Executive Summary

Patient outcomes have improved over the past ten years in some major disease areas such as cancer and cardiovascular disease. Reasons for this include strong national leadership with clear linkages being made between different policies and mechanisms designed to improve service delivery, patient care and use of medicines resulting in stronger local implementation. However, adoption of innovation in the UK is slow and low relative to other countries in important areas of public health. We have identified a number of factors which have an influence - both positive and negative - on the diffusion of innovation in the NHS which if addressed would help to energise the system to adopt innovative medicines as benchmarked by other European countries.

All factors identified lead us to an over-arching view that the current system of managing NHS medicines expenditure is no longer fit for purpose, largely because it focuses on medicines as a discrete (and very easily targeted) cost, rather than as a resource to improve the quality of NHS care and patients’ lives, as well as to save overall system costs.

Medicines managers and prescribing advisers are medicines experts and a valuable resource to the NHS but they are not consistently integral to the commissioning process and many are tasked to reduce medicines expenditure rather than support the delivery of productivity savings across the whole care pathway. Local reactions to QIPP appear to be reinforcing this approach rather than freeing up the innovative, whole-system thinking that is required to deliver £20 billion of productivity savings whilst maintaining or improving the quality of NHS care.

Recommendation Number One:

EMG believes that there needs to be a radical review of how medicines are managed across the NHS, including how the entry of new medicines is managed and how medicines managers are effectively utilised to champion high quality prescribing and good husbandry of overall system resources. This would include the setting (and implementation) of national standards for medicines evaluation and funding, together with rationalisation of the many layers of decision-making that currently exist.

NICE guidance combined with the mandatory funding direction for technology appraisals has undoubtedly accelerated uptake of some innovative medicines, although implementation is by no means consistent throughout the NHS, with many organisation introducing local restrictions and interpretations which limit uptake, as we illustrate in our evidence. The collection of data on uptake of medicines (by the NHS Information Centre giving comparisons across England and by the Department of Health, under Sir Mike Richards, giving comparisons with other health systems across the world) has provided a much clearer picture on our adoption of innovative medicines. Measures need to be introduced to provide patients with a firmer guarantee of access to medicines approved by NICE, to which they are entitled under the NHS Constitution, and to provide recourse for patients denied access. The lack of mandatory funding with
clinical guidelines enables local organisations to view adoption of treatments advocated in guidelines as discretionary.

**Recommendation Number Two:**

**EMG believes that implementation of NICE guidance should be strengthened by incorporating it into commissioning frameworks as part of the care pathway, supported by aligned incentives, backed by regular collection and publication of data on uptake of medicines, and creation of a mechanism that gives patients the right of recourse on decisions about their access to treatment.**

The approach of delivering quality and value across the system as a whole and along the patient pathway underpins best practice in commissioning. The NHS Commissioning Board will seek to promote this approach and has the potential to dramatically improve adoption and diffusion of innovative medicines as benchmarked by other European countries.

**Recommendation Number Three:**

**EMG believes that the pharmaceutical industry should be recognised as an equal partner in delivering best practice commissioning and should be represented on the NHS Commissioning Board. SHA Clusters and local organisations with commissioning responsibility should be required to have specific accountability for the adoption of innovation, backed by comparative data to illustrate performance, and including mature engagement with the pharmaceutical industry.**

We give further substance to these recommendations in the answers to Q2 below.
Introduction

The European Medicines Group (EMG) is fully supportive of this review and values highly the opportunity to submit evidence. Our focus will be on the adoption of innovative medicines by the NHS. We have compiled this evidence submission through a series of interviews with our members. Some very consistent themes have emerged on good and bad practice relating to NHS adoption of medicines innovation. We bring out these themes below using examples to illustrate the points made and have suggested solutions to address the issues raised.

The EMG is the UK voice of research-driven pharmaceutical companies headquartered in Continental Europe which develop and supply prescription medicines to the NHS. The EMG was launched in 2001 and currently has 16 members, many of whom are leaders in their field, producing treatments which tackle conditions like cancer, cardiovascular diseases, diabetes, neurological disorders such as epilepsy, Parkinson’s disease and dementia, and severe immunological disorders. Between them, our members employ over 13,000 people and invest more than £500m in Research and Development in the UK every year. We work alongside the ABPI although we are not part of the organisation; some but not all of our group are members of the ABPI. During the 10 years that the EMG has been in existence, we have focused closely on patients’ access to, and NHS uptake of, innovative medicines and so are in a good position to give insights from the perspectives of both policy and the operational realities of introducing medicines into the NHS.

