**WARNINGS AND PRECAUTIONS**

### 1. Indications

Zoledronic acid injection is indicated for:

- **Paget's Disease of Bone**
- **Benign Hypercalcemia**
- **Osteoporosis**
- **Hypocalcemia and Mineral Metabolism**
- **Multiple Myeloma**
- **Adjuvant Therapy Adjacent to Prostate Cancer**

### 2. Contraindications

Zoledronic acid injection is contraindicated in patients who are hypersensitive to zoledronic acid or any of its components.

### 3. Warnings

- **Osteonecrosis of the Jaw (ONJ)**: The risk of ONJ is increased in patients with a history of radiotherapy to the head or neck, recent dental procedures, or severe oral disease.
- **Hypocalcemia**: Caution is advised in patients with a history of hypocalcemia or those taking medications that may increase the risk of hypocalcemia.

### 4. Precautions

- **Bone Pain**: Management of bone pain may be necessary before initiating zoledronic acid injection.
- **Renal Impairment**: Adjust dosage based on creatinine clearance.

### 5. Drug Interactions

- **Hypocalcemia**: Monitor calcium levels in patients with a history of hypocalcemia.
- **Osteoporosis**: Monitor bone density in patients with osteoporosis.

### 6. Adverse Reactions

- **Musculoskeletal Pain**: Common adverse reactions include musculoskeletal pain, muscle spasms, and back pain.
- **Ocular Adverse Events**: Adverse events affecting the eye include conjunctivitis and dry eye.

### 7. Monitoring Parameters

- **Creatinine Clearance**: Monitoring creatinine clearance, including measurement of creatinine clearance, urine protein, and urine creatinine clearance, is recommended in patients at-risk for acute renal failure (ARF).

### 8. Use During Pregnancy

- **Pregnancy**: Zoledronic acid injection may cause fetal harm when administered to a pregnant woman. Use only if the potential benefit justifies the potential risk to the fetus.

### 9. Use in Lactation

- **Lactation**: Zoledronic acid is excreted in human milk. Consider the potential benefits and risks of zoledronic acid injection in breastfeeding women.

### 10. Use in Children

- **Pediatric Use**: The safety and efficacy of zoledronic acid injection in children have not been established.

### 11. Dosage and Administration

- **Adults**: The recommended dose is 5 mg administered intravenously once per year. The dose should be adjusted based on renal function.

### 12. How Supplied

- **Appearance**: Zoledronic acid injection is available as a clear, colorless solution in 5 mg/100 mL vials.

### 13. Storage

- **Storage**: Store at 2 to 8°C (36 to 46°F) protected from light.

### 14. Full Prescribing Information

- **Contents**: See the full prescribing information for Zoledronic Acid Injection 5 mg/100 mL, PI Date: 22.11.2016 Version: 00.

### 15. Other Information

- **Additional Information**: For complete information, including precautions, warnings, and contraindications, refer to the full prescribing information.
**DRUG INTERACTIONS**

A placebo-controlled, multinational study of 7736 women aged 65 to 89 years (mean age of 73) with either: a femoral neck BMD T-score less than or equal to -1.5 and at least

**Mechanism of Action**

have been caused by, drug-induced hypocalcemia.

**Impairment of Fertility:**

Although there are no data on fetal risk in humans, bisphosphonates do cause fetal harm in animals, and animal data suggest that uptake of bisphosphonates into fetal bone is greater than into maternal bone. Therefore, there is a theoretical risk of fetal harm (e.g., skeletal and other abnormalities) if a woman becomes pregnant after completing

**Experience (6.2)**

Zoledronic acid injection is not indicated for use in children.

**13 NONCLINICAL TOXICOLOGY**

In female rats given daily subcutaneous doses of zoledronic acid beginning 15 days before mating and continuing through gestation, the number of stillbirths was increased used, and the route of administration (intravenous versus oral) on this risk has not been established.

**14 CLINICAL PHARMACOLOGY**

Zoledronic acid monohydrate is a white crystalline powder. Its molecular formula is C5H10N2O7P2• H2O and a molar mass of 535.28 g/mol. Zoledronic acid injection is a clear, colorless to yellow solution that is prescribed in individual vials that contain 5 mg of zoledronic acid monohydrate, 4950 mg of mannitol, USP; and 30 mg of sodium citrate, USP.

**15 CLINICAL STUDIES**

The efficacy and safety of zoledronic acid injection in the treatment of postmenopausal osteoporosis was demonstrated in Study 1, a randomized, double-blind, placebo-controlled, multinational study of 7736 women aged 65 to 89 years (mean age of 73) with either: a femoral neck BMD T-score less than or equal to -1.5 and at least

**16 SAFETY AND TOLERABILITY**

The pharmacokinetic studies conducted in 64 cancer patients represented typical clinical populations with normal to moderately-impaired renal function. In these studies, zoledronic acid was well tolerated and no consistent trends in adverse events were observed. In a single dose, 10 mg intravenous dose, based on an AUC comparison) included an increase in pre-implantation losses and a decrease in the number of implantations and live fetuses.

**17 PATIENT COUNSELING INFORMATION**

Zoledronic acid injection is a prescription medicine used to:

- Reduce the risk of fractures (e.g., hip, spine, or wrist fractures) in women with postmenopausal osteoporosis and at least one fracture or other risk factors for fractures
- Treat Paget's disease of bone

**What are the benefits of zoledronic acid injection?**

Zoledronic acid injection can help prevent and treat fractures in women with osteoporosis by preventing bone loss and increasing bone density. It may also help reduce the risk of fractures in women with Paget's disease of bone.

**What should I know before taking zoledronic acid injection?**

Before taking zoledronic acid injection, talk to your doctor about:

- Your medical history, including any kidney problems, heart problems, or other conditions
- Your current medications, including any over-the-counter medicines you are taking

**How do I take zoledronic acid injection?**

Zoledronic acid injection is typically given once every 3 to 12 months by a healthcare professional. It is usually injected directly into a vein.

**Possible side effects of zoledronic acid injection**

Some possible side effects of zoledronic acid injection include:

- Low calcium levels in your blood (hypocalcemia).
- Bone, joint, or muscle pain.
- Fatigue.
- Diarrhea.

**Tell your doctor if you have any side effects**

If you experience any side effects, talk to your doctor or healthcare provider. They can help determine if the medication is still appropriate for you.

**Important safety information**

Zoledronic acid injection is a prescription medicine and should be used only under the supervision of a healthcare professional. Do not take it without the advice of your doctor. This guide does not take the place of talking with your doctor about your medical condition or treatment. Talk to your doctor if you have any questions about zoledronic acid injection.

**Zoledronic Acid Injection**

**Product Name:** Zoledronic Acid Injection

**Customer:** Fresenius Kabi

**Dimensions:**
- Open Dimensions: 500 x 502 x 2 mm (L x W)
- Folded Dimensions: 63 x 73 x 2 mm (L x W)

**Substrate:** Bixi Paper (40gpm ± 10%)

**Mode of Supply:** Bundles of 25’s/50’s/100’s

**Form No:** GPL/PP/F007-00/07-14

**ARTWORK NO.:** LEA-019849-00

**Supersedes No.:** NA

**PANTONE SHADE NO’S:** Black

**Varnishing/Laminating:** NA