.399	14.399	No	0	Capsule
14	Cefaclor	Distaclor	94-1	12.690	5.194	Yes	5	Tablet
15	Zopiclone	Zimovane	93-1	8.581	11.208	Yes	8	Tablet
16	Fenbufen	Lederfen	91-3	8.388	1.170	Yes	6	Tablet
17	Cephalexin	Ceporex	90-2	7.537	5.971	Yes	8	Capsule
18	Celiprolol Hydrochloride	Celectol	99-4	7.041	6.353	Yes	4	Tablet
19	Tiaprofenic Acid	Surgam	90-4	6.493	1.749	Yes	1	Capsule
20	Cholestyramine	Questran	90-4	5.719	2.272	Yes	1	Sachet
21	Bezafibrate	Bezalip	92-4	5.672	5.735	Yes	2	Tablet
22	Ketoconazole	Nizoral	97-4	4.527	3.492	Yes	1	Shampoo
23	Acarbose	Glucobay	99-3	3.938	2.827	No	0	Tablet
24	Felbinac	Traxam	98-3	3.806	3.030	No	0	Gel
25	Nabumetone	Relifex	93-3	3.715	5.375	Yes	3	Tablet
26	Metoprolol Tartrate	Betaloc	91-2	3.664	2.047	Yes	6	Tablet
27	Terazosin Hydrochloride	Hytrin	96-4	3.043	3.418	Yes	1	Tablet
28	Triazolam [2]	Halcion	90-1	3.032	0.000	No	0	Tablet
	Top 28 products (£3m+NIC)	**82.4%**			**415.582**	**22**		
	Minor products (see list below)				**88.896**	**25**		
	Total (137)				**504.478**	**47**		

[1] Number of generic suppliers as in Chemist & Druggist Generics List April - September 2001. Additional information from BNF September 2001.

[2] Products withdrawn from market.

[3] Brand name removed and marketed as generic.

8.1 List of Products that came Off-Patent between 1990-2000 *Continued*

	Chemical Name	Brand	Patent Expiry	NIC in year that patent expired (£m)	NIC in 2000 (£m)	Generic entry up to end of 2000?	No. of generic suppliers [1]	Main dosage form
	Minor Products							
29	Flecainide Acetate	Tambocor	95-1	2.833	4.931	Yes	4	Tablet
30	Clobetasol Butyrate	Eumovate	90-2	2.830	3.447	No	0	Cream
31	Betaxolol	Betoptic	96-4	2.812	2.294	No	0	Drops
32	Acemetacin	Emflex	93-3	2.777	0.780	No	0	Capsule
33	Nicardipine Hydrochloride	Cardene	99-1	2.675	2.248	Yes	1	Capsule
34	Clobetasol Propionate	Dermovate	90-2	2.637	2.640	No	0	Cream
35	Domperidone	Motilium	96-2	2.550	3.187	Yes	6	Tablet
36	Loperamide Hydrochloride	Imodium	91-2	2.521	2.777	Yes	11	Capsule
37	Amisulpride	Solian	99-4	2.366	3.854	No	0	Tablet
38	Haloperidol	Haldol	00-2	2.321	2.321	Yes	6	Tablet
39	Etodolac	Lodine	92-2	2.143	2.860	No	0	Tablet
40	Mupirocin	Bactroban	92-2	1.996	2.249	No	0	Ointment
41	Buspirone Hydrochloride	Buspar	90-4	1.982	1.840	Yes	1	Tablet
42	Fluvoxamine Maleate	Faverin	96-1	1.762	0.978	Yes	4	Tablet
43	Famotidine	Pepcid	00-3	1.589	1.589	Yes	5	Tablet
44	Flupenthixol Hydrochloride	Fluanxol	90-2	1.581	0.967	No	0	Tablet
45	Atenolol With Diuretic	Kalten	90-1	1.437	0.522	No	0	Capsule
46	Tioconazole	Trosyl	96-2	1.426	1.624	No	0	Solution
47	Alfacalcidol	One-Alpha	94-1	1.406	2.275	Yes	1	Capsule
48	Carteolol Hydrochloride	Cartrol	93-1	1.306	2.621	No	0	Drops
49	Flupenthixol Decanoate	Depixol	90-2	1.231	1.623	No	0	Injection
50	Enalapril Maleate with Diuretic	Innozide	99-4	1.051	1.013	No	0	Tablet
51	Pivampicillin [2]	Pondocillin	90-1	0.992	0.000	No	0	Tablet
52	Levobunolol Hydrochloride	Betagan	90-3	0.881	3.608	Yes	1	Drops
53	Dalteparin Sodium	Fragmin	00-3	0.848	0.848	No	0	Injection
54	Metoprolol Tartrate With Diuretic	Co-Betaloc	91-2	0.824	0.140	No	0	Tablet
55	Misoprostol	Cytotec	00-1	0.772	0.772	No	0	Tablet
56	Sulindac	Clinoril	90-3	0.739	0.289	Yes	2	Tablet
57	Glipizide	Glibenese	90-1	0.702	1.673	Yes	6	Tablet
58	Salcatonin	Miacalcic	91-2	0.687	0.284	Yes	3	Injection
59	Tripotassium Dicitratobismuthate	De-Nol	95-1	0.654	0.021	No	0	Tablet
60	Tenoxicam	Mobiflex	00-3	0.651	0.651	No	0	Tablet
61	Norfloxacin	Utinor	98-1	0.625	0.482	Yes	2	Tablet
62	Nadolol	Corgard	91-2	0.621	0.215	No	0	Tablet
63	Auranofin	Ridaura	90-4	0.501	0.125	No	0	Tablet

8.1 List of Products that came Off-Patent between 1990-2000 *Continued*

	Chemical Name	Brand	Patent Expiry	NIC in year that patent expired (£m)	NIC in 2000 (£m)	Generic entry up to end of 2000?	No. of generic suppliers [1]	Main dosage form
64	Ciprofibrate	Modalim	93-3	0.478	2.565	No	0	Tablet
65	Mebendazole	Vermox	90-2	0.477	0.299	No	0	Suspe-nsion
66	Acipimox	Olbetam	93-2	0.403	0.265	No	0	Capsule
67	Fenofibrate	Lipantil	92-4	0.376	4.136	No	0	Capsule
68	Ketotifen Fumarate	Zaditen	91-2	0.376	0.152	No	0	Tablet
69	Loprazolam Mesylate	Dormonoct	95-1	0.375	1.112	Yes	1	Tablet
70	Azelastine Hydrochloride	Rhinolast	92-1	0.357	0.998	No	0	Spray
71	Calcitriol	Rocaltrol	96-1	0.349	0.710	Yes	1	Capsule
72	Astemizole	Hismanal	99-1	0.296	0.006	No	0	Tablet
73	Rimiterol Hydrobromide [2]	Pulmadil	90-2	0.279	0.000	No	0	Inhaler
74	Propafenone Hydrochloride	Arythmol	91-3	0.272	0.764	No	0	Tablet
75	Ceftazidime Pentahydrate	Fortum	99-2	0.268	0.267	No	0	Injection
76	Mefloquine Hydrochloride	Lariam	98-2	0.251	0.343	No	0	Tablet
77	Nadolol with Diuretic	Corgaretic	91-2	0.234	0.061	No	0	Tablet
78	Gliquidone	Glurenome	90-2	0.215	0.073	No	0	Tablet
79	Alclometasone Dipropionate	Modrasone	97-4	0.174	0.141	No	0	Cream
80	Torasemide	Torem	00-2	0.162	0.162	No	0	Tablet
81	Diflucortolone Valerate	Nerisone	97-2	0.159	0.132	No	0	Cream
82	Loxapine Succinate	Loxapac	96-3	0.153	0.080	No	0	Capsule
83	Xamoterol Fumarate	Corwin	98-2	0.107	0.054	No	0	Tablet
84	Midazolam Hydrochloride	Hypnovel	95-4	0.104	0.182	Yes	2	Injection
85	Pivampicillin with Pivmecillinam [2]	Miraxid	90-1	0.088	0.000	No	0	Tablet
86	Clobetasone Butyrate	Cloburate	90-2	0.075	0.008	No	0	Drops
87	Pirbuterol Acetate [2]	Exirel	92-4	0.064	0.000	No	0	Inhaler
88	Mequitazine	Primalin	90-1	0.062	0.004	No	0	Tablet
89	Nimodipine	Nimotop	00-1	0.061	0.061	No	0	Tablet
90	Piretanide [2]	Arelix	95-2	0.059	0.000	No	0	Capsule
91	Sulconazole Nitrate	Exelderm	95-3	0.058	0.017	No	0	Cream
92	Acitretin	Neotigason	99-1	0.052	0.051	No	0	Capsule
93	Cinoxacin	Cinobac	90-1	0.051	0.010	No	0	Capsule
94	Inosine Pranobex	Imunovir	90-1	0.039	0.016	No	0	Tablet
95	Bacampicillin [2] Hydrochloride	Ambaxin	91-4	0.038	0.000	No	0	Tablet
96	Talampicillin Hydrochloride [2]	Talpen	92-2	0.031	0.000	No	0	Tablet
97	Betaxolol Hydrochloride	Kerlone	96-4	0.028	0.019	No	0	Tablet
98	Azlocillin Sodium [2]	Securopen	91-2	0.024	0.000	No	0	Infusion
99	Imipenem With Cilastatin	Primaxin	96-4	0.023	0.017	No	0	Injection
100	Gonadorelin [2]	Fertiral	93-1	0.021	0.000	No	0	Injection

8.1 List of Products that came Off-Patent between 1990-2000 *Continued*

	Chemical Name	Brand	Patent Expiry	NIC in year that patent expired (£m)	NIC in 2000 (£m)	Generic entry up to end of 2000?	No. of generic suppliers [1]	Main dosage form
101	Amikacin	Amikin	92-3	0.020	0.013	Yes	1	Injection
102	Pirbuterol Hydrochloride [2]	Exirel	92-4	0.019	0.000	No	0	Capsule
103	Fenticonazole Nitrate	Lomexin	00-4	0.019	0.019	No	0	Pessary
104	Nabilone	Cesamet	94-4	0.018	0.199	Yes	1	Capsule
105	Pivmecillinam Hydrochloride	Selexid	90-4	0.016	0.032	No	0	Tablet
106	Tocainide Hydrochloride	Tonocard	92-3	0.015	0.002	No	0	Tablet
107	Cefotaxime Sodium	Claforan	95-4	0.010	0.012	Yes	2	Injection
108	Isotretinoin	Roaccutane	90-4	0.007	0.458	No	0	Capsule
109	Piperacillin Sodium	Pipril	95-2	0.007	0.005	No	0	Injection
110	Cefsulodin Sodium [2]	Monaspar	91-2	0.004	0.000	No	0	Injection
111	Netilmicin Sulphate	Netillin	94-3	0.004	0.001	No	0	Injection
112	Isoflurane [2]	Forane	92-3	0.001	0.000	Yes	1	Anaes-thetic
113	Cephamandole	Kefadol	90-2	0.001	0.000	No	0	Injection
114	Vindesine Sulphate	Eldisone	94-1	0.001	0.000	No	0	Injection
115	Alfentanil Hydrochloride	Rapifen	98-2	0.001	0.010	No	0	Injection
116	Mitozantrone	Novantrone	98-3	0.000	0.000	No	0	Injection
117	Dobutamine Hydrochloride	Dobutrex	93-2	0.000	0.000	Yes	2	Injection
118	Etretinate [2]	Tigason	94-1	0.000	0.000	No	0	Capsule
119	Cefoxitin Sodium	Mefoxin	91-2	0.000	0.000	No	0	Infusion
120	Atracurium Besylate	Tracrium	97-1	0.000	0.000	Yes	1	Injection
121	Propofol	Diprivan	00-1	0.000	0.000	Yes	4	Injection
122	Acrosoxacin [2]	Eradacin	92-2	0.000	0.000	No	0	Capsule
123	Ceftizoxime Sodium [2]	Cefizox	97-1	0.000	0.000	No	0	Injection
124	Oxatomide [2]	Tinset	97-1	0.000	0.000	No	0	Tablet
125	Cephalothin [2]	Keflin	90-4	0.000	0.000	No	0	Injection
126	Mecillinam [2]	Selexidin	90-4	0.000	0.000	No	0	Injection
127	Mezlocillin [2]	Baypen	92-4	0.000	0.000	No	0	Tablet
128	Tribavirin	Virazid	92-2	0.000	0.144	No	0	Capsule
129	Mirtazapine	Zispin	96-1	0.000	6.758	No	0	Tablet
130	Pentostatin	Nipent	98-3	0.000	0.000	No	0	Tablet
131	Carboplatin	Paraplatin	98-2	0.000	0.000	Yes	1	Tablet
132	Epirubicin Hydrochloride	Pharmor-abacin	95-1	0.000	0.000	No	0	Tablet
133	Eformoterol Fumarate	Foradil	93-4	0.000	7.603	No	0	Inhaler
134	Gemeprost	Cervagem [3]	93-4	0.000	0.000	No	1	Tablet
135	Tizanidine Hydrochloride	Sirdalud	93-4	0.000	3.189	No	0	Tablet
136	Enoxacin [2]	Comprecin	99-4	0.000	0.000	No	0	Tablet
137	Dicobalt Edetate	Kelocyanar [3]	99-3	0.000	0.000	No	0	Tablet
	Total (minor products)					**88.896**	**25**	

8.2 Estimated Savings from Generic Competition for Products that came Off Patent 1990-2000

	Chemical name	Brand	Patent expiry	A Total NIC since patent expiry(£m)	B Total NIC at original branded price (£m)	Difference B-A (%)	Year 1 Difference (%)	Year 2 Difference (%)	Year 3 Difference (%)	Year 4 Difference (%)	Year 5 Difference (%)
1	Ranitidine Hydrochloride	Zantac	97-3	315.8	449.0	30%	9.0%	28.3%	42.2%	-	-
2	Enalapril Maleate	Innovace	99-4	76.1	102.8	26%	27.3%	-	-	-	-
3	Fluoxetine Hydrochloride	Prozac	00-1	72.2	120.4	40%	49.6%	-	-	-	-
4	Atenolol	Tenormin	90-1	313.2	781.0	60%	-	5.3%	39.9%	56.1%	59.9%
5	Cimetidine	Tagamet	92-1	228.0	408.2	44%	19.9%	38.9%	48.8%	55.4%	57.5%
6	Budesonide	Pulmicort	93-2	447.2	447.1	0%	0.0%	-2.1%	0.2%	0.2%	0.3%
7	Ciclosporin	Sandimmun	94-4	211.2	210.8	0%	-1.4%	0.0%	0.0%	0.0%	0.0%
8	Co-Amoxiclav (Amoxycillin/Clavulanic Acid)	Augmentin	95-2	134.6	119.5	-13%	-0.7%	-9.7%	-18.6%	-20.2%	-20.3%
9	Captopril	Capsuleoten	97-1	69.4	127.5	46%	41.3%	58.4%	39.8%	60.4%	-
10	Aciclovir	Zovirax	95-3	72.9	92.8	21%	-0.2%	9.4%	15.2%	26.4%	42.0%
11	Terfenadine	Triludan	92-4	56.7	63.4	11%	0.3%	3.3%	9.5%	20.6%	25.2%
12	Piroxicam [1]	Feldene	90-2								
13	Gabapentin [1]	Neurontin	00-4	8.9	8.9	0%	-	-	-	-	-
14	Cefaclor	Distaclor	94-1	71.7	88.4	19%	-0.2%	12.2%	22.9%	25.9%	28.2%
15	Zopiclone [1]	Zimovane	93-1								
16	Fenbufen	Lederfen	91-3	36.8	39.0	6%	0.0%	0.1%	2.7%	6.2%	9.9%
17	Cephalexin	Ceporex	90-2	69.0	86.6	20%	-	11.9%	13.2%	16.2%	17.0%
18	Celiprolol Hydrochloride	Celectol	99-4	9.6	9.7	1%	1.5%	-	-	-	-
19	Tiaprofenic Acid	Surgam	90-4	41.8	38.0	-10%	-1.8%	-5.4%	-5.6%	-5.3%	-5.4%
20	Cholestyramine	Questran	90-4	37.9	42.2	10%	0.0%	0.0%	2.6%	16.0%	16.1%
21	Bezafibrate	Bezalip	92-4	58.0	59.7	3%	0.4%	2.5%	2.5%	2.5%	2.5%
22	Ketoconazole	Nizoral	97-4	13.1	17.2	24%	15.1%	30.4%	30.6%	-	-
23	Acarbose	Glucobay	99-3	5.4	7.1	25%	28.3%	-	-	-	-
24	Felbinac	Traxam	98-3	9.2	9.1	0%	-0.1%	-0.2%	-	-	-
25	Nabumetone	Relifex	93-3	45.7	40.2	-14%	-4.6%	-14.7%	-15.5%	-15.5%	-15.5%
26	Metoprolol Tartrate	Betaloc	91-2	24.7	28.0	12%	-3.2%	1.3%	6.9%	13.3%	16.2%
27	Terazosin Hydrochloride	Hytrin	96-4	16.6	18.3	9%	-0.1%	-0.1%	4.8%	26.2%	-
28	Triazolam [1]	Halcion	90-1								
	Top 28 products			**2,445.3**	**3,415.0**	**28%**					
	Minor products			**524.2**	**540.9**	**3%**					
	Total			**5,414.9**	**7,370.9**	**27%**	**16.7%**	**14.7%**	**22.9%**	**23.2%**	**21.7%**

[1] Piroxicam and zopiclone excluded as market affected by ACD decisions; triazolam as withdrawn from market and gabapentin as recent patent expiry.

8.3 Products with Patent Expiry 2001 - 2004

	Generic name	Brand name	Company	Patent/SPC expiry date	NIC in 2000 £000s
1	Omeprazole	Losec	AstraZeneca	14-Apr-02	150,856
2	Simvastatin	Zocor	Merck Sharp & Dohme	05-May-03	144,098
3	Doxazosin	Cardura	Pfizer	01-Apr-02	62,559
4	Lisinopril	Zestril	AstraZeneca	05-Oct-02	56,550
5	Pravastatin	Lipostat	Bristol-Myers Squibb	09-Aug-04	41,369
6	Citalopram	Cipramil	Lundbeck	05-Jan-02	38,222
7	Ramipril	Tritace	Hoechst Marion Roussel	09-Jan-04	34,243
8	Perindopril	Coversyl	Servier	21-Jun-03	24,858
9	Loratadine	Clarityn	Schering Plough	30-Nov-02	24,408
10	Erythropoetin alfa	Eprex	Janssen-Cilag	11-Dec-04	20,645
11	Cetirizine	Zirtek	UCB Pharma	04-Feb-02	17,870
12	Lisinopril	Carace	Merck Sharp & Dohme	05-Oct-02	16,728
13	Goserelin	Zoladex	AstraZeneca	30-Nov-01	15,947
14	Ciprofloxacin	Ciproxin	Bayer	18-Jul-02	15,408
15	Meloxicam	Mobic	Boehringer Ingelheim	03-Dec-03	13,241
16	Bisoprolol	Monocor	Lederle	27-Jan-01	11,164
17	Felodipine	Plendil	AstraZeneca	20-Mar-03	10,970
18	Nicorandil	Ikorel	Rhone-Poulenc Rorer	23-Mar-02	10,116
19	Norgestimate+ ethinyloestradiol	Cilest	Janssen-Cilag	14-Jun-01	8,980
20	Nizatidine	Axid	Eli Lilly	29-Jul-02	8,806
21	Pergolide	Celance	Eli Lilly	04-Feb-04	7,020
22	Erythropoetin beta	Neo-Recormon	Roche	11-Dec-04	6,521
23	Fluconazole	Diflucan	Pfizer	07-Mar-03	6,473
24	Clarithromycin	Klaricid	Abbott	19-Nov-04	5,210
25	Leuprorelin actetate	Prostap SR	Wyeth	11-Jan-02	4,859
26	Cisapride	Prepulsid	Janssen-Cilag	19-Apr-03	3,883
27	Hepatitis B surface antigen	Engerix B	SmithKline Beecham	13-Nov-01	3,874
28	Quinapril	Accupro	Parke-Davis	13-Apr-04	3,863
29	Amisulpride	Solian	Sanofi-Synthelabo	19-Jan-01	3,852
30	Lisinopril + hydro-chlorothiazide	Zestoretic	AstraZeneca	16-Apr-04	3,759
31	Moxonidine	Physiotens	Solvay	13-Nov-04	3,147
32	Ocreotide	Sandostatin	Novartis	10-Apr-03	2,905
33	Vigabatrin	Sabril	Hoechst Marion Roussel	25-Jan-01	2,801
34	Permethrin	Lyclear	GlaxoSmithkline	19-Feb-01	2,696
35	Itraconazole	Sporanox	Janssen-Cilag	14-Dec-03	2,274
36	Carvedilol	Eucardic	Roche	06-Apr-04	2,030
37	Hepatitis B surface antigen	HB-Vax	Aventis Pasteur, MSD	15-May-01	2,011
38	Cabergoline	Dostinex	Pharmacia & Upjohn	06-Jan-02	1,948
39	Tioconazole	Trosyl	Pfizer	25-Apr-02	1,624
40	Acamprosate	Campral EC	Merck	23-Jul-02	1,550
41	Reboxetine	Edronax	Pharmacia	10-Jan-04	1,437
42	Alfuzosin	Xatral	Sanofi-Synthelabo	11-Nov-02	1,411
43	Propiverine	Detrunorm	Schering Plough	27-Sep-04	1,403
44	Olsalazine	Dipentum	Pharmacia & Upjohn	24-Sep-02	1,299
45	Leflunomide	Arava	Hoechst Marion Roussel	12-Dec-04	1,102
46	Modafinil	Provigil	Cephalon	30-Mar-03	1,097
47	Nedocromil	Tilade	Pantheon	23-Apr-01	1,065
48	Enalapril+ hydro-chlorothiazide	Innozide	Merck Sharp & Dohme	28-Dec-02	1,013

