European Medicines Agency
Evaluation of Medicines for Human Use

22 May 2006
CHMP/477258/2006

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

Atorvastatin

International Non-Proprietary Name (INN): **atorvastatin**

BACKGROUND INFORMATION*

Sortis and associated names contain atorvastatin, a HMG-CoA-reductase inhibitor (known as statin), which inhibits the synthesis of cholesterol. It is registered in the EU since 1996 through Mutual Recognition Procedure and national procedures. Atorvastatin is currently indicated as an adjunct to diet for reduction of elevated total cholesterol, LDL-cholesterol, apolipoprotein B, and triglycerides in patients with primary hypercholesterolaemia including familial hypercholesterolaemia (heterozygous variant) or combined (mixed) hyperlipidaemia (Corresponding to Types IIa and IIb of the Fredrickson classification) when response to diet and other nonpharmacological measures is inadequate. Atorvastatin is also indicated to reduce total-C and LDL-C in patients with homozygous familial hypercholesterolaemia as an adjunct to other lipid-lowering treatments (e.g. LDL apheresis) or if such treatments are unavailable.

This Referral procedure relates to a request for Arbritation concerning a type II variation for a new indication in the "*Prevention of cardiovascular events in patients estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors"*. At the end of the MRP procedure there was a discrepancy between different Member States regarding the wording of the indication that adequately reflects 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 Spain to the CHMP on 1.12.2005.

The arbitration procedure was discussed and initiated by the CHMP at its plenary meeting in December 2005, and a Rapporteur (Dr Eric Abadie) and Co-Rapporteur (Dr Bengt Ljungberg) were appointed. The questions identified pertained to:
i) the lack of a significant effect in favour of atorvastatin for the composite primary endpoint and several secondary endpoints in the female subgroup,
ii) the exclusion of non-diabetic patients at high cardiovascular risk from the proposed indication,
iii) the higher cardioprotective effect of atorvastatin when used in combination with particular antihipertensive therapies
iv) the extent to which the claimed therapeutic indication could be applied to atorvastatin doses other than those tested in the pivotal trials

The company responded to these points on 19 January 2006.

Based on the evaluation of the currently available data and the (Co-)Rapporteurs' assessment reports, the CHMP adopted an opinion on 23 March 2006 recommending the variation of the Marketing Authorisations for the addition of the following new indication:
"Prevention of cardiovascular events in patients estimated to have a high risk for a first cardiovascular event (see section 5.1), as an adjunct to correction of other risk factors."

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.europa.eu http://www.emea.europa.eu

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.

The final opinion was converted into a Decision by the European Commission on 22 May 2006.

* **Notes**:
The information given in this document and Annexes reflect only the CHMP Opinion dated 23 March 2006.
The Member States competent authorities will continue to keep the product under regular review.