Pharmacotherapeutic report on denosumab (XGEVA®) for the 'prevention of skeletal-related events in adults with bone metastases from solid tumours'

Medicine. injection fluid. Every flacon contains 120 mg denosumab in 1.7 ml solution (70 mg/ml).

Summary of the therapeutic value

Intended effects. In bone metastases from breast and prostate cancer, denosumab was statistically significantly superior compared with zoledronic acid in delaying a first skeletal-related event. In patients with bone metastases from other solid tumors, statistically denosumab was not inferior compared to zoledronic acid in delaying a first skeletal-related event. This outcome parameter is of limited clinical significance for these patients. The dropout rates in the three trials was very high (about 70%), which is usual in studies involving patients with metastases. In all 3 studies both drugs were similar with respect to disease progression and overall survival. There were no consistent differences in quality of life and pain parameters.

Unintended effects. In the three direct comparative Phase III studies in patients with bone metastases, denosumab was similar to zoledronic acid with respect to the frequency, severity and nature of side effects as well as the extent to which it was tolerated. Hypocalcemia was seen more frequently with denosumab than with zoledronic acid, while infusion reactions were seen more often with zoledronic acid. There is still insufficient clarity about possible negative effects of denosumab in the long term. The number of cases of osteonecrosis of the jaw and skin infections was slightly up with denosumab compared with zoledronic acid, though the differences in frequency were not statistically significant. Gastrointestinal symptoms are more prominent side effects with oral bisphosphonates (especially when taken incorrectly), and infusion-related reactions with intravenous bisphosphonate.

Experience. Less experience has been obtained with denosumab than with bisphosphonates.

Applicability. Similarly to the bisphosphonates, denosumab may not be used in patients with hypocalcaemia. Unlike bisphosphonates, denosumab can be used in patients with severe renal impairment (creatinine clearance <35 ml/min), although monitoring is indicated for hypocalcaemia. Creatinine clearance should be monitored after every dose of a bisphosphonate, and dose adjustment is necessary when creatinine clearance <60 ml/min. Otherwise, there are no relevant differences in applicability between denosumab and bisphosphonates.

Ease of use. The advantage of denosumab is that it is given by subcutaneous injection, while parenteral bisphosphonates need an iv infusion (zoledronic acid in > 15 min and pamedroninic acid in 2-4 hours).

Final conclusion. In the treatment of bone metastases from solid tumors, the therapeutic value of s.c. denosumab is comparable with that of i.v. zoledronic acid.

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