8.3 Products with Patent Expiry 2001 - 2004 *Continued*

	Generic name	Brand name	Company	Patent/SPC expiry date	NIC in 2000 £000s
49	Moclobemide	Manerix	Roche	14-Feb-02	814
50	Enoxaparin	Clexane	Rhone-Poulenc Rorer	07-May-01	781
51	Gestodene + ethinyloestradiol	Minulet	Wyeth	21-Jul-01	752
52	Cefixime	Suprax	Wyeth	04-Sep-03	661
53	Cefuroxime axetil	Zinnat	GlaxoSmithkline	14-Feb-02	600
54	Lofexidine	Britlofex	Britannia	04-Oct-03	572
55	Interferon alfa 2a	Roferon A	Roche	08-Nov-01	471
56	Ganciclovir	Cymevene	Roche	04-Jun-03	441
57	Lisinopril + hydro-chlorothiazide	Carace Plus	Merck Sharp & Dohme	16-Apr-04	304
58	Teicoplanin	Targocid	Aventis	26-Feb-01	296
59	Isradipine	Prescal	Novartis	02-Jan-04	255
60	Acrivastine	Semprex	GlaxoSmithkline	22-Sep-03	238
61	Rifabutin	Mycobutin	Pharmacia & Upjohn	27-May-01	163
62	Quinapril + hydro-chlorothiazide	Accuretic	Parke-Davis	13-Apr-04	153
63	Buserelin	Suprefact	Shire	31-Jul-04	107
64	Nisoldipine	Syscor MR	Pharmax	01-Nov-01	84
65	Ticlodipine	Ticlid	Sanofi- Synthelabo	Jul-01	68
66	Emedastine	Emadine	Alcon	05-Nov-02	59
67	Interferon gamma	Immukin	Boehringer Ingelheim	13-Dec-04	54
68	Toremifene	Fareston	Orion	20-Dec-03	44
69	Ciprofloxacin	Ciloxan	Alcon	18-Jul-02	44
70	Enoximone	Perfan	Aventis	26-Oct-02	34
71	Ketorolac trometamol	Toradol	Roche	10-Jul-02	25
72	Ofloxacin	Exocin	Allergan	27-Aug-01	23
73	Aztreonam	Azactam	Bristol-Myers Squibb	05-Feb-01	N/A
74	Triptorelin	De-Capsuleetyl sr	Ipsen	04-Mar-01	N/A
75	Fomivirsen	Vitravene	Ciba Vision	14-Aug-01	N/A
76	Ofloxacin	Tarvid	Hoechst Marion Roussel	27-Aug-01	N/A
77	Flumazenil	Anexate	Roche	13-Jan-02	N/A
78	Amsacrine	Amsidine	Goldshield	27-Mar-02	N/A
79	Foscarnet	Foscavir	AstraZeneca	29-Jun-02	N/A
80	Cilastatin + imipenem	Primaxin	Merck Sharp & Dohme	08-Aug-02	N/A
81	Milrinone	Primacor	Sanofi-Synthelabo	15-Oct-02	N/A
82	Gadopentetic acid	Magnevist	Schering	04-Feb-03	N/A
83	Esmolol	Brevibloc	Baxter	22-Mar-03	N/A
84	Alteplase	Actilyse	Boehringer Ingelheim	03-May-03	N/A
85	Dopexamine	Dopacard	Elan	10-Jul-03	N/A
86	Lornoxicam	Xefo	CeNeS	04-Sep-03	N/A
87	Mifepristone	Mifegyne	Hoechst Marion Roussel	27-Dec-03	N/A
88	Aldesleukin	Proleukin	Chiron	07-Feb-04	N/A
89	Vinorelbine	Navelbine	Fabre	10-Apr-04	N/A

All figures for NIC include the community sector, England only (PCA data).

Component 4:

Demand-Side Effectiveness

December 2002

Component 4

Contents

Component 4

Demand-Side Effectiveness

1. Introduction

The remit of Component 4 was to assess demand-side effectiveness, in particular the price sensitivity of prescribers, focusing on:

- Prescribers' price awareness, including how quickly perceptions respond following price changes.
- Prescribers' perceptions of quality including consistency with reviews of evidence.
- Factors that influence prescribing decisions, particularly the relative importance of price and the willingness to switch patients.

This report summarizes the three strands of research commissioned as part of Component 4:

- A review of the published literature looking at the factors affecting prescribing behaviour in the UK, with particular emphasis on the degree of price and quality awareness.
- Qualitative research into prescribers' awareness of price and quality.
- An analysis of GP prescribing patterns in the General Practice Research Database (GPRD) in an attempt to estimate the price elasticity of pharmaceutical products.

2. Executive Summary

Factors that Influence Prescribing Decisions

Overall, the research suggests that prescribers prefer to select drugs on the basis of clinical efficacy, safety, tolerability and convenience to the patient, in that order; cost is generally considered only when all of these are equal.

Prescribing decisions appear to be influenced by a wide range of factors. The decision as to whether or not to prescribe may be influenced by the doctor-patient relationship and the prescriber's knowledge and experience of the condition and the available drugs.

Similar factors also affect the decision regarding what to prescribe, although this may also be influenced by factors relating to the prescriber's colleagues, both in primary and secondary care; hospital doctors can be particularly influential regarding the use of new drugs, where GPs would generally appear to be fairly conservative. However, moves are being made by primary care organisations (PCOs), pharmaceutical advisers and secondary care prescribers to increase joint decision making on prescribing across the interface between secondary and primary care.

Research suggests that national guidance, whether in the form of guidelines or NICE directives, was generally highly influential upon prescribing decisions in primary care. Although a range of mixed views were expressed regarding NICE guidance, GPs appeared to be prepared to ignore restrictive NICE guidance where they felt it clinically appropriate. However, they welcomed the fact that it had effectively taken some difficult decisions out of their hands, allowing them a convenient 'way out' in discussions with patients.

Prescribers' Price Awareness

Although almost all GPs believed that costs should be taken into account when prescribing, there was great variation in the extent to which this was actually applied and in the extent to which they were sensitive to drug costs and price changes. All prescribers considered costs secondary to clinical efficacy, safety, tolerability and often patient compliance.

The qualitative research concluded that most prescribers do not assimilate information on drug costs and price changes. Prescribers have access to drug prices via computerised systems such as EMIS or via publications such as BNF and MIMS but these do not allow for easy comparison between medicines and most prescribers had limited knowledge of actual costs and were often unaware of prices or price changes. Prescribers considered themselves reasonably aware of comparative drug costs but in practice did not perform well in ranking relative costs of many commonly used drugs (with the exception of proton pump inhibitors and statins).

There was some evidence that prescribers are becoming more aware of cost issues around prescribing.

Most GPs reported they had conducted prescribing reviews in high volume/high cost drug classes, usually prompted by PCO and Health Authority (HA) prescribing advisers. These had generally resulted in cost-saving product changes and an improvement in the quality of prescribing.

The presence of incentive schemes and prescribing budgets per se seem to have had limited influence on initiating prescribing reviews among the GPs interviewed for this research. Visits and advice from PCO and HA prescribing advisers and national guidance seem to have been more influential, along with growing awareness of the implications of the unified budget. Overall, therefore, there seems to be a growing acceptance of 'prescribing management' than in the past.

Sensitivity of Prescribing Behaviour to Change

Prescribers are generally conservative with regard to selection of drug therapies, basing their decisions on their own clinical experience; most are reluctant to switch patients unless there is a significant advantage over the alternatives, whether in terms of efficacy, safety or cost.

The literature suggests that decisions to switch a patient from one drug are usually made only if the existing therapy is ineffective or causing adverse effects, or if new drugs offer a major therapeutic advantage. Qualitative research confirms these factors but suggests that therapeutic substitution may occur to achieve cost-minimisation in high volume/high cost areas.

While prescribers appear unwilling to trade quality and effectiveness for cost, they do seem willing to trade patient convenience for cost, and will also trade quality of evidence for cost within a drug class such as the statins.

In addition, among those GPs whose practices operated formularies, cost appeared to play a key role in selection of products listed on the formulary. However, all GPs said that no product would be prescribed in preference to a more appropriate drug simply because it was cheaper.

An econometric analysis of nine therapy areas utilizing GP prescribing data on newly instigated prescriptions from GPRD again highlighted that there is relatively little price variation and failed to show that drug prices affect prescribing behaviour.

3. Main Conclusions from the Research

3.1 Literature Review

A Literature Review was conducted by the Prescribing Research Group at the University of Liverpool under the leadership of Professor Tom Walley. This looked at the factors that affect prescribing behaviour in the UK, with particular emphasis on the degree of price and quality awareness.

The review examined the peer reviewed literature and, as the UK peer reviewed literature in certain areas was limited, also included some of the non-peer reviewed or 'grey literature' (such as Medeconomics, Pulse, GP, Doctor, British Journal of Medical Economics and Scrip), as well as specific reports prepared by academic or commercial units (e.g. reports by Scrip, IIR and other commercial enterprises providing marketing support to the pharmaceutical industry). Where appropriate, it also drew on international experience particularly in countries where the health services and cultural systems resemble those in the UK, notably Australia and New Zealand and possibly the Netherlands.

3.1.1 Overview of the Influences on Prescribing Behaviour

The decision to prescribe a drug may be influenced by a wide range of factors that vary in different circumstances. These factors include:

- the disease/condition — evidence of what treatments work, how well they work, and the risk/benefit ratio for treating this condition.

- the drug — safety, efficacy and cost considerations, as well as possible alternatives and whether or not its use is supported by local/national groups.

- the patient — the impact of the illness on the patient, their past history of treatment, and how well informed the patient is about drugs and their illness.

- the individual doctor — particularly the doctor/patient relationship, and the doctor's knowledge about the disease/treatment, and how colleagues might act.

These same factors also interact to influence the decision regarding what to prescribe. Key factors are the drug characteristics and a doctor's previous education and experience, either in general or more specifically with a particular patient. Most doctors are very conservative in their choice of drugs and are risk averse, which militates against prescribing new drugs. The pharmaceutical industry is a major player in informing doctors of what therapies are available. The final influence to prescribe a new drug is often mediated by colleagues, particularly hospital specialists.

External guidance in the form of formularies, clinical guidelines, and prescribing incentives may also be important. In the absence of external guidance on drug choice, GP choice is based on their education, knowledge of a drug, their previous experience of the patient, the drug and the whole condition, and on what effects they hope to see from drug therapies that promise to deliver that benefit, their colleagues, and price.

A decision to alter a patient's medication is usually only made if the existing therapy is ineffective or causing unsatisfactory adverse effects or new drugs offer major therapeutic advantages. A medication may be switched purely on cost grounds, but this is not always easy or appropriate; patients may be intolerant of frequent changes without good clinical reasons.

3.1.2 The Influence of Patients on Prescribing

Prescribing is governed by complex interactions and negotiation between doctor and patient. Sociological qualitative analysis has looked at the prescribing process and research, particularly into antibiotic prescribing suggests there may be a mismatch between doctor's perceptions and patients' understanding; often doctors perceive a demand for a prescription where none exists. Work pressure, particularly where there is time restriction, contributes to this problem; busier practices tend to prescribe more. Research into antibiotic prescribing indicates that withholding prescriptions alongside patient information and education reduces subsequent consultations for similar conditions by individuals.

3.1.3 The Influence of other Doctors and Education on Prescribing

Considerable research suggests that 'other doctors' particularly opinion leaders are highly influential. For GPs, consultants are the chief source of this influence but it is important to recognize that consultants may in turn be influenced by other factors. GPs are most likely to follow the lead of consultants when they are pushed for time and can fall back on

this perceived wisdom or expertise to reduce risk in prescribing. As much as 40% of long term medication use (repeat prescribing) may have been initiated by a consultant; the greatest emulation is seen in cardiovascular and central nervous system prescribing. The change to a primary care led and primary care resource driven health care service means that the effect of hospital originated prescribing requires more research.

Much postgraduate education in the UK is organized and funded by pharmaceutical companies; there are no UK data on the effect that drug company marketing has on clinical practice. To date, UK experience with policies restricting interaction with the industry is limited, although this has had little impact in Canada.

Reviews into changing clinical practice and prescribing behaviour suggest that use of opinion leaders and 'outreach visits' and 'academic detailing' has the best evidence base, although more research is still needed. Similarly, the role of prescribing advisers in health authorities has not been adequately researched. There is some evidence to show that information pharmacists working in general practice can alter prescribing behaviour and reduce prescribing costs. Researchers in the field of getting evidence into practice generally agree that that multifaceted approaches, tailored to the change required, are likely to create greater and more sustained change.

One study suggests that consultants tend to be influenced by medical journals and scientific conferences while GPs are more influenced by medical journals and postgraduate meetings. Drug bulletins are valued and read, and may change attitudes and knowledge, but require active implementation processes to alter clinical practice, although this may vary according to the complexity of the clinical context. There are concerns that GP education is dominated by the pharmaceutical industry, which may be unduly slanted towards product promotion.

3.1.4 The Influence of Pharmaceutical Promotion on Prescribing

No UK studies that look at the impact of promotion on actual prescribing behaviour (as opposed to GP perceptions of the impact) were identified. Doctors may not have much insight into the effect that drug company marketing may have on clinical practice. In the US provision of drug samples[1] has been found to effect doctors drug choice, but there is no UK data and it may not be possible to extrapolate this practice to the

[1] In the UK the ABPI Code of Practice restricts the availability of samples. Clause 17.2 states 'no more than ten samples of a particular medicine may be provided to an individual health professional during the course of a year'.

UK. Up to now experience with policies restricting interaction with the industry is limited, though in Canada, policies restricting access with the industry have not shown much impact.

3.1.5 The Influence of External Guidance on Prescribing

Observational studies suggest that doctors find formularies useful and use them to prescribe more carefully and cost-effectively. Most GPs appear to operate their own personal formularies, based in part on education, experience and historical patterns of prescribing. Where practice formularies exist, their major value seems to be in the educational exercise of their composition. There are few data on the quality of adherence to practice formularies. District formularies are rarely used in primary care, and few areas now produce them. There is little evidence yet concerning the creation of PCG formularies and their success.

Overall, formularies alone are seen as less satisfactory as increasingly doctors think of drug choice within the context of the management of the whole condition and therefore a fuller clinical guideline that includes drug choice is more acceptable.

Clinical guideline development and use has been more intensively researched; a body of literature illustrates how best to develop guidelines and support their use. When backed up with a well-constructed implementation process, guidelines can change clinical practice and improve patient outcome. GPs generally prefer local guidance, in which they have had a role and therefore ownership. Such local guidance should be based on high quality clinical evidence, and ideally be based on national guidance (for example, the British Thoracic Society guidelines).

In order to be successfully implemented in practice, clinical guidance/formularies require clinical credibility, come from a credible source and must be feasible to apply locally. It is best communicated by personal contact supported by written materials. Publicity may encourage recognition of the guidance but the decision to implement it is often mediated by colleagues. The best communication strategies include repeated use of simple messages, near-patient reminder, and use of decision support mechanisms. Good presentation is essential. More work should be conducted into how guidelines can be best incorporated into the working environment of the GP. Increasingly, computer-based decision support is used. One study suggested that GPs prescribe more cost-effectively and within guidelines where computerized prescribing support was provided. However, there is as yet no clear information on how acceptable and widely used the largest such system (PRODIGY) is.

The use of incentives to prescribe in a given way has been very effective; in general incentives must be simple and as close to the doctor as possible, and the intended prescribing must be professionally acceptable. However, incentives can have perverse effects in encouraging doctors to meet specific targets to the detriment of other aspects of patient care.

In determining drug choice, formulary developers generally take into account clinical evidence, direct drug cost and local patterns of prescribing; cost-effectiveness is less often considered. Local guideline developers take a broader but similar view. National guideline developers usually work solely from effectiveness evidence but leave local discretion in choice of drug.

3.1.6 Price Awareness among Doctors

There is no up to date UK-specific qualitative research to indicate whether or not UK doctors know the cost of drugs, although surveys conducted in the 1980s suggest that doctors are generally poor at estimating drug costs, tending to overestimate the cost of cheaper drugs and to underestimate the cost of more expensive drugs. Similarly, no good UK research was identified to indicate how doctors choose between similar drugs or whether they are aware of price changes. This is an area that needs more research.

Doctors regularly receive data on the costs of their prescribing and also performance against a set prescribing budget, but no research has been conducted to evaluate how they react to this data: some evidence suggests that feedback of data formulated to represent an assessment of quality of prescribing may influence prescribing behaviour, although it is unclear how valid these measures are without linkage to data on diagnosis or morbidity. Feedback of data on generic drug use appears to have some effect on subsequent rates of generic prescribing, but this may be related to the use of incentives.

Most studies have assessed drug cost on the basis of cost per month or, for shorter limited courses, on cost per course. No evidence was found exploring comparisons of drug costs for different lengths of time.

In general, doctors seem to be aware of a reasonable range of drugs for each major condition. The range is based on the GP's education, previous experience and promotion. Doctors will generally have views on which drugs can be substituted but these views are not always based on evidence. Within the range of drugs for any given condition, GPs are aware of very broad price comparisons.

The Literature Review found no research evidence to indicate whether GPs are more price aware for some drugs (or drugs in particular therapeutic groups) than others. Anecdotally, this has become an area of intense promotional activity and of work by prescribing advisers; price awareness will exist in areas where drugs are ostensibly at least substitutable and where there are price differentials. Where there is no competition, price awareness is minimal.

Some groups of GPs are more price aware than others, specifically former GP fundholders. There seem to be no other consistent patterns for such awareness among GPs. Dispensing doctors are aware of drug costs but are encouraged by existing incentives to be most interested in the price differential between the cost to them personally and the cost to the NHS.

3.1.7 Relative Weight given to Benefit and Price

The literature suggests that the important factors for doctors choosing a drug are clinical efficacy, safety, tolerability, and convenience to both patient and doctor, in that order. Price is generally considered only when all of these are equal. However, a doctor may decide to prescribe a low cost but potentially less effective drug initially if it is a reasonable choice in a therapeutic ladder: for example, an H_2 antagonist for a proton pump inhibitor in a previously drug naïve patient. Most clinical guidelines build in this concept of 'adequacy for purpose'.

Where patient convenience is ranked lower, a doctor may choose not to use an expensive preparation e.g. in not using modified-release preparations. This is less likely however for drugs of differing safety, where it would be less professionally acceptable to use the less safe drug on cost ground alone.

3.1.8 How GPs Perceive Quality in their Decision-making Process

In assessing the quality of a drug to prescribe, doctors accept the quality of manufacture as guaranteed by the Medicines Control Agency, and thereafter choose according to the criteria outlined above.

In judging the quality of prescribing, doctors feel that simple cost-driven criteria are inadequate, yet paradoxically they are often happy to apply such criteria to PACT data. The old rules that prescribing should be appropriate, effective, safe and cost-conscious are accepted if not always applied. But this requires better data on diagnosis and the consultation process to understand what was in each case appropriate prescribing.

It was not possible to assess the consistency of GP knowledge of relative benefits of drugs with best practice guidelines – in particular 'gold standard' benchmarks of cost effectiveness. Assuming that 'best practice' means the strict application of evidence based medicine, then prescribing practice is no more than fair. However GPs are often required to prescribe outside the licensed indications, and their prescribing while often not corresponding to evidence-based medicine, is usually defensible and reasonable. Evidence on 'gold standards' in terms of cost-effectiveness rarely exists at present.

3.1.9 What Incentivises GPs to Prescribe in a Given Way?

GPs' prescribing is incentivised by the need to fulfill professional values (that is, to prescribe in a safe and effective way to the benefit of the patient) and professional esteem (for example, to be seen as a caring doctor).

Incentivisation is also affected by the organizational environment; fundholding practices have been shown to respond to incentives but it is difficult to separate the actions of such small organisations from those of the GPs who were directly affected by the incentives available. It is not clear how incentives will operate within PCOs; some schemes may benefit individual practices while others may benefit the PCO and its patients as a whole.

Although the age, sex and ethnicity of a doctor may influence his or her choice to prescribe and to choose a particular drug, data and research are inconclusive as these factors also influence the type of patient that consults that doctor. Some evidence suggests that older doctors rely more on pharmaceutical company evidence and more on consultant advice than younger doctors, and that younger doctors prescribe more rationally. Several studies suggest that level of educational attainment is also positively associated with 'better' prescribing.

