Medicine Guideline

Zoledronic Acid for early / locally advanced breast cancer

Health
South Eastern Sydney
Local Health District

Guideline for	SESLHD Oncology Centres
Authorised Prescribers	Medical Oncologists
Indication for use	Minimisation of skeletal events and premature osteoporosis
Clinical condition	Post-menopausal women with early or locally advanced breast cancer
Proposed Place in Therapy	First line therapy after or in conjunction with standard adjuvant therapy
Adjunctive Therapy	Surgery, chemotherapy, radiotherapy, and hormonal manipulation
Contra-indications	• Osteonecrosis of the jaw • Previous anaphylaxis to zoledronic acid or its excipients • Current or recent uveitis, or a history of bisphosphonate associated uveitis • Pregnancy or breastfeeding
Precautions	Hypocalcaemia - corrected calcium level below the normal range of 2.15 to 2.65 mmol per litre. Use not recommended in patients with severe renal impairment (CrCl < 30mL/min)
Important Drug Interactions	Caution is advised when bisphosphonates are administered with aminoglycosides and loop diuretics, since both agents may have an additive effect, resulting in a lower serum calcium level for longer periods than required. Caution is indicated when zoledronic acid is used in combination with other potentially nephrotoxic drugs.
Dosage	4 mg intravenously every 6 months for 3 years
Duration of therapy	3 years (6 doses)
Prescribing Instructions	**For Outpatient Use ONLY** Prescribing on the Intravenous Adult Fluid Order Form. The infusion order should include dosage, diluent, and infusion rate, e.g., *Zoledronic acid 4 mg in 100 mL sodium chloride 0.9%, infused over at least 15 minutes*
Administration Instructions	Use either the: • 4 mg/100 mL infusion solution **or** • 4 mg/5 mL concentrated injection, dilute with 100 mL of a compatible fluid **Final concentration 4 mg/100 mL.** Infuse over at least 15 minutes.

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Adverse Effects	The most serious adverse drug reactions are: anaphylactic reaction, ocular adverse events, osteonecrosis of the jaw, atypical femoral fracture, atrial fibrillation, renal function impairment, acute phase reaction, and hypocalcaemia. **Osteonecrosis of the Jaw** is a rare but serious side effect involving the exposure of the jaw bone through lesions in the gingiva which do not heal. It can occur spontaneously but is most common following dental procedures. Symptoms can include pain, numbness, swelling, loose teeth, exposed bone and non-healing extraction sockets. Within three days after zoledronic acid administration, an **acute phase reaction** has commonly been reported, with symptoms including pyrexia, fatigue, bone pain, rigors, influenza-like illness, arthritis with subsequent joint swelling; these symptoms usually resolve within a few days.
Monitoring requirements	Due to the risk of osteonecrosis of the jaw, patients should have a full dental check-up before treatment commences and regularly throughout duration of treatment as advised by dentist and oncologist. Before starting therapy, ensure Vitamin D levels are adequate. Within the 7 days prior to the zoledronic acid infusion the following must be checked: • serum creatinine, • calcium*, • magnesium and • phosphate. * Note: Zoledronic acid can cause hypocalcaemia and therefore calcium levels need to be monitored throughout treatment. If the corrected calcium is not within range (i.e., 2.15 to 2.65 mmol/L or otherwise stated by Medical Officer), **zoledronic acid must not be administered.** Refer to treating Medical Officier for review. The Medical Officer is to advise: • whether the dose is to be administered or withheld • what dose of calcium supplements the patient needs to take to increase their calcium levels • when repeat blood test should be taken • a revised date for administration of the dose All patients will have ongoing clinical review with their medical oncologists for breast cancer surveillance (annual mammogram and ultrasound and 2-3 yearly bone mineral density)
Management of Complications	Supplementation of electrolyte deficiencies as necessary. Symptoms of acute phase reaction including pyrexia, fatigue, bone pain, rigors, influenza-like illness, arthritis with subsequent joint swelling; can be mitigated by the use of paracetamol on an as required basis.
Basis of Protocol/Guideline:	1. Dhesy-Thind et al Adjuvant Bisphosphonates and Other Bone-Modifying Agents in Breast Cancer Journal of Clinical Oncology March 6, 2017. 2. Hadji et al Adjuvant bisphosphonates in early breast cancer: consensus guidance for clinical practice from a European Panel. Annals of Oncology 2016;27(3):379. 3. Early Breast Cancer Trialists' Collaborative Group (EBCTCG) Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. The Lancet Vol 386, 03 Oct 2015

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Groups consulted in development of this guideline	Medical Oncologists, POWH Pharmacy Department, POWH

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GOVERNANCE	
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