Clinical Policy: Zoledronic Acid (Reclast, Zometa)

Reference Number: IL.PHAR.59
Effective Date: 1.1.20
Last Review Date: 4.18.2022
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Zoledronic acid (Reclast®, Zometa®) is a bisphosphonate.

FDA Approved Indication(s)

Reclast is indicated:

- Postmenopausal osteoporosis (PMO) - treatment: for the treatment of osteoporosis in postmenopausal women. In postmenopausal women with osteoporosis, diagnosed by bone mineral density (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;
- PMO - prevention: for the prevention of osteoporosis in postmenopausal women;
- Male osteoporosis - treatment: for the treatment to increase bone mass in men with osteoporosis;
- Glucocorticoid-induced osteoporosis (GIO) - prevention and treatment: for the 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;
- Paget disease: for the treatment of Paget's disease of bone in men and women with elevations in serum alkaline phosphatase (ALP) 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.

Limitation(s) 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 is indicated:

- Hypercalcemia of malignancy: For the 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);
- Multiple myeloma (MM): For the treatment of patients with multiple myeloma;

- Solid tumors: For the 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.

Limitation(s) 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

I. Initial Approval Criteria

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

1. Request is for Reclast for one of the following indications (a, b, or c):
   a. Treatment or prevention of PMO or GIO;
   b. Treatment of male osteoporosis;
   c. Paget's disease of bone;
2. Failure of a 12-month trial of an oral bisphosphonate (*alendronate is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
3. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
4. Not currently receiving therapy with Zometa;
5. Dose does not exceed 5 mg.

Approval duration:
Medicaid – osteoporosis prevention: 24 months (one infusion); 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 indications (a, b, or c):
   a. Hypercalcemia of malignancy evidenced by an albumin-corrected calcium (cCa) ≥ 12 mg/dL;
   b. MM, and member is receiving or initiating therapy (e.g., chemotherapy, transplant) for symptomatic disease;
   c. Bony metastasis from solid tumor (e.g., breast, kidney, lung, prostate, thyroid);):
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
4. Not currently receiving therapy with Reclast;
5. Dose does not exceed 4 mg.

Approval duration:
Medicaid – Hypercalcemia of malignancy: 1 week (one infusion); multiple myeloma and bone metastases: 3 months (one infusion every 3 weeks)

C. Prostate/Breast Cancer - Fracture Prevention (off-label) (must meet all)**:**
1. Request is for Zometa;
2. Diagnosis of one of the following (a or b):
   a. Prostate cancer and member is receiving androgen deprivation therapy (e.g., leuprolide (Lupron®), bicalutamide (Casodex®), Nilandron®);
   b. Breast cancer and member is receiving adjuvant endocrine therapy (e.g., tamoxifen or aromatase inhibitors such as anastrozole (Arimidex®), exemestane (Aromasin®) or letrozole (Femara®));
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
5. Zometa is not prescribed concurrently with Reclast;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 4 mg;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 12 months (one infusion for prostate cancer, two infusions for breast cancer)

D. Systemic Mastocytosis (off-label) (must meet all)**:**
1. Request is for Zometa;
2. Diagnosis of systemic mastocytosis;
3. Member has osteopenia or osteoporosis with bone pain;
4. Prescribed by or in consultation with an oncologist;
5. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
6. Zometa is not prescribed concurrently with Reclast;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 4 mg;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid – 3 months (one infusion every 3 weeks)

E. Histiocytic Neoplasms – Langerhans Cell Histiocytosis (off-label) (must meet all)**:**
1. Request is for Zometa;
2. Diagnosis of langerhans cell histiocytosis;
3. Member has multifocal bone disease;
4. Prescribed by or in consultation with an oncologist;
5. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
6. Zometa is not prescribed concurrently with Reclast;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 4 mg;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid – 3 months (one infusion every 4 weeks)

F. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Request is for Reclast;
2. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 5 mg.

