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Xgeva (*denosumab*)

An overview of Xgeva and why it is authorised in the EU

What is Xgeva and what is it used for?

Xgeva is a medicine used to prevent bone complications in adults with advanced cancer that has spread to the bone. These complications include fractures (breaks in the bone), spinal compression (pressure on the spinal cord caused by damage to the surrounding bone), or bone problems requiring radiotherapy (treatment with radiation) or surgery.

Xgeva is also used to treat a type of bone cancer called giant cell tumour of bone in adults and adolescents whose bones have fully developed. It is used in patients who cannot be treated by surgery or in whom surgery is likely to cause complications.

Xgeva contains the active substance denosumab.

How is Xgeva used?

Xgeva can only be obtained with a prescription. It is available as a solution for injection under the skin.

To prevent bone complications in cancer that has spread to the bone, 120 mg is given once every 4 weeks as a single injection under the skin in the thigh, abdomen (belly) or upper arm.

In patients with giant cell tumour of bone, 120 mg is injected under the skin once a week for 3 weeks, and then once every 4 weeks.

Patients should take calcium and vitamin D supplements while being treated with Xgeva.

For more information about using Xgeva, see the package leaflet or contact a doctor or pharmacist.

How does Xgeva work?

The active substance in Xgeva, denosumab, is a monoclonal antibody which has been designed to recognise and attach to a protein called RANKL. This protein activates osteoclasts, the cells in the body that are involved in breaking down bone tissue. By attaching to RANKL and blocking it, denosumab reduces the formation and activity of the osteoclasts. This reduces the loss of bone, making fractures and other serious bone complications less likely. The cells in giant cell tumour of bone are also activated via RANKL, and treatment with denosumab prevents them from growing and breaking down bone, allowing normal bone to replace the tumour.

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What benefits of Xgeva have been shown in studies?

Prevention of bone complications

Xgeva was compared with zoledronic acid (another medicine used to prevent bone complications) in four main studies in patients with different types of cancer which had spread to the bone.

All the studies looked at the risk of patients having a first 'skeletal-related event' (such as a fracture, pressure on the spinal cord or the need for radiotherapy or surgery to the bone) during the study period by measuring how long it took for this event to happen.

The first study involved 2,046 patients with breast cancer and the second study involved 1,901 men with prostate cancer which did not respond to hormonal treatment. In these studies, Xgeva reduced the risk of developing a first skeletal-related event by 18% compared with zoledronic acid.

The third study involved 1,776 patients with advanced solid tumours in various parts of the body or with multiple myeloma (a cancer of the bone marrow). In this study, Xgeva reduced the risk of developing a first skeletal-related event by 16% compared with zoledronic acid.

In another study involving 1,718 patients with newly diagnosed multiple myeloma, Xgeva was as effective as zoledronic acid in delaying the patients' first skeletal-related event.

Treatment of giant cell tumour of bone

In patients with giant cell tumour of bone, Xgeva was effective in controlling the disease. Two main studies looked at the effect of Xgeva in adults or full-grown adolescents with giant cell tumour of bone that was unsuitable for surgery or in whom surgery would have resulted in severe complications like amputation of a limb.

The first study involved 37 patients, 86 % of whom responded to treatment with Xgeva. A response to treatment was defined as elimination of at least 90% of the giant cells or no progression of the condition after 25 weeks of treatment.

In the second study which involved 507 patients treatment with Xgeva prevented surgery in about half (109 of 225) of the group in whom surgery would have resulted in complications. Of the remainder, 84 were able to have less extensive surgery than previously planned. About 20% of patients were able to have complete surgical removal of the cancer. For 31 patients their disease got worse during treatment.

What are the risks associated with Xgeva?

The most common side effects with Xgeva (seen in more than 1 patient in 10) are hypocalcaemia (low levels of calcium in the blood), pain in the muscles and bones, dyspnoea (difficulty breathing) and diarrhoea. Other common side effects (seen in up to 1 patient in 10) are development of another form of cancer in patients with advanced cancer, hypophosphataemia (low levels of phosphate in the blood), excessive sweating, tooth loss and osteonecrosis in the jaw (damage to the bones of the jaw, which could lead to pain, sores in the mouth and loose teeth).

Xgeva must not be used in patients with wounds from dental or mouth surgery have not yet healed, or in people with severe, untreated hypocalcaemia.

For the full list of side effects and restrictions with Xgeva, see the package leaflet.

Why is Xgeva authorised in the EU?

The European Medicines Agency decided that Xgeva's benefits are greater than its risks for patients with cancers that has spread to the bone, and it can be authorised for use in the EU. The Agency noted that there is a need for an effective treatment for bone disease in advanced cancer, particularly for patients with kidney problems since currently available treatments can be toxic for the kidneys. The Agency considered that Xgeva was effective in preventing bone-related events and was less toxic to the kidneys and easier to use than existing treatments.

For patients with giant cell tumour of bone the possibility of complete surgical removal of the tumour after treatment and the reduction in extent of the surgery in some patients were considered clinically important. The Agency considered that the benefits of Xgeva in giant cell tumour of bone were greater than the risks, and recommended that it be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Xgeva?

The company that markets Xgeva will provide a card to inform patients about the risk of osteonecrosis of the jaw and to instruct them to contact their doctor if they have symptoms.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Xgeva have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Xgeva are continuously monitored. Side effects reported with Xgeva are carefully evaluated and any necessary action taken to protect patients.

Other information about Xgeva

Xgeva received a marketing authorisation valid throughout the EU on 13 July 2011.

Further information on Xgeva can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.

This overview was last updated in 06-2018.