European Medicines Agency

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OPINION OF THE COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE PURSUANT TO ARTICLE 5(3) OF REGULATION (EC) No 726/2004, ON CONVENTIONAL ANTIPSYCHOTICS

Basis for opinion

On 23 October 2008, the United Kingdom presented to the EMEA a request for a CHMP opinion under Article 5(3) of Regulation (EC) No 726/2004 on conventional antipsychotics, as a result of recently available data on the safety of antipsychotic medicines from epidemiological studies and in more detail with regards to the risks of antipsychotics when used in elderly people with dementia.

Specifically, the Committee was requested to provide advice on the following four issues:

(1) the strength of the evidence to suggest that conventional antipsychotics are associated with excess mortality when used in elderly people with dementia;

(2) the strength of the evidence to suggest that conventional antipsychotics are associated with a greater risk of mortality compared with atypical antipsychotics;

(3) whether or not the risk can/should be extrapolated to those conventional antipsychotics not included in the studies;

(4) the need to conduct further studies, including on the possible mechanisms underlying the increase in mortality observed.

On the basis of the request made by United Kingdom, the CHMP considered that there were sufficient grounds to start the procedure.

The procedure started on 23 October 2008.

Opinion

The CHMP, having considered the matter as set out in the appended assessment report (Appendix 1), reviewed the available evidence and came to the conclusion that conventional (typical) antipsychotics are likely to be associated with increased mortality when used in elderly people with dementia. Although the results of some of the assessed studies suggest that the excess mortality observed with conventional antipsychotics may be greater than that observed for the newer atypical antipsychotics, this could not be confirmed due to the methodological limitations of these studies. No conclusion could be drawn as to whether the risk differs between individual antipsychotics within the class of conventional antipsychotics. Therefore, until and unless better evidence becomes available, it cannot be excluded that the increased risk applies to all products of the class. At present, there is no clear mechanistic basis for the observed increased risk of mortality, and further data would be needed to explore this.

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Whilst further observational studies could be performed the CHMP considered that it is unlikely that such studies would be able to provide firm evidence in relation to the underlying mechanisms. The CHMP therefore recommended that the Product Information for the conventional antipsychotics should be updated to include information on the increased risk of mortality when used in elderly patients with dementia.

The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

This opinion is forwarded to the United Kingdom, all other Member States, Iceland, Norway and to the European Commission together with its appendix.

The opinion will be published on the EMEA website with its appendix.

London, 20 November 2008

On behalf of the CHMP
Dr Eric Abadie, Chairman

Appendix 1

CHMP Assessment Report on conventional antipsychotics dated 20 November 2008.