

By email only to: [jan.olav.larsson@telia.com](mailto:jan.olav.larsson@telia.com)

1st October 2008

**Re: letter of 9th September 2008 to “Assessor responsible for Strattera”**

Dear Mr. Larsson,

Thank you for your recent correspondence to the Medicines and Healthcare Regulatory products Agency (MHRA) regarding Strattera (atomoxetine), including your latest letter of September 9th 2008.

I would also like to thank you for the information that you have provided regarding cases of psychomotor hyperactivity, akathisia, restlessness, agitation, mania and hypomania with Strattera.

Since Strattera was first authorised in 2004 the UK, together with other regulatory authorities within Europe, have kept its safety in routine clinical practice under close review. As and when new safety issues have emerged we have carefully evaluated the available data and agreed upon the appropriate course of regulatory action.

As a result major regulatory action was taken on a Europe wide basis in February 2005 (to issue new advice about the rare risk of serious liver disorders), September 2005 (to warn about the potential for an increased risk of suicidal thoughts and behaviour) and February 2006 (the conclusions of a review of its risk and benefits and to issue new advice about the potential for risk of seizure and QT interval prolongation (an irregularity of the electrical activity of the heart)). Since then the available safety data for Strattera have been reviewed in the context of the regular Periodic Safety Updates that the Marketing Authorisation holder (Eli Lilly) are legally obliged to provide and also as any new data has arisen from ongoing studies or new safety signals.

In relation to your previous correspondence of 10th and 14th August, I would like to take this opportunity to respond to the three questions that you consider remain unanswered:

1. ***“The simple question 1: How come the MHRA is delaying the issuance of the warnings even more? [Referred to the warnings about mania and psychosis with hallucinations.]”***

With regard to your concerns about reports of mania and psychosis, as stated earlier in this reply, the evaluation of these issues are currently ongoing and following an initial request in the assessment report for the Periodic Safety Update for the period (dates 27-05-2005 to 26-11-2005) we have asked Eli Lilly for more information to enable us to review this issue in more detail. These data have now been received and discussions between European Member States and Eli Lilly are ongoing to agree the most appropriate information to be included in the product information for patients and prescribers. Once this has been agreed the updated information will be reflected in the Patient Information Leaflet (PIL) and we will also consider what, if any, further communication is required to inform patients and healthcare professionals. As I am sure you will appreciate, once updates have been agreed for inclusion in the product information for prescribers and the PIL, new information will take time to appear in the packs in the market place due to movement of stock in the supply chain. We anticipate that updated patient information will be readily available in packs within the next 6 months.

2. ***“The simple question 2: Has the MHRA now done an own investigation of these extremely important reports? [Referred to the 700 reports about psychomotor hyperactivity in connection with Strattera, with the assumption that a diabetes drug that caused a heavy increase in blood sugar would right away be withdrawn from the market.]”***

The MHRA is conducting an ongoing evaluation of psychomotor hyperactivity in conjunction with concerned European member states. Since the request for further information on cases of psychomotor hyperactivity in the assessment report for PSUR 5, we have requested further information to assist our review on two more occasions. The information submitted by the MAH has been evaluated and the MAH will be requested to provide further detailed information within the next 2 months to ensure the issue has been investigated in a thorough and scientific manner.

3. ***“Will the MHRA call in question the false data given by Eli Lilly about instances of death from Strattera and has the agency now started an investigation of all the reported cases of death in connection with Strattera treatment?”***

***The last questions are answered NO in your response of August 12. As this inaction is against the very purpose of the agency my questions need to be asked again.”***

As previously stated in our correspondence of 12<sup>th</sup> August 2008, the view of the European member states where Strattera is licensed is that there are no new or unrecognised safety concerns with potentially fatal outcomes that are clearly causally associated with the use of Strattera. This conclusion has been reached following critical evaluation of all the reports with a fatal outcome and would have included reports that would have been directly reported to the FDA. In considering the total number of reports of a particular reaction or with a particular outcome, it is important to understand that a case could have been reported to the regulatory authority and also to the company

that manufactures the medicine. Therefore in order to calculate the total number of reports with a fatal outcome it is not simply a case of adding up reports with a fatal outcome mentioned in our assessment reports of the PSURs and those available on the FDA website as these different sources may contain duplicate information. We do not, therefore, consider that the figures you have compiled can be used as a basis for initiating further regulatory action. The sources of data that regulators use such as company data, spontaneous adverse reaction reports and literature are set out in European and national law. We have looked at the data you have sent us to see if they can add insight to the statutory sources of data we have received and do not think that they are of benefit as we cannot verify their source or accuracy.

In conclusion, we remain of the opinion that the benefits of use continue to outweigh the known risks of Strattera. This view is shared by all European Member States and in light of this we consider that, other than the ongoing pharmacovigilance activities already implemented and outlined above, no further action is required. As you are aware from the information we have provided in previous replies or copies of assessment reports prepared by the MHRA that you have obtained, the potential safety issues that you have mentioned in your letters are all currently being evaluated by the European member states in which Strattera is licensed.

I hope that this response addresses your outstanding questions.

Yours sincerely,

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Scientific Assessor

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