Reference number(s)
1630-A

Standard Medicare Part B Management zoledronic acid-Zometa

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Zometa	zoledronic acid

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications[1,2]

- Treatment of hypercalcemia of malignancy defined as an albumin-corrected calcium (cCa) of greater than or equal to 12 mg/dL [3.0 mmol/L] using the formula: cCa in mg/dL= calcium (Ca) in mg/dL + 0.8 (4.0 g/dL - patient albumin [g/dL]).
- Treatment of 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.

Limitations of Use

The safety and efficacy of Zometa or zoledronic acid in the treatment of hypercalcemia associated with hyperparathyroidism or with other non-tumor-related conditions have not been established.

Compendial Uses[3,4]

- Treatment in postmenopausal patients with breast cancer who are receiving adjuvant aromatase inhibition therapy to maintain or improve bone mineral density and reduce risk of fractures
- Treatment in postmenopausal patients with breast cancer who are receiving adjuvant therapy to reduce the risk of distant metastases
- Monoclonal gammopathy of uncertain significance, with osteopenia or osteoporosis
- Osteopenia prophylaxis
    - Secondary to androgen-deprivation therapy in patients with prostate cancer
    - Secondary to hormone therapy in patients with breast cancer
    - Secondary to ovarian dysfunction induced by adjuvant chemotherapy
- Treatment of osteopenia or osteoporosis in patients with systemic mastocytosis
- Langerhans cell histiocytosis with bone disease

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in the coverage criteria should be accompanied by supporting evidence from Medicare approved compendia.

Coverage Criteria

Hypercalcemia of Malignancy[1,2]

Authorization of 2 months may be granted for treatment of hypercalcemia of malignancy.

Multiple Myeloma[1,2]

Authorization of 12 months may be granted for treatment or prevention of skeletal-related events in members with multiple myeloma.

Bone Metastases From A Solid Tumor[1,2]

Authorization of 12 months may be granted for treatment or prevention of skeletal-related events in members with bone metastases from a solid tumor (e.g., breast cancer, non-small cell lung cancer, thyroid carcinoma, kidney cancer, prostate cancer).

Breast Cancer[3,4]

Authorization of 12 months may be granted for postmenopausal (natural or induced by ovarian suppression) members when either of the following criteria is met:

- The member is receiving adjuvant aromatase inhibition therapy for breast cancer and the requested medication will be used to maintain or improve bone mineral density and reduce the risk of fractures.
- The member is receiving adjuvant therapy for breast cancer and the requested medication will be used for risk reduction of distant metastasis in high-risk node negative or node positive tumors.

Monoclonal Gammopathy with Osteopenia or Osteoporosis[4]

Authorization of 12 months may be granted for treatment of osteopenia or osteoporosis associated with monoclonal gammopathy.

Osteopenia Prophylaxis[4]

- Authorization of 12 months may be granted for prophylactic treatment of osteopenia secondary to androgen-deprivation therapy in members with prostate cancer.
- Authorization of 12 months may be granted for prophylactic treatment of osteopenia secondary to endocrine therapy in members with breast cancer.
- Authorization of 12 months may be granted for prophylactic treatment of osteopenia secondary to ovarian dysfunction induced by adjuvant chemotherapy.

Systemic Mastocytosis[3]

Authorization of 12 months may be granted for treatment of osteopenia or osteoporosis in members with systemic mastocytosis.

Langerhans Cell Histiocytosis[3]

Authorization of 12 months may be granted for treatment of Langerhans cell histiocytosis with bone disease.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested drug.

Hypercalcemia of Malignancy

Authorization for 2 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested drug.
- The requested drug is being used to treat hypercalcemia of malignancy.

- The requested drug has been effective.

All Other Indications

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested drug.
- The requested drug is being used to treat an indication in the coverage criteria other than hypercalcemia of malignancy.
- The requested drug has been effective for treating the diagnosis or condition.

