European Medicines Agency
Evaluation of Medicines for Human Use

London, 23 July 2009
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CHMP ASSESSMENT REPORT

FOR

ALENDRONATE SODIUM AND COLECALCIFEROL, MSD

International Nonproprietary Name: alendronic acid / colecalciferol

Procedure No. EMEA/H/C/001180

Assessment Report as adopted by the CHMP with all information of a commercially confidential nature deleted

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1. BACKGROUND INFORMATION ON THE PROCEDURE

1.1 Submission of the dossier

The applicant Merck Sharp & Dohme Ltd. submitted on 06 May 2009 an application for Marketing Authorisation to the European Medicines Agency (EMEA) for ALENDRONATE SODIUM AND COLECALCIFEROL, MSD, through the centralised procedure falling within the Article 3(2) and point (a) of Annex of Regulation (EC) No 726/2004.

The legal basis for this application refers to:

Centralised / Article 10(c) of Directive 2001/83/EC, as amended – relating to informed consent from a marketing authorisation holder for an authorised medicinal product.

The applicant applied for the following indication:
Treatment of postmenopausal osteoporosis in patients at risk of vitamin D insufficiency.
ALENDRONATE SODIUM AND COLECALCIFEROL, MSD reduces the risk of vertebral and hip fractures.

Scientific Advice:
No scientific advice has been received for this application. The applicant received Scientific Advice from the CHMP for the initial product, FOSAVANCE on 25 July 2002, 26 June 2003 and 15 December 2004. The Scientific Advice pertained to non-clinical and clinical aspects of the dossier.

Licensing status:
The initial product, FOSAVANCE, has been given a Community Marketing Authorisation on 24 August 2005 (FOSAVANCE 70 mg / 2800 IU tablets) and 4 October 2007 (FOSAVANCE 70 mg /5600 IU tablets).

The Rapporteur and Co-Rapporteur appointed by the CHMP and the evaluation teams were:
Rapporteur: **Ian Hudson** Co-Rapporteur: **Andrea Laslop**

1.2 Steps taken for the assessment of the product

- The application was received by the EMEA on 06 May 2009.
- The procedure started on 24 May 2009.
- The Rapporteur's first Assessment Report was circulated to all CHMP members on 18 June 2009. The Co-Rapporteur's first Assessment Report was circulated to all CHMP members on 25 June 2009.
- During the meeting on 20-23 July 2009, the CHMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion for granting a Marketing Authorisation to ALENDRONATE SODIUM AND COLECALCIFEROL, MSD on 23 July 2009. The applicant provided the letter of undertaking on the follow-up measures to be fulfilled post-authorisation on 15 July 2009.

2 SCIENTIFIC DISCUSSION

2.1 Introduction

This application has been submitted as an informed consent application in accordance with Article 10c of Directive 2001/83/EC as amended.

Therefore the MAH of the reference product, FOSAVANCE has provided consent to allow access to Module 2 to Module 5 of the initial dossier and any subsequent post-marketing procedures submitted, assessed and approved. A satisfactory letter of consent, dated 19 May 2009 is provided and accepted.
FOSAVANCE had been submitted as a full application under Art 8(3) of Directive 2001/83/EC.
The dossier submitted for ALENDRONATE SODIUM AND COLECALCIFEROL, MSD consists only of Module 1 information.

As a consequence, quality, safety and efficacy of ALENDRONATE SODIUM AND COLECALCIFEROL, MSD are identical to the up to date quality, safety and efficacy profile of FOSAVANCE; the latest CHMP Opinion issued for FOSAVANCE at the time of the CHMP opinion for the current dossier was for the FOSAVANCE procedure nr EMEA/H/C/000619/II/012.
Information on the scientific discussions can be found in the FOSAVANCE CHMP assessment report and in the European Public Assessment Report (EPAR).

The approved indication is: Treatment of postmenopausal osteoporosis in patients at risk of vitamin D insufficiency.
ALENDRONATE SODIUM AND COLECALCIFEROL, MSD reduces the risk of vertebral and hip fractures.

The initially proposed invented name (IN) was refused by the NRG (Name Review Group) before the end of this procedure. The applicant will submit a type I B variation in order to change the IN (invented name) when accepted by the NRG (Name Review Group).

2.2 Quality aspects

Since this application is an informed consent of the FOSAVANCE application, the quality data in support of the ALENDRONATE SODIUM AND COLECALCIFEROL, MSD application are identical to the up-to-date quality data of the FOSAVANCE dossier which have been assessed and approved (including all post-marketing procedures).

2.3 Non-clinical aspects

Since this application is an informed consent of the FOSAVANCE application, the non-clinical data in support of the application are identical to the up-to-date non-clinical data of the FOSAVANCE dossier, which have been assessed and approved (including the ERA and all post-marketing procedures)

2.4 Clinical aspects

Since this application is an informed consent of the FOSAVANCE application, the clinical data in support of the application are identical to the up-to-date clinical data of the FOSAVANCE dossier, which have been assessed and approved (including all post-marketing procedures). Furthermore the applicant has committed to update the current dossier with ongoing/planned follow-up measures for the reference product.

- User Consultation

Since this application is an informed consent of the FOSAVANCE application, the user consultation submitted for the ALENDRONATE SODIUM AND COLECALCIFEROL, MSD application is identical to the one submitted for the FOSAVANCE dossier, which was considered acceptable by the CHMP.

2.5 Pharmacovigilance

Detailed description of the Pharmacovigilance system

The CHMP considered that the Pharmacovigilance system as described by the applicant fulfils the legislative requirements.

Risk Management Plan

The MAA submitted a risk management plan.

A referral regarding bisphosphonates and ONJ (Osteonecrosis of the Jaw; Article 5(3) of Regulation (EC) No 726/2004) is currently on-going (EMEA/H/A-5(3)/1130). The RMP should be updated according to the final outcome of this procedure. In addition, stress fractures that have been included in the SPC with FOSAVANCE variations EMEA/H/C/619/II/010 and EMEA/H/C/759/II/008 following a class review should be discussed within the next RMP update. This is included as a follow-up measure.

Table Summary of the risk management plan

Safety Concern	Proposed Pharmacovigilance Activities (routine and additional)	Proposed Risk Minimisation Activities (routine and additional)
Oesophageal Adverse Experiences	Routine pharmacovigilance	Labelling: • Special warning and precautions for use in section 4.4 of the EUSPC; section 2 “Before you take ALENDRONATE SODIUM AND COLECALCIFEROL, MSD” of the EU PPI
Osteonecrosis of the jaw	Routine pharmacovigilance and enhanced pharmacovigilance	Labelling: • Special warnings and precautions for use in section 4.4 of the SPC; Undesirable side effects in section 4.8 of the SPC;
Use during pregnancy and lactation	Routine pharmacovigilance	Labelling: • Pregnancy and lactation in section 4.6 of the SPC; Pregnancy and breast-feeding in section 2 of the EU PPI
Use in patients below 18 years of age	Routine pharmacovigilance	Labelling: • Posology and method of administration in section 4.2 of the SPC; • Children and adolescents in section 2 of the EU PPI

The CHMP, having considered the data submitted in the application, is of the opinion that no additional risk minimisation activities are required beyond those included in the product information.

2.6 Overall conclusions, risk/benefit assessment and recommendation

Since this application is an informed consent of the FOSAVANCE application the CHMP considered by consensus/majority that the risk-benefit balance of ALENDRONATE SODIUM AND COLECALCIFEROL, MSD in the treatment of postmenopausal osteoporosis in patients at risk of vitamin D insufficiency was favourable and therefore recommended the granting of the marketing authorisation.