3 to 4 weeks. The optimal duration of therapy is not known.

Standard hypercalcemia-related metabolic parameters, such as serum levels of calcium, phosphate, and magnesium, as well as markers of bone turnover, should be monitored before and during therapy. The treatment response must be reassessed every 1 to 3 months, and the treatment duration may need to be adjusted accordingly.

Hypersensitivity reactions including rare cases of urticaria and angioedema, and very rare cases of anaphylactic reaction/shock are possible. Patients should be observed for at least 2 hours after the completion of the infusion.

During treatment, serum creatinine should be measured before each zoledronic acid injection dose and treatment should be withheld if the serum creatinine level increases by more than 0.5 mg/dL.

Zoledronic acid injection is indicated for the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, including breast cancer, prostate cancer, and lung cancer.

4 CONTRAINDICATIONS

• Hypersensitivity to zoledronic acid injection or any of its components.
• Ascites, severe congestive heart failure, hepatic failure, or other severe conditions that would increase the risk of bone or tissue necrosis.
• Bone pain.
• Premenopausal women, as safety and efficacy have not been established in this population.
• Pregnancy and lactation.

5 WARNINGS AND PRECAUTIONS

1.3 Hypocalcemia: Correct before initiating zoledronic acid injection. Adequately supplement patients with calcium and vitamin D. Monitor serum calcium levels during and after therapy.

1.4 Renal Toxicity: Zoledronic acid injection is excreted intact primarily via the kidney, and the risk of adverse reactions, in particular renal adverse reactions, is increased in patients with impaired renal function. Monitor baseline and serial serum creatinine levels during and after therapy. Discontinue treatment if serum creatinine increases by more than 0.5 mg/dL above baseline.

1.5 Bone Pain, Tissue Necrosis: Bone pain and/or tissue necrosis may occur. Patients should be monitored for signs and symptoms of bone or soft tissue necrosis, and treatment should be discontinued immediately if these symptoms develop.

5.10 Hypocalcemia: Correct before initiating zoledronic acid injection. Adequately supplement patients with calcium and vitamin D. Monitor serum calcium levels during and after therapy.

6.1 Mechanism of Action

Zoledronic acid injection is a potent, highly soluble bisphosphonate that inhibits bone resorption by inhibiting osteoclast function. It is excreted primarily via the kidney and has a long half-life in bone. Treatment should be withheld if the serum creatinine level increases by more than 0.5 mg/dL above baseline levels.

6.2 Clinical Trials

A multinational, randomized, double-blind, placebo-controlled, parallel-group trial was conducted to evaluate the efficacy and safety of zoledronic acid injection in patients with hypercalcemia of malignancy (n=189). The primary endpoint was a reduction in serum calcium of at least 1.0 mg/dL at 24 hours and/or an increase of 0.5 mg/dL in renal function over baseline.

6.2.1 Hypercalcemia of Malignancy

In postmarketing experience, severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients receiving zoledronic acid injection. In some cases, this pain may occur during or after infusion. The incidence of this reaction is not known. The pain is generally managed with oral analgesics and can resolve within days to weeks after discontinuation of therapy.

7.1 Pharmacokinetics

Nephrotoxic Drugs

Zoledronic acid injection is primarily excreted intact through the kidney, and the risk of renal injury is greater in patients with mild to severe renal impairment. It is recommended to withhold treatment in patients with baseline creatinine greater than 265 μmol/L (3.0 mg/dL) and to use the reduced dose in patients with baseline creatinine of 130 to 265 μmol/L (1.5 to 3.0 mg/dL).

8.1 Drugs with Same Active Ingredient or in the Same Drug Class

No specific drug interactions have been reported with zoledronic acid injection.

8.2 Biologic and Immunologic Factors

8.3 Genetic Factors

8.4 Maternal Considerations

9.1 Pregnancy

9.2 Lactation

9.3 Children

9.4 The effects of zoledronic acid injection in children have not been established.

10.1 Mechanisms of Toxicity

10.2 Pharmacodynamic Properties

11.3 Prevention

11.4 Patient Counseling

12.1 Mechanism of Action

Zoledronic acid injection is a potent bisphosphonate that inhibits bone resorption by inhibiting osteoclast function. It is excreted primarily via the kidney and has a long half-life in bone. Treatment should be withheld if the serum creatinine level increases by more than 0.5 mg/dL above baseline levels.

12.2 Clinical Trials

A multinational, randomized, double-blind, placebo-controlled, parallel-group trial was conducted to evaluate the efficacy and safety of zoledronic acid injection in patients with hypercalcemia of malignancy (n=189). The primary endpoint was a reduction in serum calcium of at least 1.0 mg/dL at 24 hours and/or an increase of 0.5 mg/dL in renal function over baseline.

12.3 Adverse Events

The following adverse events from the two controlled multicenter HCM trials (n=189) were reported by a greater percentage of patients in the treatment group compared to the placebo group:

- Grade 3 Adverse Events:

- Pyrexia (32% vs 17%)
- Sore Throat (8% vs 4%)
- Abdominal Pain (14% vs 15%)
- Neutropenia (12% vs 15%)

- Grade 4 Adverse Events:

- Serum Creatinine (2% vs 3%)
- Serum Calcium (32% vs 31%)
- Serum Phosphorus (3% vs 2%)
- Serum Magnesium (3% vs 2%)

12.4 Laboratory Abnormalities

The following laboratory abnormalities were reported in at least 10% of patients in the two controlled multicenter HCM trials:

- Grade 3 Laboratory Abnormalities for Serum Creatinine, Serum Calcium, Serum Phosphorus, and Serum Magnesium:

- Serum Creatinine (2% vs 3%)
- Serum Calcium (32% vs 31%)
- Serum Phosphorus (3% vs 2%)
- Serum Magnesium (3% vs 2%)

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CUSTOMER APPROVAL

Customer Approval

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Date: [Date]

[Company Name]
the reported cases are in cancer patients following invasive dental procedures, such as tooth extraction. It is therefore prudent to

The following are data on the incidence of renal deterioration in patients receiving zoledronic acid injection

Grade 3 and Grade 4 laboratory abnormalities for serum creatinine, serum calcium, serum phosphorus, and serum magnesium

Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported with bisphosphonate use [see

Edema Lower Limb

Dermatitis

Insomnia

Bone Pain

Metabolism

taste disturbance, hyperesthesia, tremor;

blurred vision; uveitis;

In pregnant rats given a subcutaneous dose of zoledronic acid of 0.1, 0.2, or 0.4 mg/kg/day during gestation, adverse fetal