It is difficult to measure the effects of non-financial incentives**,** as the nature of the incentive may not be clear. In part the responses to GP fundholding were to a non-financial incentive — better care for the patients, more professional autonomy and more power. While appeals to professionalism or the wider good of the NHS may be seen as non-financial personal incentives and are undoubtedly powerful in shaping doctor behaviour in the NHS, there is little evidence to quantify this in relation to prescribing. The indicative prescribing scheme failed to encourage doctors to address their prescribing on these grounds alone.

However, financial incentives can have powerful effects on prescribing in that they make doctors more cost conscious in a broad way and encourage prescribing changes with cost-minimization (for example, generic prescribing) as the predominant feature. Doctors tend not to put in place strategic long term means to reduce prescribing costs — e.g. lowering prescribing rates or providing alternatives to the prescription, so that when savings have been achieved by cost-minimization and are 'locked in', further new savings do not occur. The most effective incentives are simple and directly impact on the doctor; their effects need to be monitored in case they are perverse to good practice.

3.1.10 Summary

The Literature Review suggests that price awareness among doctors is low. However, most of the published work identified predates GP fundholding and the more recent health service reforms that might have been expected to increase price sensitivity.

Recent policy directives have declared commitment to a quality improvement programme and clear agreed national standards for health care within the NHS. At the same time, there have been widespread organizational changes within primary care. Local health care and resource decision-making is outlined by the introduction of unified, cash limited budgets and the devolution of financial responsibility to primary care organizations (PCOs). More specifically, policies reinforce the notion of a primary care-led health service, implicitly promoting GPs as commissioners and clear drivers of health care reform. Unlike previous GP budgetary management initiatives such as fundholding, PCOs encompass all GPs within a locality. These changes place upon PCOs and all prescribers a clear onus of responsibility to improve the quality of health care and deliver changes (including through prescribing) while at the same time managing resources efficiently.

3.2 Qualitative Research: The Factors Influencing Prescribing Decisions

A programme of qualitative research into the factors that influence prescribing behaviour was conducted by the Prescribing Research Group at the University of Liverpool under the leadership of Professor Tom Walley. It aimed specifically to understand how cost awareness and drug price information relate to clinical practice, prescribing decisions and drug choice.

This research involved in-depth interviews with eight GPs, eight hospital doctors, six HA pharmaceutical advisers, four PCT prescribing advisers, four practice nurses/advanced nurse practitioners, pharmacists and PCT management to represent the range of views likely to be held by key stakeholders in the NHS. Two focus group discussions and two primary care practice group discussions were also held. In total, 60 key stakeholders were interviewed.

3.2.1 Overview of Influences on Prescribing Behaviour

The reasons for prescribing decisions are complex, often incorporating consideration of a range of factors. The most significant determinants in drug choice are:

- the clinical effectiveness and safety of a drug.
- the prescriber's experience and knowledge.

Prescribers tend to continue using drugs that they know are effective from their own clinical experience. The most important factors in deciding to prescribe a new drug are a clear therapeutic advantage over current alternatives, peer influence and absence of existing adequate alternatives.

Many GPs are cautious about using new drugs — this caution arises from the risk of potential unknown side effects and previous negative experiences of adverse effects, or unmerited expectations/claims of efficacy for new drugs. GPs tend to minimize the perceived risk of new drugs by waiting for an accumulation of information or peer prescribing, especially by hospital consultants.

Consultants are generally more confident in using new drugs where there was an expectation that it may improve the health of their patients; many see it as their role to try out new drugs.

The relative importance of other influences on drug choice was not possible to define. Other influences include:

- The pharmaceutical industry (a key source of information on new products)
- Consultants and other GPs (through peer pressure to adopt or avoid new drugs, and to contain costs)

- Patients (particularly requests for new, media-reported drugs and compliance/convenience)

- Practice nurses (who are viewed as increasingly important in patient care and chronic disease management).

There was a broad spectrum of views regarding the consideration of drug costs. Most GPs believed that costs should be taken into account when prescribing. However, there was great variation in the extent to which this was actually applied, and in the extent to which they were sensitive to drug costs and price changes. All prescribers considered cost to be secondary to clinical efficacy, safety, tolerability and often, patient compliance. Prescribers emphasize that cost consideration is dependent upon the needs of the individual patient and they promote individual patient health above other forms of rationality or notions of opportunity costs. There was no real ability to consider cost effectiveness or cost benefit – such concepts were seen as too complex for practical application by GPs although national guidance based on such evaluations was thought useful.

Factors thought to undermine a cost-considered approach included hospital-led prescribing, conflicting information, difficulty in interpreting evidence and an unwillingness to take responsibility for the implications of the 'rationing' decision or the unified budget.

Prescribers' commitment to clinically effective prescribing above cost-minimization, their motivation to make the best decisions for patients on clinical grounds and the lack of external pressure to stay within budget meant that they were generally not concerned about prescribing budget overspends.

Prescribing advisers were generally more concerned about overspends and acknowledged the inequities of budget setting and the difficulty of impressing on prescribers the nature of the fixed single budget.

Prescribing advisers, responsible for improving the quality of prescribing and limiting the growth of prescribing costs recognized a potential conflict in some areas between containing prescribing costs and effective prescribing. They were keen to contain costs but recognized and respected the GPs' primary aim of treating individual patients as well as possible. However they were also keenly aware of the opportunity costs involved and its possible detrimental effects on the ability to treat the whole population — a perspective often not shared by GPs.

Health authority and PCO prescribing strategies often adopted a cost-conscious approach. This was largely based on cost-minimization by encouraging the use of therapeutically equivalent cheaper alternatives. Some PCOs prioritised prescribing issues to be tackled on the basis of cost implications. Other factors driving prioritisation were central government policy/directives (NSFs, NICE guidance), leading to for instance an increased use of statins, where costs would increase substantially.

In general, there was little explicit promotion of one drug over another by PCOs/HAs, as it was felt that this would undermine clinicians' professional autonomy. However, the use of specific alternatives was encouraged, for example through formulary development, newsletters or written information highlighting the drug costs within a class.

To manage these competing priorities, PCOs have taken both prudent and eclectic approaches to encouraging prescribers to adopt change — employing sessional pharmacists to target 'outlying' practices, incentive payments, practical support, dissemination of information and prescribing feedback. In addition, prescribing advisers' facilitatory and non-confrontational approach is a key influence in shaping prescribers' views and behaviour. Pharmaceutical advisers appear to be working effectively with most practices and achieving measurable gains, while GPs recognize them as facilitators of prescribing behaviour change. Advisers reported encountering very few hostile or apathetic responses. These strategies seem to be contributing to a much greater acceptance of 'prescribing management' than in the past.

3.2.2 GPs' Awareness of Drug Costs

Most prescribers did not assimilate information on drug costs and price changes and were often unaware of prices or price changes. Prescribers had little awareness of absolute drug costs and tended to overestimate their awareness of comparative drug costs. In the in-depth interviews with GPs, HA pharmaceutical advisers and PCO prescribing advisers, most claimed to have no real awareness of costs. A few prescribers claimed an awareness of costs (primarily from information on their computer system, which gives absolute costs).

Prescribers performed poorly in ranking relative costs of many commonly used drugs. A list of statins, ACE inhibitors, SSRIs and Proton Pump Inhibitors was compiled and GPs asked to estimate either the cost of prescribing these drugs at a specified dose for 28 days or to rank the drugs in each class in order from most expensive to least expensive. All

GPs chose to rank the drugs as they mostly had no idea on the individual prices. The rankings were good for the PPIs and the statins but poor for the other drug classes. GPs felt that drug prices change frequently and most expected their impression of price to be out of date. They rely on price information from the PCOs and HAs, and from drug company representatives. However, such information is rarely sought out, unless GPs were carrying out informal reviews of cost-effectiveness within a therapeutic segment, when they would ask representatives about the cost of new drugs or look it up in MIMS, the BNF or on their computers.

Prescribers and advisers were willing to undertake simple cost-minimisation prescribing strategies, e.g. generic and lower cost, therapeutically equivalent substitution although cost savings need to be either substantial or sustained (not less than 10%, mostly around 30%). In addition, GP prescribers are reluctant to undertake systematic therapeutic substitution with entire patient groups since this is onerous and may undermine the doctor-patient relationship. Experience had suggested that attempts to do this were often more trouble than they were worth, and they thought that their efforts were sometimes undermined by changes in company pricing strategies.

Prescribers were happy to 'cost-minimize' so drug cost was accepted as an appropriate element in consideration. There was little evidence of willingness to trade quality and effectiveness for cost. By contrast, there was some evidence of willingness to trade cost for patient convenience, and also a willingness to trade cost for quality of evidence within a drug class (e.g. to use atorvastatin instead of simvastatin). Several GPs interviewed were prepared to change hospital-generated prescriptions to more 'cost-effective' options in the same drug class.

While broad prescribing decisions were made with cost in mind (for example, to prescribe generically) more specific GP prescribing decisions involving a cost component were based on external guidance usually from the PCO or a pharmaceutical company representative rather than personal decisions or actively seeking cost data.

There was, in general, little awareness and understanding of health economic concepts such as cost effectiveness and cost utility - cost-minimization was the only practical example of the application of health economics. However, GPs generally believed they prescribe cost-effectively rather than simply minimizing costs.

PCO policies generally followed patterns of cost-minimization, advocating a policy of 'least necessary force' for therapeutic outcome. Specific promotion of individual products by prescribing adviser or the PCO was rare except as part of a policy (including other drugs) or in discussion with individual practices.

However, PCOs appear to strive for a long term outlook in their advice to GPs on preferred first line therapies; they are increasingly likely to recommend therapies that are approaching the end of their patent so that greater, longer term savings can be made.

3.2.3 The Influence of Pharmaceutical Promotion on Prescribing

While accepting the marketing approach of pharmaceutical representatives, none of the prescribers in the survey considered their prescribing to be influenced by it - GPs claimed to ignore pressure to give commitment to prescribe certain drugs. Both health authority and PCO advisers largely saw themselves as a foil to the pharmaceutical industry's efforts to influence prescribing and were highly selective in which representatives they saw, being only willing to see those promoting new products or those with new indications.

A proportion of the GPs don't see pharmaceutical representatives or severely limit access, but the majority of GPs do receive visits from representatives and their appeal to prescribers and practice nurses was as a means of keeping up-to-date and gaining knowledge on new products. They were also regarded as useful information providers for practical data such as dosage, indications, administration and mode of action, and also product modification, new licensing indications, and price changes. However GPs views were mixed - this was invariably coupled with a perspective that information was selective and biased towards the promotion of the company's own product and this limited the confidence respondents had in the evidence presented, especially when it conflicted with information received from other sources.

In addition to information provision, hospital doctors also found pharmaceutical representatives useful for funding educational meetings and clinical trials. Practice nurses had also attended educational events or courses funded by the industry. However, it was perceived that the influence of these on prescribing practice was limited.

3.2.4 Awareness of Local and National Guidelines / Frameworks

GPs were generally aware of the general content of major national guidelines, and also of local guidelines, but were often weak on specifics. Advisers were very aware of such guidelines and tried to implement them actively wherever possible.

In general there were concerns about the workload that National Service Frameworks (NSFs) imposed among GPs and advisers; this guidance was thought to increase costs and thereby pressure on GPs. There was some cynicism about the Government's aims and its 'unrealistic' approach of creating expectation and demand without providing adequate resources to meet these. Nevertheless, national advice was usually influential upon prescribing, as was local advice.

Similarly, awareness of NICE guidance was high but views were mixed; all approved of the aim of removing variations in NHS practice, but there were concerns about several NICE evaluations where these did not accord with personal impressions and about the failure to provide resources to meet NICE directives.

In terms of applicability of guidance, the individual patient was always the main concern of the doctor; they were happy to use facilitative NICE guidelines to provide therapy, although concerns about resource issues were common among advisers and PCT CEOs. GPs were prepared to ignore restrictive NICE guidelines if they felt it clinically appropriate. GPs welcomed the fact that decisions that were often difficult with patients (e.g. to refuse a drug) had been taken out of their hands by NICE.

3.2.5 Formularies and Choice of Drug

The impact of hospital formularies was mixed. Most hospital physicians state that prescribing from formulary only is not well controlled. However, new drugs do have to go through the Drug and Therapeutics Committee (D&TC) before they are available in the hospital. Cost efficacy of the drug is examined closely at these meetings; formulary pharmacists tend to conduct the research into the drug for the committee. If the pharmacist concludes there is little evidence that the drug is better than competitors and that it is not the cheapest in the therapeutic group at that time, it is unlikely to get on to the formulary. But, physicians can get round lack of formulary availability by prescribing on a case-by-case basis.

The work of NICE had a great impact on formularies/D&TCs. NICE guidance had sometimes been used as a 'stalling tactic' if it had not yet reviewed a drug that a clinician was interested in getting on to the formulary.

Few practices had formal practice formularies. Those that had them rarely updated them, and they fell into disuse. Since formularies were often based on common prescribing, it is difficult to say whether the formulary influenced the prescribing or vice versa. Formularies were generally internalized; the development process was seen as valuable. There were no attempts to impose external formularies, e.g. from PCOs.

Influences on drug choice where no formulary was available or in areas not covered by formulary were cited as (in order): efficacy, tolerability, and cost. If a drug offered something unique and important, cost became less of an issue in the decision to use it. But for 'me-too' drugs, cost became the most important decision criteria.

Important influences included the doctors' assessment of efficacy, based in part on information received but most importantly on personal experience of using a drug or observation of the drug being used, particularly by a hospital doctor. Other influences, in less certain order, came from colleagues, patients, promotion by drug companies, local peer pressure/PCO adviser pressure.

The influence of patients was relatively small but growing and was more on the decision to prescribe than on the choice of therapy/preparation, although this was slowly changing. GPs were generally reluctant to tell patients when cost cutting decisions/changes made, although a small number were very keen that patients should have these decisions put clearly to them. Some GPs were reluctant to change drugs on cost grounds alone, but most were happy where clinical equivalence was assured. Some valued patient compliance highly and would pay extra for it in terms of sustained release and once-daily preparations — others would trade cost against patient convenience.

All GPs believed that antibiotics were overused by other doctors. Most were happy to refuse antibiotics to patients in order to reduce use. This was seen as a quality issue, rather than as an important area for cost savings.

3.2.6 Attitudes to Prescribing Budgets and Incentive Schemes

Only CEOs and advisers gave serious consideration to prescribing budgets — these were seen as largely irrelevant by GPs and there was no external pressure to apply them other than by incentive schemes.

There was little understanding or awareness of the opportunity costs in prescribing — those services that may or may not be purchased because of prescribing costs/management — there were few concrete examples of which GPs were aware. Advisers were more aware of services not developed rather than services withdrawn.

GPs were not bothered by budget overspends, whether at practice or PCO level. It was thought to be up to the Government to provide an adequate budget to meet needs. There was little awareness of areas where services had actually been lost because of overspends. Such loss of services seemed rare — HAs seemed to have contingency funds. Hospital doctors in particular were not convinced of the reality of 'fixed' budgets for services. Advisers were more concerned about overspends, and more aware of areas where services had been lost as a result of prescribing overspends. They felt that for the moment at least, the HAs/ government would provide funds to limit effects of overspends.

In reality, budgets appear to be largely ignored at practice level. Even at PCO level there was a feeling that the PCO would be bailed out if budgets were so far exceeded that services might be severely compromised. Many practices seemed to deliberately overspend to inflate future budgets — this was reinforced by past experience of having budgets cut when underspent, while seeing overspending practices 'gaining'.

Opinions differ on the role and success of current prescribing incentive schemes, although these schemes have been part of the motivation for some practices to review the appropriateness of their prescribing. Overall they seem to be considered to be fairly popular and worth a moderate effort. Most were not solely cost based. Even where cost targets were exceeded, if this could be justified practices still received payments. There was some disillusionment among GPs who undertook attempts to contain costs only to see advantages shared among others or lost because of others.

All PCOs had local prescribing incentive schemes in place. For incentive schemes to achieve success the payment or health benefit to patients has to be seen to be worthwhile or significant enough to motivate compliance. Additionally, they had to be realistic, achievable, based on quality prescribing, not just cost reduction, and targeted at individual practices so that there was opportunity for all practices to implement change. If objectives were too onerous or complex to apply, then this limited the opportunity for successful change.

PCOs were seen by interviewees to have been relatively well received, influential and successful in their attempts to change prescribing behaviour. On the other hand, prescribers appear suspicious and wary about a cost-driven agenda; many were unwilling to acknowledge the implications of the unified budget and had failed to grasp 'the big picture'. Nevertheless, there would appear to be a gradual transition in general practice culture, from relative autonomy towards increasing acceptance of management, collaboration and accountability within the new NHS organizational structures.

However, the lack of sanctions to tackle 'deviating' GPs and limited resources available to promote prescribing strategies is a key concern for some PCOs. In addition, questions remain over the methods used to evaluate appropriate prescribing, in addition to the sustainability of prescribing change.

3.2.7 Summary

The qualitative research concluded that most prescribers had little awareness of absolute prices of drugs, and performed poorly in ranking the relative costs of many commonly used drugs (with the exception of proton pump inhibitors and statins and for generics as a general principle).

The qualitative research suggests some evidence within primary care whereby GPs are increasingly open to the process of 'managed prescribing'. It seems there is a growing realization that it is an important part of their role to manage the cost of prescribing.

GPs are increasingly relying on PCOs and NICE to help them in their efforts to prescribe 'appropriately'. This concept of 'appropriateness' includes both quality and cost issues.

Cost is inextricably linked with the clinical effectiveness and safety of a product when it is assessed by GPs; GPs will not prescribe a drug that they feel lacks clinical efficacy or will compromise a patient's safety, just because it is cheaper.

The presence of incentive schemes and budgets per se have had a limited influence on initiating prescribing review within the sample interviewed. Visits and advice from the PCO and HA prescribing advisers, the NSFs and NICE guidance have been more influential in initiating prescribing cost reviews. However awareness of a unified budget is increasing among GPs and there are some indications that this is beginning to make an impact on GPs' likelihood to select products more cost effectively.

3.3 General Practice Research Database (GPRD) Analysis

3.3.1 Terms of Reference

Stage 2 of Component 4 states that 'the study will examine actual prescribing behaviour as a check on the effectiveness of the demand and supply sides of the market and will include:

- How sensitive prescribing behaviour is to price changes, for example, following modulation, whether the "elasticity" of demand varies between prescribers and/or between products and treatment strategies.'

3.3.2 Background

This analysis was contracted out to the Sheffield Health Economics Group (SHEG), part of the School of Health and Related Research at the University of Sheffield (ScHARR). The work was undertaken by Jennifer Roberts (SHEG) who was the lead researcher and Nigel Rice (Centre for Health Economics, University of York).

More specifically the study aims were:

- to estimate GP price elasticity of demand for pharmaceuticals.

- to investigate the sensitivity of prescribing behaviour to the entry of new drugs.

The study would focus, in the main, on newly instigated prescriptions, as it is reasonable to assume that new prescriptions are more likely to be effected by price than repeat prescriptions.

The research used data from the General Practice Research Database (GPRD) to analyse the sensitivity of prescribing behaviour to events such as the entry of new drugs and price changes of existing drugs. The database contains over six million anonymised and validated patient medical records captured at the time of the GP consultation. The GPRD holds comprehensive prescription and disease information for use in medical research. Prescriptions are particularly well recorded as GPs use the computerised system to generate the prescription form. Crucially, the database allows new and repeat prescriptions to be separately identified.

3.3.3 Markets Analysed

The main phase of the EER analysis (Component 2) covered 27 therapeutic areas or "markets". The markets chosen were those with the highest – or most rapidly growing – expenditure within the 18 broad (ATC2) therapeutic categories specified by the DH and ABPI. The 27 markets covered 17 of the original 18 ATC2 categories giving a broad coverage of the major areas of NHS expenditure on pharmaceuticals. Informed by the results of the main phase of the EER analysis, DH/ABPI agreed that the GPRD analysis should focus on therapeutic groups that were most likely to prove amenable to econometric analysis. That is, those groups where price changes were evident, and where new products entered the market over the period to be covered (September 1995 to September 2000).

Nine markets were initially identified, however a finer breakdown of some of the markets was undertaken, as it became apparent that these markets contained sub-groups of drugs which were unlikely to be generally substitutable.

1. Proton pump inhibitors

2. SSRI anti-depressants

3. Migraine treatments:
   a) Triptans
   b) Other

4. Anti-rheumatics

5. Loop diuretics

6. Anti-psychotics:
   a) Ordinary anti-psychotics
   b) Atypical anti-psychotics
   c) Long-term depot injections

7. Broad spectrum penicillins and cephalosporins:
   a) Penicillins
   b) Cephalosporins

8. Tricyclic anti-depressants

9. Calcium antagonists

3.3.4 Analysis

The broad aim is to estimate how sensitive GP prescribing is to certain events using data from GPRD. The events analysed are the entry of a new product within a therapeutic class and changes in price of existing products.