The UK is generally a low and slow adopter of modern medicines compared with equivalent health systems in Europe. The Richards report1 ‘Extent and causes of international variations in drug usage’ (2010) cited HTA, service planning, organisation and direction setting, and clinical culture as key determinants of the level of prescribing in England, and comparisons with other health systems showed relatively low UK uptake of innovative medicines in important areas of public health.

Medicines are an essential part of the delivery of high quality NHS care. The appropriate use of modern medicines will play an important part in delivering the outcomes that the NHS wishes to achieve and the length and quality of life that patients wish to enjoy. Medicines represent about £1 in every £10 of NHS expenditure and many contribute to major savings in hospital care, which is the most expensive element of the health service, for example through reducing the incidence of many life-threatening and debilitating complications of long term conditions. The pharmaceutical industry is being challenged to deliver value to the NHS and to demonstrate how that value can be realised, a challenge that we fully recognise and are engaging with. The system as it stands, however, is unable to fully realise the value of our medicines and the skills and resources that industry can bring to support the NHS.

Our evidence is given below in sections according to the questions posed in the call for evidence:

- An overall commentary on the processes used by the NHS to decide on adoption of innovative medicines
- Learnings (both positive and negative) from experience of the adoption and spread of innovation
- Recommended actions for the NHS Commissioning Board, other national bodies, local NHS organisations, and industry


**Medicines Decision-Making in the NHS**

The factors affecting decisions by NHS organisations on what medicines will be made available to patients are extremely complex and often vary from one locality to another. The ultimate expression of that decision-making is the local formulary. Whilst clinicians retain the freedom to prescribe whatever medicines they believe suit their patients best, there are a broad range of mechanisms that restrict that freedom, involving a complex web of influences from overarching national policy and guidance, to mechanistic system levers, to local processes and the attitudes and behaviours of the individuals involved in prescribing and funding decisions. The schematic below is an attempt to illustrate this web. Our evidence below will set out how many of these factors are working, either individually or together, against adoption of medicines innovation.

**Factors affecting Access to Medicines**

[Diagram of factors affecting access to medicines, including national priorities, local factors, formularies, levers, and people & behaviours.]

European Medicines Group response to the call for evidence to the NHS Chief Executive Innovation Review. August 2011
Q1. Learning about Adoption and Spread of Innovation

1.1 Positive experience

NICE

The combination of positive NICE guidance and the mandatory funding direction to implement it has undoubtedly enabled uptake of some innovative medicines more quickly than might otherwise have been the case. Whilst there is a case that NICE has recommended against the use of many medicines in the NHS that are readily available to patients in other health systems, and that much of its guidance restricts use within the product licence, where it is positive and accompanied by mandatory funding it has accelerated adoption of innovation in an NHS that would otherwise have been slow to respond.

The mandatory funding support for NICE technology appraisal guidance has proved essential, however, to stimulating adoption of innovation. In the case of NICE clinical guidelines, for example, where there is no mandatory element, adoption of treatments advocated by NICE is largely viewed as discretionary.

It must not be assumed, however, that mandatory funding is synonymous with 100% uptake and implementation. As we shall see from some of the examples below, many organisations put their own local restrictions and interpretations on it in order to limit uptake.

Data collection on uptake of medicines

The Government has published some very useful data on uptake of medicines. The Richards report 'Extent and causes of international variations in drug usage' (2010) was a comprehensive analysis of international variations covering medicines in 14 different categories across 14 different countries and showed that the UK ranked highly in the use of medicines in three disease areas, but low in new cancer medicines, dementia, hepatitis C, multiple sclerosis, rheumatoid arthritis and second-generation antipsychotics. The Information Centre’s second experimental analysis of uptake in England of NICE-recommended treatments, Use of NICE-appraised medicines in the NHS in England - 2009, Experimental statistics, looked at 47 medicines in 18 groups relating to 29 technology appraisals. Analyses of local practice showed major variations in uptake of NICE-approved medicines.

These analyses provide some welcome, thorough and transparent data on uptake of medicines by the NHS and are a potentially valuable resource for managers at all tiers in the health system to understand and assess their relative performance.

Cancer Drugs Fund

Set up partly to address the deficiencies of the NICE methodology to assess the clinical and cost effectiveness of cancer medicines and partly to bridge the gap between availability of cancer medicines in the UK compared with other health systems in Europe, the dedicated funding provided in the Cancer Drugs Fund has enabled access to and uptake of cancer medicines that would otherwise have been denied. Management of the Fund has varied hugely across the country, with use of the money allocated to the Interim Fund after six months ranging from 25% to 100% (a reflection of the effectiveness of local decision-making processes). Overall, adoption of innovation has been benefited by the Fund. However, we believe that the Fund is a short term measure and that a sustainable solution to the issues which the Fund seeks to address, such as the NICE methodology not being appropriate for oncology medicines, is necessary.

