Clinical Policy: Zoledronic Acid (Reclast, Zometa)

Reference Number: ERX.SPA.66
Effective Date: 10.01.16
Last Review Date: 02.21
Line of Business: Commercial, Medicaid

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 - prevention and treatment: For the treatment and prevention of GIO 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

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It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Reclast and Zometa are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Osteoporosis (must meet all):
1. Request is for Reclast;
2. Prescribed for one of the following uses (a or b):
   a. Treatment or prevention of PMO or GIO;
   b. Treatment of male osteoporosis;
3. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
4. Failure of a 12-month trial of oral bisphosphonate therapy *(see Appendix B; alendronate is preferred)* at up to maximally indicated doses, unless all are contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for oral bisphosphonates*
5. Reclast is not prescribed concurrently with Zometa;
6. Dose does not exceed 5 mg.

Approval duration: osteoporosis treatment: 12 months (one infusion); osteoporosis prevention: 24 months (one infusion)

B. Paget Disease (must meet all)**:**
1. Request is for Reclast;
2. Diagnosis of Paget disease of the bone;
3. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
4. Failure of a 12-month trial of oral bisphosphonate therapy *(Appendix B; alendronate is preferred)* at up to maximally indicated doses, unless all are contraindicated or clinically significant adverse effects are experienced *(Appendix E)*;
   **Prior authorization may be required for oral bisphosphonates*
5. Reclast is not prescribed concurrently with Zometa;
6. Dose does not exceed 5 mg.

Approval duration: 12 months (one infusion)

C. Hypercalcemia of Malignancy (must meet all)**:**
1. Request is for Zometa;
2. Diagnosis of hypercalcemia of malignancy:
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
5. Albumin-corrected calcium ≥ 12 mg/dL;

7. Zometa is not prescribed concurrently with Reclast;
8. Dose does not exceed 4 mg.

Approval duration: 1 week (one infusion)

D. Multiple Myeloma or Solid Tumor (must meet all)**:**
1. Request is for Zometa;
2. Diagnosis of one of the following (a or b):
   a. MM, and member is receiving or initiating therapy (e.g., chemotherapy, transplant) for symptomatic disease;
   b. Bony metastasis from solid tumor (e.g., breast, kidney, lung, prostate, thyroid);
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. Dose does not exceed 4 mg.

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

E. 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: 12 months (one infusion for prostate cancer, two infusions for breast cancer)

F. 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: 3 months (one infusion every 3 weeks)

G. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Osteoporosis and Paget Disease of Bone (must meet all)**:**
1. Request is for Reclast;

2. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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: osteoporosis treatment and Paget disease: 12 months (one infusion); osteoporosis prevention: 24 months (one infusion)

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

1. Request is for Zometa;
2. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BMD: bone mineral density
FDA: Food and Drug Administration
GIO: glucocorticoid-induced osteoporosis
MM: multiple myeloma
PMO: postmenopausal osteoporosis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oral bisphosphonates		
alendronate (Fosamax®)	Treatment/prevention: PMO Treatment: GIO, male osteoporosis Treatment: Paget disease *See prescribing information for dose.*	Varies
Fosamax® Plus D (alendronate / cholecalciferol)	Treatment: PMO, male osteoporosis *See prescribing information for dose.*	

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
risedronate (Actonel®, Atelvia®)	Actonel: Treatment/prevention: PMO, GIO Treatment: male osteoporosis Treatment: Paget disease Atelvia: Treatment: PMO *See prescribing information for dose.*	
ibandronate (Boniva®)	Treatment/prevention: PMO *See prescribing information for dose.*	

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

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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

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Oncology

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Added maximum dose to continued therapy. 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. Added contraindication of CrCl < 35 as it can lead to hospitalization. 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). Added requirement for member to continue to be receiving oral calcium and vitamin D to continued therapy.	06.17	08.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Converted to new template. Modified diagnoses and removed requirements for evidence of diagnoses for Reclast indications. Removed age requirement. Modified criteria to add specialist requirement or trial and failure of a bisphosphonate (alendronate is preferred) for osteoporosis-related indications. Removed definition of treatment failure.Modified approval duration of 24 months to apply only to postmenopausal osteoporosis prevention. Removed requirements for calcium and vitamin D supplementation. Added requirement for continuation of standard antineoplastic therapy for multiple myeloma and bone metastases. Modified approval duration for Other diagnoses/indications to 6 months. Updated appendices.	11.17.17	02.18
1Q 2019 annual review: no significant changes; added geriatrician prescriber option; removed previous requirement that physiatrist prescriber applies only to postmenopausal osteoporosis; references reviewed and updated.	11.01.18	02.19
1Q 2020 annual review: Reclast: closed epiphyses added if less than 18 years; Paget diease - specialists added: endocrinologist and rheumatologist, continuation criteria removed for individualization of therapy; Zometa: oncology - examples of skeletal related event and solid tumor added; oncologist and age added; NCCN recommended breast/prostate cancer and systemic mastocytosis uses added/updated; hypercalcemia continuation of therapy criteria removed given response fluidity; references reviewed and updated.	11.19.19	02.20
1Q 2021 annual review: the MM/solid tumor common criteria line item, at risk for skeletal related event, is removed for solid tumor and for MM is replaced with receiving or initiating therapy for symptomatic disease per pivotal trials/NCCN; 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 updated.	11.03.20	02.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.