European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

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QUESTIONS AND ANSWERS ON THE SAFETY OF PROTELOS/OSSEOR (strontium ranelate)

As part of its continuous monitoring of medicines, the European Medicines Agency (EMEA) has become aware of new safety information on Protelos/Osseor (strontium ranelate), concerning the risk of a severe allergic reaction to the medicine called 'drug rash with eosinophilia and systemic symptoms' (DRESS).

The EMEA's Committee for Medicinal Products for Human Use (CHMP) has concluded that a warning on the risks of DRESS should be introduced in the medicine's prescribing information, stating that patients showing symptoms of the syndrome should stop treatment and contact their doctor immediately.

What is Protelos/Osseor?
Protelos/Osseor is a medicine containing the active substance strontium ranelate. It is used to treat osteoporosis (a disease that makes bones fragile) in women who have been through the menopause, to reduce the risk of fractures (broken bones) in the spine and the hip. It is taken daily as a long-term treatment.

Osteoporosis happens when not enough new bone grows to replace the bone that is naturally broken down. Gradually, the bones become fragile and more likely to break. The active substance in Protelos/Osseor, strontium ranelate, acts on the bone structure. Once in the gut, strontium ranelate releases strontium, which is similar to calcium. Like calcium, it gets absorbed into the bone, where it stimulates bone formation and reduces bone breakdown. The mechanism of action of strontium is not fully understood but it stimulates bone formation and reduces bone breakdown.

What is DRESS?
DRESS, also known as drug hypersensitivity syndrome, is a rare but serious and life-threatening type of allergic reaction to some medicines. It starts with a skin rash, accompanied by a fever, swollen glands, increased numbers of white cells in the blood and effects on the liver, kidneys and lung. It can result in kidney or liver failure. Stopping treatment, together with corticosteroid therapy (medicines that reduce the activity of the immune system), usually results in the symptoms improving, but recovery can be slow and there is a risk of symptoms returning during the recovery period.

What were the concerns of the CHMP?
In November 2007, as part of its continuous monitoring of the safety of this medicine, the CHMP became aware of an increasing number of reports of DRESS in patients taking Protelos/Osseor. Since the medicine was first marketed in Europe in 2004, 16 cases of the syndrome have been reported following a total of around 570,000 'patient-years of exposure', which is equivalent to 570,000 patients each having taken the medicine for a year.

In the 16 cases reported to the CHMP, symptoms of DRESS appeared within three to six weeks after the patients started to take Protelos/Osseor. All of the cases were severe, requiring hospital treatment. Two of the patients died. The link between Protelos/Osseor treatment and DRESS was not recognised immediately, and there was a delay before the medicine was stopped. This could have made the outcome worse in these patients.

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What were the conclusions of the CHMP?
The CHMP concluded that the use of Protelos/Osseor is linked to an increased risk of DRESS syndrome and that there is a need for prompt action. In the light of this, the Committee recommended that a warning on DRESS should be immediately introduced into the prescribing and patient information for Protelos/Osseor. Doctors and patients are warned of the risk of severe allergic reactions with the medicine, and of the need for patients who develop a rash while taking Protelos/Osseor to stop taking the medicine and contact their doctor immediately.

This warning has been provisionally introduced through an urgent regulatory procedure. The Committee also requested that the company provide a letter to be sent to healthcare providers explaining the changes in recommendations of use for Protelos/Osseor.

What is the advice to patients and prescribers?
- Women who start to experience symptoms of DRESS, such as rash, while taking Protelos/Osseor should stop taking the medicine and consult their doctor immediately. These patients should not take Protelos/Osseor again.
- Doctors should only prescribe Protelos/Osseor according to the updated prescribing information.
- Women who are taking Protelos/Osseor and have questions or concerns should talk to their doctor or pharmacist.

For further information, see the updated Product Information adopted by the CHMP on 15 November 2007.