Clinical Trials

It is generally acknowledged that, where clinical trials are conducted in the UK, NHS uptake of the medicine concerned is accelerated. Clinical trials are essential to fuelling the engine of medicines innovation in the NHS: they not only provide early access to new treatments for patients, but also give
NHS clinicians the opportunity to work with the latest developments in their fields, increasing their expertise and keeping them and their employers at the forefront of modern medical practice.

The Government and NHS are making efforts to reverse the decline in pharmaceutical industry investment in clinical trials in the UK and we applaud these efforts.

The EMG will be submitting a supplementary evidence paper specific to this issue in the near future.

Patient Access Schemes

The introduction in the PPRS of 2009 of Patient Access Schemes (along with flexible pricing) as a pragmatic and systematised mechanism to improve the value of new medicines has enabled patient access to medicines in serious conditions such as rheumatoid arthritis, cancer and macular degeneration that would otherwise not have been recommended by NICE. The system allows companies to propose a scheme that is designed according to the specific clinical and economic circumstances of the medicine and the condition it treats. Much has been learned about the design of these schemes over time, with a welcome trend to greater simplicity and respect for commercially confidential information. Thousands of patients have benefited and the international standing of the UK as a market more open to the adoption of innovative medicines has been enhanced amongst global company decision-makers.

1.2 Barriers to adoption of innovative medicines and examples of real world experience

The following paragraphs set out the recurring issues that have been reported by our members, with examples to illustrate the points made and demonstrate how uptake of innovative medicines is being impaired by the system. Our aim here is to bring to life the challenges faced by companies in bringing innovative medicines to patients, with a view to working with Government and the NHS to find solutions that benefit patients, the NHS and the pharmaceutical industry. Solutions are suggested below.

Cost effectiveness, cost, budget impact or affordability?

There is no consensus or shared understanding across the NHS, at national or local level, as to what constitutes value for money and how decisions are taken with regard to funding for medicines. Different parts of the system are working to different parameters: NICE is the recognised national authority on guidance in the use of medicines and evaluates a medicine’s impact on health, quality of life and health and social care costs using strict definitions of effectiveness and cost effectiveness and a cost per quality of life year (QALY) gained as its measure of value. Local NHS organisations generally do some analysis of evidence of efficacy, safety and cost, and the focus is more on relative cost and budget impact, usually within the limitation of a discrete medicines budget. Our experience also suggests that considerations of the patient-experience, health-economy-wide or longer-term benefits of the medicine are frequently secondary to straight cost considerations.

These opposing forces present often insuperable barriers to adoption of valuable innovation.

Local interpretation of NICE guidance

By law, funding for medicines approved as a cost effective use of NHS resources by NICE in its Single or Multiple Technology Appraisal process is mandatory within a 90-day period from the publication of guidance. The NHS Constitution gives a commitment that patients are entitled to NICE-approved medicines and NICE clearly sets out the conditions under which the medicine should be used cost effectively.
Yet there are many instances where local NHS organisations, in efforts to save money, have put further conditions on the use of the medicine beyond those outlined by NICE, slowing down or preventing their use.

**Introducing complex internal processes before NICE guidance can be implemented**

Ebixa (memantine, Lundbeck) was approved by NICE in March 2011\(^6\), with mandatory funding coming into operation by the end of June 2011. NICE guidance states that Ebixa is recommended for patients with moderate Alzheimer’s disease, who are intolerant or have a contraindication to acetyl cholinesterase inhibitors, or with severe Alzheimer’s disease, with treatment to be initiated by a specialist. Yet some local organisations have continued since June 2011 to put in place significant hurdles before releasing funding. In one example the local PCT refused to authorise a shared care protocol, so a process was introduced whereby Consultants had to gain funding approval by completing a form, which was sent to the Chief Pharmacist and then reviewed by an approval panel which included two local consultants. (This process has recently been removed to allow appropriate access to Ebixa following discussions with Lundbeck.) In another example a hospital pharmacist prepared a 12-page business case for approval by commissioners to justify the generation of a shared care protocol. Time will be taken to approve this and develop the protocol, further delaying the implementation of national guidance. Similar behaviour is being seen in other localities which are now well beyond the 90 day statutory period.

**Additional local restrictions on use of medicines beyond those specified by NICE**

Multaq (dronedarone, Sanofi) was the first new medicine for atrial fibrillation (AF) for 20 years. It is indicated for adult patients with a history of, or current non-permanent, AF to prevent recurrence of AF or to lower ventricular rate. AF is the most common heart rhythm disorder and occurs in 1-2% of people. It significantly increases a person’s risk of cardiovascular morbidity and mortality, which are an expensive drain on NHS resources, especially in secondary care.

