European Medicines Agency
Evaluation of Medicines for Human Use

London, 14 July 2008
EMEA/CHMP/151554/2008

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

OPINION FOLLOWING AN ARTICLE 29(4)[1] REFERRAL FOR

Alvesco and associated names

International Non-Proprietary Name (INN): ciclesonide

BACKGROUND INFORMATION

Alvesco and associated names, 40 µg, 80 µg and 160 µg pressurised inhalation, solution is a glucocorticoid used to treat obstructive airway disease. The product contains ciclesonide which is delivered by a pressurized metered dose inhaler containing ethanolic hydrofluoroalkane-134A as a propellant.

Altana Pharma AG submitted applications for mutual recognition of **Alvesco** and associated names, 40µg, 80 µg and 160 µg pressurised inhalation, solution on the basis of the marketing authorisation granted by United Kingdom on 14 April 2004. The Mutual Recognition Procedure started on 2 May 2007. The Reference Member State was United Kingdom and the Concerned Member States were:
First wave: Belgium, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, The Netherlands, Norway, Poland, Slovak Republic, Slovenia and Sweden
Repeat use: Austria, Bulgaria, Cyprus, Spain, France, Italy, Malta and Portugal

These Member States and the applicant / MAH were not able to reach an agreement in respect of the Mutual Recognition of the Marketing Authorisation granted by the Reference Member State. The United Kingdom referred the reasons of disagreement to the EMEA on 25 October 2007.

Significant difference have been identified with regard to the currently approved posology for the control of exacerbations in severe asthma, and the need for a study comparing 160 µg, 320 µg and 640 µg/daily to demonstrate a reduction in the frequency of exacerbations in patients with severe asthma at the higher doses. The data supporting this application, as interpreted according with the CHMP guidance, did not support authorization of regular daily doses in excess of 160 µg in the treatment populations, and this was considered to be of serious public health concern.

The arbitration procedure started on 15 November 2007 with the adoption of a list of questions. The Rapporteur was Dr Ian Hudson and Co-Rapporteur was Dr Pierre Demolis. The Marketing Authorisation Holder provided written explanations on 16 January 2008.

During their March 2008 meeting, the CHMP, in the light of the overall data submitted and the scientific discussion within the Committee, was of the opinion that the benefit/risk ratio is favourable for **Alvesco** and associated names, that the objections raised by France should not prevent the granting of a Marketing Authorisation and that the Summary of Product Characteristics, labelling and package leaflet of the Reference Member State should be amended. A positive opinion was adopted by consensus on 19 March 2008.

[1] Article 29(4) of Directive 2001/83/EC, as amended.

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In particular, the proposed wording for Section 4.2 at the end of CMDh procedure was amended to reflect that in severe asthmatics, a 12 week study provided by the applicant/MAH has shown that a dose of 640µg/d (given 320µg/d twice daily) demonstrated a reduction in the frequency of exacerbations but without an improvement in lung function. The applicant/MAH also accepted an updated wording for Section 5.1, which includes more detail on Study M1-140, at the end of the CMDh procedure, and a fully updated Package Leaflet.

Additionally, the applicant/MAH was requested to commit to obtaining scientific advice in relation to exploring a suitable study design, and executing such study(ies) to provide further information on the use of the higher dose of Alvesco in the control of severe asthma. In light of this, the applicant/MAH proposed a study which would resolve the outstanding question on the long term use of 320 µg and 640 µg daily.

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

The final opinion was converted into a Decision by the European Commission on 11 July 2008.