European Medicines Agency

London, 14 August 2008
EMEA/CHMP/524135/2008

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP) OPINION FOLLOWING AN ARTICLE 6 (12) REFERRAL

Actira and associated names

International non-proprietary name (INN): moxifloxacin

BACKGROUND INFORMATION *

Actira film-coated tablets contain 400 mg moxifloxacin as hydrochloride. It is approved for the treatment of the following bacterial infections if they are caused by bacteria susceptible to moxifloxacin: acute exacerbation of chronic bronchitis; community acquired pneumonia, except severe cases; acute bacterial sinusitis (adequately diagnosed).

The tablets have to be taken orally once daily for up to 10 days, depending on the indication. In clinical trials the tablets have been studied for up to 14 days treatment. Actira was initially approved in June 1999.

This Referral procedure relates to a request for arbitration concerning a type II variation for a new indication to include treatment of mild to moderate pelvic inflammatory disease (PID), i.e. infections of upper genital tract, including salpingitis and endometritis.

At the end of the mutual recognition procedure there was a discrepancy between different EU Member States regarding the wording of the indication that should adequately reflect the clinical data submitted by the company, and an official referral for arbitration according to Article 6(12) of Commission Regulation EC No 1084/2003, as amended, was notified by Belgium to the CHMP on 19 October 2007.

The main unresolved areas of concern identified by Belgium were in terms of efficacy the emergence of moxifloxacin-resistant strains of *N. gonorrhoeae* and the feasibility of the treatment in the proposed indication in clinical practice. In terms of safety the longer treatment duration, the risk of effects on cartilage in young patients and the risk of QT-prolongation were of concern.

The arbitration procedure was discussed by the CHMP at its plenary meeting in November 2007 and a Rapporteur (Dr Harald Enzmann) and Co-Rapporteur (Dr. Pieter Neels) were appointed. The Referral procedure was initiated on 15 November with the adoption of a CHMP List of Questions to be addressed by the MAHs.

Written explanations were provided by the Marketing Authorisation Holders (MAH) on 18 January 2008 and 27 February 2008.

The CHMP considered that moxifloxacin cannot be used in the setting of PID in empirical monotherapy due to the increasing incidence of fluoroquinolone-resistant *N. gonorrhoeae*, unless a resistant strain can be excluded. Moxifloxacin should therefore be given in combination with another appropriate antibacterial agent (e.g. a cephalosporin) for the treatment of mild to moderate PID, unless moxifloxacin-resistant *N. gonorrhoeae* can be excluded.

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The Committee further considered that the benefit/risk balance concerning the use of moxifloxacin up to 14 days in the PID indication remains positive, and that information and recommendations on the use of moxifloxacin, and the measures that should be taken before it is prescribed, are adequately addressed in the 'contraindications' and 'special warnings and precautions for use' sections of the EU SPC.

In view of the data provided on efficacy and safety, the benefit/risk of the proposed extended indication "mild to moderate pelvic inflammatory disease" was therefore considered to be positive by the CHMP as the initially proposed wording was adequately revised to reflect the current knowledge.

On 19 March 2008, the CHMP recommended the variation to the Marketing Authorisations to include this indication.

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

The final opinion was converted into a Decision by the European Commission on 14 July 2008.

∗ Notes: the information given in this document and its annexes reflects only the CHMP opinion dated 19 March 2008. The Member States' competent authorities will continue to keep the product under regular review.

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