Zoledronic Acid Monotherapy[i]

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Adjuvant treatment of breast cancer in endocrine depleted pre- or post menopausal women	C50	00545a	Hospital

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Zoledronic acid is administered once every six months for up to 5 years or until disease progression or unacceptable toxicity develops

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Zoledronic acid	4 mg	IV infusion	100 mL 0.9% NaCl Over 15 minutes	Every 6 months for 5 years
Patients should receive oral calcium supplementation of at least 500 mg and at least 400 IU oral vitamin D supplementation daily unless hypercalcaemia is present Patients must be well hydrated prior to and following administration of zoledronic acid. Overhydration should be avoided in patients at risk of cardiac failure					

ELIGIBILITY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to zoledronic acid, to other bisphosphonates or to any of its excipients
- Patients with hypocalcaemia
- Severe renal impairment
- Breast feeding
- Pregnancy

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Serum calcium, phosphate and magnesium
- Dental examination as clinically indicated

Regular tests:

- Serum calcium, phosphate and magnesium prior to each cycle
- Renal profile prior to each cycle
- Dental examination as clinically indicated*
  *See also Adverse Effects/Regimen specific complications re osteonecrosis of the Jaw

Disease monitoring:
Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

Renal and Hepatic Impairment:

Table 1: Dose modification of Zoledronic acid in renal and hepatic impairment

Renal Impairment		**Hepatic Impairment**
Cr Cl (ml/min)	**Recommended dose**	Limited clinical data in hepatic insufficiency, therefore no specific recommendations
>60	4 mg	
50-60	3.5 mg	
40-49	3.3 mg	
30-39	3 mg	
<30	Not recommended	
Treatment should be withheld for deterioration in renal function (increase of serum creatinine greater than 44 micromol/L in patients with normal baseline (serum creatinine less than 124 micromol/L) or increase of serum creatinine greater than 88 micromol/L in patients with abnormal baseline). Resumption of therapy may be considered when serum creatinine returns to within 10% of baseline.		

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: None

PREMEDICATIONS:
None required

OTHER SUPPORTIVE CARE:
No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Osteonecrosis of the Jaw:** Cases of osteonecrosis have been reported. A dental examination with appropriate preventive dentistry and an individual benefit-risk assessment is recommended prior to treatment with bisphosphonates in patients with concomitant risk factors.
- **Hypocalcaemia-related adverse effects:** Hypocalcaemia has been reported in patients treated with zoledronic acid. Caution is advised when zoledronic acid is administered with medicinal products known to cause hypocalcaemia, as they may have a synergistic effect resulting in severe hypocalcaemia. Serum calcium should be measured and hypocalcaemia must be corrected before initiating zoledronic acid therapy. Patients should be adequately supplemented with calcium and vitamin D.
- **Renal function impairment:** Zoledronic acid has been associated with reports of renal dysfunction.

DRUG INTERACTIONS:

- Caution is advised when zoledronic acid is administered alongside anti-angiogenic medicinal products as an increase of osteonecrosis of the jaw has been observed in patients treated concomitantly with these medicinal products.
- Caution is indicated when zoledronic acid is used with other potentially nephrotoxic medicinal products. Attention should also be paid to the possibility of hypomagnesaemia developing during treatment.
- Current drug interaction databases should be consulted for more information.

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP

Patient alert card:
https://www.hpra.ie/img/uploaded/swedocuments/edumat_auto_16e09ff2-9f00-4215-b2c6-e335178dff43.pdf

REFERENCES:

1. Gnant M et al. Zoledronic acid combined with adjuvant endocrine therapy of tamoxifen versus anastrozol plus ovarian function suppression in premenopausal early breast cancer: final analysis of the Austrian Breast and Colorectal Cancer Study Group Trial 12. Annals of oncology 2015; 26: 313-320
2. Nuzzo F et al. Bone effect of adjuvant tamoxifen, letrozole or letrozole plus zoledronic acid in early-stage breast cancer: the randomized phase 3 HOBOE study. Annals of Oncology 2012; 23(8): 2027-2033
3. Wilson C et al. Adjuvant zoledronic acid reduces fractures in breast cancer patients; an AZURE (01/04) study. European Journal of Cancer 2018; 94: 70-78
4. Zoledronic acid (Zometa®). Summary of Product characteristics. Accessed January 2021. Available at: https://www.ema.europa.eu/en/documents/product-information/zometa-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	11/02/2019		Prof Maccon Keane
2	03/02/2021	Reviewed	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This is an unlicensed indication for the use of zoledronic acid in Ireland. Patient's should be informed of this and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be fully aware of their responsibility in communicating any relevant information to the patient and also ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy