Zoledronic Acid

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.

Adjuvant therapy for postmenopausal women with node-positive invasive breast cancer or node-negative invasive breast cancer and at high risk of recurrence.

Please refer to 'Bone Protection Myeloma 2020' protocol for myeloma patients

ICD-10 codes

Codes with a prefix C15-C80

Regimen details

Day	Drug	Dose	Route
1	Zoledronic acid	4mg*	IV infusion

* dose to be reduced in renal impairment (CrCl ≤60mL/min) – see renal impairment section.

Cycle frequency

Palliative therapy: 21-28 days
Adjuvant therapy for breast cancer: 6 monthly

Number of cycles

Palliative therapy: as indicated
Adjuvant therapy for breast cancer: up to 3 years

Administration

Zoledronic acid is administered by IV infusion in 100mL 0.9% sodium chloride over 15 minutes.

Pre-medication

Ensure patients are well hydrated prior to treatment.

Emetogenicity

This regimen has low emetic potential

Additional supportive medication

Oral calcium and vitamin D supplements – UK chemotherapy board guidelines recommend 1000mg calcium and 800IU vitamin D daily. Dose adjusted according to calcium levels.
Paracetamol for flu-like symptoms as required.
Antiemetics if required.

Extravasation

Zoledronic acid is not vesicant

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
Dental examination	3 months, unless ongoing dental issues
U+E (including creatinine)	14 days
Calcium	28 days
Phosphate	28 days
Magnesium	28 days
Vitamin D	28 days

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
U+E (including creatinine)	14 days
Calcium	14 days
Phosphate	14 days
Magnesium	3 months
Vitamin D	3 months

6 monthly dental assessment is recommended.

Standard limits for administration to go ahead

If blood results within normal range, administer Zoledronic acid as planned. If outside of normal limits refer to table below:

Investigation	**Result**	**Action**
Calcium	<2.2 mmol/L corrected	DO NOT ADMINISTER – inform prescriber/consultant
	>2.6 -3.0mmol/L corrected	Administer Zoledronic acid and advise patient to stop calcium supplement
	>3.0mmol/L corrected	DO NOT ADMINISTER – refer for urgent management of hypercalcaemia
Magnesium	0.5-0.7mmol/L	Administer Zoledronic acid
	<0.5mmol/L	DO NOT ADMINISTER – Inform prescriber/consultant
Phosphate	0.6-0.8 mmol/L	Administer Zoledronic acid
	<0.6mmol/L	DO NOT ADMINISTER – Inform prescriber/consultant
Vitamin D (prior to 1st dose only)	<35nmol/l	DO NOT ADMINISTER - Inform prescriber, commence high dose replacement as per local practice, delay treatment to allow at least 2 weeks high dose replacement. No need to recheck level.
	35-50nmol/l	Administer Zoledronic acid. Inform prescriber - consider increasing calcium/vitamin D supplementation to twice daily.
	>50nmol/l	Administer Zoledronic acid
Dental work	Check with patient prior to each treatment. If they have had any dental work done since previous treatment, do not administer zoledronic acid and inform consultant. It is recommended that patients should have a 6 monthly dental assessment	

Dose modifications

- **Renal impairment**

Creatinine clearance should be calculated prior to each dose. The dose should then be adjusted as per table below. If CrCl < 30mL/min Zoledronic acid is contra-indicated.

CrCl (mL/min)	Zoledronic Acid dose
>60	4mg
50-60	3.5mg
40-49	3.3mg
30-39	3.0mg
<30	Omit

- **Hepatic impairment**

Limited clinical data are available in patients with severe hepatic insufficiency, no specific recommendations can be given for this patient population.

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

- **Serious side effects**

Osteonecrosis of the jaw (dental assessment prior to treatment and withhold zoledronic acid for 4 weeks pre and post any dental intervention). If dental extractions are required the patient should be referred to a specialist dental hospital
Atrial fibrillation

- **Frequently occurring side effects**

Flu like symptoms
Pain flare
Bone pain, myalgia, arthralgia
Hypocalcaemia
Hypophosphataemia
Nausea

- **Other side effects**

Numbness around mouth (sign of low calcium)
Conjunctivitis
Headache
Renal impairment
Anaemia

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

Thalidomide: Increased risk of renal impairment with concomitant thalidomide
Aminoglycosides: Increased risk of renal impairment
Anti-angiogenics: increased incidence of osteonecrosis of the jaw has been reported

Additional comments

Note the onset of treatment effect is 2-3 months.

References

- Summary of Product Characteristics Zoledronic acid (Seacross) accessed 7 Oct 2021 via medicines.org.uk
- UK Chemotherapy Board. *Medication-related osteonecrosis of the jaw. Guidance for the oncology multidisciplinary team.* Report of a working party on behalf of the UK Chemotherapy Board. UKCB, 2019.

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