NICE guidance for Multaq\(^7\), issued in 2010, recommended its use, with a cost per QALY of less than £10,000, and showed that use of Multaq would reduce hospital admissions. Yet, at the end of the 90 day statutory period when NICE guidance was supposed to have been fully implemented, one in four eligible patients was denied funding\(^8\). 70% of the guidelines developed by local organisations had restricted prescribing to Cardiologists and Electrophysiologists\(^9\) (even though 40% of patients do not see a Cardiologist).

‘Red lighting’ is common and causes further delays due to local opinion and re-examination of NICE guidance. For example, Cambridgeshire Joint Prescribing Committee\(^10\) stated ‘*The relative effectiveness and cost-effectiveness of dronedarone versus amiodarone remains subject to a number of areas of uncertainty in terms of informing current NHS practice. Will not be funded until implementation plans agreed.*’
One of the original objectives of NICE was to promote innovation and in many cases it has supported faster uptake of new medicines. However, local NHS organisations appear to be spending considerable resource in further interpreting NICE guidance. Importantly, there is little transparency on the costs of this bureaucracy, which directly contributes to slowing the uptake of new medicines and calls into question whether the original objective of NICE will be met.

NHS organisations clearly feel it is legitimate to spend resource on re-interpretation and review of NICE guidance: a reason for this may be that there appears to be little recourse where there is a failure to implement the mandatory funding direction.

Black and red lists

Victoza (liraglutide, Novo Nordisk) is a highly innovative treatment for Type 2 diabetes. As a long-acting glucagon-like peptide-1 (GLP-1) analogue, it represents a new way of treating Type 2 diabetes, and was recommended by NICE in September 2010\textsuperscript{11}, with mandatory funding coming into operation at the end of December 2010. NICE guidance states that Victoza is recommended as an option for the treatment of people with type 2 diabetes under particular conditions: if the person is intolerant of either metformin or a sulphonylurea, or treatment with metformin or a sulphonylurea is contraindicated, and the person is intolerant of thiazolidinediones and dipeptidyl peptidase-4 (DPP-4) inhibitors, or treatment with thiazolidinediones and DPP-4 inhibitors is contraindicated. Yet in Buckinghamshire\textsuperscript{12}, it is black-listed as ‘awaiting application’, and in Cambridgeshire\textsuperscript{10} it is red-listed for hospital use only. Both the Mid-Essex\textsuperscript{13} formulary and the draft Greater Manchester formulary\textsuperscript{14} list it as second choice to exanetide, which has no NICE technology appraisal guidance and is not subject to the mandatory funding direction.
Multiple layers of decision-making

The schematic on page 4 above shows the complexity of the decision-making processes for NHS medicines use and funding.

The complex decision-making matrix

The adoption of innovative medicines is subject to an array of evaluations and decision-making processes which will involve a combination of the following:

- Appraisal by NICE
- Evaluation by the National Prescribing Centre
- Evaluation by one or more of the regional drug evaluation groups that exist all over England (e.g. North East Technology Advisory Group, London New Drugs Group, Greater Manchester Medicines Management Group, Oxford Priority Setting Group, Midlands Therapeutic Review and Advisory Committee (MRTRAC), North Yorkshire Drugs and Therapeutics Centre, SW Peninsula Health Technology Commissioning Group, East of England Prescribing Advisory Group
- Additional evaluations commissioned by local organisations from UKMi or local pharmacists
- Consideration by local Drugs and Therapeutics Committees for decisions on inclusion in local formularies

The necessity for all these layers of evaluations and decision-making bodies has to be questioned, particularly in an NHS that is facing unprecedented financial challenges.

It is extremely difficult to estimate the cost of all this activity and of the duplication involved, but for companies it represents a vast matrix of potential hurdles to jump before adoption of innovation is allowed.
Quality of local medicines evaluation

The example above illustrates some of the issues around the quality of local medicines evaluation.

There is no consistent process or set of standards for conducting medicines evaluation, which can vary from full health technology appraisal by NICE to a day’s work by a medicines management pharmacist.

- The purpose, nature of evaluations, ways of working and outputs are highly variable; whether this is solely a reflection of differences in local needs and priorities is questionable.
In most organisations, the processes that are used, the rigour with which data are synthesised, and processes for peer review are unclear. Some outputs are in the public domain; others are not. Accountability for quality is generally unclear.

Interaction with the companies that developed the medicines is highly variable, ranging from collaborative to none at all: issues being lack of engagement in the gathering of evidence; lack of dialogue during evaluations or interactions left until very late in the process; lack of sight of evidence reviews before they are published to check for factual accuracy; evaluations taking place with little or no disease context.

