NOVARTIS

ZOMETA®

(zoledronic acid)

4 mg/5 mL concentrate for solution for infusion
4 mg/100 mL solution for infusion

Basic Succinct Statement (BSS)

CODE: BSS RD 7 Oct 2016; APPR 2 Aug 2017

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Important note: Before prescribing, consult full prescribing information.

Presentation: Zoledronic acid. Vials as a 4 mg/5 mL liquid concentrate for further dilution prior to use. The 'ready to use' presentation contains bottles of Zometa® 4 mg/100 mL solution for infusion

Indications: ♦Prevention of skeletal related events (pathological fractures, spinal compression, radiation or surgery to bone, or tumour-induced hypercalcemia) in patients with advanced malignancies involving bone. ♦Treatment of hypercalcemia of malignancy (HCM).

Dosage:

♦Zometa 4 mg/5 mL concentrate should be further diluted with 100 mL 0.9% w/v sodium chloride or 5% w/v glucose solution before infusion. The final Zometa solution for infusion, should be given as an intravenous infusion of no less than 15 minutes. Zometa must not be mixed with calcium or other divalent cation-containing infusion solutions, such as Lactated Ringer's solution, and should be administered as a single intravenous solution in a line separate from all other drugs.

♦The Zometa 4 mg/100 mL solution for infusion is a "ready to use" presentation and must not be further diluted or mixed with other infusion solutions except for patients with renal impairment. It should be administered as a single intravenous solution in a separate infusion line of no less than 15 minutes.

♦For *'prevention of skeletal related events in patients with advanced malignancies involving bone',* the recommended dose is 4 mg Zometa infusion given every 3 to 4 weeks. Dose reduction is recommended in patients with pre-existing mild to moderate renal impairment.

♦For *'treatment of HCM',* the recommended dose is 4 mg given as a single infusion. No dose adjustment is necessary in patients with mild to moderate renal impairment.

♦Patients without hypercalcemia should also be administered an oral calcium supplement of 500 mg and 400 IU vitamin D daily.

Contraindications: ♦Pregnancy. ♦ Breast-feeding women. ♦Patients with clinically significant hypersensitivity to zoledronic acid or other bisphosphonates or any of the excipients in the formulation of Zometa.

Warnings and precautions: ♦All patients must be assessed prior to administration of Zometa to ensure that they are adequately hydrated. ♦Overhydration should be avoided in patients at risk of cardiac failure. ♦Monitoring of standard hypercalcemia-related metabolic parameters such as serum levels of calcium, phosphate and magnesium, and particularly, serum creatinine. ♦ In view of the potential impact of bisphosphonates on renal function, and the lack of extensive clinical safety data in patients with severe renal impairment with Zometa, its use in this population is not recommended. ♦Dose reduction in patients with pre-

existing mild to moderate renal impairment. ♦In patients requiring repeated administration of Zometa, serum creatinine should be evaluated prior to each dose. If renal function has deteriorated, the dose should be withheld. ♦Limited clinical data in patients with severe hepatic insufficiency; no specific recommendations can be given for this patient population. ♦Osteonecrosis of the jaw has been reported predominantly in adult patients with cancer receiving bisphosphonates, including Zometa. Post-marketing experience and the literature suggest a greater frequency of reports of ONJ based on tumour type (advanced breast cancer, multiple myeloma), and dental status (dental extraction, periodontal disease, local trauma including poorly fitting dentures). Therefore, patients should avoid invasive dental surgery during treatment with Zometa, maintain good oral hygiene and should have a dental examination with preventive dentistry prior to treatment with bisphosphonates. Patients should inform their dentist while under dental treatment or if dental surgery is foreseen. Cases of osteonecrosis of other anatomical sites including the hip, femur and external auditory canal have been reported.

