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IMPORTANT SAFETY INFORMATION

11th July 2005

Dear Health Care Professional,

Re: European Commission Decision on Committee for Medicinal Products for Human Use (CHMP) review of paroxetine-containing products

Further to discussions with the Irish Medicines Board (IMB), GSK wishes to inform you of revisions to the product information for Seroxat resulting from the EU-wide review of paroxetine containing medicines.

A re-evaluation of the benefit-risk assessment of paroxetine-containing medicines was initiated in June 2003 following a request by the UK's regulatory authority. This request arose from safety concerns relating to the potential for emotional changes (including self-harm, suicidal thoughts, attempted suicide and hostility) and withdrawal reactions associated with the use of paroxetine. The CHMP issued its Opinion on 8 December 2004, concluding that the benefit-risk balance for these products remains positive across all approved indications in adults, but recommended a number of changes to the product information.

The European Commission recently accepted the recommendations from the CHMP and associated changes to the product information for paroxetine on an EU-wide basis (see attached Summaries of Product Characteristics). This letter is intended to give you brief details of the review and notification of the resulting changes to the **SEROXAT** labelling that will be implemented shortly.

These changes include:

- A warning to remind prescribers that paroxetine should not be used in children and adolescents. Data from controlled clinical trials in paediatric patients showed paroxetine to be associated with an increased risk of adverse events associated with suicidal behaviour and hostility, and that efficacy has not been adequately demonstrated.

- Strengthened disease related warnings, recommending close monitoring of patients at high risk of suicidal behaviour. These include patients with a known history of suicidal behaviour or suicidal thoughts prior to starting treatment and young adults.

- Strengthened warnings around withdrawal symptoms, indicating that withdrawal symptoms upon stopping treatment are common, particularly if discontinuation is abrupt, and that patients must not stop their treatment abruptly except on medical advice. Generally withdrawal symptoms are mild to moderate and self-limiting, however in some patients they may be severe and/or prolonged.

- Strengthened warnings regarding a risk of serotonin syndrome, akathisia, gastrointestinal bleeding and hyponatraemia.

- Additional information regarding use during pregnancy and lactation relating to potential neonatal complications.

In addition, the indications for use of paroxetine in adults were harmonised across all EU Member States and include treatment of depression and anxiety disorders (obsessive-compulsive disorder, generalised anxiety disorder, post traumatic stress disorder, panic disorder and social anxiety disorder).

Any suspected adverse drug reactions (ADRs) should be notified to the company and /or the IMB in the usual way.

If you have any further questions or wish to discuss this letter, please contact GlaxoSmithKline on 1800 244 255.

Yours sincerely,

Martina Dempsey PhD
Director of Medical & Regulatory Affairs