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Zometa and zoledronic acid.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- NCCN guideline: Histiocytic neoplasms
- NCCN guideline: Prostate cancer
- NCCN guideline: Multiple myeloma
- NCCN guideline: Non-small cell lung cancer
- NCCN guideline: Breast cancer
- NCCN guideline: Thyroid carcinoma
- NCCN guideline: Systemic mastocytosis
- NCCN guideline: Kidney cancer

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Zometa and zoledronic acid are covered in addition to the following:

- Breast cancer
- Monoclonal gammopathy with osteopenia or osteoporosis
- Prophylaxis against osteopenia
- Treatment for osteopenia/osteoporosis in patients with systemic mastocytosis
- Langerhans cell histiocytosis

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Zometa and zoledronic acid in patients with breast cancer can be found in two metanalyses.

In a meta-analysis by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) of bisphosphonate use in women with early breast cancer (26 trials; number of participants = 18,766), overall risk of recurrence of any breast cancer was not significantly reduced. However, there were borderline significant reductions in distant recurrence (10-year risk, 20.4% with bisphosphonates vs 21.8% with control), and breast cancer mortality (10-year risk, 16.6% vs 18.4%, respectively). The effect on distant recurrence was primarily related to a significant reduction in bone recurrence of 17%. In subgroup analysis, risk reductions in recurrence (14%), distant recurrence (18%), bone recurrence (28%), and breast cancer mortality (18%) were highly significant in postmenopausal women who received bisphosphonate treatment compared with controls, but the same benefits were not observed in premenopausal women. No treatment benefit was observed for either menopausal subgroup for first distant recurrence at sites other than bone. Benefits for bone recurrence were similar between the non-aminobisphosphonate, clodronate, and the 2 most widely tested aminobisphosphonates, zoledronic acid and ibandronate. The majority (97%) of women were in trials lasting 2 to 5 years and the median follow-up period was 5.6 woman-years.

In a systematic review and meta-analysis, adjuvant zoledronic acid therapy compared with nonuse, placebo, or delayed use, significantly reduced the risk of death by 19% (5 studies, 6414 patients) and the risk of fracture by 21% (7 studies, 7967 patients). However, therapy did not significantly affect disease-free survival, locoregional or distant recurrence, or the incidence of bone metastases. Osteonecrosis of the jaw developed in 0.52% of patients with zoledronic acid and 0% of patients in control groups.

Support for using Zometa and zoledronic acid for treatment of breast cancer can be found in the National Comprehensive Cancer Network's guideline for breast cancer. The NCCN Guideline for breast cancer supports the use of Zometa and zoledronic acid in postmenopausal patients with ductal carcinoma in situ (DCIS) receiving adjuvant aromatase inhibitor therapy along with calcium and vitamin D supplementation to maintain or improve bone mineral density and reduce the risk of fractures. In patients with invasive breast cancer, Zometa and zoledronic acid can be used in postmenopausal patients receiving adjuvant therapy along with calcium and vitamin D supplementation to either: a) maintain or improve bone mineral density and reduce the risk of fractures or b) for risk reduction of distant metastases for three to five years in high-risk node negative or node positive tumors. In patients with invasive breast cancer or inflammatory breast cancer, Zometa and zoledronic acid can be used with calcium and vitamin D supplementation in addition to systemic therapy or endocrine therapy for bone metastases in patients with an expected survival of at least three months and adequate renal function. In patients with inflammatory breast cancer, Zometa and zoledronic acid can be considered in postmenopausal patients receiving adjuvant aromatase inhibition therapy along with calcium and vitamin D supplementation to maintain or improve bone mineral density and reduce risk of fractures.

Support for using Zometa and zoledronic acid in monoclonal gammopathy of uncertain significance can be found in a study of 54 patients with monoclonal gammopathy of undetermined significance with

