24th October 2011

Circular No. P 14/2011

Dear Healthcare Professional,

Re: Review of the Benefit-Risk ratio of Protelos and Osseor has started at the European Medicines Agency

Protelos, or Osseor (strontium ranelate) as it is called in some European countries and manufactured by Les Laboratoires Servier, were authorised via the European centralised procedure in 2004 and are indicated for treatment of postmenopausal osteoporosis to reduce the risk of vertebral and hip fractures.

Venous thromboembolism (VTE) and drug rash with eosinophilia and systemic symptoms (DRESS) are known risks of these medicines. The risk of VTE was identified in clinical trials and the risk of DRESS through spontaneous reporting soon after the granting of the initial marketing authorisation, and warnings are included in the product information. The risks are addressed in the product's risk-management plan and have been kept under close review by the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP).

A study analysing the side effects associated with strontium ranelate that were spontaneously reported in France from January 2006 to March 2009 to Les Laboratoires Servier or the French competent authority (Afssaps) noted 199 severe adverse reactions, of which 52% were cardiovascular (most frequently VTE events) and 26% were cutaneous. The authors concluded that DRESS syndrome is unpredictable, but that the VTE risk could be reduced by adding a contraindication for patients with a history of VTE and by stopping treatment if a new VTE risk situation occurs. Based on a recent pharmacovigilance update and pending an EU-wide review, Afssaps recommended restricting the use of strontium ranelate to those patients who are under 80 years of age, at high risk of fractures and who cannot take bisphosphonates.

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An EU wide review has been therefore initiated at the European Medicines Agency's CHMP. The Committee is now reviewing all relevant data on the cardiovascular and cutaneous safety concerns, taking into account existing risk-minimisation measures and their impact on the benefit-risk balance for Protelos and Osseor. The Committee will issue an opinion on measures necessary to ensure the safe and effective use of these medicines and whether or not the marketing authorisations for these medicines should be changed, suspended or revoked.

While this assessment is ongoing no changes to the conditions for use of Protelos and Osseor are being recommended Europe-wide.

Healthcare professionals are encouraged to maintain vigilance on Protelos. Suspected adverse drug reactions may be reported using the Medicines Authority yellow card scheme or online at http://www.medicinesauthority.gov.mt/pub/adr.doc or to the marketing authorisation holder or their local representatives.

The Medicines Authority has participated in the discussions held at the EMA and is in agreement with the full **press release** issued by the EMA, attached here for your perusal.

Healthcare professionals are encouraged to check the Medicines Authority website regularly for product safety updates as these are issued on an ongoing basis.

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