Zoledronic Acid Monotherapy

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant treatment of breast cancer in endocrine depleted pre- or post menopausal women</td>
<td>C50</td>
<td>00545a</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

*If the reimbursement status is not defined*, the indication has yet to be assessed through the formal HSE reimbursement process.

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 patient's individual clinical circumstances.

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

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Zoledronic acid</td>
<td>4 mg</td>
<td>IV infusion</td>
<td>100 mL 0.9% NaCl Over 15 minutes</td>
<td>Every 6 months for 5 years</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Recommended dose</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr Cl (ml/min)</td>
<td></td>
<td>Limited clinical data in hepatic insufficiency, therefore no specific recommendations</td>
</tr>
<tr>
<td>&gt;60</td>
<td>4 mg</td>
<td></td>
</tr>
<tr>
<td>50-60</td>
<td>3.5 mg</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>3.3 mg</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>3 mg</td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>Not recommended</td>
<td></td>
</tr>
</tbody>
</table>

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.

ATC CODE:
Zoledronic acid M05BA08

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_4f687cb6-afdd-4f08-979a-28258a75af65.pdf

REFERENCES:


NCCP Chemotherapy Regimen

Version Date Amendment Approved By
1 11/02/2019

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1 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

2 ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at; http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/