The analysis aims to estimate *price elasticities* of GP prescribing for different drugs. Put simply in this context, price elasticity measures the change in the prescribed volume of a drug associated with a change in price of either that drug (own price elasticity) or of other drug(s) within the same therapeutic category (cross price elasticity). The analysis also aims to measure the effect on volume prescribed of the entry of new drugs, either branded or generic, within a class.

The analysis initially treats new and repeat prescriptions separately with a view to testing whether GP prescribing responses to events vary significantly between newly instigated and repeat prescriptions.

3.3.5 The Model

The modelling exercise is built on a demand system that focuses on the quantity response to price changes and other events within a defined market.

The quantity prescribed of a given drug will be determined by a number of explanatory variables:

- The price of that drug (own price elasticity)[2]

[2] The aggregate prices used here are based on two-step Divisia prices indexes, derived by Europe Economics (2001).

- The prices of other drugs in the same market (cross price elasticity)[3]
- The entry of a new brand into the market
- The characteristics of patients – e.g. age and sex
- Practice characteristics

In the event, no data was available on practice characteristics, and data on patient characteristics was limited to age and sex aggregated to practice level.

Standard panel data techniques[4] are used to identify the coefficients for each of these variables.

Model Specifications

Alternative specifications are used to illustrate the investigative process and also to provide information on the robustness of the elasticity estimates obtained. The biggest problem with specifying equations of this type, is that there is very little guidance on the dynamics of the relationship between quantity prescribed, price variation and the entry of new drugs, either from economic theory or from empirical data. As a result most of the specifications are alternative methods of modelling the dynamic relationship between price and quantity[5]. Also, a number of other modifications were tried for a sub set of markets. Again, these modifications were undertaken to check on the general robustness of the findings.

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[3] Different presentations are merged to form an aggregate quantity measure using standardised daily-defined doses (DDDs). The focus of the analysis is on newly instigated prescriptions. That is, if a patient had received any prior prescription for any drug in the same therapeutic class, those prescriptions would be excluded from the analysis. Thus, both repeat prescriptions, and prescriptions that relate to patients being switched from one drug to another drug in the same class are excluded.

[4] This technique is a combination of time series and cross sectional analysis.

[5] The alternative models tested are as follows:-
a) Postulates a simple relationship between current prices and quantities,
b) Both the own and other price variables are lagged by one quarter. New product entry variable is included, but not lagged,
c) As b) but the new entry variables are lagged,
d) As b) but new entry variables are omitted,
e) The same as the basic model in a) except that it allows for a first order autoregressive - AR (1) - error term i.e. errors in one period are correlated with errors from the previous period. This is a general dynamic specification that is often useful in defining economic relationships, and is used here in the absence of any other firm guidance on lags in the relationship between price and quantity.
f) Includes two variables to reflect patient characteristics at the practice level. The average age of patients and the proportion of patients who are male.

Analysis by Modal Presentation – The price variable used in the analysis is an average price averaged across all presentations of a given product. An alternative approach is to use prices (and volumes) for the modal strength. Analysis using modal strength presentation was undertaken for PPIs and SSRIs.

Analysis for all Prescriptions – As noted above, the focus of this analysis has been on newly instigated prescriptions. The analysis was also replicated using all prescriptions for the PPI market.

Analysis Pre and Post Generic Entry – In a number of markets generic versions of some of the brands enter during the period of the analysis. As this may introduce a structural break in the series – i.e. market conditions post generic entry are unlikely to be the same as before generic entry, the analysis was split into two periods, pre and post generic entry. This was carried out for SSRIs, Penicillins, and Cephalosporins.

Alternative Time Periods - Finally, alternative periods were modelled – for example, at the beginning of the sample period only one product was available in the triptan market. Thus the analysis also looked at a sub period when more than one (three) products were available (beginning in May 1997). A similar issue arises for loop diuretics and Zyprexa (Atypical Anti-psychotics).

3.3.6 Results

While the markets vary in complexity and the results vary somewhat across markets, the overwhelming finding for all markets is that few of the estimated price effects are significant, and those that are, are not robust to different ways of specifying the demand models. In particular, the results are not robust to whether lagged or current prices are used as the appropriate explanatory variable in the demand models. There is little theoretical guidance as to which form of prices are the most appropriate, hence it is important to investigate the sensitivity of the results to different specifications. The lack of robustness to the specification of prices is cause for concern and caution should be applied when determining policy on the basis of these results.

There is relatively little price variation in most of the markets we analysed. Where price variation does exist it seems unrelated to variations in quantity, which are often dominated by trends, which are determined by factors other than price. The conclusions that can be drawn for the extent of competition in the nine drug markets must be

tentative. Price elasticity is determined by the ease with which a product can be substituted for another good that fulfils approximately the same function. Given a particular product market, price elasticity of demand is a reflection of the extent of demand side competition.

In those markets with a reasonable amount of price variation, some statistically significant price effects were found. For PPIs, Losec had a significant cross price elasticity with respect to Zoton – i.e. when the price of Zoton falls, the quantity of Losec falls. However, no significant own price elasticity was found – i.e. the volume of Losec is unrelated to the price of Losec. The opposite is the case for Zoton – a significant own price elasticity was found (i.e. when the price of Zoton falls, the quantity of Zoton rises), but no significant cross price effect with respect to Losec was found (i.e. the quantity of Zoton is unrelated to the price of Losec).

In the SSRI market statistically significant own price elasticities were found for both Cipramil and Lustral – i.e. when the price of these products falls volume rises. However, in the main there was little evidence of cross price effects – i.e. a price change of one product did not have an effect on the volume of the other product[6].

This suggests some price sensitivity in the quantity of newly instigated prescriptions (i.e. excluding repeats) to prices in these two markets. However, the fact that significant own price effects were found without cross price effects (vice versa for Losec) is contrary to prior expectations – so one should be cautious in drawing conclusions.

However, a complex set of factors, on both the demand and supply side, interact to determine the extent of competition in the supply of branded medicines to the NHS. This study has looked only at the demand side factors, which are largely concerned with the extent to which the relevant agents are well informed about the choice of alternative products that are available, and also the relative prices of these products. However, the extent of demand side competition is an important determinant of supply-side behaviour because the more GPs' prescribing behaviour responds to relative prices, the greater the incentives to pharmaceutical companies to compete in terms of price.

[6] The exception here is that Citolapram had a significant cross price elasticity with respect to the price of Sertraline when lagged one period.

The markets we have analyzed are regulated by the PPRS - while price reductions are not restricted, there are constraints placed on price increases[7]. The lack of price variation is the main reason for the insignificant price elasticity estimates. Whether or not this can then be interpreted as a reflection of weak demand side competition is beyond the scope of this study.

A secondary aim to estimate the effect of new product entries on the demand for existing products was also unsuccessful. Again results are very sensitive to model specification.

A summary of the results for each market is attached at Appendix 4.

3.3.7 Summary

This analysis examined the relationship between price and the volume of newly instigated prescriptions issued by GPs. Newly instigated prescription were chosen in an attempt to isolate that sub set of prescribing which is most likely to be affected by price.

Across the markets the analysis found few price effects that were significant and robust to alternative model specifications. This may be attributable to a lack of price variation, though where price variation does exist it seems unrelated to variation in quantity.

Of the nine markets analysed, two exhibited some statistically significant volume relationship with price (PPIs and SSRIs). However these relationships were not entirely internally consistent in that own price effects were found when cross price effects were absent, and vice versa. In other words, if a price of a given product changed, one would expect both the volume of that product and other competing products to change, in most cases this consistency of impact was not observed.

[7] Under the Pharmaceutical Price Regulation Scheme (PPRS) companies have freedom of pricing for major new products placed on the market but thereafter NHS prices may only be raised with the Department's agreement. Companies are permitted to modulate the prices of products provided that the effect of the modulation is cost neutral. The 1999 scheme also allows companies to make temporary reductions to NHS prices.

4. Appendix – Summary Results for Individual Markets

4.1 Proton Pump Inhibitors

This is the simplest market; it has 2 incumbent brands (Losec and Zoton) and experiences 3 new branded entries. The market has not been subdivided. There is a reasonable amount of price variation.

New Prescriptions

There are strong trends in demand for both products (positive for Zoton and negative for Losec), which do not appear to be explained by relative price changes. These trends are likely to dominate the results. The models have very low explanatory power and the estimated price effects are very sensitive to model specification. For Losec we found a significant cross price elasticity but the size of the effect is sensitive to whether or not lagged prices are used. For Zoton the general finding is of a significant own price elasticity estimate, but no robust finding for cross price elasticity.

All Prescriptions

The downward trend in Losec prescribing is not as pronounced here as for new prescriptions. The explanatory power of the Losec models is very low, about half that of those for first ever prescriptions and no significant own or cross price effects are identified. For Zoton the results are similar to those for first ever prescriptions. The explanatory power of these models is very good at nearly 0.60, although this is largely due to the strong upward trend in the data.

Modal Quantities

The downward trend in the demand for Losec appears stronger for modal quantity than for the original aggregate measure. We find a cross price elasticity consistently greater than one, but the actual size varies considerably with the specification of the model. The explanatory power (at around 10%) is low and very similar to the original results.

The results for modal strength of Zoton are very similar to original results. The explanatory power, at around 15-18% is slightly worse than when aggregate quantity was used.

4.2 SSRI Anti-depressants

This market has not been sub-divided. It contains seven incumbent branded products and experiences five new entries during the estimation period; two are generic versions of incumbents. Only two products exhibit sufficient price variation to include their prices as right hand variables.

The general finding here is of very elastic demand for citalopram, with no cross price effect (in relation to sertraline). However, the elasticity estimate is very sensitive to model specification and in many cases is unfeasibly large. The explanatory power of these models is good at around 0.40. These results are likely to be dominated by the large price reduction in October 1998, which did seem to speed up the already positive trend in quantity prescribed. For sertraline the general finding is of a significant own price elasticity estimate (near unity) but no robust significant finding for cross price elasticity. However, the explanatory power of these models is extremely poor at under 0.01.

Models for the five other incumbent products produced no significant coefficients on anything but the year dummies.

Pre-generic Entry

Two molecules in this market experience generic entry during the estimation period, and since the majority of prescriptions are written generically from the start, we cannot distinguish a quantity response to price change. For these products we curtail the estimation period at March 1999 (the date of the first generic entry) and estimate models for the original brands only.

The modelling is not successful. Where coefficients are significant, they are not robust across model specification and explanatory power is very low. The problems noted in the original modelling are exacerbated here by the reduced number of observations available for estimation.

Modal Quantities

For Cipramil and Lustral the results are very similar to those produced when aggregate quantities based on Defined Daily Doses (DDDs) were used, both in terms of significance and size of the coefficients. There are no significant own or cross price elasticities. Despite the statistical insignificance of most of the coefficients the estimates are robust across specifications. Explanatory power is low for all models, and especially so for the Lustral models.

For Prozac and Seroxat again these results are very similar to those produced when aggregate quantities based on DDDs were used. The main difference is in relation to the effects of new product entries on the demand for Seroxat. The coefficients on the new entry dummies are much larger when modal quantities are used as the dependent variable. No significant cross price effects are found. Explanatory power is very low for all models.

4.3 Migraine Treatments

This market is subdivided into two sectors, triptans and 'others'. Many of the products in the `others' sector are combination products, which cause problems for analysis based on DDDs.

Triptans

The analysis starts in May 1997, as prior to this there is only one incumbent. By May 1997 there are three brands, and there is a new entry in July 1998. Only one of these products exhibits any price variation during the analysis period, and this is simply a price reduction of 25% in October 1999. As expected, due to the lack of price variation, there are no significant price terms in any of the models. The explanatory power of all models is poor.

Alternative Analysis Period

We also estimated models for the entire data period (September 1995 to September 2000). At this time the triptans sector contained only one product, Imigran. The results showed no significant coefficient estimates except for year dummies.

Others

The analysis for this market covers the entire time period. There are five incumbent products and three new entries. There is very little price variation except for Paramax. Results should be treated with caution due to the problems in defining DDDs for combination products. As expected due to limited price variation, there are few significant estimates and explanatory power is poor for all models.

4.4 Antirheumatics

There are a large number of products in this highly genericised market. For many products original, branded generic and unbranded generic versions exist. The original data file contained data on 41 products. For 22 of these products there are a relative small number of prescriptions so they are excluded from the analysis. In addition for 20 products there is no price variation.

Models were estimated for 11 products but no significant results (except for coefficients on the year dummies) were found for any molecules except the two COX1 NSAIDS diclofanec and ibuprofen. The results are very weak and any significant price effects should be treated with caution, as few are robust to changes in model specification.

4.5 Loop Diuretics

This market is analysed as the total market with no sub-divisions. The estimation period starts in February 1997 to cope with the problem of generic entry of bumetanide. At this time there were nine products in the market, but only five have a reasonable number of prescriptions.

For the entire market there are very few significant price effects, and those that do exist are very sensitive to whether current or lagged prices are used in the model. In addition most of the significant price effects are unfeasibly large, and the explanatory power of all the models is very poor at around 0.01.

A further problem with this market arises from the entry of the branded generic Frusol, which did not enter the market until October 1998, and yet we appear to have prescriptions for this product throughout the entire analysis period.

4.6 Antipsychotics

The market had been divided into three sub-sectors:

- ordinary antipsychotics;
- atypical antipsychotics;
- long-term depot injections.

Ordinary antipsychotics

This data set contains information on 22 products including a large number of branded and unbranded generic versions of drugs. No new products enter the market during our analysis period. For 14 of the 22 products there are less than 300 prescriptions throughout the analysis period, and for eight products there was no price variation. Demand models are estimated for seven products. The explanatory power of all models is very poor and there are no significant price effects.

Atypical antipsychotics

During the entire analysis period September 1995 to September 2000 there are seven drugs (all branded) in this market, however, only three are prescribed in meaningful quantities, and of these only one is available at the start of the period. In addition there is also very little price variation. Five of the seven products do not change price at all during the analysis period and the remaining products change price only once. We can only present meaningful results for Zyprexa with an estimation period starting in October 1996. There is no significant own price elasticity and the explanatory power of the models is very poor.

Long-term depot injections

There are five products in this market but the only product with a meaningful number of prescriptions is flupentixol. In addition there is very little price variation for any of the products, and where prices do change the price changes tend to be collinear. The demand equations for flupentixol have very poor explanatory power and produced no significant price effects.

4.7 Broad Spectrum Penicillins and Cephalosporins

The market had been divided into two sub-sectors:

- penicillins;
- cephalosporins.

Penicillins

There are a large number of products available at the start of the analysis period, and a generic version of co-amoxiclav, enters in January 1999. For a number of products there are only a small number of prescriptions. In addition, there is very little price movement and only three products exhibit enough price variation to be included as explanatory variables.

Pre-generic entry
We firstly estimate demand equations for September 1995 to December 1998 aggregating all Augmentin and co-amoxiclav prescriptions. The overwhelming finding is of results that are very sensitive to whether current or lagged prices are used. The explanatory power of all the models, except those for amoxicillin with current prices, is very poor.

Post-generic entry
The models estimated for January 1999 to September 2000, when the generic version of co-amoxiclav had entered the market, produce results that are very similar to those presented above, in terms of extreme sensitivity to model specification.

Cephalosporins

There were nine molecules in this sub-sector at the start of the analysis period. One new molecule enters in August 1998, branded generics enter in February 1997 and September 1998, and unbranded generics of cefradine enter in October 1998. Only two products exhibit any price variation.

The results for cephalexin appear sensible when current prices are used. Unfortunately the explanatory power of these models is poor and there are substantial changes to the results when lagged instead of current prices are used. For most other products the explanatory power of all the models is very low and there are no significant price effects.

Post-generic entry
In addition to the models reported above which use data for the entire time period September 1995 to September 2000, we also estimated models for October 1998 onwards, where all products have then entered the market. The results show no substantive differences to those presented here.

4.8 Tricyclic Anti-depressants

The market has not been sub-divided; it contains 13 molecules and is highly genericised. The market experiences exit events for five of the original brands. A number of products are excluded from the analysis due to small numbers of prescriptions.

There is some price variation in this market, but it has no obvious link with changes in the mean quantities prescribed. Demand equations are estimated for nine products. There are a small number of significant coefficients but these are not robust to the use of lagged or current prices and often have signs, which are contrary to economic theory. The explanatory power of all models is very poor.

4.9 Calcium Antagonists

This market is analysed as the total market with no sub-divisions. At the start of the analysis period (September 1995) there are eight molecules in the market. Both diltiazem and nifedipine have a large number of branded generic and unbranded generic versions. The quantities prescribed of a number of products are very small and there is very little price variation.

There are very few significant price effects in any of the models, and those that do exist are often unfeasibly large. In addition the price effect estimates are extremely unstable across the specifications i.e. depending on whether current or lagged prices are used. For most models the explanatory power is low.

Component 5:

International Perspective

December 2002

Component 5

Contents

Component 5

International Perspective

1. Introduction

This paper describes the work comparing the prices of medicines in the UK with prices in other countries carried out for component 5.

The terms of reference were as follows:

'Prices in other countries are often compared with prices in the UK. The Department already carries out an analysis of UK prices against prices in ten countries for a 'basket' of products. This analysis will continue, and be supplemented by increasing understanding of the impact on these price comparisons of exchange rate movements and of pharmaceutical policy implementation in other countries.

An additional study will be established to monitor the prices of future new products (and spending thereon). This will involve both a comparison of UK launch prices against those in other countries and, where possible, the spending on new products against these in other countries, so the relationship between prices and volumes can be more readily understood.

Both DH and the ABPI will undertake co-ordinated work in this area.'

2. Executive Summary

The work comprised three parts:

- ***Comparison of the prices of the best selling branded medicines supplied to the NHS with prices elsewhere in Europe and in the USA in the period 1996 to 2000.***

The Department of Health carries out an annual exercise comparing the prices of the best selling branded medicines to the NHS in the UK with those in Austria, Belgium, Finland, France, Germany, Ireland, Italy, Netherlands, Spain and the USA.

The most recent exercise for 2000 shows that prices in the UK are significantly lower than those in the USA but higher than those in the other nine European countries. This is based on bilateral comparisons (i.e. form and strength matches occurred between the UK and another country) using average annual exchange rates.

The UK's position has changed since 1996, largely as a result of sterling appreciation. For the countries for which we have 2000 data, the average sterling appreciation was 26%[1]. If the five-year average exchange rate for the period 1996-2000 is used, UK prices are broadly comparable with Germany, Finland, Ireland and France and higher than the other EU countries.

- ***Analysis of the launch prices of major new products***

This compared prices of the ten best-selling major new products (new chemical entities) launched in the UK in each of the six years 1995 to 2000 with the launch prices of the same products in nine other EU countries (Belgium, Denmark, France, Germany, Italy, Netherlands, Portugal, Spain and Sweden) plus Switzerland and the USA.

A bilateral price comparison, using annual average exchange rates, shows that for new products launched in the UK, the UK is ranked 9th (out of 12 countries) for those introduced in 1995, 5th in 1996 and 1997, 2nd in 1998 and 5th in 1999 and 2000.

A bilateral comparison at annual average exchange rates for 2000, for a multilateral product basket of the sample of new product launches for 1995 – 2000 shows that in 2000, the UK is the most expensive country in Europe and second only to the USA. Analysis of products launched between 1995 and 2000 shows that prices in the UK tend to be relatively higher for those launched at the beginning of the period than those launched more recently. Exchange rate movements may explain this phenomenon, as prices set at the beginning of the period and not subsequently changed would have appreciated by the end of the period.

- ***Analysis of the prices of off-patent molecules***

UK prices of the top 100 molecules (by value in 2000) that were off-patent in the UK and which had unbranded generic sales were compared over the six year period 1995 to 2000 with the average prices of the same molecules in nine other EU countries plus Switzerland and the USA. It is important

[1] This figure is based on all countries in the comparison over the period quarter 4 1996 to quarter 4 2000 and is not strictly comparable with figures in the last paragraph of section 3 which uses a slightly different time period and differentiates between EU and non EU countries.

to note that this analysis compares average prices for the molecule, which includes the original brand, branded generics, and unbranded generics. Thus they do not represent the prices of unbranded generics alone.

Bilateral comparisons at annual average exchange rates show that at the beginning of the period, UK prices for off-patent molecules were the cheapest apart from in Spain. By 2000, off-patent molecules in the UK are more expensive than in the other nine EU countries but significantly less expensive than in Switzerland and the USA.

Using six-year average exchange rates Portugal and Spain and in some years Italy and/or Denmark have lower prices than the UK. Other EU countries have higher prices than the UK with Switzerland and the USA substantially more expensive than the UK.

3. Issues in Making International Price Comparisons

International price comparisons for medicines that are valid are not easy to make and hence such analyses need to be interpreted with some caution, particularly when they are used to compare prices over time.

The comparisons can be significantly affected by:

- the relative level of sales in each country of the products used in the comparison;
- the movement in exchange rates; and
- the proportion (and mix) of medicines expenditure included in the analysis, which will vary from country to country and over time.

