

Guidance on the Management of Withdrawal from Seroxat (Paroxetine) and Other SSRIs

Notes of a meeting held at MHRA on 2 September 2008

Present:

Robert (Bob) Fiddaman (RF), Campaigner, Author of Seroxat Sufferers Blog

Prof. Kent Woods (KW), Chief Executive, MHRA

Sarah Morgan (SM), Head of Pharmacovigilance Risk Management, MHRA

John Watkins (JW), Communication Manager, MHRA, acting as secretary

1. RF said he would like to discuss problems of withdrawing from Seroxat. He said that though his concerns centred around Seroxat, he recognised that other SSRIs posed similar problems which ought also to be addressed.
2. He produced copies of the Patient Information Leaflet (PIL) for Seroxat in which he had highlighted the 32 places where patients were told to talk with their doctor about various issues. He felt that too much of an onus was put on doctors, many of whom did not know enough about withdrawal problems and their management.
3. In answer to a question from KW, RF agreed that the focus of the meeting should be on the information going to doctors and perhaps also on their training.
4. KW noted that doctors do not generally refer to the PILs, nor indeed to the similar but more technical Summaries of Product Characteristics (SPCs). Instead, they use the British National Formulary (BNF), revised twice each year, and guidance produced by NICE. The NICE guidance on the management of depression was currently being revised; a draft is due to go out for public consultation in December 2008 with a view to publication in June 2009.
5. He emphasised that MHRA controls neither the BNF nor NICE in any of the matters they cover, but the Agency can and does make suggestions to both organisations about the information they provide.
6. RF illustrated the practical problems encountered by patients in withdrawing. He offered each of the others a jelly baby and asked them to bite off one-third. No problem. He then produced some Tic-Tacs (mints). It was immediately acknowledged that biting off a third was very difficult. Likewise with a Seroxat tablet, said RF. The liquid preparation was much better suited to dose tapering but doctors seemed largely unaware of it. He outlined his own experience of withdrawing over a period of 21 months. The liquid, administered through a syringe, helped that process, though – for him – not even tapering took him beyond the point where he felt he had to “go cold turkey”. He did that because he did not want the drug to continue to have a hold over him.
7. During withdrawal he experienced severe “zaps” in his brain. He described his dependence on the drug as an addiction, and exemplified that by relating his feelings of wanting to “rip the shop apart” if it turned out that they were out of stock.
8. KW noted that the term “addiction” ought to be reserved for circumstances which typically entailed cravings leading to increase in dosage, but suggested it was less important to argue about terminology than to acknowledge, as he did, that there are significant problems associated with withdrawal; the issue was how best to manage withdrawal. He noted that, as with benzodiazepines, those SSRIs which both act and disappear more quickly are more likely to pose problems with withdrawal. He did not know whether a switch to slower acting SSRIs had been researched as a potential solution, as it had proved to be for benzodiazepines.

