

Clinical Policy: Zoledronic Acid (Reclast, Zometa)

Reference Number: CP.PHAR.59

Effective Date: 03/11

Last Review Date: 03/17

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for zoledronic acid (Reclast®, Zometa®).

Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® that zoledronic acid is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Osteoporosis and Paget's Disease of the Bone (must meet all):

1. Request is for Reclast for one of the following indications (a, b, c, or d):
 - a. Treatment of osteoporosis and both of the following (i and ii):
 - i. Diagnosis is evidenced by one of the following (a or b):
 - a) T-score ≤ -2.5 [dual energy X-ray absorptiometry (DXA)] at the femoral neck, spine, or total hip;
 - b) History of osteoporotic fracture confirmed by radiographic imaging;
 - ii. Meets one of the following (a or b):
 - a) Postmenopausal woman;
 - b) Male (if hypogonadal osteoporosis, member is receiving testosterone but remains at high risk for fracture or has a contraindication to testosterone);
 - b. Prevention of osteoporosis in postmenopausal woman with T-score < -1.0 (DXA) at the femoral neck, spine, or total hip, and one of the following (i or ii):
 - i. A 10-year probability of hip fracture $\geq 3\%$ per the WHO Fracture Risk Assessment Tool (FRAX);
 - ii. A 10-year probability of a major osteoporosis-related fracture $\geq 20\%$ per the FRAX;
 - c. Treatment or prevention of glucocorticoid-induced osteoporosis in members either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to ≥ 7.5 mg of prednisone and are expected to remain on glucocorticoids for at least 12 months;
 - d. Treatment of Paget's disease of the bone and one of the following (i, ii, or iii):
 - i. Serum alkaline phosphatase is elevated ≥ 2 times the upper limit of the age-specific normal reference range;
 - ii. Member is symptomatic;
 - iii. At risk for complications from the disease;
2. For osteoporosis-related indications, failure (decline in BMD of $\geq 5\%$ or continued fractures) of a one-year trial of an oral bisphosphonate (e.g., alendronate, risedronate) unless contraindicated or clinically significant adverse effects are experienced;
3. Not currently receiving therapy with Zometa;

4. Prescribed dose of Reclast does not exceed 5 mg;
5. Member has none of the following contraindications:
 - a. Hypocalcemia (serum calcium (Ca) or albumin-corrected calcium (cCa) is within normal limits);
 - b. Creatinine clearance (CrCl) < 35 mL/min.
**Labs should be recent (within the past 90 days)*

Approval duration:

For osteoporosis prevention – 24 months (one infusion)

For all other indications – 12 months (one infusion)

B. Hypercalcemia, Multiple Myeloma, and Bone Metastases (must meet all):

1. Request is for Zometa for one of the following diagnoses (a, b, or c):
 - a. Hypercalcemia of malignancy defined as an albumin-corrected calcium (cCa) of \geq 12 mg/dL per Appendix B;
 - b. Multiple myeloma when used in conjunction with both of the following (i and ii):
 - i. Standard antineoplastic therapy;
 - ii. An oral calcium supplement of 500 mg and a multiple vitamin containing 400 international units of vitamin D daily;
 - c. Bone metastases from solid tumors and both of the following (i and ii):
 - i. Used in conjunction with both of the following (a and b):
 - a) Standard antineoplastic therapy;
 - b) An oral calcium supplement of 500 mg and a multiple vitamin containing 400 international units of vitamin D daily;
 - ii. If prostate cancer, documented evidence that prostate cancer has progressed after treatment with at least one hormonal therapy;
2. Not currently receiving therapy with Reclast;
3. Prescribed dose of Zometa does not exceed 4 mg.

Approval duration:

For hypercalcemia of malignancy – 1 week (one infusion)

For multiple myeloma and bone metastases – 3 months (one infusion every 3 weeks)

C. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Osteoporosis and Paget's Disease of the Bone (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Request is for Reclast;
3. For osteoporosis-related indications, documentation of positive response to therapy;
4. For Paget's disease, member meets one of the following (a, b, or c):
 - a. Disease relapse based on increases in serum alkaline phosphatase;
 - b. Failure to achieve normalization of serum alkaline phosphatase;
 - c. Member is symptomatic;

5. Prescribed dose does not exceed 5 mg.

Approval duration:

For osteoporosis prevention – 24 months (one infusion)

For all other indications – 12 months (one infusion)

B. Hypercalcemia, Multiple Myeloma, and Bone Metastases (must meet all):

1. Currently receiving the medication via Centene benefit or member has previously met all initial approval criteria;
2. Request is for Zometa;
3. For hypercalcemia of malignancy, member meets both of the following (a and b):
 - a. At least 7 days have elapsed since last treatment;
 - b. Documented evidence that serum calcium has not returned to normal or remained normal after initial treatment;
4. For multiple myeloma and bone metastases, member meets both of the following (a and b):
 - a. Documentation of positive response to therapy;
 - b. Currently receiving an oral calcium supplement of 500 mg and a multiple vitamin containing 400 international units of vitamin D daily;
5. Prescribed dose does not exceed 4 mg.

Approval duration:

For hypercalcemia of malignancy – 1 week (one infusion)

For multiple myeloma and bone metastases – 6 months (one infusion every 3 weeks)

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Zoledronic acid is an inhibitor of osteoclastic bone resorption. Although the anti-resorptive mechanism is not completely understood, several factors are thought to contribute to this action. In vitro, 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.

