

SUMMARY OF REGULATORY ACTION

The safety profile of the SSRIs is a topic which has been the subject of considerable public interest and scientific debate over recent years. In May 2003, in response to continued public concern, the Government established an Expert Working Group of the independent scientific advisory committee, the Committee on Safety of Medicines (CSM), to further investigate the safety of SSRIs, with a particular focus on suicidal behaviour and withdrawal reactions. This comprehensive review considered a large body of evidence including data from clinical trials, published literature, post-marketing studies, reports of patients' experiences and feedback from meetings with patient groups.

Upon the advice of the Expert Group and CSM, the Medicines and Healthcare products Regulatory Agency (MHRA) took action ahead of other regulators to issue clear advice in 2003 on the risks and benefits of treatment with Seroxat and other SSRIs in the under 18 age group; It was recommended that, with the exception of fluoxetine, SSRIs should not be used in children and adolescents aged less than 18 years with depressive illness. This advice followed receipt of clinical trial data showing an increased rate of suicidal thoughts and behaviour in this population. Only fluoxetine has been shown to have a favourable balance of risks and benefits for the treatment of major depressive disorder in under 18s.

An MHRA funded study published in February 2008 has shown that antidepressant prescribing in under 18s doubled between 1999 and 2003 but fell to the 1999 level between 2004 and 2005. The significant reduction in prescribing of antidepressants since the 2003 regulatory action does not appear to have resulted in an increase in suicidal behaviour.

From the beginning of the review the Expert Working Group and MHRA were conscious of the need to ensure that the workings of the Group were entirely transparent and the basis for the recommendations of the Group were clearly set out. Importantly, responding to feedback from clinicians and others, summaries of the clinical trial data on which the advice was based were released to ensure total transparency for healthcare professionals, patients and the public. Throughout the course of this review, action was taken to ensure that patients and healthcare professionals were provided with updated advice as and when new data arose.

The conclusions and key findings of the Expert Group were communicated to health professionals on 6 December 2004. Overall it was concluded that SSRIs are effective medicines in the treatment of depression and anxiety conditions, and that the balance of risks and benefits of all SSRIs in adults remains positive in their licensed indications. The Expert Working Group's conclusions and the supporting evidence base were detailed in the Group's

comprehensive report published on 6 December 2004 –available on the MHRA website (www.mhra.co.uk). The publication of the report was timed to coincide with the publication of guidelines on the treatment of depression by the National Institute of Health and Clinical Excellence.

Since the completion of the review and publication of its findings in December 2004, every effort has been made to issue updated advice as appropriate. In December 2005, new advice was issued about the safety of use of Seroxat during pregnancy. In May 2006, prescribers were informed about a new analysis of the risk of suicidal behaviour in the adult population by the US Food and Drug Administration – the overall conclusions that review were consistent with those of the UK review – ie, that adults who receive SSRIs are not at an overall increased risk of suicidal thoughts or behaviour but that young adults (ie, those younger than 25 years) may have an increased risk of suicidal behaviour. In August 2007, an article was include in the MHRA drug safety bulletin, Drug Safety Update, providing further information to prescribers about the risk of suicidal behaviour with antidepressants and advising particularly close monitoring of young adults.

Most recently discussions within Europe have led to a decision that the product information for prescribers and the Patient Information Leaflets for all antidepressants, not only SSRIs, should be updated to contain clear warnings with respect to the increased risk of suicidal thoughts and behaviour in young adults and the need for close monitoring of patients. The updates to the product information are ongoing in accordance with implementation timelines agreed within Europe.

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