♦Atypical subtrochanteric and diaphyseal femoral fractures have been reported with bisphosphonate therapy, including Zometa, primarily in patients receiving long-term treatment for osteoporosis. Discontinuation of Zometa therapy should be considered pending evaluation of the patient. During Zometa treatment patients should be advised to report any thigh, hip or groin pain. ♦Severe and occasionally incapacitating bone, joint, and/or muscle pain have been reported in patients taking bisphosphonates. ♦Patients treated with Zometa (zoledronic acid) should not be treated with Aclasta®. Zometa should also not be given together with other bisphosphonates since the combined effects of these agents are unknown. ♦Asthmatic patients who are sensitive to acetylsalicylic acid should not take Zometa. ♦ Patients who have received doses higher than those recommended should be carefully monitored, since renal function impairment (including renal failure) and serum electrolyte (including calcium, phosphorus and magnesium) abnormalities have been observed. In the event of hypocalcemia, calcium gluconate infusions should be administered as clinically indicated. ♦ Pre-existing hypocalcemia must be effectively treated by adequate intake of calcium and vitamin D before initiating therapy with Zometa. ♦The safety and efficacy of Zometa in pediatric patients have not been established. ♦Hypocalcemia has been reported in patients treated with Zometa. Cardiac arrhythmias and neurologic adverse events (seizures, tetany, and numbness) have been reported secondary to cases of severe hypocalcemia. In some instances, the hypocalcemia may be life-threatening. ♦ Caution is advised when Zometa is administered with other drugs causing hypocalcemia , as they may have a synergistic effect, resulting in severe hypocalcemia. ♦ Serum calcium should be measured and hypocalcemia must be corrected before initiating Zometa therapy. Patients should be adequately supplemented with calcium and vitamin D.

Women of child-bearing potential: Women of child-bearing potential should be advised to avoid becoming pregnant and advised of the potential hazard to the fetus while receiving Zometa.

Pregnancy: See Contraindications.

Breast-feeding: See Contraindications.

Interactions: ♦Caution is advised when bisphosphonates are administered with aminoglycosides or calcitonin or loop diuretics since these agents may have an additive effect, resulting in a lower serum calcium level for longer periods than required. ♦ Caution is advised when used with other potentially nephrotoxic drugs. ♦Caution is advised when Zometa is administered with anti-angiogenic drugs as an increase in incidence of ONJ has been observed in patients treated concomitantly with these drugs.

Adverse reactions: Common adverse reactions are usually mild and transient and similar to those reported for other bisphosphonates:

In adult patients: ♦Very common (>10%): hypophosphatemia

♦Common (1 to 10%): acute phase reaction consisting of fever, fatigue, chills, and influenza-like illness; bone-, joint, and/or muscle pain, joint stiffness; generalised body pain, hypertension; headache; paresthesia; sleep disorder; peripheral edema; hyperhidrosis; constipation, elevation of serum creatinine and blood urea; renal impairment; anemia; asthenia, conjunctivitis; gastrointestinal reactions, such as nausea and vomiting, decreased appetite, hypocalcaemia;

♦Uncommon (0.1 to 1%): thrombocytopenia, leukopenia; hypersensitivity reactions; hypotension; shortness of breath (dyspnea), cough; dizziness, dysgeusia, hypoesthesia, hyperesthesia, tremor; anxiety; blurred vision; diarrhea, abdominal pain, dyspepsia, stomatitis, dry mouth; local reactions at the infusion site, such as redness or swelling;, weight increased, chest pain; rash and pruritus;osteonecrosis of jaw, muscle spasm; acute renal failure, hematuria, proteinuria, hypomagnesemia, hypokalemia;

♦Rare (0.01 to 0.1%): pancytopenia, confusional state, uveitis, interstitial lung disease, acquired Fanconi syndrome, bradycardia, angioneurotic edema, hyperkalemia, hypernatremia, arthritis and joint swelling as a symptom of acute phase reaction.♦ Cardiac arrhythmia (secondary to hypocalcemia)

♦Very rarely (<0.01%) or Unknown: episcleritis, bronchoconstriction, somnolence, atrial fibrillation, anaphylactic shock/reaction, urticaria, scleritis and orbital inflammation, severe and occasionally incapacitating bone, joint, and/or muscle pain, atypical subtrochanteric and diaphyseal femoral fractures (bisphosphonate class adverse reaction, including Zometa), convulsion, hypoesthesia and tetany (secondary to hypocalcemia).

Packs and prices: Country specific.

Legal classification: Country specific.