Adronic 4

Zoledronic Acid INN 4mg

COMPOSITION

Adronic 4 Concentrated Solution for IV Infusion: Each vial contains Zoledronic Acid Monohydrate INN 4.264 mg equivalent to Zoledronic Acid 4 mg supplied as 5 ml concentrated solution for IV infusion.

CLINICAL PHARMACOLOGY

Mechanism of action: The principal pharmacologic action of Zoledronic acid is inhibition of bone resorption. Several factors are thought to contribute to this antiresorptive action. Zoledronic acid inhibits osteoclastic activity and induces osteoclast apoptosis. Zoledronic acid also blocks the osteoclastic resorption of mineralized bone and cartilage through its binding to bone. Zoledronic acid inhibits the increased osteoclastic activity and skeletal calcium release induced by various stimulatory factors released by tumors.

Pharmacokinetics: Zoledronic acid shows low affinity for the cellular components of human blood, the plasma protein binding is low. Zoledronic acid does not inhibit human P450 enzymes and does not undergo biotransformation. This drug is eliminated intact via the kidney.

INDICATIONS

Zoledronic Acid is a bisphosphonate indicated for the treatment of:

- Hypercalcemia of malignancy.
- Patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. Prostate cancer should have progressed after treatment with at least one hormonal therapy.

Limitation of use: The safety and efficacy of Zoledronic Acid has not been established for use in hyperparathyroidism or nontumor-related hypercalcemia.

DOSAGE AND ADMINISTRATION

Hypercalcemia of malignancy

- 4 mg as a single-use intravenous infusion over no less than 15 minutes.
- 4 mg as retreatment after a minimum of 7 days.

Multiple myeloma and bone metastasis from solid tumors

- 4 mg as a single-use intravenous infusion over no less than 15 minutes every 3-4 weeks for patients with creatinine clearance of greater than 60 ml/min.
- Reduce the dose for patients with renal impairment.
- Coadminister oral calcium supplements of 500 mg and a multiple vitamin containing 400 international units of Vitamin D daily.

Administer through a separate vented infusion line and do not allow to come in contact with any calcium or divalent cation-containing solutions.

PREPARATION AND ADMINISTRATION

Zoledronic Acid 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.

Zoledronic Acid concentrate should be diluted in 100 ml of sterile 0.9% Sodium Chloride, USP, or 5% Dextrose Injection, USP, following proper aseptic technique, and administered to the patient by infusion. Undiluted concentrate should not be stored in a syringe, to avoid inadvertent injection.

To prepare reduced doses for patients with baseline Creatinine Clearance less than or equal to 60 ml/min, volume specified at the following table should be withdrawn-

Remove and Use Adronic Volume (ml)	Dose (mg)
4.4	3.5
4.1	3.3
3.8	3.0

The withdrawn concentrate must be diluted in 100 mL of sterile 0.9% Sodium Chloride, USP, or 5% Dextrose Injection, USP.

If not used immediately after dilution with infusion media, for microbiological integrity, the solution should be refrigerated at 2-8°C. The refrigerated solution should then be equilibrated to room temperature prior to administration. The total time between dilution, storage in the refrigerator, and end of administration must not exceed 24 hours.

CONTRAINDICATIONS

Contraindicated in patients with known hypersensitivity to Zoledronic Acid.

ADVERSE EFFECTS

The most common adverse events (greater than 25%) are nausea, fatigue, anemia, bone pain, constipation, fever, vomiting, and dyspnea.

PRECAUTIONS

Pregnancy: Zoledronic Acid may cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

Nursing mothers: It is not known whether Zoledronic Acid is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from Zoledronic Acid, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Zoledronic Acid binds to bone long term and may be released over weeks to years.

Pediatric use: Zoledronic Acid is not indicated for use in children.

Geriatric use: No significant differences in response rate or adverse reactions have been observed in patients aged 65 years or older receiving Zoledronic Acid as compared to younger patients. Because decreased renal function occurs more commonly in the elderly, special care should be taken to monitor renal function.

DRUG INTERACTIONS

Aminoglycosides may have an additive effect to lower serum calcium for prolonged periods. Concomitant use of Loop diuretics with Zoledronic Acid may increase risk of hypocalcemia.

OVERDOSE

Overdosage may cause clinically significant hypocalcemia, hypophosphatemia, and hypomagnesemia. Clinically relevant reductions in serum levels of calcium, phosphorus, and magnesium should be corrected by intravenous administration of calcium gluconate, potassium or sodium phosphate, and magnesium sulfate, respectively.

STORAGE

Store below 30°C. Keep in a dry place away from light.

Keep out of the reach of children.

PRESENTATION

Adronic 4 Concentrated Solution for IV Infusion: Each box contains a single-dose glass vial of Zoledronic Acid 4 mg.

Manufactured by:
ARISTOPHARMA LTD.
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