The National Prescribing Centre has issued several guidance documents to support local decision-making on medicines use, including guiding principles (2009), a handbook of good practice (2009) and a fitness-for-purpose framework for area prescribing and medicines management committees (2010). These are useful documents and have contributed to greater consistency of process and transparency but there is a long way to go before best-practice standards are consistently adopted.

Greater Manchester formulary

To implement one of the five QIPP priorities in Greater Manchester, the Greater Manchester Medicines Management Group initiated the development of a formulary for all 10 PCTs in the Greater Manchester area to ‘promote clinically cost effective prescribing across Greater Manchester’. The work to evaluate all medicines in 15 of the BNF chapters and select a first choice followed by 1-2 alternatives started in 2010 and consultation on conclusions of eight of the chapters began with the NHS in April 2011 and with industry in June 2011. A ‘do-not-prescribe’ list had already been published. The aim is that compliance with the formulary will be monitored, with an expectation of a compliance rate in 80% of the medicines prescribed to new patients and an explanation given by prescribers for non-compliance. In future, inclusion of new medicines on the formulary will have to be initiated by clinicians using evidence of superiority over an existing formulary medicine.

Evaluations have been carried out by local pharmacists (many conducted by the North Yorkshire Drugs and Therapeutics Centre), taking into account criteria of clinical effectiveness, cost effectiveness, patient acceptability and safety; some allowance may be made for local practice and preference. No formal process for evaluation or product selection, details as to the methods or rigour of assessment, or benchmarks for the selection criteria have been published. Evaluations have been based on data published before April 2010 and companies were only offered the opportunity to submit clinical or cost effectiveness evidence in July 2011. The definition of cost effectiveness used is unclear, i.e. whether this is cost comparison, budget impact, or taking account of whole-system costs and benefits, such as reductions in hospital admissions.

The costs of developing the formulary and anticipated costs of keeping it up to date have not been published.
Issues with use of evidence

Movicol (polyethylene glycol plus electrolytes, Norgine) is an osmotic laxative, costing from 23p per day. Following its launch it has been further researched and developed to extend its licensed indications and expand the age of patients for whom it is appropriate. It is a modern solution to a problem that affects millions of people in the UK. Unlike older products, such as lactulose that has been in use for many years and is the most commonly prescribed laxative, Movicol is supported by Grade A evidence\(^{29,30}\). The NICE guideline\(^{31}\) on the management of constipation in children and young people, published in May 2010, clearly recommends Movicol/Movicol Paediatric Plain as first-line treatment. A systematic review conducted by the Cochrane Collaboration in 2010\(^ {32}\), which examined 10 randomised controlled trials, concluded ‘Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation’. A subsequent Cochrane Quality and Productivity Topic\(^ {33}\), published by NICE in November 2010 and intended to help the NHS identify practices which could be significantly reduced or stopped completely, releasing cash and/or resources without negatively affecting the quality of NHS care, was accompanied by a NICE comment: ‘Using polyethylene glycol in preference to lactulose in the treatment of chronic constipation is likely to improve the quality of patient care by reducing the use of a less effective treatment’. A further comment stated ‘It is possible that because of Movicol’s better efficacy, relative to lactulose, that patients may need less of this particular laxative. Costs may not necessarily increase and they may even decrease from switching from lactulose to Movicol. Overall this may be a cost neutral event but there are anticipated benefits to quality of patients’ care.’

The draft Greater Manchester formulary\(^ {34}\) puts lactulose as first choice osmotic laxative with Movicol as second choice. The up-to-date NICE publications, which post-date the April 2010 cut-off for evidence, were not factored into the draft published in April 2011, even though development of the guideline was in the public domain and a draft guideline was on the NICE website; nor was the company given the opportunity to highlight the forthcoming final guideline to reviewers. The Greater Manchester Medicines Management Group, responsible for producing the draft formulary, are taking feedback from interested parties, but may reserve the right to consider following the NICE guideline as optional (in contrast to the mandatory technology appraisal guidance).

It is not known what the cost of the original work to Greater Manchester was, nor of the work involved in factoring in the work of NICE.

Silo budgeting and perverse incentives

As we have said above, many medicines when used appropriately can save overall system costs. However, some NHS financial systems and incentives work to prevent patients getting innovative treatments that would make a significant impact on their lives and which would create overall savings in the system.

