Denosumab

Indication
Palliative therapy for and prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumours, other than prostate cancer, if bisphosphonates would otherwise be prescribed.

(NICE TA265)

ICD-10 codes
Codes with a prefix C80

Regimen details

Day	Drug	Dose	Route
1	Denosumab	120mg	SC

Cycle frequency
28 days
In some circumstances, to coincide with cycles of chemotherapy it is acceptable to administer every 42 days (unlicensed – discuss with consultant)

Number of cycles
As long as clinical benefit.

Administration
Denosumab is administered as a single subcutaneous injection into thigh, abdomen or upper arm. Before administration, the denosumab solution should be inspected visually. The solution is a clear, colourless to slight yellow solution and may contain trace amounts of translucent to white proteinaceous particles. Do not inject the solution if it is cloudy or discoloured. Do not shake excessively.

To avoid discomfort at the site of injection, allow the vial to reach room temperature (up to 25^{o}C) before injecting and inject slowly. Inject the entire contents of the vial.

Pre-medication
Nil

Emetogenicity
Nil

Additional supportive medication
Oral supplement of 500 mg calcium and 400 IU vitamin D daily. Dose adjusted according to calcium levels.

Extravasation
N/A

Investigations – pre first cycle

ALL PATIENTS ARE RECOMMENDED TO HAVE A DENTAL ASSESSMENT PRIOR TO COMMENCING TREATMENT BECAUSE OF THE POTENTIAL RISK OF OSTEONECROSIS OF THE JAW. ANY DENTAL WORK SHOULD BE COMPLETED BEFORE STARTING DENOSUMAB

Investigation	**Validity period** (or as per local policy)
FBC	28 days
U+E (including creatinine)	14 days
Corrected calcium	14 days
Vitamin D level	14 days
Phosphate	14 days
Magnesium	14 days

Any pre-existing hypocalcaemia or low vitamin D levels must be corrected before treatment is given. If corrected calcium is < 2.0mmol/L, withhold treatment until hypocalcaemia has resolved. If vitamin D < 35nmol/L withhold treatment until the patient has had at least 2 weeks of high-dose treatment
If hypophosphatemia; phosphate replacement should be prescribed.
If hypomagnesaemia; magnesium replacement should be prescribed.

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC*	As indicated
U+E (including creatinine)	Every 2-3 months, more frequently if renal impairment.
Corrected calcium	2 weeks after first dose and then prior to each subsequent dose.
Phosphate	Prior to each dose.
Magnesium	As required.

* treatment may go ahead without FBC

In addition 6 monthly dental assessment is recommended.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant. Ensure patient is not hypocalcaemic.

Dose modifications

- **Renal impairment**

No dose reduction is required in patients with mild- moderate renal impairment.
If Cr Cl<30mls/min, consultant must give go ahead to proceed as greater risk of hypocalacaemia. Closer monitoring of calcium levels will be required.

- **Hepatic impairment**

The safety and efficacy of denosumab has not been studied in patients with hepatic impairment, denosumab is not thought to be eliminated via hepatic mechanisms.

- **Other toxicities**

Withhold treatment for any Grade 3 or 4 adverse events, or for osteonecrosis of the jaw. If osteonecrosis is suspected or any dental extractions are required whilst on denosumab refer to dental hospital.

If corrected calcium is < 2.0 mmol/L, withhold the denosumab until hypocalcaemia resolved.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Osteonecrosis of the jaw (dental assessment prior to treatment and withhold denosumab for at least 3 weeks pre and post dental intervention)
Hypersensitivity

- **Frequently occurring side effects**

Flu like symptoms
Pain flare
Hypocalcaemia
Hypophosphataemia
Diarrhoea

- **Other side effects**

Numbness around mouth (sign of low calcium)
Renal impairment
Drug related hypersensitivity reaction
Atypical femoral fracture

Significant drug interactions – for full details consult product literature/ reference texts

No interaction studies have been performed.

In clinical trials, there were no clinically-relevant alterations in trough serum concentration and pharmacodynamics of denosumab by concomitant chemotherapy and/or hormone therapy or by previous intravenous bisphosphonate exposure.

Additional comments

Patients with fructose intolerance should not receive denosumab.
Patients should be advised to use adequate contraception methods during treatment.

References

- Summary of Product Characteristics Denosumab (Xgeva) accessed 10 May 2017 via www.medicines.org.uk
- NICE TA265 accessed 10 May 2017 via www.nice.org.uk
- Stopeck, AT et al; Journal of Clinical Oncology 2010; 28:5132-5139

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