Prices can be compared between the UK and one other country (a bilateral comparison) or between the UK and a number of other countries (a multilateral comparison). In practice medicines are not all available in the same presentations in the same strengths in all countries, resulting in a multilateral comparison being based on a much smaller sample of medicines than a bilateral comparison. In some bilateral comparisons the index is driven by price differences in a very limited number of strengths. However, in 2000 the market coverage in the comparison of the prices of the best selling branded medicines by the Department ranged between 25% and 49% of England spend on branded medicines, similar to previous years, which represents a significant proportion of medicine expenditure.

Relative positions, particularly between European countries, will be affected by the development of different price control policies in these countries. The different regulatory regimes will have an effect on the price of a molecule over its product life cycle i.e. pre and post-patent.

Price comparisons are usually made on list prices, which may not reflect the actual prices at which products are sold. In the UK, the discount 'clawback'[2] from pharmacists effectively reduces the prices paid by the NHS and in the USA large buyers obtain discounts from list prices. Other European countries (Austria, Italy, Germany, Netherlands and Spain) also regulate the profit margins of pharmacies in a way that leads to institutional buyers paying lower prices than published list prices.

Some countries e.g. France link volumes to price implicitly or explicitly in negotiations with companies.

Using average annual exchange rates, the pound has appreciated considerably (by circa 40%[3]) between 1995 and 2000 against most European countries, but depreciated slightly (by 4%) against the US dollar. The picture is similar between 1996 and 2000, with the pound appreciating against most European countries by circa 36%[4], and depreciating a little against the dollar by 3%.

4. Results of Analysis

4.1 Annual International Price Comparisons 1996-2000

The Department undertakes an annual price comparison of the best selling branded medicines in the NHS with prices elsewhere in Europe and in the USA using IMS data on prices and NHS volume weights from PPA data. The results of the latest exercise were published in the 5th PPRS Report to Parliament.

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2 The reimbursement system is designed to secure cost-effective purchasing and value for money for the NHS by encouraging pharmacists to buy lower than the reimbursement price. Pharmacists are reimbursed the Drug Tariff price of the item dispensed less an assumed level of discount. Recovery of the estimated discount, by means of a scale of deductions using the results of a Discount Inquiry, aims to determine the difference between the actual cost of the products purchased by pharmacies and the amount they are reimbursed.

3 The actual rate of appreciation varies a little depending on the country concerned, but 40% is fairly typical.

4 This figure differs from that in section 4.1, which uses a slightly different time period and does not differentiate between EU and non-EU countries.

In 2000 it compared the prices of all preparations for the top 150 branded medicines in the UK with those in Austria, Belgium, Finland, France, Germany, Ireland, Italy, Netherlands, Spain and the USA. There were 128 drugs for which data were available and at least one other country match was found. The list of products and exchange rates are at Appendix 5.1.

The study concluded:
'Previous reports showed that UK prices were in the middle range of the countries in this study over the period 1992 to 1996 but the UK's position has changed since 1996, largely as a result of sterling appreciation. For the countries for which we have 2000 data, the average sterling appreciation was 26%[5].

The 2000 weighted index, based on bilateral comparisons, and based on 2000 market exchange rates showed prices in the UK to be:

- significantly lower than those in the USA;
- higher than those in the other European comparator countries.

However, if a longer-term five-year average exchange rate is used, prices in the UK are broadly comparable with Germany, Finland, Ireland and France and higher than the other European Union countries.'

[5] This figure is based on all countries in the comparison over the period quarter 4 1996 to quarter 4 2000 and is not strictly comparable with figures in paragraph 10 which uses a slightly different time period and differentiates between EU and non-EU countries.

Table 1 shows the bilateral comparison for the years 1996 to 2000 using annual exchange rates and using the five-year average exchange rate.

At that year's market exchange rate						
Country	1996	1997	1998	1999	2000	2000 (using 5 year average exchange rate*)
France	112	86	85	84	80	96
Germany	124	108	108	97	91	103
Italy	91	82	81	83	79	90
Netherlands	112	93	N/A	N/A	81	93
Spain	88	71	71	67	64	74
UK	100	100	100	100	100	100
USA	183	175	174	184	209	189
Austria			81	83	77	88
Belgium			86	84	78	89
Finland			86	85	83	95
Ireland			90	88	83	96

* Uses 2000 price information but converted to sterling using the average exchange rate for the period 1996-2000

Using annual exchange rates, the UK position has changed from 5th (out of seven countries) in 1996 to 2nd (out of 11 countries) in 2000. Using the longer-term five-year average exchange rate, UK position is 3rd in 2000 (after USA and Germany) but within 5 points of Ireland, Finland and France but 10 to 12 points higher than Italy, Austria and Belgium and 24 points higher than Spain.

Table 2 shows the results of the multilateral comparisons of ex-manufacturer prices at market exchange rates. The results are very similar with the UK position changing from 5th (out of seven countries) in 1996 to 2nd (out of 11 countries) in 2000. Using the longer-term five-year average exchange rate, the UK position is 3rd (after USA and Germany).

Country	1996	1997	1998	1999	2000	5 year average*
France	105	85	85	86	83	94
Germany	125	101	109	103	94	108
Italy	93	86	88	82	82	93
Netherlands	108	93	-	-	-	-
Spain	89	74	77	72	70	80
USA	191	184	188	213	243	220

* Uses 2000 price information but converted to sterling using the average exchange rate for the period 1996-2000

The next stage of the study was to look at the prices of the newer and older products separately - the launch prices of major new products (NCEs) and the prices of molecules post-patent expiry.

4.2 Analysis of the Launch Prices of Major New Products (NCEs)

The ten best-selling major new products (new active substances/new chemical entities) launched in the UK in each of the six years 1995 to 2000 were identified from IMS data. UK prices were compared over the six-year period 1995-2000 with the launch prices of the same products in nine other EU countries plus Switzerland and the USA. The 60 products are listed at Appendix 5.2.

Several types of analyses were performed using annual average exchange rates set out at Appendix 5.3.

4.2.1 Bilateral Price Indices Weighted by UK Volumes by Year for Available Form/Strengths for Brands Launched in the UK 1995-2000.

Table 3 shows indices for the launch year of each cohort, using the exchange rates in Appendix 5.3. The UK is 100. The term n/a means that no bilateral comparison was available.

Country	1995	1996	1997	1998	1999	2000
Belgium	97	n/a	n/a	92	n/a	84
Denmark	112	112	92	97	100	87
France	96	100	57	88	118	95
Germany	107	90	87	93	99	85
Italy	105	79	127	88	75	105
Netherlands	130	104	102	87	95	105
Portugal	n/a	n/a	107	88	88	81
Spain	105	82	87	98	87	80
Sweden	109	121	96	92	102	97
Switzerland	128	130	85	83	103	105
USA	110	88	139	138	133	148

For NCEs launched in the UK, the UK was ranked 9th in 1995, 5th in 1996 and 1997, 2nd in 1998 and 5th in 1999 and 2000.

Appendix 5.4 shows price indices for a maximum of three annual periods for each cohort of brands.

4.2.2 Bilateral Price Indices Weighted by UK Volumes for 2000 for a Multilateral Product Basket

This sample uses the 60 products in the analysis above and consists of products available in all countries in the sample in 2000.

The price comparisons are then based on bilateral comparisons where matches at form/strength were found. The price comparisons show the relative prices of products launched in a given country in a given year by the year 2000 compared to the same products in the UK. Details of the number of form strengths and brands included are at Appendix 5.5.

Table 4 shows the indices by year (i.e. the contribution made to the 2000 price index by products launched in 1995, 1996 and so on) at 2000 exchange rates. For example, the table shows that, in 2000, the products launched in Belgium in 1995 cost 77 compared to 100 - the cost of the same products in the UK in 2000; products launched in Belgium in 1996 cost 75 relative to UK =100 etc.

Country	1995	1996	1997	1998	1999	2000
Belgium	77	75	76	84	93	84
Denmark	87	79	84	90	97	85
France	76	70	75	75	97	95
Germany	89	75	76	78	93	83
Italy	77	64	89	76	88	106
Netherlands	82	79	83	80	95	110
Portugal	77	65	80	70	94	81
Spain	72	62	72	73	89	80
Sweden	93	91	89	92	99	97
Switzerland	97	90	77	78	102	106
USA	129	160	156	166	187	148

In 2000, products launched between 1995 and 1998 are more expensive in the UK than in any other country except the USA. For products launched in 2000, the UK is ranked 5th.

This shows that in 2000, there is a tendency for older "new" products to be relatively more expensive in the UK (compared to other countries) than more recent "new" products (significant at 10% level). However this may be due to exchange rate movements rather than any tendency for newer products to be priced more cheaply (compared to other countries).

Table 5 shows the price indices by launch year of each cohort in the year 2000 (i.e. the contribution made to year 2000 price index) but adjusted for year of launch exchange rates (e.g. the 1995 cohort is the index of prices for this cohort in the year 2000 at 1995 exchange rates).

Country	1995	1996	1997	1998	1999	2000
Belgium	110	103	86	96	101	84
Denmark	118	107	96	104	101	87
France	107	94	85	99	110	96
Germany	127	102	86	103	98	84
Italy	96	88	98	97	91	105
Netherlands	119	108	92	106	99	105
Portugal	130	89	91	98	101	81
Spain	98	86	81	94	93	80
Sweden	114	120	98	101	99	97
Switzerland	132	119	84	105	106	105
USA	125	155	150	177	149	150

The UK is the 10th most expensive for the 1995 cohort, 8th for the 1996 cohort, 2nd for the 1997 cohort, 7th for the 1998 and 1999 cohorts, and, as above, 5th most expensive for the 2000 cohort of products. The impact of exchange rate movements on new product prices over the period can thus be seen by comparing Table 5 with Table 4.

As in Table 3, this would suggest that there is little trend in the impact of the launch price of new products launched over 1995 and 2000 on 2000 price comparisons after allowing for exchange rate movements over the period.

Table 6 shows the results for all products in the sample which were available in the year 2000, using 2000 exchange rates shown in Appendix 5.4:

Country	2000
Belgium	79
Denmark	85
France	75
Germany	81
Italy	78
Netherlands	82
Portugal	75
Spain	71
Sweden	92
Switzerland	87
USA	153

The UK is the most expensive in Europe and second only to the USA.

To conclude, therefore, there seems to be little in the trends in pricing of new products over the 1995 to 2000 period which would explain the rising prices in the UK (relative to other countries) over time.

4.3 Analysis of the Prices of Off-Patent Molecules 1995-2000

4.3.1 Top 100 Off-Patent Molecules in 2000

The prices of the top 100 molecules by value in 2000 that were off-patent in the UK and which had unbranded generic sales were identified from IMS data. The average UK prices of these molecules (sales value divided by IMS standard unit measurement of volume) were compared over the six year period 1995-2000 with the average prices of the same molecules in nine other EU countries plus Switzerland and the USA. It is important to note that this analysis compares average prices for the molecule, which includes the original brand, branded generics, and unbranded generics. Thus they do not represent the prices of unbranded generics alone. The molecules included in the analysis are at Appendix 5.6.

Table 7 shows the results of bilateral comparisons at annual average exchange rates. The exchange rates used are at Appendix 5.3. The UK is 100.

Country	1995	1996	1997	1998	1999	2000
Belgium	154	147	117	113	104	96
Denmark	146	132	109	103	90	85
France	129	130	108	107	99	96
Germany	149	149	120	114	106	99
Italy	106	117	99	99	92	90
Netherlands	159	136	102	102	96	90
Portugal	129	105	88	90	83	78
Spain	99	99	80	79	72	68
Sweden	110	122	103	95	92	91
Switzerland	220	206	161	144	134	128
USA	189	202	205	229	223	237

For the year 2000 at annual average exchange rates molecules that are off-patent in the UK are more expensive than in all the EU comparator countries. Switzerland and the USA are substantially more expensive than the UK. At the beginning of the period, UK prices were the cheapest apart from those in Spain.

The general price trend relative to the UK was downwards. The USA was an exception to this. To put this in context we looked at the price trend within the UK for these molecules. We calculated a Paasche index for UK prices over the six-year period, which was as follows:

Paasche Index for UK

1995	1996	1997	1998	1999	2000
100	104	107	109	116	116

Although the 100 molecules comprise a combination of branded and generic products it shows the impact of the increases in generic prices in the UK on the indices in 1999. Thus part of the explanation for the relative price movements shown in Table 7 is that UK prices of these molecules were increasing over the period.

In the case of the US we sought to understand why there was an upward trend in prices relative to the UK despite the existence of a competitive generics market. It was not possible with the data set we had to identify

the precise contribution of US brand price rises to the increases in the US price indices. It was however possible to illustrate that price rises in brand form/strengths post patent expiry occur despite the availability of a comparable generic form/strength.

Examples are provided in the tabulation below:

		1996	1997	1998	1999	2000	2001
Brand	Proventil (salbutamol)						
Form/ Strength	Solution for nebln Price per SU £	0.68	0.72	0.82	0.88	0.96	1.04
	Index	100	107	122	130	141	154
Brand	Cardizem (diltiazem)						
Form/ Strength	240mg retard caps Price per SU £	0.96	0.99	1.05	1.10	1.15	1.22
Index		100	103	109	114	119	127
Brand	Procardia (nifedipine)						
Form/ Strength	10mg capsules Price per SU £	0.33	0.34	0.35	0.36	0.37	0.38
	Index	100	103	106	109	112	114

Prices are provided in £ and converted using a constant exchange rate

It may be that the post patent market is effectively segmented into brand and generic users and prices therefore rise in the post patent branded sector. This is clearly part of the reason for the upward trend in the US index relative to the UK.

Table 8 shows the results at period average exchange rates. The UK is 100.

Country	1995	1996	1997	1998	1999	2000
Belgium	126	125	121	120	112	112
Denmark	122	113	111	108	96	98
France	109	112	111	112	106	111
Germany	122	127	123	120	114	115
Italy	97	101	99	102	97	103
Netherlands	130	116	105	108	104	105
Portugal	92	91	92	97	91	93
Spain	83	84	82	83	77	80
Sweden	100	102	103	101	98	101
Switzerland	182	176	169	153	144	145
USA	187	198	211	238	226	225

This shows the impact of exchange rates over the period, which are set out in Appendix 5.3. Using six-year average exchange rates Portugal and Spain and in some years Italy and/or Denmark have lower prices than the UK. Other EU comparator countries have higher prices than the UK. Switzerland and the USA are substantially more expensive than the UK.

4.3.2 Molecules Off-Patent throughout the Six Year Period

Further analysis was carried out excluding those molecules with patent expiry during the period 1995 to 2000. The ten molecules excluded are asterisked in 5.6. The results for this subset are very similar. **Table 9** shows the results of bilateral comparisons at annual exchange rates. The UK is 100.

Country	1995	1996	1997	1998	1999	2000
Belgium	129	128	126	125	113	111
Denmark	133	124	123	117	100	103
France	113	115	112	112	104	106
Germany	123	127	124	121	114	115
Italy	101	105	101	104	101	105
Netherlands	130	119	108	111	106	105
Portugal	95	95	96	103	96	93
Spain	85	86	88	89	80	79
Sweden	98	103	104	106	103	104
Switzerland	186	182	174	166	152	147
USA	187	201	216	248	228	219

For the year 2000 at annual average exchange rates molecules that are off-patent in the UK are more expensive than in all the EU comparator countries. Switzerland and the USA are substantially more expensive than the UK.

Table 10 shows the results using period average exchange rates. It shows the impact of exchange rates. Using six-year average exchange rates only Portugal and Spain have lower prices than the UK.

Country	1995	1996	1997	1998	1999	2000
Belgium	158	150	123	118	105	95
Denmark	159	145	120	111	94	89
France	134	134	110	107	97	92
Germany	150	149	120	114	106	99
Italy	109	121	101	101	95	92
Netherlands	160	140	105	105	98	90
Portugal	133	109	93	95	86	78
Spain	102	102	86	84	75	68
Sweden	108	123	104	100	96	94
Switzerland	225	213	166	156	141	130
USA	189	206	210	238	225	230

5. Appendices

5.1 List of Products used in 2000 International Price Comparison

Actraphane Hm
Adalat
Adizem
Alna*
Aprovel
Arimidex
Arthrotec
Asacol
Atrovent
Avaxim
Axid
Becotide
Betnelan
Blopress
Bricanyl
Cabaser
Calcichew
Carace
Cardura
Casodex
Cerezyme*
Cilest
Cipramil
Ciproxin
Claritine
Combivent
Coracten*
Coversyl
Cozaar
Creon
Daivonex
Depakine
Detrusitol
Diane
Diclomax*
Didronel
Diflucan
Diovan
Diprobase
Duragesic
E 45
Effexor
Epogam
Erypo
Estraderm
Famvir
Flixonase
Flixotide
Flomax*
Fosamax
Fucicort*
Fybogel
Gaviscon
Genotropin
Gopten
Harnal*
Havrix
Ikorel
Imdur
Imigran
Inderal
Klacid
Kliogest
Lamictal
Lamisil
Lanzo
Lescol
Lipitor
Lipobay
Livial
Losec
Madopar
Medocodene
Microgynon 30
Minocin
Mobic
Molipaxin
Monocor
Monosorb*
Moscontin*
Motens
Naramig
Neurontin
Norvasc
Oilatum
Oxis
Pariet
Permax
Plavix
Plendil
Pravachol
Premarin
Prempak C*
Premphase
Prograf
Proscar
Prostap Sr
Protium
Prozac
Pulmicort
Recormon
Remeron
Requip
Risperdal
Sandimmun
Sandostatin
Seretide
Serevent
Seroquel
Seroxat
Singulair
Staril
Systen
Tegretol
Telfast
Tildiem
Topamax
Triatec
Trusopt
Tylenol Codeine*
Typhim
Ventolin
Viagra
Vioxx
Voltaren
Winadeine
Xalatan
Xatral
Xenical
Zantac
Zestril
Zocor
Zoladex
Zoloft
Zomig
Zyban
Zydol
Zyprexa
Zyrtec

* IMS data was provided for these products but no matches of form/strength were found.

Note that the product names are the international names provided by IMS

Quarter 4 2000 Average Exchange Rates used in 2000 Price Comparison

Country	
Austria	22.93
Spain	277.32
Finland	9.91
Belgium	67.24
Germany	3.26
Italy	3,227.23
Ireland	1.31
France	10.93
USA	1.45
Netherlands	3.67

5.2 Major New Products (NCEs) 1995-2000

The new chemical entities (NCEs) included in the analyses are shown below. The brand names are 'international names' with the UK brand name shown in brackets where it differs from the 'international name'.

1995	1996	1997	1998	1999	2000
Effexor	Zyprexa	Lipitor	Viagra	Vioxx	Celebrex
Cipramil	Harnal (Flomax)	Xalatan	Plavix	Sustiva	Zyban
Cozaar	Diovan	Lipobay	Pariet	Ziagen	Avandia
Casodex	Protium	Aprovel	Detrusitol	Remicade	Nexium
Arimidex	Mobic	Seroquel	Xenical	Arava	Actonel
Fosamax	Zerit	Aricept	Blopress (Amias)	Eloxatine (Eloxatin)	Levonelle/ Levonelle 2
Reopro	Epivir	Remeron (Zispin)	Singulair	Mirapexin	Oxycontin (Oxynorm)
Topamax	Cellcept	Telfast	Viramune	Nebilet	Mononine
Merrem (Meronem)	Taxotere	Nasonex	Viracept	Aggrastat	Trizivir
Trusopt	Requip	Solian	Evista	Integrilin	Enbrel

5.3 Annual Average Exchange Rates Utilised in Analyses of Major New Products (NCEs) and Off-Patent Molecules

Country	1995	1996	1997	1998	1999	2000
Belgium	46.5	48.40	58.59	60.18	61.39	66.27
Switzerland	1.87	1.93	2.38	2.40	2.44	2.56
Germany	2.26	2.35	2.84	2.92	2.98	3.21
Denmark	8.84	9.06	10.82	11.11	11.31	12.25
Spain	196.55	197.93	239.81	247.68	253.19	273.32
France	7.87	7.99	9.56	9.78	9.98	10.78
Italy	2,570.57	2,409.64	2,788.65	2,879.36	2,946.40	3,180.63
Netherlands	2.53	2.64	3.20	3.29	3.36	3.62
Portugal	196.55	241.02	287.14	298.78	305.19	329.33
Sweden	11.27	10.48	12.51	13.18	13.39	13.87
USA	1.58	1.56	1.64	1.66	1.62	1.52

5.4 Major New Products (NCEs): Bilateral Price Indices weighted by UK Volumes by Year for available form strengths for brands launched in the UK 1995-2000. Price indices for a maximum of three annual periods for each cohort of brands.

Table 1 shows the indices for the brands launched in the UK in 1995:

Country	1995	1996	1997
Belgium	97	94	80
Denmark	112	107	90
France	96	95	86
Germany	107	117	96
Italy	105	102	88
Netherlands	130	118	93
Portugal	n/a	103	82
Spain	105	97	80
Sweden	109	110	92
Switzerland	128	118	96
USA	110	115	111

The UK is 100. The table shows that NCEs launched in the UK in 1995 were the 3rd cheapest after Belgium and France in 1995, 4th cheapest after Belgium, France and Spain in 1996 but the most expensive after the USA by 1997.

