Zoledronic acid is a bisphosphonate with a long duration of action.\(^1\) Bisphosphonates have an important role in the treatment of osteoporosis.\(^2\)

Zoledronic acid is available on Special Authority (SA)\(^3\) for Paget’s disease, osteoporosis including prevention of glucocorticoid-induced osteoporosis, and for the prevention of additional fractures after low-trauma hip fractures.\(^4\) Zoledronic acid is best used for patients who are likely to have poor tolerance or compliance with oral bisphosphonates, because of gastrointestinal problems, or if they cannot remain upright for 30 minutes, which is necessary with oral alternatives.\(^4\) Patients with a SA for alendronate will also be eligible for a SA for zoledronic acid.\(^3,4\)

Note: There are 2 forms of zoledronic acid, Aclasta\(^®\) (5mg) for osteoporosis, and Zometa\(^®\) (4mg) for oncology patients. This bulletin will focus on the 5mg preparation for osteoporosis.

**CHECK RENAL FUNCTION**

Check creatinine clearance (CrCL) prior to every infusion, and if it is below 35mL/min, do not administer zoledronic acid.\(^1\) Regularly review other medicines that may compromise renal function such as diuretics, and ask about NSAID (non-steroidal anti-inflammatory drug) use. Other oral bisphosphonates must be discontinued prior to treatment,\(^1\) but no wash-out period is required.\(^1\)

Renal impairment has been observed following a single dose of zoledronic acid.\(^1\) Risk factors for renal impairment include advanced age, and concomitant medicines that can compromise renal function such as aminoglycoside antibiotics, or diuretics that can cause dehydration.\(^1\) A rapid infusion time (less than 15 minutes), or high dose will also increase the risk. Never exceed 5mg per year.\(^4\)

**ENSURE THE PATIENT IS ADEQUATELY HYDRATED**

To reduce the risk of renal impairment, two glasses of water (500mL) should be consumed a few hours before, and after the infusion.\(^1\) Advise patients to maintain adequate fluid intake especially if they are elderly, or if they are also taking diuretics.\(^1\)

**CHECK CALCIUM AND VITAMIN D STATUS**

All patients with osteoporosis should have an adequate dietary intake of calcium, and receive sufficient vitamin D. Zoledronic acid is contraindicated if patients have hypocalcaemia. Check serum calcium is within the normal range (2.0–2.6mmol/L) and treat pre-existing hypocalcaemia before initiating zoledronic acid.\(^1\) Risk factors for hypocalcaemia include vitamin D deficiency, recent thyroid surgery, and intestinal calcium malabsorption (eg coeliac disease). If the patient is not receiving regular vitamin D, prescribe supplements prior to administration.\(^1\)

Cholecalciferol 2x 1.25mg tablets during week before the infusion and 1.25mg per month thereafter\(^1\)

Note: Patients with a recent low-trauma hip fracture should be given vitamin D prior to the first infusion and prescribed calcium and vitamin D supplements to prevent further fractures.\(^1\)

**ASK THE PATIENT TO ARRANGE A DENTAL CHECK-UP**

Osteonecrosis of the jaw (ONJ) has been associated with bisphosphonates. It is very rare and has mostly been reported in cancer patients who are also receiving chemotherapy and corticosteroids, and in those with poor oral hygiene or undergoing dental procedures such as tooth extraction.\(^1\) The onset of ONJ typically occurs 10 months or more after receiving zoledronic acid.\(^8\) While on treatment, patients should avoid invasive dental procedures if at all possible. A dental examination (with preventive dentistry) is recommended prior to therapy for those with risk factors.\(^1,8\) Regularly ask the patient about any loose teeth and pain, swelling or numbness in their jaw.

**GIVE OVER AT LEAST 15 MINUTES, NO MORE THAN ONCE A YEAR**

The 5mg/100mL ready-to-infuse solution is to be administered intravenously via a vented infusion line (at constant rate) over at least 15 minutes.\(^1\) (Consider a longer infusion time if CrCL is approaching 35mL/min). Monitor the patient during the infusion;
SAFER USE OF HIGH RISK MEDICINES

Zoledronic Acid

allow for an appointment time of 30-45 minutes. Funding does not routinely include the cost of giving the infusion.

For the treatment of osteoporosis, zoledronic acid should be given no more than once a year. Some patients may only require infusions every 2-3 years, depending on the results of clinical assessments such as bone turnover markers and DEXA scans. Patients with Paget’s disease are likely to require infusions much less frequently; assess and re-treat as per individual patient requirement. Recent evidence suggests that the most benefit from bisphosphonates is gained within the first 5 years of treatment. After that, it may be beneficial to have a ‘drug holiday’ for a period of 2-3 years, to allow bone resorption to recover, and potentially reduce the risk of rare adverse effects such as osteonecrosis of the jaw.

Note: For patients with recent low trauma hip fracture, the first dose should be given 2 or more weeks following hip fracture repair.

INFORM THE PATIENT ABOUT POST-DOSE SYMPTOMS

Within the first 3 days following the infusion, many patients experience flu-like symptoms (7.8%), fever (18%), myalgia (9.4%), arthralgia (6.8%) and headache (6.5%). These symptoms usually decrease with subsequent doses, and may be relieved with paracetamol, which can be given following the infusion. In case these symptoms arise, the patient may wish to have a carer drive them home, especially after the first infusion. Although rare, bisphosphonates have been associated with inflammatory eye disorders including uveitis and scleritis which tend to occur within one month of treatment. If redness, photophobia, blurred vision, eye pain or floating spots in the visual field occur, refer to an ophthalmologist.

There have been some reports of atypical femoral fractures during treatment with bisphosphonates; however causality has not been fully established. As a precaution, patients should be advised to report any hip, thigh, or groin pain.

Note: Zoledronic acid has been associated with an increase in the incidence of serious atrial fibrillation (1.3%) compared to placebo (0.5%). The mechanism of this is unknown, but in the majority of the cases the events occurred more than 30 days after the infusion. Zoledronic acid is contraindicated during pregnancy and breastfeeding.

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