Local commissioning organisations need to adopt a longer term and integrated approach towards funding for patient care in order to deliver productivity savings whilst maintaining or improving quality of care and patient outcomes.
**Silo budgeting: preventing patients receiving innovative medicines because savings are realised in a different part of the NHS budget**

Exjade (desferasirox, Novartis) is an oral treatment for chronic iron overload in adults and children with beta thalassaemia major (BTM) requiring frequent blood transfusions, for whom treatment with desferrioxamine is contraindicated or inadequate. Thalassaemia is an inherited blood disorder that affects the body’s ability to create red blood cells and BTM is the most common and severe form requiring patients to have blood transfusions throughout their lives.

Prior to the introduction of Exjade in 2006, treatment was limited to desferrioxamine which has been on the market for over 10 years. Desferrioxamine is administered five to seven times per week via painful nightly infusions lasting eight to 12 hours. Exjade is a soluble tablet, offering substantial quality of life improvements for patients many of whom are young children. It was awarded the Prix Galien prize for innovation in 2008. When the total cost of the intervention is taken into account (including pumps, needles, etc.), the acquisition cost of Exjade (£12,761 for a 52kg patient) is less than that for desferrioxamine (£14,350 for a 52kg patient). However, the uptake of Exjade has been slow because the costs of desferrioxamine are split across the medicines and devices budgets and so the savings in total treatment cost not recognised.

Whilst uptake of this medicine has improved, this has been the consequence of individual dialogue initiated by Novartis at local level. Unless the silo-budgeting approach to care is addressed and the cost of these medicines examined in the round and in the context of the patient care pathway, the problem is likely to persist in areas where Novartis has been unable to make the case to decision-makers.

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**Perverse incentives: financial incentives to retain treatment in specialised hospital facilities rather than short courses of an oral medicine under specialist supervision**

Toctino (alitretinoin, Basilea) is the first and only treatment licensed for severe chronic hand eczema (CHE). It is a highly innovative once-a-day oral therapy for patients unresponsive to treatment with potent topical corticosteroids. An average treatment course of 13 weeks will result in clear or almost clear hands in nearly 50% of patients and improvement in 80%, with no relapse within six months in 65% of patients. On average, Toctino treatment requires five clinic visits per year and NICE estimated that the cost per patient per year of treatment as £2,176. The favoured alternative therapy for people with severe CHE is PUVA (psoralen and ultraviolet A) light therapy which requires an average of 46 visits to specialised hospital facilities per year at a cost per year estimated by NICE of £3,468.

The clinical and cost saving benefits of Toctino were recognised by NICE guidance in July 2009 (TA 177), which recommended it as first-line therapy. At that time, NICE actively informed the NHS that Toctino was 13th in the league of treatments that could save the NHS money, namely £6million if 20% of PUVA use was replaced by Toctino.

Visits for PUVA generate income for hospitals; the Toctino drug cost comes out of the medicines budget and as such it is perceived as comparatively expensive. Hence there is little incentive for hospitals to reduce PUVA treatment in favour of innovative drug therapy that saves money for the overall health economy.
Rarity vs. exceptionality

There are some innovative medicines that, because of the prevalence of the disease they aim to treat, fall into a system vacuum in terms of commissioning and funding decisions. Most diseases affecting up to 500 patients in England will be covered by national specialised commissioning, which has well developed processes for provider accreditation, care pathway development and, more recently, a body that is evolving to consider the clinical and cost effectiveness of innovative medicines (Advisory Group for National Specialised Services - AGNSS). Ten Specialised Commissioning Groups commission services for uncommon diseases on behalf of their regional populations (covering 2.8-7.5 million people) for less rare conditions. More common conditions are of course commissioned by PCTs.

However, some rare conditions are not actively commissioned by any of these arrangements and therefore rely on Individual Funding Requests or Exceptional Funding Requests. By definition, these are designed for patients who have an exceptional presentation or are likely to benefit in an exceptional way. Disease rarity is not synonymous with exceptionality and so applications that come through for more than a few patients no longer fall into the exceptional category and funding is denied.

Rare but not exceptional

Tracleer (bosentan, Actelion) is an endothelin receptor antagonist which has two indications: Pulmonary Arterial Hypertension and prevention of digital ulcers in people with systemic sclerosis (SSC). Tracleer is the only licensed medicine for prevention of digital ulcers. SSC affects three people in 10,000 and only a small percentage of them will get digital ulcers. The rarity of digital ulcers, coupled with low awareness and perception of severity, make it unlikely that a full NICE appraisal will ever be conducted. The number of patients with digital ulcers is also too high for consideration by AGNSS. Regional commissioning does not cover this condition as it is outside the specialised services definition set. There is no active work programme to consider the disease area in any PCT or successor body.

