DRAFT: LOROS Guideline for Zoledronic Acid

Zoledronic acid is a bisphosphonate acting primarily on bone as a potent inhibitor of osteoclastic bone resorption

Indications

Treatment of:

- Bone pain in advanced malignancy (unlicensed)
- Tumour –induced hypercalcaemia (TIH)

(In the oncology setting it is used to prevent skeletal-related events in cancer-patients with bone involvement (pathological fracture, spinal compression, radiation/surgery to bone) NB onset of action for this indication is 2-3 months).

Prior to Administration

NB: DO NOT USE: in pregnancy or breastfeeding
if allergic to zoledronic acid or product excipients
if allergic to other bisphosphonates

- Clinical assessment – include hydration status-
rehydate with IV fluid if indicated (see below)

- Blood tests / Renal function tests:– within the week prior to each dose obtain serum calcium, creatinine, and urea levels

- Ask about dental problems – look for tooth or jaw pain. If there are any concerns, particularly if tooth extraction is needed, refer to a dentist for preventive dentistry before zoledronic acid treatment due to the uncommon risk of osteonecrosis of the jaw particularly if treating for > 12 months (see side-effects)

- Review drug treatment for interactions: Caution if using with thalidomide, or nephrotoxic drugs due to risk of further renal damage, and if using with aminoglycosides due to risk of prolonged hypocalcaemia

Rehydration in TIH - where indicated: 2 litres IV Sodium Chloride 0.9% over 12 hours prior to zoledronic acid dose (adjust according to patient's clinical condition)

Zoledronic Acid Dosage in Normal Renal Function

Indication: BONE PAIN (unlicensed) & skeletal–related events in malignancy:
Dose: 4mg (reconstituted & further diluted) intravenous infusion over a minimum of 15 minutes every 3 to 6 weeks

Ask GP to prescribe oral Calcium (500mg) & Vitamin D (400iu) supplement daily
(E.g. Calcichew D3 Forte)

Indication: TUMOUR-INDUCED HYPERCALCAEMIA
(Corrected serum calcium >3.0mmol/L or > 2.6 mmol/L and symptomatic)

Dose: 4mg (reconstituted & further diluted) as a SINGLE intravenous infusion over a minimum of 15 minutes

Dose Adjustment in Renal Impairment

Make dosage adjustments when estimated creatinine clearance is < 60ml/min:

Baseline Creatinine Clearance (ml/min) or Estimated GFR (ml/min)	Recommended dose	Volume of concentrate used to prepare infusion
> 60	4.0mg	5ml
50 - 60	3.5mg	4.4ml
40 - 49	3.3mg	4.1ml
30 - 39	3.0mg	3.8ml
< 30 or if serum creatinine : > 265 micromol/litre (bone pain or Ca with bone mets) > 400 micromol/litre in TIH	AVOID or use with caution - discuss with senior and pharmacy. Consider pamidronate instead.	

If renal function deteriorates following zoledronic acid treatment in patients with bone metastases withhold dose until serum creatinine returns to within 10% of baseline value. Re-initiate at same dose.

Preparing Zoledronic Acid Infusion:
Zoledronic acid is supplied as a 4mg in 5ml concentrated solution. Dilute it further with 100ml of a calcium-free solution: either 0.9% Sodium Chloride or 5% Glucose Use prepared solution immediately, (it can be stored in a refrigerator at 2-8 C, but is given at room temperature.) Discard any un-used prepared solution after 24 hours.

Monitoring Treatment
After treatment monitor renal function, serum calcium, phosphate and magnesium (NB Calcium levels reduce over 3 to 5 days)
Consider supplementation in hypocalcaemia, hypophosphataemia or hypomagnesaemia.

Potential Side-effects
The most common (<10%) side effects are usually mild and do not last long:
Nausea & vomiting, fatigue, anaemia, pyrexia, constipation, diarrhoea, dyspnoea, myalgia, anorexia, cough, arthralgia, lower limb oedema & others – see data sheet.

Osteonecrosis (bone damage) of the jaw is uncommon, but more likely after 12 months of treatment. Look for pain in mouth, teeth or jaw & for swelling / sores in the mouth, numbness or a feeling of heaviness in the jaw or loosening of teeth.
NB: There is no good treatment for osteonecrosis of the jaw at present.