osteopenia or osteoporosis by Berenson et al. Treatment with zoledronic acid significantly improved lumbar-spine bone mineral density (BMD) in patients with monoclonal gammopathy of undetermined significance (MGUS) in a open-label, single-arm, phase 2 study (n=54). Patients (median age, 67 years; range, 50 to 91 years) diagnosed with monoclonal gammopathy of undetermined significance with osteopenia or osteoporosis at the lumbar-spine (LS) or total hip (TH) (defined as a T-score less than -1), a Karnofsky Performance Status score of greater than 60%, no evidence of lytic lesions, anemia, hypercalcemia or renal insufficiency related to the M protein were eligible for the study. Enrolled patients were scheduled to receive zoledronic acid 4 mg IV infusion over 15 minutes on day 0 and repeated at 6 and 12 months. The median baseline LS-BMD T-score was -1.7 (range, -3.97 to +2.1), and the median TH-BMD T-score at baseline was -1.65 (range, -3.5 to +1.4). The primary endpoint was the percent change from baseline (compared with 13 months) in the postero-anterior lumbar-spine (LS) bone mineral density (BMD) T-scores. Although the a priori sample size was planned to be 80 patients, the study was closed early due to difficulty in enrolling patients. Of the 54 patients enrolled, 10 patients (including 6 patients who discontinued) were not evaluable for efficacy due to lack of LS-BMD or TH-BMD assessments at final follow-up. Among the evaluable patients (n=44) after 13 months of treatment, the median percent improvement of the LS-BMD T-score was +21.8% with a median change from baseline of +0.3 (range, -0.38 to +3.91; p less than 0.0001). In the subset group of patients with osteopenia or osteoporosis (n=32), the median percent improvement of the LS-BMD T-score was +16.2% with a median change from baseline of +0.3 (range, -0.38 to +3.91; p less than 0.0021). The TH-BMD T-scores in the group of evaluable patients (n=44) did not show significant change from baseline (median change, +0.19; range, -2.4 to +2.03; p=0.1684). However, in patients with osteopenia or osteoporosis (n=33), the median percent improvement of the TH-BMD T-score (secondary endpoint) was statistically significant at +8.7% with a median change from baseline of +0.2 (range, -0.6 to +2.03; p less than 0.002). The most commonly reported adverse events were fatigue, arthralgia, fever, and generalized hurt. Six patients discontinued the study due to consent withdrawal, 1 death (cause of death unknown), arthralgia, physician's request, progression to chronic lymphocytic leukemia, and development of primary amyloidosis. There were no reports of osteonecrosis of the jaw, new fractures, or progression to multiple myeloma.

Support for the use of Zometa and zoledronic acid to prevent osteopenia in patients receiving androgen deprivation therapy for nonmetastatic prostate cancer can be found in a randomized, double-blind, placebo-controlled, multicenter trial by Smith et al. Zoledronic acid increased bone mineral density (BMD) significantly in the hip and spine in men receiving androgen deprivation therapy (ADT) for prostate cancer. One hundred six men with nonmetastatic prostate cancer (stage M0) were randomized to receive zoledronic acid 4 mg (n=55) IV over 15 minutes every 3 months or placebo (n=51) for 1 year. Analysis of primary efficacy variables were preplanned in 4 subgroups; patients receiving a gonadotropin-releasing hormone (GnRH) agonist alone, receiving a GnRH agonist and antiandrogen, baseline BMD T-score -1 or greater, and baseline BMD T-score less than -1 to-3. By week 12, mean total testosterone decreased to castrate level (less than 50 nanograms/deciliter). All patients were instructed to take calcium 500 mg and multivitamin containing 400 international units of vitamin D daily. Forty-seven patients in the zoledronic acid group and 43 in the placebo group completed the trial. Lumbar spine BMD in the zoledronic group was increased from baseline at 1 year compared with a decrease of BMD in the placebo group; this change reflected a mean percent change at 1 year between the groups of 7.8% (95% CI, 5.6% to 10%; p less than 0.001). Zoledronic acid was effective regardless of ADT regimen. Intragroup comparisons from

baseline were found to be statistically significant: the lumbar spine BMD in the zoledronic group increased 5.6% from baseline (p less than 0.001) and decreased 2.2% from baseline (p=0.0012) in the placebo group. Subgroup analysis of patients with normal baseline lumbar spine BMD and those with low baseline lumbar spine BMD also demonstrated a significant difference in change between the zoledronic acid and placebo groups. Significant hip BMD increases were seen in the zoledronic acid group in the femoral neck, trochanter, and total hip with corresponding decreases seen in the placebo group (femoral neck mean differences, 3.3%, 95% CI, 1.4 to 5.2, p less than 0.001; trochanter mean differences, 4.9%, 95% CI, 2.9 to 6.9, p less than 0.001; and total hip mean differences, 3.9%, 95% CI, 2.5 to 5.3, p less than 0.001, respectively. Differences noted in the nondominant forearm were not statistically significant. Grade 3 or 4 toxicities were reported in both groups; 24% in the zoledronic group and 39% in the placebo group. Five patients withdrew from the study due to adverse effects (3 from the zoledronic group and 2 from the placebo group). The most common toxicities reported in the zoledronic and placebo groups, respectively, were hot flushes (58% vs 51%), fatigue (38% vs 35%), arthralgias (22% vs 14%), constipation (16% in each group), and urinary frequency (15% vs 22%).

