Zoledronic acid Intravenous for Adults

Who can administer

May be administered by registered competent doctor or nurse/midwife

Important information

- There are **two preparations/strengths available**- with different indications for each - check carefully that the correct product is being used
- Dental checks required- **Osteonecrosis of the jaw can occur**- see SPC
- Ensure **adequate hydration** before and after administration to try and prevent renal adverse reactions
- See '**Monitoring** requirements' below
- Local protocols may be in place
- See under 'Dose' for adjustments required in **renal** impairment

Available preparations

Zerlinda 4mg per 100ml Solution for Infusion (Teva)

Zoledronic acid (Mylan) 4mg per 5ml

Aclasta 5mg per 100ml infusion

Reconstitution

Already in solution

Infusion fluids

Zerlinda (Teva), Aclasta: Not required - product ready for infusion

Zoledronic acid (Mylan) 4mg per 5ml - add to 100ml Sodium chloride 0.9% or Glucose 5%

Methods of intravenous administration

Intermittent intravenous infusion (administer using an electronically controlled infusion device)

Zoledronic acid (Mylan and Teva brands)

- Administer required dose over at least 15 minutes

Aclasta

- Administer over at least 15 minutes via a vented infusion line
- Precautions need to be taken during administration to **prevent possible air embolism** - particularly in central line administration.
- Bottles **must be vented** in one of two ways
  - Directly by means of a filter needle into the bottle which goes through the rubber stopper and opens into the air, or

- Direct air vent on the air inlet of the administration set, located between the drip chamber and piercing pin, it is covered with a bacterial retentive filter to reduce the chance of contamination

Dose in adults

DOSE DEPENDS ON INDICATION - Note: Must use correct brand for each indication

Zoledronic acid (Teva, Mylan)

1: Prevention of skeletal related events (SRE) in patients with malignancies involving bone

2: Treatment of Tumour Induced Hypercalcaemia (TIH)

Zoledronic acid (Aclasta)

3: Treatment of osteoporosis in men or post-menopausal women at increased risk of fracture

4: Treatment of Paget's disease of the bone

<table>
<tr><th colspan="4">Zoledronic acid (Mylan, Teva)</th></tr>
<tr><th colspan="4">1: Prevention of skeletal related events (SRE) in patients with malignancies involving bone</th></tr>
<tr><th>Dose</th><th colspan="2">According to renal function</th><th>Every three to four weeks</th></tr>
<tr><td rowspan="6">Baseline renal function abnormal</td><td colspan="2">Baseline eGFR (ml per minute/1.73m^2)</td><td>Dose to give</td></tr>
<tr><td colspan="2">Greater than 60</td><td>4mg</td></tr>
<tr><td colspan="2">50 to 60</td><td>3.5mg *</td></tr>
<tr><td colspan="2">40 to 49</td><td>3.3mg *</td></tr>
<tr><td colspan="2">30 to 39</td><td>3mg *</td></tr>
<tr><td colspan="2">Less than 30</td><td>Not recommended</td></tr>
<tr><td>Subsequent doses - measure serum creatinine prior to each dose</td><td colspan="3">Hold further doses if renal function has deteriorated:
• Patient whose baseline serum creatinine is less than 124micromol per litre when there has been an increase in serum creatinine of 44micromol per litre.
• Patient whose baseline serum creatinine is greater than 124micromol per litre when there has been an increase in serum creatinine of 88micromol per litre.
In clinical studies, the drug was resumed only when the creatinine level returned to within 10% of the baseline level.
Treatment should be resumed at the same dose as that prior to treatment interruption</td></tr>
<tr><td rowspan="4">* Preparation of infusion for doses less than 4mg (this is necessary so that the final infusion ends up as 100ml)</td><td>Dose of zoledronic acid (mg/100mL)</td><td>Volume to be removed from ready-to-use bottle (mL)</td><td>Replace with following volume of sodium chloride 0.9% or glucose 5% (mL)</td></tr>
<tr><td>3.5mg/100mL</td><td>12ml</td><td>12ml</td></tr>
<tr><td>3.3mg/100mL</td><td>18ml</td><td>18ml</td></tr>
<tr><td>3mg/100mL</td><td>25ml</td><td>25ml</td></tr>
</table>

Zoledronic acid (Mylan, Teva)	
2: Treatment of tumour induced hypercalcaemia (TIH)	
Dose	4mg stat dose
	Median time to normocalcaemia - 4 days
Renal impairment	No dose adjustment for serum creatinine less than 400micromol per litre No data for use in patients where serum creatinine is greater than 400micromol/l (risk benefit evaluation)

Aclasta	
3: Treatment of osteoporosis in men or in post-menopausal women at increased risk of fracture	
Dose	5mg, once a year
Renal impairment	Do not use if eGFR is less than 35ml per minute/1.73m2

Aclasta	
4: Treatment of Paget's disease of the bone	
Dose	The recommended dose is a single intravenous infusion of 5 mg of Aclasta After a single treatment with Aclasta in Paget's disease, an extended remission period is observed in responding patients. Retreatment consists of an additional intravenous infusion of 5mg Aclasta after an interval of one year or longer from initial treatment in patients who have relapsed. Limited data on re-treatment of Paget's disease are available (see SPC)
Renal impairment	Do not use if eGFR is less than 35ml per minute/1.73m2

Hepatic impairment

Zoledronic acid (Mylan, Teva): Due to limited data, no recommendations can be given

Aclasta: No dosage adjustment required

Monitoring

- Monitor serum electrolytes, calcium, phosphate, magnesium
- Maintain adequate hydration prior to and after administration of zoledronic acid
- Assess renal function prior to each dose (monitor serum creatinine, urea and sodium) (ref 1)

Further information

Pre-existing hypocalcaemia

- Pre-existing hypocalcaemia must be treated by adequate intake of calcium and vitamin D before initiating treatment with **Aclasta.** In Paget's disease it is advised that supplemental calcium corresponding to at least 500mg elemental calcium twice daily is given for at least 10 days post infusion
- Patients on Zoledronic acid (Actavis brand) should also be administered an oral calcium supplement of Calcium 500mg/Vitamin D3 400 units per day
- Patients receiving treatment with Zoledronic acid (Actavis) should not be treated with Aclasta

Renal insufficiency

- There are **different cut-off points** for patients with renal impairment for the **different indications**. This is because some indications require **more urgent treatment**, for example treatment of Tumour Induced Hypercalcaemia is urgent- and so a risk benefit evaluation will allow it to be administered even where there may be renal impairment.

Other

- Paracetamol or ibuprofen (caution if renal impairment) pre-treatment may be required shortly after an Aclasta dose to minimise adverse effects which can occur for up to three days post-administration
- In patients with a recent low-trauma hip fracture, Aclasta should be given two or more weeks following hip fracture repair
- Before first infusion of Aclasta give 50,000 to 125,000 units of Vitamin D orally or by IM injection
- Hydration must be maintained prior to, and following administration of zoledronic acid

Storage

- Store below 25^{0}C

References

Zoledronic acid (Mylan) November 2021

Aclasta SPC March 2020

Zoledronic acid (Teva) SPC accessed online via EMA website 13th Dec 2021

1: Injectable Medicines Administration guide- downloaded from Medusa 13th Dec 2021

Search synonym: Zometa

Therapeutic classification

Bisphosphonates