Table 2 shows indices for the brands launched in 1996:

Country	1996	1997	1998
Belgium	n/a	81	79
Denmark	112	90	86
France	100	81	79
Germany	90	79	78
Italy	79	54	58
Netherlands	104	82	82
Portugal	n/a	86	76
Spain	82	72	71
Sweden	121	96	93
Switzerland	130	112	94
USA	88	97	106

The table shows that NCEs launched in the UK in 1996 increased from mid-range in 1996 to the most expensive after Switzerland in 1997 and the USA in 1998.

Table 3 shows indices for the brands launched in 1997:

Country	1997	1998	1999
Belgium	n/a	88	85
Denmark	92	93	91
France	57	82	80
Germany	87	84	82
Italy	127	101	96
Netherlands	102	94	89
Portugal	107	90	86
Spain	87	84	81
Sweden	96	91	91
Switzerland	85	83	79
USA	139	136	143

The table shows that NCEs launched in the UK in 1997 increased from 5th most expensive in 1997 to the most expensive after the USA in 1999.

Table 4 shows indices for the brands launched in 1998:

Country	1998	1999	2000
Belgium	92	84	73
Denmark	97	100	92
France	88	79	77
Germany	93	88	84
Italy	88	78	78
Netherlands	87	79	85
Portugal	88	80	74
Spain	98	97	74
Sweden	92	99	94
Switzerland	83	90	88
USA	138	177	186

NCEs launched in the UK in 1998 were 2nd most expensive after the USA in each of the three years.

Table 5 shows indices for the brands launched in 1999:

Country	1999	2000
Belgium	n/a	93
Denmark	100	93
France	118	102
Germany	99	91
Italy	75	85
Netherlands	95	92
Portugal	88	94
Spain	87	86
Sweden	102	96
Switzerland	103	101
USA	133	159

NCEs launched in the UK in 1999 were 5th most expensive in 1999 and 4th most expensive in 2000.

Table 6 shows indices for the brands launched in 2000:

Country	2000
Belgium	84
Denmark	87
France	95
Germany	85
Italy	105
Netherlands	105
Portugal	81
Spain	80
Sweden	97
Switzerland	105
USA	148

NCEs launched in 2000 in the UK were 5th most expensive out of 12 countries in the study.

5.5 Major New Products (NCEs): Coverage by Country by Year

1995 NCEs	Form/strengths			Brands		
	1995	1996	1997	1995	1996	1997
Belgium	1	3	8	1	3	6
Denmark	9	10	17	5	6	10
France	2	3	6	2	3	6
Germany	4	10	10	3	8	8
Italy	8	11	12	5	8	8
Netherlands	6	9	10	4	7	8
Portugal	0	3	5	0	3	4
Spain	3	8	9	1	6	7
Sweden	9	16	17	6	10	10
Switzerland	3	12	14	3	9	9
USA	8	12	17	5	8	9

1996 NCEs	Form/strengths			Brands		
	1996	1997	1998	1996	1997	1998
Belgium	0	6	10	0	4	6
Denmark	13	18	21	7	8	9
France	10	18	18	5	7	7
Germany	13	19	22	7	8	8
Italy	7	16	18	4	7	7
Netherlands	11	20	21	5	8	8
Portugal	0	4	8	0	1	4
Spain	4	14	16	2	6	5
Sweden	9	16	17	4	6	7
Switzerland	8	14	16	5	7	7
USA	11	18	19	4	6	6

1997 NCEs	Form/strengths			Brands		
	1997	1998	1999	1997	1998	1999
Belgium	0	7	10	0	5	6
Denmark	10	14	15	7	8	8
France	2	13	14	1	6	7
Germany	14	14	17	7	7	9
Italy	6	14	15	4	8	8
Netherlands	10	14	15	5	7	8
Portugal	3	8	10	2	5	6
Spain	2	12	12	2	7	7
Sweden	12	13	14	6	6	7
Switzerland	7	12	13	4	7	8
USA	11	12	12	6	6	6

1998 NCEs	Form/strengths			Brands		
	1998	1999	2000	1998	1999	2000
Belgium	6	8	11	4	7	8
Denmark	9	12	12	6	8	8
France	12	14	18	6	8	10
Germany	18	17	17	10	10	10
Italy	10	14	17	5	8	10
Netherlands	9	9	14	5	6	9
Portugal	4	7	10	2	5	7
Spain	5	10	12	2	6	9
Sweden	10	13	14	6	9	9
Switzerland	12	16	17	6	9	10
USA	12	14	14	9	10	10

1999 NCEs	Form/strengths		Brands	
	1999	2000	1999	2000
Belgium	0	7	0	3
Denmark	5	8	3	5
France	6	13	4	7
Germany	12	16	7	8
Italy	5	16	4	9
Netherlands	1	11	1	7
Portugal	1	3	1	2
Spain	9	18	6	8
Sweden	6	10	4	6
Switzerland	9	11	4	6
USA	10	11	4	4

2000 NCEs	Form/strengths	Brands
	2000	2000
Belgium	3	2
Denmark	7	4
France	2	2
Germany	13	7
Italy	3	3
Netherlands	3	3
Portugal	2	2
Spain	2	2
Sweden	11	5
Switzerland	7	5
USA	14	7

Multilateral	Form/strengths	Brands
All markets	**22**	**15**

5.6 Off-Patent Molecules

Acetylsalicylic Acid
Aciclovir
Allopurinol
Amiodarone
Amitriptyline
Amoxicillin
Amphotericin B
Atenolol
Azathioprine
Beclometasone
Bendroflumethiazide
Betahistine
Bisoprolol
Captopril
Carbamazepine
Carboplatin
Ceftazidime
Cefuroxime*
Chlorhexidine
Cimetidine
Ciprofloxacin
Clotrimazole
Codeine
Cromoglicate
Cyproterone
Desmopressin
Dexamethasone
Diclofenac
Dihydrocodeine
Diltiazem
Dosulepin
Doxorubicin
Enalapril*
Erythromycin
Estradiol
Factor VIII
Fentanyl
Flucloxacillin
Fluoxetine*
Furosemide
Fusidic Acid
Gamolenic Acid*
Gentamicin
Gliclazide*
Heparin
Human Insulin
Human Insulin Isophane
Hyaluronic Acid*
Hydrocortisone
Ibuprofen
Ipratropium
Isoflurane
Isosorbide Mononitrate
Ketoprofen
Lactulose
Levothyroxine
Lisinopril
Mebeverine
Mesalazine*
Metformin
Metronidazole
Minocycline
Morphine
Naproxen
Nicotine
Nifedipine
Nitroglycerin
Nizatidine
Oxybutynin
Pancreatin
Paracetamol
Prednisolone
Prochlorperazine
Propofol*
Propranolol
Ranitidine*
Salbutamol
Tamoxifen
Terbutaline
Timolol
Tramadol
Valproic Acid
Vancomycin
Verapamil
Warfarin
Zopiclone*

* molecules with patent expiry 1995 to 2000.

Component 6:

Hospital Sector

December 2002

Component 6

Contents

Component 6

Hospital Sector

1. Introduction

The terms of reference for this component of the study were:

'to improve understanding of the supply/demand of pharmaceuticals in the hospital sector, and whether there are important links to the community sector. Key issues are:

- the balance of hospital sales between products that are predominantly sold to hospitals and those predominantly sold to the community;
- assessment of the competitiveness of the market for those products that are predominantly sold to hospitals, including number of potential suppliers and the efficiency of the procurement process;
- comparisons between discounted prices in hospitals and in the community for products sold predominantly to the community.'

The work took four strands:

a) An analysis of the balance of sales between hospital and community (setting the context).

b) An analysis of firm concentration in the main pharmaceutical markets in the hospital sector.

c) A workshop with hospital and industry participants followed by in depth interviews with senior pharmacists from five trusts in England to explore the efficiency of the procurement process. The trusts covered a wide range of hospitals providing different types of services.

d) An analysis of discounts offered in the hospital sector relative to the community sector.

2. Executive Summary

Summaries of the four strands of work are shown below.

2.1 Balance of Sales between Hospital and Community, using IMS Data on Drug Spend

Hospital sales account for 19% of total sales. Nearly half of sales to hospitals are in markets where hospital sales predominate (i.e. where hospital sales account for more than 80% of total sales). These tend to be fairly niche markets accounting for only 9% of total (hospital plus community) sales.

2.2 Concentration of Hospital Sector

The hospital sector is less concentrated than the community sector. The top ten (branded) firms account for 45.2% of hospital sales compared to 58.8% in the community, reflecting the greater use of generics in the hospital sector.

Within individual markets[1] 47% of markets have (at least) one company supplying more than 40% of the market (the OFT benchmark for potential dominance) – accounting for 44.4% of total sales. This is lower than in the community sector where 61% of markets are above the 40% threshold (accounting for 55.6% of sales).

The top markets by value are also less concentrated in the hospital sector. For example, only three of the top ten markets by value have a concentration index of greater than 40% compared to five of the top ten in the community.

2.3 Hospital Pharmacist Interviews

The interviews with pharmacists revealed variation in purchasing practice. For example, though most trusts have some form of formulary there is considerable variation in their coverage and the degree of restriction on prescribing (and the degree to which they are enforced). Purchasing strategies also varied considerably. The interviews suggest that any interaction between the community and hospital markets is likely to be diminishing because of the medicines management policies of PCTs.

[1] Defining a market is not a straightforward task. For ease of analysis a working definition at BNF sub-chapter level (or the next level up if sub-chapter is not available) has been assumed when defining a market. That is not to say that all products in each category will be substitutable and part of the same market, nor that products in different categories need never be substitutes and part of the same market.

2.4 Hospital Discounts

There is considerable variation in discounts across products and for individual products across trusts. The modelling work suggests that, for a given drug, the level of discount is associated with the presence of other drugs in the class which are heavily discounted and where there is a generic version of the product available. Generic presence appears to have a greater influence on discounting of the brand where the chemical entity concerned has high sales value. However, only a quarter of the variation is explained by these factors - variation in purchasing practice may help to explain the inability of the statistical analysis to explain more of the variation. Our analysis found little evidence of a statistically significant relationship between the size of the combined hospital and community market and levels of discount in the hospital sector – other than via the impact of generic availability on prices.

On the whole, both the statistical analysis and the interviews are suggestive of a fairly competitive environment with respect to some trusts across some products. However, both the analysis and the interviews confirm that this is not necessarily the case across the board.

3. Main Conclusions

3.1 Balance of Sales between Hospital and Community

Hospital sales account for 19% of total sales (IMS data).

44% of sales to hospitals are for drugs that are largely only used in hospitals (i.e. where hospital sales account for more than 80% of total sales). These drugs are concentrated in 52 markets (at ATC 3 level) out of a total of 232. These are largely niche markets accounting for only 9% of total sales (hospital plus community). A further 21% of hospital sales are in markets where hospital sales are between 40 – 80% of the total and the remaining 36% of sales are in markets where the hospital share of total sales is less than 40%.

Hospital ATC sales as % of total ATC sales	100-80%	80-60%	60-40%	40-20%	<20%
Proportion of Hospital sales Value by Hospital share of total Sales					
Percentage of hospital sales	44%	9%	12%	17%	19%
Proportion of Total Sales Value By Hospital share of Total Sales					
Percentage of total sales	9%	2%	5%	10%	74%
No. of (ATC3) Markets By Hospital share of Total Sales					
Number of markets	52	16	22	25	117
(Percentage %)	(22%)	(7%)	(9%)	(11%)	(51%)

3.2 Concentration of Hospital Sector

3.2.1 Aggregate Company Concentration

The analysis for this indicator used IMS data for the year to April 2002. Market shares of the top ten companies are expressed as a percentage of total sales (including generics).

The analysis in table 1 below shows various measures of market concentration. Note that this analysis is based on UK hospital sales.

Table 1 – Market Share of the Top Ten Companies – Year to April 2002

	Company	Sales (£m)	Share (%)	Cumulative Share (%)
1	GlaxoSmithkline	176		9.2%
2	Aventis	108		14.9%
3	Roche	94		19.8%
4	Novartis	91		24.5%
5	Pharmacia	74		28.4%
6	AstraZeneca	72		32.2%
7	Bristol Myers Squibb	69		3.6%

Overall concentration levels are lower than for the community sector at 45.2% for the top ten companies compared to 58.8% in the community sector.[2]

3.2.2 Concentration Index at Market Level

Value and percentage of sales in markets supplied by only one manufacturer/where one manufacturer has 40% or more of sales

For each market (defined as a BNF sub-chapter where available, or the next level of aggregation if not available) the company with the largest sales was identified and the market share for that company was calculated (Concentration Ratio 1 – CR1 - in table 2 below).[3]

[2] The data sets are not strictly comparable as IMS data was used for the hospital calculation and PCA data for the community market.

[3] When the largest company in a given market was 'generic', the CR1 was set to zero, on the assumption that this figure for 'generic' represents several manufacturers. This is likely to under-estimate the degree of concentration, as it assumes all markets where most sales are generic are in effect *perfectly* competitive. This is likely to exaggerate the effect of generics. It is also entirely possible that a single manufacturer does indeed supply the generics in any given market in at least some of the smaller markets.

Table 2 - Value and Share of Sales by Concentration of Market, Year to April 2002

CR1	Value	Value Share	Number of Markets	% of Markets
1	10	0.6%	20	9%
>0.9	97	5.7%	36	16%
>0.8	168	9.8%	47	21%
>0.7	243	14.2%	58	26%
>0.6	370	21.6%	76	34%
>0.5	472	27.6%	87	38%
>0.4	762	44.4%	106	47%
>0.3	952	55.5%	114	50%
>0.2	1,116	65.1%	118	52%
>0.1	1,116	65.1%	118	52%
>0.0	1,716	100.0%	226	100%

This table shows the number of markets where concentration is above a certain threshold. The table also shows the proportion of sales value that these markets account for.

CR1 refers to the 1-firm concentration ratio – in other words the market share held by the top firm in that market (a market is defined here as a BNF sub-chapter, or the next level of aggregation if not available at sub-chapter level).

The top row therefore refers to 100% concentrated markets (i.e. with only one manufacturer), and a look at the table will show there are 20 such markets (9% of all markets).

The row for CR1>0.4 indicates figures for markets where (at least) one firm has 40% or more of the market. There are 106 such markets (47% of the total), accounting for 44.4% of total sales– this is somewhat lower than in the community sector where 61% of markets (accounting for 55.6% of sales) have a concentration index of greater than 40%. A market share of 40% or more for the top firm is one of the indications used by the OFT as a standard benchmark for market dominance.

Table 3 shows another summary of these figures:

Table 3 – Concentration by Size of Market, Year to April 2002

Top	Proportion of NIC	Number of markets With CR1>0.4	Ave. CR1
5	27.3%	1	26.3%
10	40.8%	3	23.3%
20	58.2%	11	39.8%
50	83.4%	25	36.0%
100	95.6%	47	34.9%
226	100.0%	106	36.9%

This table shows the proportion of total sales accounted for by the top 5, 10, 20, 50 and 100 markets (by market value), as well as the number of markets with a CR1 higher than the benchmark of 0.4 and a weighted average of the CR1 for each category. So for instance, three of the ten largest markets, accounting for 40.8% of sales, have a CR1>0.4 and the weighted average of the CR1 of the ten is 23.3%. This compares with five out of the top ten markets in the community sector (accounting for 42.1% of sales with an average CR1 of 40.8%).

3.3. Hospital Pharmacist Interviews

3.3.1 Background

Interviews were carried out with senior pharmacists from five different trusts throughout England to understand the efficiency of the procurement system. Of those interviewed, three were Directors of Pharmacy, responsible for all pharmaceutical services within their trusts, while the other two were more specifically involved in procurement. Several had Regional responsibilities.

The trusts covered a wide range of hospitals providing different types of services, and included district general hospitals, teaching hospitals and hospitals specialising in particular areas such as oncology and mental health.

3.3.2 Selection of Drugs for Hospital Use (Formularies)

The use of formularies varied throughout the different trusts, as did their purpose. Some hospitals had extensive formularies, while others had no formulary at all, or a very minimal list.

The purpose of formularies ranged from providing therapeutic guidelines, to exerting firmer control over prescribing. Several pharmacists said that in their trust, formularies were mainly used as a prescribing guide for junior doctors by specifying what can be prescribed for particular conditions. One trust operated a system of highlighting "preferred" drugs in the BNF, and linking them to treatment protocols. Often, formularies did not include specialist drugs such as oncology drugs. Senior doctors were generally able to prescribe non-formulary drugs, especially, for example, where a patient was referred from another hospital.

The general view was that formularies tended to follow practice rather than lead it. Most were reviewed regularly but it was unusual to make significant changes, as the savings could be small and the effort involved in switching, huge. Changes were usually made against a clinical background, rather than for cost reasons.

Antibiotics were usually treated as a special case.

3.3.3 New Drugs

All of the trusts in the study had formal procedures for adding new drugs to a formulary or otherwise endorsing their use in the hospital(s) concerned. In some cases, there was a New Drugs Committee, while in others, new drugs were considered by the main Drug and Therapeutics Committee (D&TC). Submissions were generally made by the consultant in the clinical area concerned, often in conjunction with a clinical pharmacist.

Cost was taken into account in reaching a decision, but all those interviewed said that clinical considerations took priority. Cost of a particular treatment in the community was also taken into account by most hospitals.

Pharmacoeconomic data was considered where it was available. One trust expressed reservations in accepting at face value pharmacoeconomic data supplied by the industry.

NICE guidance was generally taken into consideration, but sometimes had to be phased in gradually (or not at all) due to funding problems. (N.B. these interviews predated the decision of the Secretary of State for Health to require trusts to make funding available for the implementation of NICE decisions.)

3.3.4 Drug and Therapeutics Committees

The make up of the committees making decisions on the use of new medicines tended to be well balanced, with representatives from different clinical directorates, pharmacy, nursing, Health Authority representatives and GPs among others. Most tended to have a financial representative, but where this was not the case, finance divisions were consulted separately.

3.3.5 Existing Treatment

All of those interviewed said that patients were not generally switched from their own medication, and there was an increasing tendency to use patients' own medication while they were in hospital. If necessary, non-formulary products would be ordered in for them.

3.3.6 Medicines to take Home

The situation varied. Sometimes consultants specified a class of drug, and sometimes a particular drug. The situation was similar with out-patients.

3.3.7 Pharmaceutical Company Representatives

Pharmaceutical company representatives tended to target clinicians, some of whom were more swayed than others. The decision to use a drug still had to be approved by the D&TC.

3.3.8 Budgets

Budgets were held by clinical directorates, though in most cases, the pharmacy department played a role in monitoring and managing them. Budgets were cash limited and were almost always overspent, since they were based on historical spend, and it was difficult to predict the effect of a new drug entering the market, or an existing drug being licensed for new indications. The overspend could be managed in-house, or the Health Authority approached for more funds.

3.3.9 Purchasing Arrangements

Purchasing was done at various levels:

- by trusts
- by consortia (groups of seven or eight hospitals)
- by Division, through NHS Purchasing and Supply Agency (PASA) (there are five supplies divisions in England).

Drugs were either purchased on contract, or from wholesalers or through deals with individual companies. Some companies would only deal with individual trusts.

3.3.10 Class Tendering

Tendering on a class basis did take place, but in varying degrees, and only in specific therapeutic categories. Some found it difficult to get agreement throughout the trust, while others encountered differences in clinical practice across the region.

3.3.11 Discounts

Hospitals rarely paid the list price for drugs, but some companies were beginning to reduce the discounts they were offering. Larger discounts tended to be offered in more crowded markets.

Companies did offer support to the NHS e.g. provision of nursing or medical staff, but some wanted a quid pro quo, in the form of lower discounts. The view of several of the trusts interviewed was that the two should be kept separate.

As far as loss leading is concerned, the general view was that with prescribing advisers, prescribing leads and PCGs, GPs were much less likely to slavishly follow hospital prescribing.

3.3.12 Parallel Imports

All of those interviewed used parallel imports, and all said that use of parallel imports had resulted in some affected manufacturers reducing their prices. Significant penalties for parallel importers who fail to maintain continuity of supply had prevented speculative tendering.

3.4 Analysis of Hospital Discounts

Currently, no comprehensive data on hospital drug contract prices is collected centrally. However, in March 2000 the Department collected information on hospital drug prices from a sample of trusts for a sample of drugs in the process of examining the impact of the 4.5% price reductions[4] on hospital prices. 38 responses were received but two of those provided only partial information and one has been unusable. A sample of 108 pharmaceuticals covering 160 presentations was obtained.

It should be stressed that as the data is some two years old it may not reflect current market conditions - it is becoming apparent that some manufacturers are currently reviewing their pricing strategies in the hospital sector.

Nevertheless, the data showed that:

- The mean (unweighted) discount was 28%.

- There is considerable variation in the amount of discount offered across products. The discount also varies for the same drug across trusts, (e.g. between 0% and 95% for one product across trusts) and for the same manufacturer across their product range (of a similar magnitude).