Support for using Zometa and zoledronic acid to prevent osteopenia in patients receiving hormone therapy for breast cancer can be found in an open-label, multicenter, randomized, phase 3, (ZO-FAST) trial (n=1065). Improvement in lumbar spine bone mineral density (BMD) was maintained in postmenopausal women with hormone receptor-positive early-stage breast cancer receiving adjuvant letrozole who were treated with immediate compared with delayed zoledronate therapy. This trial enrolled postmenopausal women with hormone-responsive stage I, II, or IIIA breast cancer with Eastern Cooperative Oncology Group (ECOG) scores less than or equal to 2 and baseline lumbar spine and total hip T-scores greater than or equal to -2. Women with preexisting lumbar spine or hip fractures or with a history of low-intensity fractures were excluded. All patients received letrozole 2.5 mg orally daily for a median of 60 months (range, 0 to 67.8 months) and were randomized to either immediate (initiated within 1 month of randomization) or delayed (only initiated if the patient had a fracture or a decrease in T-score to less than -2) zoledronate 4 mg IV every 6 months. In the immediate group (n=532), a median of 11 infusions of zoledronate were administered to each patient. In the delayed group (n=533), 144 (27%) patients began zoledronate therapy at a median of 12.8 months. At 60 months, mean lumbar spine BMD was increased by 4.3% in the immediate-zoledronate group compared with a 5.4% decrease in the delayed-zoledronate group (p less than 0.0001). In recently postmenopausal women, lumbar spine BMD was preserved, but not improved, in the immediate zoledronate group and was significantly decreased in the delayed zoledronate group (change compared with baseline, -0.3% [p=0.7] and -9.3% [p less than 0.0001], respectively; treatment difference, 9%). However, in established postmenopausal patients, lumbar spine BMD was significantly improved with immediate treatment (change compared with baseline, 5.3%; p less than 0.0001), and was decreased in the delayed-treatment group (change compared with baseline, -4.2%; p less than 0.0001; treatment difference, 9.5%). In analysis of a secondary endpoint, the immediate-zoledronate group had a statistically significant reduction of 34% in risk of disease-free survival events (defined as disease recurrence or death) compared with those in the delayed-zoledronate group (hazard ratio, 0.66; 95% CI, 0.44 to 0.97; p=0.0375).

In an open-label, multicenter, randomized (n=602) study, zoledronic acid given upfront compared with delayed administration prevented cancer treatment-induced bone loss (CTIBL) in postmenopausal

