Denosumab (XGEVA™)
Prevention of skeletal-related events from bone metastases of solid tumours (except prostate)

Background: Denosumab is a fully human monoclonal antibody that reduces osteoclast-mediated bone destruction. NICE has approved denusomab for the 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 (except prostate) where a bisphosphonate would normally be indicated (NICE TA 265).

Patient Group:

Prevention of skeletal-related events from bone metastases in patients with breast cancer and other solid tumours (excluding prostate cancer) where a bisphosphonate is indicated.

Life expectancy>12 weeks

Hypocalcaemia must be corrected prior to treatment.

Patient must be referred for preventative dentistry prior to treatment to prevent Osteonecrosis of the Jaw.

Pre-treatment Assessment:
Weight, FBC, U&E, LFTs
Calcium and Phosphate serum levels
Preventative dentistry

Regimen Details:

Day 1

Denosumab 120mg s/c injection into thigh, abdomen or upper arm once every 4 weeks.
Administration:

- Denosumab should be administered by a qualified healthcare professional.

- It should be administered into the thigh, abdomen or upper arm.

- Before administration, the denosumab solution should be inspected visually. The solution 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°C) before injecting and inject slowly. Inject the entire contents of the vial.

- A 27 gauge needle is recommended for the administration of denosumab. Do not re-enter the vial.

Pre meds: None

Anti-emetics: None.

Additional Medication: All patients should receive supplementation of at least 500 mg calcium and 400IU vitamin D is required in all patients, unless hypercalcaemia is present.

Monitoring and Assessment:

- Hypocalcaemia can occur at any time during therapy with denosumab and most commonly occurs within the first 6 months of dosing. Patients with severe renal impairment (creatinine clearance < 30 ml/min) or receiving dialysis are at greater risk of developing hypocalcaemia. If hypocalcaemia occurs while receiving denosumab, additional calcium supplementation may be necessary.

- U&E (Calcium and phosphate) – prior to each dose for the first 6 months then every 3 months. Patients with creatinine clearance < 30mL/min are at greater risk of hypocalcaemia and calcium levels should be monitored monthly in these patients.

Dose Modifications:
Renal Impairment

No dose modification required.

Hepatic Impairment

No dose modification required.

Pharmaceutical Care:

- Patients on denosumab should not be treated concomitantly with bisphosphonates.
- Advise patients about the importance of maintaining good oral hygiene.
- Denusomab may be stored at room temperature (up to 25°C) for up to 30 days in the original container. Once removed from the refrigerator, denusomab must be used within this 30 day period.
- Patients with rare hereditary problems of fructose intolerance should not use denosumab.
- Denosumab may be suitable for shared care under a formal shared care agreement.

Most Common Toxicities:

- Hypocalcaemia
- Hypophosphataemia
- Osteonecrosis of the jaw
- Cellulitis
- Diarrhoea
- Dyspnoea
- Excessive sweating

References:

1. SPC XGEVA™ Amgen Ltd. www.medicines.org.uk [accessed 2nd December 2012]