Formulations:

Reclast:

- 5 mg/100 mL (single-use ready-to-infuse solution)

Zometa:

- 4 mg/5 mL (single-use vial of concentrate to be diluted)
- 4 mg/100 mL (single-use ready-to-use bottle)

FDA Approved Indications:

Reclast (zoledronic acid) is a bisphosphonate/intravenous infusion solution indicated for:

- Treatment of osteoporosis in postmenopausal women. In postmenopausal women with osteoporosis, diagnosed by BMD or prevalent vertebral fracture, Reclast reduces the incidence of fractures (hip, vertebral, and non-vertebral osteoporosis-related fractures). In patients at high risk of fracture, defined as a recent low-trauma hip fracture, Reclast reduces the incidence of new clinical fractures.
- Prevention of osteoporosis in postmenopausal women.
- Treatment to increase bone mass in men with osteoporosis.
- Treatment and prevention of glucocorticoid-induced osteoporosis in men and women who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and who are expected to remain on glucocorticoids for at least 12 months.
- Treatment of Paget's disease of bone in men and women. Treatment is indicated in patients with Paget's disease of bone with elevations in serum alkaline phosphatase of two times or higher than the upper limit of the age-specific normal reference range, or those who are symptomatic, or those at risk for complications from their disease.

Limitations of use:

- The safety and effectiveness of Reclast for the treatment of osteoporosis is based on clinical data of three years duration. The optimal duration of use has not been determined. All patients on bisphosphonate therapy should have the need for continued therapy re-evaluated on a periodic basis. Patients at low-risk for fracture should be considered for drug discontinuation after 3 to 5 years of use. Patients who discontinue therapy should have their risk for fracture re-evaluated periodically.

Zometa (zoledronic acid) is a bisphosphonate/intravenous infusion solution indicated for:

- 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: $cCa \text{ in mg/dL} = Ca \text{ in mg/dL} + 0.8 (4.0 \text{ g/dL} - \text{patient albumin [g/dL]})$.
- Treatment of patients with multiple myeloma.
- Treatment of 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 in the treatment of hypercalcemia associated with hyperparathyroidism or with other non-tumor-related conditions have not been established.

Appendices

Appendix A: Abbreviation Key

BMD: bone mineral density

Ca: calcium

cCa: albumin-corrected calcium

CrCl: creatinine clearance

DXA: dual energy X-ray absorptiometry

FDA: Food and Drug Administration

FRAX: WHO Fracture Risk Assessment Tool

MM: multiple myeloma

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WHO: World Health Organization

Appendix B: Formula for Albumin-Corrected Calcium Level

$$cCa \text{ in mg/dL} = Ca \text{ in mg/dL} + 0.8 (4.0 \text{ g/dL} - \text{patient albumin [g/dL]})$$

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3489	Injection, zoledronic acid, 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date
<p>Zometa criteria</p> <p>Hypercalcemia of malignancy initial – renal dose adjustment and co-administration with saline hydration criteria removed; max dose added; re-auth - max total doses removed; signs of jaw osteonecrosis removed; renal deterioration removed; approval changed from 3 to 6 months.</p> <p>Multiple myeloma initial - definition of MM active (symptomatic) disease added; modified dosing criteria to max of $\leq 4\text{mg}$; lytic destruction of bone/spine compression/osteopenia criteria removed-; re-auth - 2 year treatment limit criteria removed- ; signs of jaw osteonecrosis criteria removed; renal deterioration criteria removed since tx interruption vs. hard stop; approval changed to 6 months.</p> <p>Bone metastases from solid tumors - initial: modified dosing criteria to max dose of $\leq 4\text{mg}$; criteria for prostate cancer added as noted in PI; re-auth: 2 year treatment limit criteria removed; signs of jaw osteonecrosis criteria removed-; renal deterioration criteria removed; approval changed to 6 months.</p>	01/16	2/16
<p>Reclast criteria split from CP.PHAR.20.Osteoporosis Inj policy.</p> <p>For men, criteria changed to require testosterone only for hypogonadal rather than primary osteoporosis, removed year-long testosterone therapy prior to Reclast.</p> <p>Added “at femoral neck or spine” for T score.</p> <p>Removed requirement must be > 50 in cases where osteoporosis diagnosis relies on history of an osteoporotic fracture.</p> <p>Certain conditions representing potential contraindications to therapy are and other safety criteria removed as the PI does not instruct that they be ruled out prior to initiating therapy or specify a test and measureable outcome by which to do so.</p>	3/16	03/16

Reviews, Revisions, and Approvals	Date	Approval Date
<p>Retained contraindication that are objective and verifiable and should be checked prior to therapy per PI (Hypocalcemia & CrCl) Added additional criteria if purpose is prevention of osteoporosis per UpToDate and FRAX. Added definition of bisphosphonate trial failure and, if contraindication/intolerance, that it be to one of the two oral drugs listed Calcium/vitamin D requirement language edited to be less specific. Approval duration broken up across indications. Edited to allow continued therapy for Paget’s disease in some cases per PI.</p>		
<p>Removed age restriction. Added maximum dose to continued therapy. Certain conditions representing potential contraindications to therapy and other safety criteria removed. Osteoporosis and Paget’s disease: Removed high risk of fracture (recent low-trauma hip fracture). Added “at total hip” to T score. Added requirement for T score/history of fracture to confirm diagnosis of male osteoporosis, and combined treatment of osteoporosis of postmenopausal women and males. Removed requirement for administration of calcium/vitamin D if appropriate. For Paget’s disease, removed requirement for trial/failure of an oral bisphosphonate. Hypercalcemia, multiple myeloma, and bone metastases: Removed requirement that multiple myeloma must be active, and deleted appendix C (definition of active MM). Removed CrCl < 30 (a warning) and hypercalcemia associated with hyperparathyroidism (a limitation of use) from contraindications. Added requirement for member to continue to be receiving oral calcium and vitamin D to continued therapy. Added reasons to discontinue to continued therapy</p>	02/17	03/17

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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