women (PMW) with early breast cancer receiving adjuvant letrozole (Let). The Zometa-Femara Adjuvant Synergy Trial (Z-FAST), enrolled PMW with stage I-IIIa estrogen receptor (ER) and/or progesterone receptor (PR) positive breast cancer and baseline lumbar spine (LS) and total hip (TH) T-scores of -2 or greater. Patients were randomized to receive Let 2.5 mg orally once daily for 5 years with either upfront zoledronic acid 4 mg IV infusion every 6 months (n=301; median age, 60 years; range, 35 to 83 years) or delayed zoledronic acid 4 mg IV infusion every 6 months (n=301; median age, 60 years; range, 41 to 89 years) initiated when either LS and TH T-scores decreased to less than -2 or a nontraumatic fracture occurred. All patients received daily calcium 1000 to 1200 mg and vitamin D 400 to 800 international units. At 12 months, zoledronic acid had been administered to 25 (8.3%) patients (mean time to zoledronic acid initiation, 8.8 months; range, 0.03 to 24.15 months) in the delayed zoledronic acid group. Of 500 evaluable patients, the upfront zoledronic acid group had a positive percent change in bone mineral density (BMD) and the delayed zoledronic acid group had a negative percent change in BMD with an overall BMD mean percent difference between the groups of 4.4% (95% CI, 3.7% to 5%; p less than 0.0001) for LS (primary endpoint) and 3.3% (95% CI, 2.8% to 3.8%; p less than 0.0001) for TH after 12 months of treatment. In a subset of 212 patients, the difference in percent change of serum bone turnover markers between the upfront and delayed zoledronic acid groups was -35% for N-telopeptide (NTx) and -33% for bone-specific alkaline phosphatase (BSAP) at 12 months, with both markers significantly increasing over baseline in the delayed zoledronic acid group (NTx, p less than 0,0001; BSAP, p=0.0006) and significantly decreasing over baseline in the upfront zoledronic acid group (NTx, p=0.013; BSAP, p less than 0.0001). In 300 patients evaluated in the safety analysis, the incidence of adverse events and treatment-related withdrawals were similar between groups; however, bone pain occurred more frequently in the upfront zoledronic acid group compared with the delayed zoledronic acid group (11.3% vs 4%). No patients developed significant renal dysfunction (grade 3 or 4) or jaw osteonecrosis. One patient in the upfront zoledronic acid group developed a grade 1 increase in serum creatinine.

A randomized, phase 3, open-label, prospectively defined bone mineral density (BMD) subprotocol analysis (n=401) in premenopausal women on adjuvant endocrine therapy demonstrated that the addition of zoledronic acid prevented cancer treatment-induced bone loss (CTIBL) compared with patients on adjuvant endocrine therapy alone. Patients with stage I to II, estrogen receptor (ER) and/or progesterone receptor (PR) positive breast cancer with no prior adjuvant therapy were randomized to subcutaneous (subQ) goserelin 3.6 mg every 28 days and tamoxifen 20 mg orally daily with (n=100; median age, 43.8 years (yr)) or without (n=103; median age, 46.6 yr) IV zoledronic acid 4 mg every 6 months or goserelin 3.6 mg subQ every 28 days and anastrozole 1 mg orally daily with (n=104; median age, 44.7 yr) or without (n=94; median age, 45.7 yr) zoledronic acid 4 mg IV every 6 months. At 36 months, results from 114 patients showed that the treatment groups without zoledronic acid had significant decreases in BMD (lumbar spine observed data, -14.4%, p less than 0.0001; trochanter observed data, -8.2%, p=0.0005) and T-scores (lumbar spine observed mean difference, -1.4, p less than 0.0001; trochanter observed mean difference, -0.6, p=0.0017) compared with baseline. In the treatment groups containing zoledronic acid, BMD remained stable compared with baseline and T-scores significantly improved (p less than 0.0001) compared with adjuvant endocrine therapy alone. Patients receiving the combination of anastrozole and goserelin had significantly greater (p less than 0.0001) overall BMD loss compared with patients receiving tamoxifen and goserelin (lumbar spine observed data, -17.4% vs -11.6%; trochanter observed data, -11.3% vs -5.1%). T-score changes over baseline were greater for the anastrozole/goserelin group (lumbar spine

observed mean difference, -2.6; trochanter observed mean difference, -0.8) compared with the tamoxifen/goserelin group (lumbar spine observed mean difference, -1.1; trochanter observed mean difference, -0.1). Adverse events were mild to moderate in severity and were consistent with known toxicities associated with each drug. Zoledronic acid use was not associated with renal dysfunction and the addition of zoledronic acid did not add significant toxicity to the other treatment groups. No patient experienced bone fractures or jaw osteonecrosis.

