LES LABORATOIRES SERVIER

Direct Healthcare Professional Communication

New restricted indication and monitoring recommendations for the use of Protelos (strontium ranelate)

Dear Healthcare Professional,

This letter is to inform you of the new restricted indication and monitoring recommendations for Protelos following the European Medicines Agency's full evaluation of the benefits and risks of strontium ranelate. Available data does not show evidence of an increased cardiovascular risk in patients without contra-indications introduced in April 2013. This letter is sent in agreement with the European Medicines Agency (EMA) and the Malta Medicnes Authority.

Summary:

- **The use of Protelos/Osseor is now restricted to the treatment of severe osteoporosis:**
  - **in postmenopausal women,**
  - **in adult men,**

  at high risk of fracture, for whom treatment with other medicinal products approved for the treatment of osteoporosis is not possible due to, for example, contraindications or intolerance. In postmenopausal women, strontium ranelate reduces the risk of vertebral and hip fractures.
- **The current cardiovascular contraindications remain in place. Patients with established, current or past history of ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease or uncontrolled hypertension should not be treated with Protelos/Osseor.**
- **Prescribers are advised to:**
  - **assess patients' risk of developing cardiovascular disease before starting treatment.**
  - **monitor patients' cardiovascular risk on a regular basis, generally every 6 -12 months.**
  - **stop treatment if the patient develops ischaemic heart disease, peripheral arterial disease, cerebrovascular disease or if hypertension is uncontrolled.**
- **Treatment should only be initiated by a physician with experience in the treatment of osteoporosis.**
- **Educational materials regarding the current indications and restrictions of Protelos/Osseor will be provided for healthcare professionals and patients.**

Merci d'adresser toute correspondance au :
Siège social : 50, rue Carnot • 92284 Suresnes cedex • Tél.: 01.55.72.60.00
S.A.S. au capital de 34.590.852 euros • 085 480 796 RCS Nanterre

Further information on the review of Protelos/Osseor:

The review by the European Medicines Agency was initiated following concerns about cardiovascular safety.

These final recommendations from the Agency's Committee for Medicinal Products for Human Use (CHMP) come after initial advice from the Pharmacovigilance Risk Assessment Committee (PRAC) to suspend the medicine due to its cardiovascular risk. However, the CHMP considered that the cardiovascular risk identified by the PRAC can be sufficiently reduced to allow the medicine to be used in patients who do not have an alternative treatment.

Strontium ranelate is associated with an increased risk of cardiovascular disorders, including myocardial infarction. This conclusion is predominantly based on data from pooled placebo-controlled studies in postmenopausal osteoporotic patients (3,803 patients treated with strontium ranelate, corresponding to 11,270 patient-years of treatment, and 3,769 patients treated with placebo, corresponding to 11,250 patient-years of treatment). In this data set, a significant increased risk of myocardial infarction was observed in strontium ranelate treated patients as compared to placebo (1.7% versus 1.1 %), with a relative risk of 1.6 (95% CI = [1.07 ; 2.38]). There was also an increased risk of venous thrombotic and embolic events compared to placebo (1.9% versus 1.3 %), with a relative risk of 1.5 (95% CI = [1.04 ; 2.19]).

However available data does not show evidence of an increased cardiovascular risk in patients without contra-indications (established, current or past history of ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease or uncontrolled hypertension).

Regarding the benefits, the efficacy data showed an effect in preventing fractures, including in patients at high risk of fracture.

Call for reporting

As a reminder, there is a need to report any suspected adverse reactions in accordance with the national spontaneous reporting system to:
GALEPHARMA Ltd - Tel: +(356) 21 247 082 - 14-15, Strait Street, Valletta, VLT1430, Malta.

Alternatively any suspected adverse reactions can be reported to the Medicines Authority Post-licensing Directorate by filling in an ADR form and sending by post to 203, Level 3, Rue D' Argens, Gzira GZR 1368, MALTA, or by email to postlicensing.medicinesauthority@gov.mt or submitting online at www.medicinesauthority.gov.mt/adrportal.

Communication information

For further inquiries concerning this information, please contact GALEPHARMA Ltd
Tel: +(356) 21 247 082 – 14-15, Strait Street, Valletta, VLT1430, Malta.

Patricia MAILLERE
General Director
Worldwide Regulatory Affairs
Les Laboratoires Servier

Graziella GRECH
Field Sales Manager
for Les Laboratoires Servier
medicinal products in Malta
Responsible Person for Pharmacovigilance
Galepharma Ltd