Approval duration:
Medicaid – osteoporosis prevention: 24 months (one infusion); **a**ll other indications: 12 months (one infusion)

B. Oncology-Related Indications (must meet all)**:**

1. Request is for Zometa;
2. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Zometa for a covered indication and has received this medication for at least 30 days;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 4 mg;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

- Hypercalcemia of malignancy: 1 week (one infusion)
- Prostate cancer and breast cancer: 12 months (one infusion for prostate cancer, two infusions for breast cancer)
- All other indications: 12 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.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALP: alkaline phosphatase
BMD: bone mineral density
cCa: albumin-corrected calcium
GIO: glucocorticoid-induced osteoporosis
MM: multiple myeloma
PMO: postmenopausal osteoporosis
CrCl: creatinine clearance
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

The drugs listed here may not be a formulary agent and may require prior authorization.

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
alendronate (Fosamax®)	Osteoporosis 10 mg PO QD or 70 mg PO q week Glucocorticoid-induced osteoporosis 5 mg PO QD or 10 mg PO QD (in postmenopausal women not receiving estrogen) Osteoporosis prophylaxis 5 mg PO QD or 35 mg PO q week Paget's disease 40 mg PO QD for 6 months; may re-treat if needed	Osteoporosis 10 mg/day or 70 mg/week Glucocorticoid-induced osteoporosis 5 mg/day or 10 mg/day (in postmenopausal women not receiving estrogen) Osteoporosis prophylaxis 5 mg/day or 35 mg/week Paget's disease 40 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to any product component
  - Reclast: hypocalcemia, creatinine clearance < 35 mL/min, acute renal impairment
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Zoledronic acid (Reclast)	Treatment: PMO, male osteoporosis Treatment/prevention: GIO	5 mg IV once a year	5 mg/year
	Prevention: PMO	5 mg IV once every 2 years	5 mg/2 years
	Paget disease	5 mg IV once; retreatment may be considered	5 mg
Zoledronic acid (Zometa)	Hypercalcemia of malignancy	4 mg as a single-use IV infusion; may re-treat with 4 mg after a minimum of 7 days	4 mg/infusion
	MM Solid tumor - bone metastasis	4 mg as a single-use IV infusion every 3 to 4 weeks	4 mg/3 weeks

VI. Product Availability

Drug Name	Availability
Zoledronic acid (Reclast)	Ready-to-infuse solution: 5 mg/100 mL
Zoledronic acid (Zometa)	Ready-to-infuse solution: 4 mg/100 mL Single-use vial concentrate: 4 mg/5 mL

VII. References

1. Reclast Prescribing Information. East Hanover, NJ: Novartis Pharmaceutical Corporation; April 2020. Available at http://www.reclast.com. Accessed November 03, 2021.
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Osteoporosis Diagnosis, Fracture Risk, and Treatment

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7. National Osteoporosis Foundation Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporosis International 2014. Available at: https://cdn.nof.org/wp-content/uploads/2016/01/995.pdf. Accessed November 5, 2021.
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Male Osteoporosis

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Glucocorticoid-Induced Osteoporosis

12. Buckley L, Guyatt G, Fink HA, et al. 2017 American College of Rheumatology guideline for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Rheumatol. 2017; 69(8): 1521-1537.

Paget Disease

13. Singer FR, Bone HG, Hosking DJ, et al. Paget's disease of the bone: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2014; 99(12): 4480-4422.

Oncology

14. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 02, 2021.
15. National Comprehensive Cancer Network. Multiple Myeloma Version 3.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed November 02, 2021.
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17. National Comprehensive Cancer Network. Prostate Cancer Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed November 02, 2021.
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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	P&T Approval Date
New policy created, adapted from CP.PHAR.59 Zoledronic Acid (Reclast, Zometa) policy.	12.12.19	1.7.20
1Q 2021 review and Changes: added Age ≥ 18 years or documentation of closed epiphyses on x-ray; added criteria for prostate and breast cancer; revised approval duration and frequency of treatment for prostate/breast cancer fracture prevention from once every 3 weeks for 3 months to once every year for prostate cancer and twice a year for breast cancer; references reviewed and update; added criteria Prostate/Breast Cancer - Fracture Prevention (off-label); updated continued therapy request that Member is responding positively to therapy; references reviewed and updated	3.11.2021	
2Q2022 – added oncologist to indication Hypercalcemia, Multiple Myeloma, Bone Metastases, and Prostate and Breast Cancer**;** revised diagnosis for Multiple Myeloma**;** Zometa - added criteria for off label indication of Systemic Mastocytosis and histiocytic neoplasms per NCCN guidelines; Removed *Appendix D* General information; references reviewed and updated.	4.18.22	

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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.