Clinical Policy: Zoledronic Acid (Reclast, Zometa)

Reference Number: PA.CP.PHAR.59
Effective Date: 03/11
Last Review Date: 01/19

Coding Implications
Revision Log

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

FDA Approved Indication(s)
Reclast is indicated:

- 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;
- For the prevention of osteoporosis in postmenopausal women;
- For the treatment to increase bone mass in men with osteoporosis;
- 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;
- 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:

- 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);
- For the treatment of patients with multiple myeloma;
- 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
It is the policy of health plans affiliated with Pennsylvania Health and Wellness® 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, or c):
   a. Osteoporosis;
   b. Prevention of osteoporosis;
   c. Paget's disease of bone;
2. For osteoporosis-related indications, member meets one of the following (a or b):
   a. Prescribed by or in consultation with one of the following specialists: a gynecologist, endocrinologist, rheumatologist, geriatrician, orthopaedist, or physiatrist;
   b. 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. Not currently receiving therapy with Zometa;
4. Dose does not exceed 5 mg.

Approval duration:
***For osteoporosis prevention* – 24 months (one infusion)**
Glucocorticoid-induced osteoporosis – 12 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 indications (a, b, or c):
   a. Hypercalcemia of malignancy evidenced by an albumin-corrected calcium (cCa) ≥ 12 mg/dL (*see Appendix D)*;
   b. Multiple myeloma when used in conjunction with standard antineoplastic therapy;
   c. Bone metastases from solid tumors and both of the following (i and ii):
      i. Member is currently receiving standard antineoplastic therapy;
      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. Dose 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 PA.CP.PMN.53

II. Continued Approval

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

1. Currently, receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
2. Request is for Reclast;
3. For osteoporosis-related indications, documentation of positive response to therapy;
4. For Paget's disease, disease has relapsed or progressed (e.g., increases in or failure to achieve normalization of serum ALP, radiographic progression of disease);
5. If request is for a dose increase, new dose does not exceed 5 mg.

Approval duration:
***For osteoporosis prevention* – 24 months (one infusion)**
Glucocorticoid-induced osteoporosis – 12 months (one infusion)
***For all other indications* – 12 months (one infusion)**

B. Hypercalcemia, Multiple Myeloma, and Bone Metastases (must meet all):
1. Currently, receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
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 continues to receive standard antineoplastic therapy and is responding positively to therapy with Zometa (e.g., no significant toxicity);
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 Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
2. Refer to PA.CP.PMN.53

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)

Appendices

Appendix A: Abbreviation/Acronym Key

ALP: alkaline phosphatase
BMD: bone mineral density
cCa: albumin-corrected calcium
CrCl: creatinine clearance
FDA: Food and Drug Administration

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	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
Fosamax® Plus D (alendronate/ cholecalciferol)	Osteoporosis 70 mg alendronate/2,800 units cholecalciferol or 70 mg alendronate/5,600 units cholecalciferol PO q week	Osteoporosis 70 mg alendronate/5,600 units cholecalciferol/week
risedronate (Actonel®, Atelvia®)	Osteoporosis (including prophylaxis) 5 mg PO QD or 35 mg PO q week or 75 mg PO QD for 2 consecutive days for 2 doses/month or 150 mg PO q month	Osteoporosis (including prophylaxis) 5 mg/day or 35 mg/week or 75 mg/day for 2 days per month or 150 mg/month

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
	Glucocorticoid-induced osteoporosis 5 mg PO QD Paget's disease 30 mg PO QD for 2 months; may re-treat if needed after 2 months	Glucocorticoid-induced osteoporosis 5 mg/day Paget's disease 30 mg/day
ibandronate (Boniva®)	Osteoporosis 150 mg PO q month or 3 mg IV q 3 months Osteoporosis prophylaxis 150 mg PO q month	Osteoporosis 150 mg/month or 3 mg/3 month Osteoporosis prophylaxis 150 mg/month
etidronate disodium (Didronel®)	Paget's disease 5 to 10 mg/kg/day PO (not to exceed 6 months) or 11 to 20 mg/kg/day PO (not to exceed 3 months); may re-treat if needed	20mg/kg/day
pamidronate disodium (Aredia®)	Paget's disease 30 mg IV over 4 hours QD for 3 consecutive days (total dose of 90 mg); may re-treat if needed	30 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; Reclast only – hypocalcemia, creatinine clearance < 35 mL/min and in those with evidence of acute renal impairment
- Boxed warning(s): none reported

Appendix D: General Information

- The World Health Organization uses the following classifications for osteoporosis and osteopenia:

Category	T-score
Normal	-1.0 or above
Low bone mass (osteopenia)	Between -1.0 and -2.5
Osteoporosis	-2.5 or below

- Formula for albumin-corrected calcium level: cCa in mg/dL = Ca in mg/dL + 0.8 (4.0 g/dL - patient albumin [g/dL])
- Hormonal therapy for prostate cancer includes regimens containing luteinizing hormone-releasing hormone (LHRH) agonists (e.g., goserelin, histrelin, leuprolide, triptorelin), LHRH antagonists (e.g., degarelix), antiandrogens (e.g., nilutamide, flutamide, bicalutamide, enzalutamide), and/or an androgen biosynthesis inhibitor (e.g., abiraterone) per NCCN guidelines.

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
Modified diagnoses and removed requirements for evidence of diagnoses for Reclast indications. Modified age requirement. Modified criteria to add specialist requirement or trial and failure of a bisphosphonate (alendronate is preferred). Removed definition of treatment failure. Removed contraindication of hypocalcemia. Modified approval duration of 24 months to apply only to postmenopausal osteoporosis prevention; modified approval duration for other diagnoses/indications to 12 months. Removed requirements for calcium and vitamin D supplementation. Modified definitions for positive response to therapy. Added requirement for continuation of standard antineoplastic therapy for multiple myeloma and bone metastases. References reviewed and updated.	02/18	
1Q 2019 annual review: modified Paget's disease to only require diagnosis; added geriatrician prescriber option; removed previous requirement that physiatrist prescriber applies only to postmenopausal osteoporosis; references reviewed and updated.	01/19	

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