All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG Secretariat Assessment Report – Limited submission

Denosumab (Xgeva®▼) 120 mg solution for injection

Company: Amgen Limited

Licensed indication under consideration:
Denosumab (Xgeva®▼) for the treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity

Marketing authorisation date: 1 September 2014

Comparator(s):

The applicant company suggest that there are no suitable comparators for unresectable giant cell tumour of bone (GCTB).

Limited submission details:

The limited submission criteria were met as the anticipated usage of denosumab in NHS Wales is considered to be of minimal budgetary impact.

Clinical effectiveness:

- GCTB is a rare tumour with limited treatment options. Surgery is the standard of care for patients with resectable disease; while it can be associated with severe morbidity, recurrence, and malignant transformation.
- Denosumab is the only licensed therapeutic option for the treatment of adults and skeletally mature adolescents with GCTB that is unresectable or where surgical resection is likely to result in severe morbidity. Clinical expert opinion sought by AWTTC also highlights localised radiotherapy as a treatment option however it is associated with adverse events which are difficult to justify in this patient population.
- Denosumab is recommended as an option for preventing skeletal-related events in adults with bone metastases from breast cancer and from solid tumours other than prostate. The evidence submitted by the company for the treatment of GCTB is from a retrospective independent review of tumour response from two open-label, single-arm, phase II studies.
- Overall, the majority (136/190 [72%]) of patients had a response in this analysis (based on the best response using any tumour response criteria). The European Medicines Agency highlights several lines of evidence that support the intended biological and clinically meaningful effect of denosumab, including a reported reduction in both the frequency and severity of surgery. However, there are limitations in the evidence owing to the rarity of the disease and the studies being uncontrolled.
- The safety profile is consistent with the known safety profile of denosumab. However, compared to the original licensed setting, this indication includes a younger patient population and longer duration of treatment. As such, further follow up is required to exclude effects related to long term treatment and known rare events such as osteonecrosis of the jaw and malignant transformation.

Budget impact:

- The company highlights an annual incidence of GCTB of one person per million in the UK, equating to three patients in Wales. Year one of the company's budget impact analysis is based on a prevalence of nine patients and an incidence of three patients a year thereafter. The company have assumed that in addition to unresectable patients, all prevalent resectable patients will become eligible for denosumab treatment due to recurrence. The company considers this is likely to be a small overestimate of the eligible patient population.
- The budget impact is estimated to be £34,425 in year one, £13,770 in year two and £12,240 in subsequent years.
- The budget impact estimates include medicine acquisition costs based on the approved Department of Health Patient Access Scheme and associated administration costs.
- The company estimates are based on the assumption that all eligible patients will receive treatment with denosumab due to a lack of effective licensed alternatives, and that each patient will receive a total of 16 doses based on the median observed in the studies. Budget impact calculations are based on patients receiving 15 doses in their first year of treatment and one further dose in the following year.

Additional information:

AWTTC is of the opinion that, if recommended, denosumab (Xgeva®▼) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

The company do not anticipate that denosumab (Xgeva®▼) will be supplied by a home healthcare provider.

Evidence search:

Date of evidence search: 9 June 2015.
Date of range of evidence search: No date limits were applied to database searches.

Further information:

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as:
All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Denosumab (Xgeva®▼) 120 mg solution for injection. Reference number: 1870. October 2015.