9. KW said he was aware that RF had had some very good support from his doctor and wondered how widespread such support would be. RF believed that many doctors would not be able to provide that level of help, due to not knowing how to manage withdrawal. RF had sent the Agency a very large number of personal testimonies about difficulties that others had experienced during withdrawal.
10. RF pointed to guidance on withdrawal produced by Dr David Healy; KW said he had seen it but his concern about any guidance would be whether “one size fits all”, given the range and diversity of withdrawal experiences. That should not however prevent the development of authoritative guidance.
11. RF asked what authority MHRA had to issue warnings. Could it for example require warnings to be put on packaging like those on packets of cigarettes?
12. KW replied that the place for warnings to patients is within the PIL. If they were very prominent on the packaging then that might well deter patients who really needed the medicine from taking it. The Agency has control over PILs. KW outlined the improvements to PILs in recent years, largely due to testing them with users; a programme which will end very soon has been reviewing and revising the PILs for all medicines. RF acknowledged that there had been significant recent improvements in the Seroxat PIL. KW noted that there is still room for improvement in PILs but the Agency is now starting to explore other initiatives relating to PILs. It might for example become feasible to ensure that PILs are available to patients beforehand rather than at the time they start to take their medicines.
13. RF wondered whether MHRA had thought of including Yellow Cards with or in the PILs. SM replied that we had considered asking pharmacists to include them in the bag holding the package. KW noted that every edition of the BNF had a Yellow Card at the back but there was no obvious place for making it available to patients other than placing them in pharmacies and GP surgeries. Reports from patients were still relatively new. So far only about 10% of all reports come from them, but the quality of the information they contain is every bit as good as that from healthcare professionals.
14. KW asked RF what he thought of the Seroxat PIL’s Section 5, “Stopping Seroxat”. Early in the section it says “When stopping Seroxat your doctor will help you to reduce the does slowly ...”. RF felt that this was over-optimistic. He also felt that the advice about dosage reductions of 10mg a week (which SM noted was based on clinical trials) was too large an increment in view of his own experience – he needed to reduce by 1mg a week, only practicable with the liquid – and the experiences of others. And he felt that the signposting to the liquid form, “It may be easier for you to take Seroxat liquid during the time that you are coming off the medicine” was inadequate. SM agreed that steering patients towards the liquid could be made more obvious; and it could be helpful if such a steer was also given to doctors, in some document such as the NICE guidance¹.
15. Referring again to the management of withdrawal in relation to benzodiazepines, KW read out the advice on management of withdrawal for that class of drugs that is in the current edition of the BNF. RF said he would have found it very helpful if that kind of advice, but about Seroxat / SSRIs had been available to him at the time he started to withdraw. He wondered how many doctors used the BNF. KW reckoned that almost every doctor will use it, with many of them referring to it frequently. When he was a clinician, he always carried around a copy of the BNF in his coat pocket.
16. KW thought that the inclusion of similar advice in relation to SSRIs could be suggested to the BNF. It might also be suggested to NICE for their guidance. And a potentially useful way of

¹ There was also some discussion about how to interpret the list under “Likely to affect up to 1 in 10 people”. JW wondered whether each effect in the list would affect up to 1 in 10 but SM said it meant that up to 1 in 10 could expect to experience one or more of the effects in the list.

drawing prescribers attention to any new advice that emerged would be MHRA's monthly Drug Safety Update. KW again stressed that though we might make suggestions about this to the BNF and to NICE, it would be for them to decide. While MHRA's primary role is to regulate industry – with no jurisdiction over doctors, it is within the remit of both the BNF and NICE to inform and indeed to influence doctors.

17. RF asked whether MHRA would talk with David Healy. KW said he would be happy to have that happen. But it would be useful if others with experience of managing withdrawal were also consulted. Those present at the meeting could not immediately identify anybody else in the UK but MHRA would try to do that, perhaps with the help of one of its Board members.
18. RF asked whether the management of withdrawal could be covered in the training of doctors. KW explained the difficulty any organisation would have in influencing medical schools when each school determines its own curriculum.
19. RF enquired how the Agency kept up to date on research and indeed legal issues surrounding Seroxat. Had the Agency for example been aware of the "Glenmullen report" before he drew attention to it at a time when the Agency was still investigating GSK? KW could not recall at exactly what stage he personally became aware of the document but assured RF that the Agency kept track of developments generally, not just in the context of a particular investigation. SM described how her group undertake a weekly review of the literature in respect of all drugs, covering all the major journals. And pharmacovigilance also takes account of clinical trials and trends in Yellow Card reports.
20. The meeting concluded by recognising that though the focus had been on Seroxat, there were other SSRIs that posed similar problems, and that changes in prescribing practices, such as a reduction in prescriptions for Seroxat in recent years and increases for other drugs, for example Venflaxine, mean that some of the issues deserve to be dealt with in terms of the class of drugs rather than in relation to individual members of that class.