Further statistical analysis of the data shows that the observed discount for a given product is associated with the level of discounting of other competitor products in the same market[5], and whether or not there is a generic version of the product available. The latter variable may be modified however, in that the presence of a generic appears to have greater impact in markets where there is significant spend (in the combined community and hospital market) compared to smaller markets. That is, the impact of generic availability on the level of discount is significantly greater where there are high sales in the community.

Tables 4 and 5 summarise the findings[6].

[4] Implemented in October 1999 as part of the 1999 PPRS agreement.
[5] Where the market is defined at the BNF sub-chapter level.
[6] This fairly crude presentation of the results serves simply to illustrate, in a non-technical way, the results of regression analysis. The variables listed are those which were found to be significant (at 95% confidence).

Table 4 - Average[7] Discount (%) By Market Value[8] and Whether a Generic is Available

	No Generic Available	Generic Available
Low Value Market	16.2	28.3
High Value Market	22.7	44.3

Table 5- Average[7] Discount (%) By Size of Competitor Discount[9]

Low Competitor Discount	High Competitor Discount
9.2	66.6

We also tested for whether the size of the overall market (community and hospital) - measured by the total NIC for the BNF sub-chapter in which the drug is to be found or by the total NIC for the chemical entity, or by the ratio of the latter to the former - was a factor in explaining discounts. We found no significant independent effects for overall market size (community and hospital) over and above the interaction with the availability of generics variable discussed above.

However, there remains a large amount of unexplained variation, in that only about a quarter of the variation is explained by these variables. Either a key variable is missing from the analysis, or there is a lot of randomness in the setting of hospital discounts.

7 Average excludes one outlier with a reported discount of 1231%.
8 High NIC is NIC in the BNF sub-chapter over £17.5m (median NIC of sample).
9 High competitor discount is where a drug sells in a market (BNF sub-chapter) where the cheapest drug on the market (or the second cheapest if the drug concerned has the largest discount) sells at a discount of more than 35% (the average 'competitor' discount).

Component 7:

Less Regulated Markets

December 2002

Component 7

Contents

Component 7

Less Regulated Markets

1. Executive Summary

In **Germany** funding for pharmaceuticals for patients is provided by statutory or private health insurance with cover for the unemployed paid by the state and co-payments are charged. Pharmaceutical companies are free to set and vary the prices of their products as they see fit, with automatic reimbursement. For all products except patented medicines launched since 1996 their pricing decisions are, however, affected by the fact that reimbursement is at reference price levels.

The reference price for any medicine is based on the prices charged for all the products in the group to which that medicine is allocated. If the price is above the reference price, the patient must pay the difference in addition to the normal co-payment. Patients dislike paying additional co-payments, and will, in this situation, choose an alternative medicine where possible. Doctors dislike telling patients they have to pay additional co-payments. Hence, companies tend to price medicines at or below the reference price.

The drugs bill in Germany is impacted by higher levels of generic utilisation (largely higher priced branded generics) than in the UK, a list of non-reimbursed drugs i.e. negative list, (to be replaced with a positive list in 2003) and, since January 2002, individual physician expenditure volumes.

Prices in the hospital sector are negotiated between the hospitals and the pharmaceutical companies and depend on market factors such as volumes and the range of competitors. The products purchased are on a formulary determined by a committee, chosen largely on the basis of clinical criteria, but taking account of economic considerations where alternative products are considered medically interchangeable.

The medicines market in the **US** falls into two parts – the private sector (patients covered by private insurance, usually via their employer, that provide health plans and the uninsured) and the regulated public sector (Medicaid, Veterans Administration (VA) etc).

Most private insurance companies develop formularies for the management of medicine provision; these usually admit NCEs when they come to market, and then decide which product should be in the formulary when second and third entrants arrive. Prices, or price discounts, are set by negotiation between the pharmaceutical company and the insurance company's Pharmacy Benefit Managers. Most plans include some form of co-payment, and these typically vary from $7 to $35 according to the type of medicine. Prices in the regulated public sector are negotiated with manufacturers by the VA (they average less than half the published prices) or reimbursed at agreed levels by the Medicaid programme. Manufacturers must make drugs available to organisations covered by the VA negotiations as a condition of eligibility for Medicaid reimbursement. Research by Patricia Danzon has found list prices lower and discounts larger where the number of competitors is large.

Non-insured individuals, and those on Medicare (which does not cover the cost of medicines) pay the retail price – a mark-up on the price set by the manufacturer. In some States, Medicare patients can get assistance or purchase supplemental insurance.

Hospitals purchase drugs through wholesalers or directly from manufacturers, joining together in purchasing consortia to maximise purchasing power. Very significant discounts are common.

2. Introduction

The terms of reference for this component were:

'To examine the experience of less regulated markets in the US (and possibly elsewhere such as Germany) to see if there are any lessons for the UK. This will focus on:

- level and growth of prices in a less regulated environment, adjusted for other factors;
- evidence that competition does constrain prices at reasonable levels across the market as a whole;
- other effects of deregulation, for example on innovation.'

3. Germany

3.1 Healthcare Funding

The Gesetzliche Krankenversicherung (GKV), statutory health insurance is at the centre of the German healthcare system. GKV policies cover some 90% of the population. Most of the rest have private insurance. Employees, their partners and children are covered by GKV. There are fixed contributions as a percentage of monthly salary paid equally by the employee and employer. Pensioners and the unemployed are also covered. Contributions for the unemployed are paid by the state and statutory pension plans currently subsidise GKV contributions by 6.7% of the pension (i.e. pensioners do not pay any contributions). The GKV covers a wide range of healthcare services including hospital care and medicines. Healthcare is provided free of charge other than co-payments.

The state governments only pay directly for hospital capital investments. The pressure to constrain healthcare expenditure comes from its effect on German non-wage costs and consequently its impact on German competitiveness.

3.2 Outline of System

- Free pricing for all products with automatic reimbursement;
- Reimbursement control through reference pricing for mostly off-patent products;
- Patented medicines launched since the beginning of 1996 are outside the reference price system.

3.3 Medicines Market: Key Features

- Growth in medicines expenditure by the GKV increased by 16% between 1992 and 2000 compared to 23.3 % increase in total GKV expenditure (between 1992 and 1999: 11% for medicines and 20.5 % in total GKV expenditure);
- Prescribed medicines are covered 82% by GKV, 8% co-payment and 10% private prescriptions paid either by patient or private insurance;

- In the former West Germany generics accounted for 41% of total GKV drug spend and 56% of volume in 2000;
- Parallel imports are 2.5% of market by value. Imports had a 3.2% share of sales in 2000 and 4.6% in 2001;
- Wholesale and pharmacy margins are regulated by law. Generally margins are on a percentage sliding scale with higher value packs attracting lower margins;
- Wholesale network is highly concentrated with only three major firms;
- There are a large number of pharmacists relative to the population – 3804 people per pharmacy (3667 in the former West Germany and 4658 in the East).

3.4 Prices

Price comparison to the UK at ex-manufacturer prices. UK=100.

Germany	1996	1997	1998	1999	2000	5 year average exchange rate
Bilateral	124	108	108	97	91	103
Multilateral	125	101	109	103	94	108

Source: PPRS 5th Report to Parliament

3.5 Patented Medicines Launched Since 1996

Patented medicines launched onto the German market since the beginning of 1996 have been outside the reference price system. There is freedom of entry on launch and companies are able to vary prices thereafter subject to the constraints of the market.

3.6 Generics

Germany is Europe's largest generics market. Generics account for around 41% of drug expenditure and around 56% of volume. Generics are more often "branded generics" rather than the "true generics" available in the UK. But this changed from February 2002 when a new

law on containment of drug expenditure requires pharmacists to dispense generics from the lowest third of the price range.

3.7 Reference Price System

The reference price system (RP) was introduced in 1989. It sets a reference price for each medicine, based on the price of all products in the group into which the product is allocated. The RP is the maximum amount reimbursed. If the price is higher the patient must pay the difference in addition to the normal co-payments. Normal co-payments are DM8, DM9 or DM10 depending on the size of the pack.

Companies retain the right to set their own prices, but 94% of products are priced at or below the reimbursement level. This is because:

- Patients dislike paying co-payments, especially where alternative products are available;

- GPs dislike explaining to patients that they have to pay an additional co-payment.

Where prices are above the reimbursement level this is usually because the product concerned has a major OTC market, or where it has a small German market but a large European market, where German prices are used as a reference in other pricing systems.

At its maximum some 65% of the market was covered by the RP system. However, the coverage of the system has declined since 1996 as a result of the exemption of patented products launched since that time. When products go off patent they become subject to the RP system.

The reference prices are set by the Krankenkassen (federal health insurance funds) along an economic rationale but the RP must be high enough to give GPs a choice of a number of products. Generally the RP is no higher than the lower third of the product range in the group. The reference groups were constructed by a committee of Krankenkassen staff and doctors.

During the last couple of years, product groups and respective reference prices have regularly been reviewed and in most cases prices have repeatedly been reduced. As a result of legal uncertainty surrounding the reference pricing system, further price adjustments were stopped in 1999. The opinion of a number of regional administrative courts was that the German system - with sick funds ultimately establishing the

reference prices - violates EU cartel law. A conclusive judgement is awaited from the European Court of Justice. The German Parliament has passed interim reference pricing legislation ('Festbetragsanpasssungsgesetz' - FBAG), which enabled the Ministry of Health to fix the reference prices by a legal ordinance effective in February 2002 and limited until 2003.

3.8 Formularies

A negative list of non-reimbursed drugs has existed since 1983. Medicines on the current list are primarily:

- Fixed combinations of drugs with more than 3 active ingredients – but may be prescribed for special treatments;
- Drugs with disputed therapeutic efficacy – these may be prescribed under exceptional circumstances to named patients.

Medicines for minor conditions such as colds and flu are only reimbursed when prescribed for children under 18.

Work is currently in hand to produce a positive list to replace the negative list. Publication is expected in 2003.

3.9 Drug Budgets

A system of regional global budgets for prescribed medicines dates from 1993. An upper limit of expenditure for each regional association of Krankenkassen physicians is determined annually on the basis of historical expenditures and negotiations. Doctors are financially liable for over spending up to 5% over budget. These regulations are theoretical, as no compensation has been paid.

Legislation to replace this system came into effect in January 2002. A new law ('Arzneimittelbudget-Ablösungsgsgesetz' - ABAG) revised this collective liability system:

- The capped drug budget has been withdrawn and replaced by expenditure volumes, which are negotiated regionally by sick funds and physicians associations. These expenditure volumes are backed by agreements on targets for cost-effectiveness and quality ('Zielvereinbarung') including higher prescription rates of generics and imported drugs and less prescriptions of 'me-toos' and disputed drugs.

- Drug budgets will be replaced by individual prescribing limits for each doctor, based on the status (working or pensioner) of the doctor's patients.

- The Krankenkassen will be responsible for informing doctors and regional associations of Krankenkassen physicians of expenditure patterns on a monthly basis.

- In event of doctors over prescribing, provisions will exist for a procedure involving negotiation and advice. If these procedures fail, doctors may be subject to a financial penalty.

- A bonus option will be available for doctors who stay below their set-prescribing limit.

3.10 Hospitals

Pharmaceutical prices for the hospital sector are set freely. Hospitals, usually represented by their pharmacists, negotiate directly with the sales force of manufacturers. Prices depend on volumes, therapeutic value of a product and competition. Hospitals consider the outcomes of such negotiations confidential and are not keen to disclose prices. However, retail price discounts and rebates of 50% and over are common. Hospitals limit purchases to products on their formulary. Inclusion on a formulary is usually decided by a committee of doctors, pharmacologists, pharmacists and administrators, largely on the basis of clinical criteria. Economic considerations, mainly price, play a role when alternative products are considered medically interchangeable (such as different drugs within a class of antibiotics).

Diagnosis Related Groups (DRGs) are to be introduced to all German hospitals from 1 January 2003. Currently in 80% of cases costs are reimbursed on a per diem basis, and in the remaining 20% on a lump sum basis.

3.11 OTC Sales

Prices are unregulated but for medicines available only at pharmacies there is a uniform retail price.

3.12 Parallel Trade

In 2002 parallel trade penetration is estimated at 5.5%.

4. United States

4.1 Background

4.1.1 Healthcare Funding

The main sources of healthcare funding are:

Private insurance	47%
Private out of pocket	19%
Public federal	34%
Public State and local	12%
Other	10%

These exceed 100%, because there is overlap of funding. For example, those in the "Public Federal" bucket may purchase additional insurance to supplement pharmaceutical coverage. Also, those eligible for 'Public Federal' may also be eligible for funding from 'Public State' funds.

4.1.2 Outline of System

- Within the unregulated sector manufacturers negotiate prices with Health Maintenance Organisations (HMOs) and Pharmacy Benefit Managers (PBMs), usually to gain entry to formularies;

- Price controls are limited to Medicaid, Veterans Administration, and some state pharmaceutical assistance programmes.

4.1.3 Medicines Market: Key Features

- Growth in medicines expenditure increased by 17.3% in 2000 (from 1999) compared to a 6.9 % increase in health care expenditure.

- Inflation in medicine prices is 3.5% to 5.5% per annum.

- In primary care 70% of scripts are paid for by insurance; 20% out of pocket; and 10% are paid for by Medicaid.

- Generic prescriptions are approx. 11% of total prescriptions by expenditure and 47% (2000) by volume. The latter has increased from 19% in 1994.

- There are about 100 PBMs, of which the top three process 45% of prescriptions processed by PMGs.

- Wholesale sector dominated by four firms that have 80% of market.

- There are 51,000 pharmacies, of which 21,000 are community, 21,000 part of a chain and 9,000 mass market (located in supermarkets).

4.1.4 Pricing

Pricing is complex and results from the segmentation of the market. Some prices are public but many are not. The main price categories are:

- Retail price: the price charged by retail pharmacist to individuals without insurance.

- Average Wholesale Price (AWP) is a publicly available price published by independent pricing services. It is an average of the suggested wholesale list prices used by national drug wholesalers. This price is typically marked up 20% to 25% by wholesalers above the manufacturer list price, or wholesale acquisition cost (WAC), for branded products. However, almost no one actually pays AWP price. AWP is established through a survey of the national wholesalers by the pricing services. This survey typically represents over two thirds of wholesaler total dollar volume for the product surveyed. Because individual wholesalers may mark up a product differently, price services may use a weighted average based on wholesaler market share, not a consensus average, to calculate AWP. Additionally, AWP forms the basis of much retail pricing and reimbursement.

- Average manufacture price (AMP): average price paid to a manufacturer by the retail class of trade (including wholesalers).

- Medicaid rebate: the effective out patient drug price represents the greater of 15.1% off AMP or AMP-BP (Best Price) offered in the marketplace after manufacturer rebate to state net price.

- Federal supply schedule (FSS): a list of products and prices that are available to federal organisations that purchase prescription drugs. These prices usually offer substantial discounts off market prices. FSS prices are publicly available.

- Non-Federal Average Manufacturer Price (Non-FAMP): the average price paid to a manufacturer by wholesalers for drugs distributed to non-federal purchasers. It is not publicly available.

- Federal Ceiling Price (FCP): the maximum price manufacturers can charge for FSS-listed brand-name drugs to federal agencies such as the Veterans Administration (VA) and the Department of Defence (DoD). FCP must be at least 24% lower than NFAMP. FCP is not publicly available.

- Federal national contract: the price VA and/or DoD obtain through competitive bids from manufacturers for selected drugs in exchange for inclusion in the VA formulary. Prices are publicly available.

4.1.5 Price Comparison to UK

Price comparison to UK at ex-manufacturer prices. UK = 100.

USA	1996	1997	1998	1999	2000	5 year average exchange rate
Bilateral	183	175	174	184	209	189
Multilateral	191	184	188	213	243	220

Source: PPRS 5th Report to Parliament

The USA prices do not take account of discounts offered in the market place and therefore in reality the difference between UK and USA is not as great as these indices suggest. As information on discounts is not publicly available a comparison on the basis of market prices is not possible.

4.2 Private – The Insured Sector

4.2.1 Health Plans

- There are a large number of health plans. The American Association of Health Plans alone has over 1000 members representing HMOs, PPOs (Preferred Provider Organisations), UROs (Utilization Review Organisations), and other network-based plans that provide care for over 100 million Americans nationwide.

- Most employers have health insurance as part of their employment package. The extent of choice and benefits available vary between employer and between health plans.

- Costs are rising in excess of inflation and provision of health insurance is becoming increasingly significant to employers. Many small and medium-size employers are considering decreasing the pharmacy benefit offered to employees, and some are either reducing or are considering limiting and/or discontinuing pharmacy benefits for retirees.

- Most insurance companies have formularies for the management of medicine provision. These are overseen by a Pharmacy & Therapeutics (P&T) committee with advice from the plan's PBM when it has one. The sophistication of formulary arrangements varies between insurers.

- Health plans generally admit NCEs when they come to market. When second and third entrants in the therapeutic category arrive P&T committees decide which product(s) should be in the plan's formulary.

- Compliance with each formulary by GPs is complicated by the number of plans and relatively poor use of IT by GPs. Litigation by patients where a specific medicine is requested by the patient and then not prescribed is also a factor.

- Most plans have some form of co-payment – typically $7-10 for a generic medicine, $15 for a brand medicine on the plan's formulary; and $20-35 for a branded medicine not in the plan's formulary. Some insurers are starting to introduce a fourth category for life style medicines and/or make co-payment a percentage of the price rather than a flat fee.

- Many plans have formally moved to a tiered pricing system as a way to manage drug spending and simultaneously offer more product choice to beneficiaries. In 2001, approx. 40% of all insured people were enrolled in tiered systems for pharmaceuticals. Generic products are generally on the first tier and have an approximate $7 copayment. Second-tier products generally have a $15 copayment, and third-tier products a $35 copayment. Some plans have more tiers. Life style products may not be reimbursed at all.

- In many states substitution of generic medicines for prescribed branded medicines is allowed by the pharmacist with the patient's permission.

4.2.2 Pharmacy Benefit Managers

- Pharmacy Benefit Managers (PBMs) handle the administrative functions of pharmacy benefit plans for Managed Care Organisations (MCOs). About 60% of all HMOs hire PBMs. A PBM may perform any or all of the following:
    - Create drug formularies;
    - Negotiate national contracts with pharmaceutical manufacturers to obtain drug discounts;
    - Negotiate with chain pharmacies to create preferred provider networks;
    - Reimburse pharmacies;
- PBMs originated from a need in the private primary care sector to improve the processing of prescriptions.
- Over time PBMs moved into the procurement of medicines obtaining discounts from manufacturers and pharmacies and into the operation of mail order supply. Most health plans require a lower payment of prescriptions, which are dispensed by mail order or e-commerce.
- The price paid to a retail pharmacy for a given drug is negotiated by the PBM and the pharmacy. Typically the PBM will take into account its estimate of the cost to the pharmacy of acquiring the drug and offer a dispensing fee above that amount. Because some PBMs cover a large share of the market, a pharmacy will often accept a price that is less than it would charge to cash customers. PBM payments to retail pharmacies for branded medicines are probably in the range of AWP minus a percentage plus a dispensing fee. For generic drugs the majority are reimbursed using limits known as the maximum allowable cost (MAC). These limits are established by PBMs based on the lowest estimated acquisition cost for any generic. MAC tends to be 50% to 60% below AWP. Because of HMOs increasing use of PBMs, the latter

have increasing leverage over pharmacies that are left with the option of refusing a large share of business, raising their prices for cash customers or reducing their operating margins.

- PBMs also obtain a negotiated rebate paid directly by the manufacturer to the PBM. It does not affect the price paid by a wholesaler or the retail pharmacist, but is a separate transaction between the PBM and manufacturer. A key factor in determining whether rebates are available and how large they are is the use of formularies. Manufacturers of branded products that treat conditions for which an alternative brand name treatment is available have a strong incentive to grant discounts to PBMs in return for inclusion of their drug in the formulary. If there are generic equivalents, larger rebates may be available. There is little data on the size of rebates but the HHS report quotes industry representatives as saying that rebates on selected drugs can be as much as 35%. PBMs that operate under contract to an insurer are required to pass on most of the rebates. In addition a PBM will often guarantee a minimum per prescription rebate in case actual manufacturer rebates received are lower than expected. PBMs may also receive further rebates from manufacturers in return for agreements with regard to the content of their communications with physicians about the use of certain drugs.

4.2.3 Private: Payment Out of Pocket

- This category covers those that do not have insurance coverage (estimated at some 40 million) and those on Medicare, which does not cover the cost of medicines. Non-insured individuals pay the retail price of medicines. Those covered by Medicare will also meet the full price unless they live in a State that has an assistance programme or purchase supplemental government insurance (Medigap) to cover prescriptions.

4.3 Regulated Sector

4.3.1 Pricing for Federal Facilities and Agencies

- Federal departments and agencies, and other federal agencies are able to purchase prescription drugs at substantially lower prices than many other purchasers. Prices paid to these entities are set by the Federal Supply Schedule (FSS). Under the Veterans Health Care Act 1992, manufacturers must make drugs available to organisations covered by the FSS as a condition of eligibility for

Medicaid reimbursement. Thus, although manufacturers are not required to list their drugs on the FSS, they have a financial incentive to do so because Medicaid accounts for approximately 10% of US drug sales.