Clinicians have to apply for funding via Individual or Exceptional Funding Requests, not all of which will be successful. The panels established to review these requests are strong in terms of assessing exceptionality where a specific request is likely to be highly individual. For patients with digital ulcers the requests are very similar, i.e. the patients share the same characteristics and are likely to benefit in the same way. The decisions made are, nonetheless, different from one panel to another. Once Funding Panels have received a number of these requests from specialist centres for patients with digital ulcers, their ‘exceptional’ status ceases and no funding via this route ceases. Effectively patients are discriminated against on the basis of rarity.

Cultural factors

The review recognises that in a large and complex public service system like the NHS, diffusion of innovation may be blocked by cultural barriers.

Clinical practice in the NHS is conservative compared with other countries and, whilst this can be viewed as a way to protect patient safety, the norm is to use old and cheaper medicines even where the evidence suggests that newer ones offer greater patient benefit. In other countries, there is a willingness to use the recognised best option first. This culture has to some extent been fuelled by years of cost restrictions from PCTs and other agencies leading clinicians in many disease areas to accept that newer therapies should only be considered for patients who have cycled through older, less effective treatments.
**Epilepsy**

In epilepsy, the approach is generally to use older, cheaper, generic medicines as first-line treatment and wait for breakthrough seizures before moving on to something more modern. Many senior clinicians continue to refer to lamotrigine and levetiracetam as ‘the newer agents’. Lamotrigine and levetiracetam are both products that have no patent protection and were discovered and developed some 30 years ago in the 1980s. More recent agents in epilepsy are used in patient management later in the UK than in similarly developed health economies.

The graph below shows the use of a new epilepsy agent, lacosamide, launched in September 2008. As can be seen, the use of lacosamide (as measured by treatment day share) is the same in France after eight months as in the UK after nearly three years. In Spain the picture is starker with patients there receiving the same level of use after just three months of the medicine being available. Culturally there is a drive in the UK to use new therapies last, regardless of the benefits that new treatments will bring to patients.

![Graph showing treatment days shares launch curves by country](source: IMS, UCB calculations)
**Rheumatoid arthritis**

Whilst there is a good history over the last five years of using TNF inhibitors to treat severe rheumatoid arthritis their use has been restricted in the UK by guidance from NICE to only those patients who have a DAS (disease activity score) higher than 5.1 which reflects a high level of disease.

The impact of this restriction is that patients in the UK must fail on two older therapies and then wait (with only pain control as an active therapy) until their condition progresses far enough to qualify for a TNF inhibitor. By delaying treatment patients accumulate damage.

This increased damage can lead to:
- Joint damage
- Increased disability with high rates of joint replacement surgery
- Lack of treatment causes increased severity and frequency of symptoms
- Increased Pain
- Decreased quality of life
- Cardiovascular and other co-morbidities
- Loss of employment

The 2010 British Society of Rheumatology (BSR) guidelines and 2010 European EULAR guidelines both recommend treatment for moderate patients (with a disease activity score of between 3.2 and 5.1) and this is practised in other developed health economies such as Germany, France and US.

There are many benefits to extending the usage of TNF inhibitors into moderate patients. Similar improvements can be seen in both moderate and severe patients and these include slowing or stopping of joint damage, reduction in pain and improvement in quality of life.
Q2. Recommendations for Action

2.1 For the NHS Commissioning Board and other national bodies

a) Radical overhaul of NHS medicines management

The NHS Commissioning Board should undertake a radical overhaul of how medicines are managed by the NHS. The skills of medicines managers and prescribing advisers should be maximised to enable them to become champions of quality, clearly accountable for improved patient outcomes and productivity across the care pathway, rather than focused on guardianship of a discrete medicines bill. Medicines management should become an integral part of the commissioning process, rather than be seen as a separate element.

We would suggest that the overhaul should include:

i) Rationalisation of the tiers of national, regional and local evaluation to reduce the current complexity and eliminate unnecessary duplication

ii) Work with NICE and the National Prescribing Centre to set standards (that are implemented) for local medicines evaluation to include methods of evidence synthesis and use of best-practice processes that are transparent and open to stakeholder input. Standards should include accreditation criteria for local organisations that want to conduct such evaluations to ensure their skills, methods, processes and outputs are transparent and to the appropriate standard. NICE and/or the National Prescribing Centre could take responsibility for accreditation

iii) Routine collection and publication of data on uptake and use of medicines at national, regional and Primary Care Organisation levels, including compliance with NICE guidance, that allow for mature comparisons and peer review; data collection on UK performance vs. other countries should also continue, building on the Richards report

iv) A fundamental examination of the purpose and role of medicines management, including:
   a) Positioning and organisational setting
   b) Purpose, role, job description
   c) Performance assessment and management
   d) Effective management of budgets to prevent silo budgeting and perverse decisions
   e) Implementation of NICE guidance
   f) Good practice in working with pharmaceutical companies: focused on collaboration to improve the quality and productivity of care and decision-making rather than procedures to prevent malpractice; thereby reflecting a more mature relationship
   g) Reducing medicines wastage and improving adherence to medication
   h) Design of local incentives to improve the quality of care
   i) Championing and implementing best practice standards of medicines evaluation and related processes
   j) Cultural issues

v) Creation of a clear route to funding for medicines that are neither evaluated by NICE nor AGNSS, including medicines for rare conditions
b) **Strengthening implementation of NICE guidance**