Support for using Zometa and zoledronic acid as prophylactic treatment of osteopenia secondary to ovarian dysfunction induced by adjuvant chemotherapy is supported by a prospective study (n=404) of a randomized, open-label, phase 3 study (n=1803) (Austrian Breast and Colorectal Cancer Study Group trial-12 (ABCSG-12)). Premenopausal women (19 years or older) who underwent surgery for stage I/II estrogen receptor-positive or progesterone-receptor-positive (or both) breast cancer, had a Karnofsky Index of 70 or greater, had fewer than 10 positive lymph nodes, and were scheduled to receive goserelin for 3 years were stratified by tumor stage and grade, hormone-receptor status, and lymph node involvement, and subsequently randomized to 1 of 4 treatments. The treatment regimens were 3 years of either goserelin 3.6 mg subQ every 28 days plus tamoxifen 20 mg/day orally with or without zoledronic acid 4 mg IV every 6 months or goserelin 3.6 mg subQ every 28 days plus anastrozole 1 mg/day orally with or without zoledronic acid 4 mg IV every 6 months. The median follow-up was 60 months (range, 15.5 to 96.6 months). After 3 years of treatment, endocrine therapy alone caused significant loss of BMD at the lumbar spine (-11.3%, mean difference -0.119 g/cm(2) [95% CI -0.146 to -0.091], p<0.0001) and trochanter (-7.3%, mean difference -0.053 g/cm(2) [-0.076 to -0.030], p<0.0001). In patients who did not receive zoledronic acid, anastrozole caused greater BMD loss than tamoxifen at 36 months at the lumbar spine (-13.6%, mean difference -0.141 g/cm(2) [-0.179 to -0.102] vs -9.0%, mean difference -0.095 g/cm(2) [-0.134 to -0.057], p<0.0001 for both). 2 years after the completion of treatment (median follow-up 60 months [range 15.5-96.6]), patients not receiving zoledronic acid still had decreased BMD at both sites compared with baseline (lumbar spine -6.3%, mean difference -0.067 g/cm(2) [-0.106 to -0.027], p=0.001; trochanter -4.1%, mean difference -0.03 g/cm(2) [-0.062 to 0.001], p=0.058). Patients who received zoledronic acid had stable BMD at 36 months (lumbar spine +0.4%, mean difference 0.004 g/cm(2) [-0.024 to 0.032]; trochanter +0.8%, mean difference 0.006 g/cm(2) [-0.018 to 0.028]) and increased BMD at 60 months at both sites (lumbar spine +4.0%, mean difference 0.039 g/cm(2) [0.005-0.075], p=0.02; trochanter +3.9%, mean difference 0.028 g/cm(2) [0.003-0.058], p=0.07) compared with baseline. Although there was partial recovery 2 years after completing treatment, patients receiving endocrine therapy alone did not recover their baseline BMD levels. Concomitant zoledronic acid prevented bone loss during therapy and improved BMD at 5 years.

Support for using Zometa and zoledronic acid to treat osteoporosis and osteopenia in patients with systemic mastocytosis can be found in the National Comprehensive Cancer Network's guideline for systemic mastocytosis. The NCCN Guideline for systemic mastocytosis supports the use of Zometa when used for the treatment of osteoporosis or osteopenia.

Support for using Zometa and zoledronic acid for Langerhans cell histocytosis can be found in the National Comprehensive Cancer Network's guideline for histiocytic neoplasms. The NCCN Guideline for histiocytic neoplasms supports the use of Zometa and zoledronic acid as preferred first-line or subsequent therapy for unifocal Langerhans cell histiocytosis with isolated bone disease or multifocal bone disease.

Support for using Zometa and zoledronic acid for kidney cancer can be found in the National Comprehensive Cancer Network's guideline for kidney cancer. The NCCN Guideline for kidney cancer supports the use of Zometa and zoledronic acid as a component of best supportive care for bony metastases.

Support for using Zometa and zoledronic acid for non-small cell lung cancer can be found in the National Comprehensive Cancer Network's guideline for non-small cell lung cancer. The NCCN Guideline for non-small cell lung cancer supports the use of Zometa and zoledronic acid in those with bony metastases.

Support for using Zometa and zoledronic acid for thyroid carcinoma can be found in the National Comprehensive Cancer Network's guideline for thyroid carcinoma. The NCCN Guideline for thyroid carcinoma supports the use of Zometa and zoledronic acid in papillary carcinoma, follicular carcinoma, oncocytic carcinoma, and medullary carcinoma in patients with bony metastases. In patients with anaplastic carcinoma, Zometa and zoledronic acid can be used as palliative care for bone metastases.

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