



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

15 April 2014  
EMA/235924/2014

## Protelos/Osseor to remain available but with further restrictions

The European Medicines Agency has concluded its review of Protelos/Osseor and has recommended further restricting the use of the medicine to patients who cannot be treated with other medicines approved for osteoporosis. In addition these patients should continue to be evaluated regularly by their doctor and treatment should be stopped if patients develop heart or circulatory problems, such as uncontrolled high blood pressure or angina. As recommended in a previous review, patients who have a history of certain heart or circulatory problems, such as stroke and heart attack, must not use the medicine.

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.

'The CHMP agreed with the PRAC's overall assessment of the risks of Protelos/Osseor. Both committees worked in close collaboration and the PRAC's recommendation was instrumental for us to fully assess the benefit-risk profile of the medicine', said Tomas Salmonson, chair of the CHMP. 'However, the CHMP considered that, for patients who have no alternative treatment, regular screening and monitoring to exclude cardiovascular disease will sufficiently reduce the risk identified by the PRAC so that these patients can continue to have access to the medicine.'

In arriving at its conclusions, the CHMP noted that study data showed a beneficial effect in preventing fractures, including in patients at high risk of fracture. In addition, available data do not show evidence of an increased cardiovascular risk with Protelos/Osseor in patients who did not have a history of heart or circulatory problems.

The CHMP considered that the cardiovascular risk in patients taking Protelos/Osseor can be managed by restricting its use to patients with no history of heart and circulatory problems and limiting its use to those who cannot take other medicines approved for the treatment of osteoporosis. In addition, patients treated with Protelos/Osseor should be screened and monitored regularly, every 6 to 12 months.

Additional risk minimisation measures include providing educational material to prescribers to ensure that only the appropriate patients are treated with the medicine. Importantly, the company is required to conduct further research to demonstrate the effectiveness of the new measures. The Committee concluded that given the benefits seen in preventing fractures in patients at high risk, Protelos/Osseor



should remain an option for patients with no history of cardiovascular disease who cannot take other medicines.

In deciding on how Protelos/Osseor should be used, the CHMP took into account the PRAC's analysis of its benefits and risks as well as advice from osteoporosis experts that there is a group of patients who could benefit from the medicine.

'The PRAC has worked closely with the CHMP throughout the procedure and while we acknowledge that the recommendations of the two committees differed, our understanding of the medicine's benefit-risk profile is closely aligned and we share a common view of the importance of effective monitoring of cardiovascular risk', said June Raine, chair of the PRAC. 'The PRAC will continue to monitor the safety of Protelos /Osseor and the effectiveness of risk minimisation in long term use.'

The CHMP's recommendations were sent to the European Commission, which endorsed them and issued a final legally binding decision valid throughout the EU.

### **Information to patients**

- Protelos/Osseor will only be prescribed for preventing fractures in post-menopausal women and men with severe osteoporosis who have a high risk of fracture and cannot be treated with other medicines approved for osteoporosis.
- Before starting treatment, your doctor will assess your risk of heart disease and high blood pressure and continue to check your risk at regular intervals during treatment.
- You should not take Protelos/Osseor if you have or have had heart or circulatory problems such as stroke, heart attack, or obstruction of the blood flow in the arteries.
- Your treatment with Protelos/Osseor will be stopped if you develop heart or circulatory problems during treatment.
- If you have any questions, speak to your doctor or pharmacist.

### **Information to healthcare professionals**

- Protelos/Osseor should only be used to treat severe osteoporosis in postmenopausal women and 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;
- Protelos/Osseor must not be used in patients with established, current or past history of ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease, or those with uncontrolled hypertension;
- Doctors should continue to base their decision to prescribe Protelos/Osseor on an assessment of the individual patient's risks. The patient's risk of developing cardiovascular disease should be evaluated before starting treatment and on a regular basis thereafter, generally every 6 to 12 months;
- Protelos/Osseor should be stopped if the patient develops ischaemic heart disease, peripheral arterial disease or cerebrovascular disease, or if hypertension is uncontrolled;
- Doctors should review their patients currently on Protelos/Osseor as necessary.

This final EMA recommendation on the use of Protelos/Osseor was based on an analysis of pooled data from randomised studies in around 7,500 post-menopausal women with osteoporosis. The results showed an increased risk of myocardial infarction with Protelos/Osseor as compared with placebo (1.7% versus 1.1 %), with a relative risk of 1.6 (95% CI, 1.07 to 2.38), and an increased risk of venous thrombotic and embolic events — 1.9% versus 1.3 % with a relative risk of 1.5 (95% CI, 1.04 to 2.19).

Available data do not show evidence of an increased cardiovascular risk in patients without established, current or past history of ischaemic heart disease, peripheral arterial disease or cerebrovascular disease, or in those without uncontrolled hypertension.

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

---

### **More about the medicine**

Protelos/Osseor (strontium ranelate) is authorised in the EU to treat severe osteoporosis (a disease that makes bones fragile) in women who have been through the menopause and who are at high risk of fracture (broken bones) to reduce the risk of fractures of the spine and the hip. It is also used to treat severe osteoporosis in men who are at high risk of fracture.

The current recommendations add to EMA recommendations made in April 2013 not to use Protelos/Osseor in patients with known circulatory problems. More information can be found [here](#).

### **More about the procedure**

The review of Protelos/Osseor was initiated in May 2013 at the request of European Commission under Article 20 of Regulation (EC) No 726/2004.

The first stage of this review was conducted by the Pharmacovigilance Risk Assessment Committee (PRAC), the committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. The PRAC's recommendations were then sent to the Committee for Medicinal Products for Human Use (CHMP) responsible for all questions concerning medicines for human use, which adopted the Agency's final opinion.

Further information on the PRAC recommendation and the background to this review can be found on Agency's website.

The CHMP opinion was forwarded to the European Commission, which endorsed it and issued a final legally binding decision valid throughout the EU on 15 April 2014.

---

### **Contact our press officers**

Monika Benstetter or Martin Harvey

Tel. +44 (0)20 3660 8427

E-mail: [press@ema.europa.eu](mailto:press@ema.europa.eu)