**Implementing the mandatory funding direction**

i. Measures to ensure that mandatory funding for NICE guidance is properly released and that there is effective recourse against non-compliance with positive NICE guidance. Measures should include automatic inclusion of medicines recommended by NICE on local formularies, without additional conditions being imposed.

ii. Introduction of an appeal process for patients when access to NICE-recommended medicines is denied or restricted: to strengthen the implementation of NICE guidance, where there is currently no recourse for patients, honour the right in the NHS Constitution for patients to receive NICE-recommended medicines and support the Government’s commitment to ‘no decision about me without me’.

iii. Routine collection and publication of data on compliance with NICE guidance that allow for mature comparisons and peer review.

**NICE support tools**

NICE has made good progress in developing implementation support for local NHS organisations. We believe this could be strengthened further to support the commissioning of high quality and cost effective services. For example, NICE could develop:

- Care pathways for each quality standard, outlining the role of each intervention in delivering overall value
- Pro-forma business cases for each of the medicines it recommends

**NICE support team**

NICE has a team of individuals whose role it is to support local organisations to implement its guidance and we believe that this function could be strengthened. The incorporation of the NPC into NICE in April 2010 offers further opportunities to strengthen implementation of guidance and standards relating to medicines as the NPC has its own team of pharmacists to support local organisations in implementing good practice in decision-making about medicines use.

c) **Improving incentives to deliver quality and productivity across the care pathway/health economy**

The Board should review the incentives in the system so that they promote the delivery of quality; for example more widespread use of CQUIN and systems for sharing rewards where organisations work together to improve quality and productivity.

d) **Industry representation on the NHS Commissioning Board**

EMG believes that the pharmaceutical industry, as a major source of innovation, and with considerable therapy area, business and organisational expertise to contribute to the commissioning process, should be recognised as an equal partner in delivering best practice commissioning and should be represented on the NHS Commissioning Board.
2.2 For local NHS organisations

a) Creating clear accountability for diffusion of innovation at all tiers of the NHS commissioning system

In addition to the work of the NHS Commissioning Board to promote diffusion of innovation in the NHS, SHA Clusters and local organisations with commissioning responsibility should be required to have specific accountability for the adoption of innovation, which would include accountability for engagement with the pharmaceutical industry and other innovative partners.

b) Working with the pharmaceutical industry

There is scope for local NHS organisations to work much more constructively and usefully with pharmaceutical companies. Relationships are often based on old paradigms with resistance and sometimes direct bans on any contact. This is not helpful to either the NHS or the industry. A more mature relationship is required, and industry is playing its part in improving its understanding of customer needs and deploying personnel skilled to meet those needs. Local organisations should be open to dialogue on:

- Up-to-date evidence on new and existing medicines and their impact on the shape, quality and productivity of local services
- Skills and support that companies can offer to supplement or fill gaps in local organisational skills or expertise
- Joint working to meet shared objectives that improve quality and productivity of patient care

2.3 For industry

Industry has an important role to play in supporting the NHS to deliver innovation to patients. Industry recognises it must play its part and wants to work with the NHS to ensure that the value of its medicines is realised by local NHS organisations. As well as making direct efforts themselves, companies need the NHS to help them engage effectively and constructively with local NHS organisations.

Areas where the industry can add particular value are:

- As a member of the NHS Commissioning Board and through engagement with local SHA Clusters and local organisations with a commissioning responsibility
- Providing information on medicines relevant for NHS forward planning
- Supporting the NHS in tackling key areas of inefficiency relating to medicines, such as medicines wastage and poor patient adherence to treatment
- Providing resources and expertise to support local managers in getting the most value out of individual medicines
- Joint working, partnerships and collaborations where local NHS organisations and companies work together and pool resources to achieve shared objectives that improve the quality and productivity of patient care and the patient experience. There are many examples where joint working on ‘win-win’ projects has reduced overall system costs (e.g. by reducing unplanned hospital admissions) whilst increasing the potential market for medicines. The ABPI in its evidence submission has given a series of case examples of this type of work which is relatively widespread.
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