28 April 2004
CPMP/1333/03

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP)

OPINION FOLLOWING AN ARTICLE 31 REFERRAL

loratadine

International Non-Proprietary Name (INN): loratadine

BACKGROUND INFORMATION*

Loratadine is an anti-histamine compound belonging to the H-1 antagonist group.

Loratadine has been authorised nationally and through MRP in the EU Member States.

In early 1999, the Medical Products Agency (MPA) was made aware of data from the Swedish Medical Birth Registry (SMBR), which indicated that use of loratadine in the first trimester of pregnancy might be associated with an increased risk of hypospadia in the male newborn. The database consisted of 1,020 infants born to women who reported use of loratadine before the first antenatal visit.

During 1999, this signal was evaluated by the MPA, the SMBR and the MAH of the product in Sweden, Schering Plough, both by review of the clinical cases, and from a preclinical point of view. This evaluation resulted in the conclusion that this may have been a random finding. Furthermore, data from a preclinical study performed by the MAH in 1999 did not indicate that loratadine has an anti-androgenic effect, which could be one possible mechanism.

In an analysis from November 2001, the previous signal appeared reinforced. Among 2,780 exposed pregnancies there were in total 15 cases of hypospadia vs. the expected incidence of 6-7 cases. Based on these data, the MPA considered that it could not be excluded that the use of loratadine during the first trimester of pregnancy may be associated with an increased risk of hypospadia.

On 25 April 2002, Sweden triggered a referral to the EMEA under Article 31 of Directive 2001/83/EC, as amended, based on the data from the Swedish Medical Birth Registry, which could not exclude that the use of loratadine during the first trimester of pregnancy may be associated with increased risk of hypospadia.

The referral procedure started 26 April 2002. The Rapporteur and Co-Rapporteur appointed were: Dr P Neels and Dr T Salmonson, respectively. Written explanations were provided by the Applicants/Marketing Authorisation Holders by 14 August 2002, 24 January 2003, 2 May 2003, 4 August 2003 and 10 October 2003.

Based on evaluation of the currently available data and the Rapporteurs' assessment reports, the CPMP considered that the benefit/risk profile of loratadine containing medicinal products remains favourable, and therefore adopted an opinion on 20 November 2003 recommending

that the Applications/Marketing Authorisations for loratadine containing medicinal products should be granted or maintained in accordance with the SPC set out in Annex III of the Opinion.

in the indication:

"relief of symptoms associated with Allergic Rhinitis and Chronic Idiopathic Urticaria".

The list of product names concerned is given in the Annex I. The scientific conclusions are provided in the Annex II, together with the amended Summary of Product Characteristics in the Annex III.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 86 68
E-mail: mail@emea.eu.int http://www.emea.eu.int

The final opinion was converted into a Decision by the European Commission on 28 April 2004.

* **Notes**: The information given in this document and Annexes reflect only the CPMP Opinion dated 20 November 2003. The Member States competent authorities will continue to keep the product under regular review.

