European Medicines Agency
Evaluation of Medicines for Human Use

London, 12 September 2008
EMEA/CHMP/496102/2008

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

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

Activelle and associated names

International Non-Proprietary Name (INN): Estradiol and norethisterone acetate

BACKGROUND INFORMATION

Activelle and associated names, estradiol 0.5mg and norethisterone acetate 0.1 mg film-coated tablets is a continuous combined hormone replacement therapy (HRT) for oestrogen deficiency symptoms in women more than one year after menopause.

Novo Nordisk A/S submitted applications for mutual recognition of **Activelle** and associated names, estradiol 0.5mg and norethisterone acetate 0.1 mg film-coated tablets on the basis of the marketing authorisation granted by Sweden on 3 August 2007. The Mutual Recognition Procedure started on 20 September 2007. The Reference Member State was Sweden and the Concerned Member States were Austria, Belgium, Bulgaria, Czech Republic, Germany, Denmark, Estonia, Spain, Finland, France, Hungary, Ireland, Iceland, Italy, Lithuania, Luxembourg, Latvia, Netherlands, Norway, Portugal, Romania, Slovenia, Slovak Republic and United Kingdom. These Member States were not able to reach an agreement in respect of the Mutual Recognition of the Marketing Authorisation granted by the Reference Member State. Sweden referred the reasons for disagreement to the EMEA on 3 March 2008.

Significant difference has been identified with regard to clinical safety. This refers to endometrial safety of Activelle 0.5 mg/0.1 mg, which had been insufficiently demonstrated according to the CHMP guideline for HRT products (EMEA/CHMP/021/97 rev 1) and this was considered to be of serious public health concern.

The arbitration procedure started on 19 March 2008 with the adoption of a list of questions. The Rapporteur was Dr Pierre Demolis (FR) as Rapporteur and Co-Rapporteur(s) was Dr Ingemar Persson (SE). The Marketing Authorisation Holder provided written explanations on 5 May 2008.

During their June 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 **Activelle** and associated names, that the objections raised by France and Germany 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 majority on 26 June 2008.

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 September 2008.

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

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