- FSS prices are negotiated with manufacturers by the VA. Generally they may be no higher than the lowest contractual price charged by the manufacturer to any non-federal purchaser under similar terms and conditions. To determine this price, manufacturers supply the VA with information on price discounts. According to the US General Accounting Office (in 1997), average FSS prices are more than 50% below the published catalogue prices. For certain drugs (branded name drugs without competition or innovator multiple source drugs) the manufacturer must charge the lesser of the FSS or a 'federal ceiling price'. This is set at 76% of the non-Federal average manufacturers' price. The FCP may be higher or lower than the FSS.

- The VA also tenders for some drugs and has been able to obtain prices lower than FSS prices. It contracts following competitive bids, with manufacturers for products that are therapeutically equivalent, on the basis of those that provide best value, based on medical effectiveness and price. In exchange these products are included in the VA's national formulary and used throughout the VA's health care system.

4.3.2 Pricing for Medicaid Programmes

- Medicaid programmes pay retail pharmacies using fixed cost limits and fixed dispensing fees. For single-source drugs reimbursement is based on a calculation that includes AWP. For multiple-source drugs the limit is based on a maximum allowable cost (MAC) – similar to the MAC principle used by PBMs. The Medicaid MACs are published every 6 months and are set at 150% of the lowest published price for any equivalent drug, plus a dispensing fee.

- Medicaid programmes must also by law receive rebates from manufacturers. For single source drugs and 'innovator multiple source drugs' the rebate must equal the difference between the average manufacturer price (the average price paid by wholesalers) and the manufacturers' best price (the lowest price offered by the manufacturer during the year, excluding federal and disproportionate share hospital (DSH) sales). The minimum

rebate is 15.1% of the AMP. For non-innovator multiple source drugs, the rebate is 11% and the best price arrangement does not apply. The rebates are paid to the state Medicaid agencies following the submission of confidential information by each manufacturer to Centers for Medicare and Medicaid Services (CMS-formerly 'HCFA').

4.4 Hospital Sector

- More frequently used medicines are purchased through wholesalers, and others are procured directly from manufacturers. Hospitals frequently join together as purchasing consortia to maximise purchasing power. Each hospital has a formulary and there is strong competition for medicines to be included or remain in each formulary. Very significant discounts are common.

4.5 Recent U.S Research on Competitive Pricing Environment

Attached at Appendix 1 is a summary of recent (as yet unpublished) research undertaken by Professor Danzon which provides evidence on the degree of discounting off wholesale invoiced prices in the US market.

The analysis undertakes to explain discounts in the most price sensitive part of the private insurance market (i.e. the sub market dominated by HMOs and PBMs).

Using information on Best Contract Price (BCP), which as noted above, is not normally in the public domain, the research looked at the impact of competition on discounts from Wholesale Acquisition Cost (WAC).

The study found evidence that discounts were positively related to the number of competing molecules in a therapy class; off-patent products facing generic competition had significantly lower prices than in-patent products; higher Medicaid market share reduces discounts as the 'best price' rule reduces the incentive to reduce discounts offered to private buyers**.**

However, these findings should be put in the context of the competitive environment engendered by HMOs and PBMs. Other parts of the private market will not obtain such large discounts as they are not as price sensitive.

Appendix 1

Price Competition between brands in the U.S. Pharmaceutical Industry: Empirical Evidence[1,2]

1. Structural Determinants of Competition

A traditionally price-insensitive market for drugs has changed in recent years due to the growth of managed pharmacy benefits and the growth of generic competition. There have been three major changes in the market.

Managed Pharmacy Benefits

Here drug coverage can be either managed directly by HMOs or (more commonly) contracted out to pharmacy benefit managers (PBMs). The objective is to negotiate lower prices and make physicians and patients more cost-conscious and hence control overall drug expenditures, in addition to monitoring quality, drug interactions etc. Key features are that the PBM establishes a formulary of preferred drugs, which are selected based on price and efficacy; non-preferred drugs are either not reimbursed (closed formularies) or require a higher patient co-payment than preferred drugs (tiered formularies). Preferred drugs tend to gain market share relative to non-preferred drugs, because they carry lower co-payments for patients and because physicians are encouraged to use preferred drugs. This ability of PBMs to move market share towards preferred drugs enables the PBM to negotiate discounts from drug manufacturers.

Generic Competition

The second recent stimulus to price competition in the US pharmaceutical market is statutory and other changes that have encouraged generic competition. All states have adopted generic substitution laws that authorize pharmacists to dispense a generic in place of the brand, unless the physician specifically notes "brand required." A further stimulus to price competition in the off-patent sector results from the widespread use of a form of reimbursement that is

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[1] Patricia M. Danzon, Michael F. Furukawa. The Wharton School, University of Pennsylvania

[2] The research reported here is supported by a grant from Merck & Co. Inc. to the University of Pennsylvania.

equivalent to generic referencing, although not called reference pricing. Specifically, in the late 1980s and 1990s most HMOs, PBMs and Medicaid programs adopted "maximum allowable cost" (MAC) reimbursement for off-patent products. The MAC is the fixed reimbursement that the plan pays to the pharmacy for an off-patent drug, regardless of the actual price of the drug dispensed. The MAC is usually set at the price of low-priced generic. If the patient wants the brand, he or she must pay the difference. Thus MAC programs create strong incentives for patients to be price-sensitive in their choice between brands and generics, and very strong incentives for pharmacies to be price sensitive in their choice of which generic to dispense. This in turn creates strong incentives for generic manufacturers to compete on price.

Medicaid Best Price

Price competition between on-patent drugs in the form of discounts to PBMs and other private purchasers has been constrained by the federal requirement (OBRA 1990) that manufacturers give to Medicaid and certain other public payers the "best price" given to any private buyer or a 15.1 percent discount off the average manufacturer price (AMP), whichever is lower. This applies to all originator products, both on and off-patent. Generics are required to give a flat 11 percent discount to Medicaid, with no best price provision.

The effect of the best price provision for branded products has been to reduce incentives for competitive discounting to private purchasers. The Medicaid best price requirement has the effect of tying a large and relatively price inelastic market segment to the more price-elastic private market segment. The predicted effect is to reduce discounts given to private buyers, which in fact occurred. (CBO 1993; GAO, 1994)

2. Predictions

Price competition is more likely, the greater the number of competitors in the market. One focus is on therapeutic substitutes, which compete on list price to all customers and on discounts off list price to PBMs, HMOs and other customers that use formularies, such as federal and non-federal hospitals. We predict that competition is even more intense for off-patent products, because for these the primary customer is the pharmacist who has strong financial incentives to dispense the lower priced generics, due to MAC reimbursement.

Theory predicts that the best price provision could act as a floor on discounts at the mandated minimum discount, depending on the size and elasticity of demand in the non-Medicaid market relative to the Medicaid market.[3] Thus in general, discounts are less likely, the larger the Medicaid share of sales.

3. Data: Best Contract Price (BCP) Dataset

For a limited period of time, a publicly available website published data on the best price discounts available to Medicaid for a sample of leading products. This sample included 81 single source, branded products, that is, originator products that face competition only from other on-patent originator products but not from generics, and an additional 51 off-patent products. We use these data to analyze the effect of competition on best prices and on percentage discounts. We analyze actual prices because payers, patients and manufacturers are concerned about the final price, regardless of how this was achieved through a combination of list price and discount off list. We also analyze percent discounts off wholesale average cost (WAC) to test the hypothesis that discounts are inversely related to Medicaid share of sales.

Variables

Price — measured as price per standard unit (which is a proxy for a dose). We use two measures of price:

- Best Contract Price (BCP) – the lowest reported price given to customers and reported to the HRSA under the 340b program.

- Ex-manufacturer price – represents the average wholesaler acquisition cost (WAC) based on the IMS audit of invoices, and does not reflect "off-invoice" discounts given in the form of rebates and chargebacks.

Discount:

- Discount off WAC – the percentage discount off the wholesaler acquisition cost for the BCP, calculated as (WAC – BCP) / WAC.

[3] With the best price provision, the manufacturer would rationally consider the volume-weighted average demand elasticity over the private and Medicaid sectors.

Therapeutic substitutes—the number of therapeutically-similar molecules within the same therapeutic/pharmacologic subgroup, based on the third level of the IMS Anatomical Therapeutic Classification system (ATC3). The current measure is based on our sample of the leading 249 molecules in the US market, by volume of units. This sample accounts for over 60 percent of sales in the US. It includes the major competitors but understates the total number of therapeutic substitute molecules. Such measurement error in explanatory variables generally biases coefficient estimates towards zero; if so, the estimates here may underestimate the effect of number of competitors.

Generic availability indicator—dummy variable indicating the availability of a generically-equivalent version of the molecule.

Generic competitors—the number of manufacturers selling generically-equivalent versions of the molecule.

Molecule age—the number of months since launch of the molecule (active ingredient) in the U.S.

Medicaid share—the share of new prescriptions filled by Medicaid consumers relative to Cash and Third-party. Data were only available at the product level and represent the average share across all manufacturers in the molecule.

4. Results

Table 1 reports multivariate analysis for price and discount, both measured in logs. The first equation for each dependent variable includes the full sample of products, the second equation includes only single source (presumably on-patent) products.

Best Contract Prices (i.e. after discounts) are significantly negatively related to the number of therapeutic substitute molecules.

For single source products, a doubling of the number of competitors leads to a 56 percent reduction in price (elasticity of – 0.556)

For the full sample, which includes some generic products, the elasticity is slightly lower (-0.430), prices for products with generic competition are significantly lower than prices for on-patent products.

Discounts off list price (the latter measured by WAC) are positively related to number of competitors.

For single source products, a doubling of the number of competitors leads to a 28 percent increase in the discount off list price (elasticity of –0.28).

Medicaid share tends to reduce discounts off list prices, but is unrelated to Best Contract Price. This could be reconciled if list prices are lower for products with high Medicaid shares. This is the subject of ongoing research.

Table 1: Best Price (340b) Regressions

Sample:	All	Single source	All	Single source
Dependent variable:	(ln) Price	(ln) Price	(ln) Discount	(ln) Discount
Explanatory variables:	Estimate (t-stat)	Estimate (t-stat)	Estimate (t-stat)	Estimate (t-stat)
Intercept	2.758	1.956	-1.414	-1.409
	(2.26)**	(2.21)**	(-3.62)***	(-3.61)***
(ln) # Therapeutic - substitutes	0.430	-0.556	0.196	0.284
	(-2.38)**	(-3.16)***	(3.39)***	(3.66)***
Generic availability indicator	-2.444		0.679	
	(-5.57)***		(4.82)***	
(ln) Molecule age	-0.433	-0.196	-0.011	-0.044
	(-1.67)*	(-1.08)	(-0.14)	(-0.55)
Medicaid share	1.142	1.165	-1.188	-1.327
	(0.77)	(0.83)	(-2.50)**	(-2.15)**
N:	132	81	132	81
Adjusted R-squared:	0.502	0.090	0.324	0.134
***Significant at the .01 level				
**Significant at the .05 level				
*Significant at the .10 level				

Appendices:

Terms of Reference

Glossary

December 2002

Appendix 1

Terms of Reference

Pharmaceutical Price Regulation Scheme (PPRS)

The Study into the Extent of Competition in the Supply Of Branded Medicines to the NHS

Project Outline

Background

The 1999 PPRS specifies that the Department and the ABPI are agreed that an assessment of the scope, pace of change and practical impact of competition in the supply and use of medicines for NHS should be undertaken. The details of the arrangements for this assessment are to be agreed by March 2000. The results will inform the PPRS mid-term review should either side request this no earlier than April 2002.

Components of the study

The main components of the project are set out below.

Component 1: Performance Management Framework

To establish a set of key indicators aimed at monitoring the conditions for an efficient and competitive pharmaceuticals market. This will focus on demand side measures, but will also include indicators for the areas covered by other components. The list of indicators will be developed in consultation, but will need to cover where relevant Primary Care Groups, NICE, and CHIMP. Full use will be made of information already being collected by the Department. These indicators will provide a 'baseline' for assessing progress over the period of the new PPRS scheme. DH will be mainly responsible for the completion of this work.

Component 2: Competition in the in-patent sector

A scoping exercise has been undertaken providing an initial overview of competition in the pharmaceuticals market. This examined:

- the size and growth of different sub-markets concentrating on the top 40 or so classes, which account for around 80% of sales, and others considered relevant to understanding the full picture;
- numbers of competitor companies and products, market shares, and changes in market shares over time (including entry/exits) for each of the leading classes;
- price dynamics between products.

This material was presented to a Peer Review Workshop in November 1999, which considered the available evidence and made recommendations for a more detailed analysis of the extent of competition.

Taking these recommendations into account, the Department and the ABPI will jointly agree a methodology for selecting and analysing sub-markets for closer investigation, covering a range of market conditions. This analysis, based on the agreed approach, will be contracted out to one or more independent consultants.

The specification for the work will be developed through the initial stages of Component 2, but is likely to cover:

- an overview of each market, identifying close substitutes and 'grey areas' (where there are links between product classes, even though they may not be direct substitutes);
- substitutability between products in each market, in particular, whether changes in relative prices lead to (or would be expected to lead to) significant changes in demand for these products;
- price differences between competing products and whether these reflect prescribers' perceptions of relative price differences;
- timing and impact of new products entering these markets, including, whether originator products appear to hold a significant first mover advantage (e.g. because of inertia created by repeat prescribing of a product);

- an understanding of whether prices are at competitive levels, taking account of the need for companies to achieve a return on investment in R&D over the life cycle of a product portfolio.

The Department and ABPI will agree a specification for a project that will be contracted out to a third party. The contractor will have relevant experience, for example, in competition economics. The arrangement will provide objectivity while still allowing judgement to be exercised by the Department and ABPI on the meaning of the findings.

Component 3: Out-of-patent sector analysis

To chart the speed of availability and penetration of generics for products that have recently come off patent or which come off patent during the new scheme. It will look at:

- information on those products due to expire during the new scheme;

- whether/how long before generics enter the market, particularly for the more significant products;

- fall in market share and/or price of branded products, including calculation of a sales-weighted post-patent price index;

- assessment of 'barriers to entry' where generic entry does not occur or is slow.

This work will be carried out by DH and ABPI although both parties may carry out work in this area independently. The detailed terms of reference for this work will be drawn up to complement the review by the Oxford Economic Research Associates Ltd (OXERA) announced by Ministers to the Health Committee on 4 November 1999.

Component 4: Demand-side effectiveness

To assess the effectiveness of the demand side, in particular the price sensitivity of prescribers, and feed into the assessment of relevant markets (see Component 2). The first stage will examine prescribers' awareness of price and quality and it will cover:

- prescribers' price awareness, including how quickly perceptions respond following price changes;

- prescribers' perceptions of quality, including consistency with the reviews of evidence by NICE (and/or other pharmacological evidence);

- factors prescribers take into account in making prescribing decisions, in particular the weight they attach to price as against other factors and their willingness to switch patients.

Some of this work has already been commissioned by ABPI following discussion with DH.

Stage 2 will examine actual prescribing behaviour as an overall check on the effectiveness of the demand and supply sides of the market and will include analysis of:

- how sensitive prescribing behaviour is to price changes, for example following modulation, whether the "elasticity" of demand varies between prescribers and/or between products and treatment strategies;

- trends in generic prescribing levels.

This work will be undertaken by DH and the ABPI, with some external contract work.

Component 5: International perspective

Prices in other countries are often compared with prices in the UK. DH already carries out an analysis of UK prices against prices in ten countries for a 'basket' of products. This analysis will continue, and be supplemented by increasing understanding of the impact on these price comparisons of exchange rate movements and of pharmaceutical policy implementation in other countries.

An additional study will be established to monitor the prices of future new products (and spending thereon). This will involve both a comparison of UK launch prices against those in other countries and, where possible, the spending on new products against these in other countries, so the relationship between prices and volumes can be more readily understood.

Both DH and the ABPI will undertake co-ordinated work in this area.

Component 6: Hospital sector

This component will seek to improve understanding of the supply/demand of pharmaceuticals to the hospital sector, and whether there are important links to the community sector. Key issues are:

- the balance of hospital sales between products that are predominantly sold to hospitals and those sold predominantly to the community;

- assessment of the competitiveness of the market for those products that are predominantly sold to hospitals, including number of potential suppliers and the efficiency of the procurement process;

- comparison between discounted prices in hospitals and the community for products sold predominantly to the community sector.

This work will be undertaken by DH and ABPI.

Component 7: Experience of less regulation.

To examine the experience of less regulated markets in the US (and possibly elsewhere such as Germany) to see if there are any lessons for the UK. This will focus on:

- level and growth of prices in a less regulated environment, adjusted for other factors;

- evidence that competition does constrain prices at reasonable levels across the market as a whole;

- other effects of deregulation, for example on innovation.

It will be undertaken principally by means of a literature study and would be an external contract.

For each of the above components the study will take into account changes in the structure of the pharmaceutical market as they may affect the supply of medicines to the NHS and any amendments or developments to Government policy and management arrangements for the NHS that may occur during the course of the current PPRS agreement.

March 2000

Appendix 2

Glossary

ABAG	Arzneimittelbudget-Ablösungsgesetz
ABPI	Association of the British Pharmaceutical Industry
ACD	Advisory Committee on NHS Drugs
ACE	Angiotensin-Converting Enzyme
AFR	Annual Financial Return
AMP	Average Manufacture Price
ASTRO-PU	Age, sex and temporary resident originated prescribing unit (Units of prescribing adjusted for the age, sex and other characteristics of the population)
ATC	Anatomical Therapeutic Class
AWP	Average Wholesale Price
BAEPD	British Association of European Pharmaceutical Distributors
BAI	Breath Actuated Inhaler
BCP	Best Contract Price
BNF	British National Formulary
CBO	Congressional Budget Office
CEO	Chief Executive Officer
CFC	Chloro Fluoro Carbon
CHD	Coronary Heart Disease
CHE	Centre for Health Economics
CHIMP	Commission for Health Improvement
CIA	Calcium antagonists
CMS	Centres for Medicare and Medicaid Services (formerly HCFA)
Cox	Cyclooxygenase
CR	Concentration ratio
DDD	Defined Daily Dose
DH	Department of Health, also referred to as "the Department"
DoD	Department of Defence
DRG	Diagnosis Related Group
DSH	Disproportionate Share Hospital
D&TC	Drug and Therapeutics Committee
DT	Drug Tariff
EER	Europe Economics Research
EU	European Union
FBAG	Festbetragsanpassungsgesetz
FCP	Federal Ceiling Price
FHSA	Family Health Service Authority

FSS	Federal Supply Schedule
GAO	General Accounting Office
GKV	Gesetzliche Krankenversicherung
GP	General Practitioner
GPRD	General Practice Research Database
HA	Health Authority
HCFA	Health Care Financing Administration (now called CMS)
HMG CoA	3-hydroxy-3-methylglutaryl co-enzyme A
HMO	Health Maintenance Organisation
HRT	Hormone Replacement Therapy
HSC	Health Service Circular
IMS	Intercontinental Marketing Services
LLS	Lipid Lowering Statins
MAC	Maximum Allowable Cost
MAOI	Monoamine Oxidase Inhibitor
MCA	Medicines Control Agency
MCOs	Managed Care Organisations
MDI	Metered Dose Inhaler
MIMS	Monthly Index of Medical Specialities
MR	Modified Release
N/A	Not Appropriate
NAS	New Active Substance
NCE	New Chemical Entity
NHS	National Health Service
NIC	Net Ingredient Cost
NICE	National Institute for Clinical Excellence
Non-FAMP	Non-Federal Average Manufacture Price
NSAID	Non-Steroidal Anti-Inflammatory Drug
NSF	National Service Framework
OFT	Office of Fair Trading
OTC	Over The Counter
PASA	Purchasing and Supply Agency
PBM	Pharmacy Benefit Manager
PCA	Prescription Cost Analysis. (Data for England, community only)
PCG	Primary Care Group
PCO	Primary Care Organisation
PCT	Primary Care Trust
PICTF	Pharmaceutical Industry Competitiveness Task Force
PPA	Prescription Pricing Authority
PPI	Proton Pump Inhibitor
PPO	Preferred Providers Organisation
PPRS	Pharmaceutical Price regulation Scheme
P&T	Pharmacy & Therapeutics

PU	Prescription Unit
QPP	Quantity per Prescription
R&D	Research and Development
ROC	Return on Capital
ROS	Return on Sales
RP	Reference Price
ScHARR	School of Health and Related Research
SHEG	Sheffield Health Economics Group
SPC	Supplementary Protection Certificate
SSRI	Specific Serotonin Reuptake Inhibitors
SU	Standard Unit
UK	United Kingdom
URO	Utilisation Review Organisation
VA	Veterans Administration
WAC	Wholesale Acquisition Cost
WHO	World Health Organisation
WTE	Whole Time Equivalent
VAT	Value Added Tax

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Copies are available from:
Department of Health
Pricing and Supply Branch
Room 130
Richmond House
79, Whitehall
London SW1A 2NS
Telephone: 020 7210 5655
or email Anna.Jean@doh.gsi.gov.uk