Clinical Policy Title:	zoledronic acid
Policy Number:	RxA.263
Drug(s) Applied:	Reclast®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Zoledronic acid (Reclast®) is a bisphosphonate.

Reclast® is indicated:

- Treatment and prevention of postmenopausal osteoporosis
- Treatment to increase bone mass in men with osteoporosis
- Treatment and prevention of glucocorticoid-induced osteoporosis
- Treatment of Paget's disease of bone in men and women.

Limitation(s) of use: Optimal duration of use has not been determined. For patients at low-risk for fracture, consider drug discontinuation after 3 to 5 years of use.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
zoledronic acid (Reclast®)	Treatment of postmenopausal osteoporosis, treatment to increase bone mass in men with osteoporosis, and treatment and prevention of glucocorticoid-induced osteoporosis	5 mg IV once a year	5 mg/year
	Prevention of postmenopausal osteoporosis	5 mg IV once every 2 years	5 mg/2 years
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
	Treatment of Paget's disease of bone	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
	Multiple myeloma and bone metastases from solid tumors	4 mg as a single-use IV infusion every 3 to 4 weeks	4 mg/3 weeks

Dosage Forms

- 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.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Osteoporosis;
   b. Prevention of osteoporosis;
   c. Paget's disease of bone;
2. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
3. 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;
4. Dose does not exceed 5 mg.

Approval Duration
Commercial: 6 months
Medicaid: Postmenopausal 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 (*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 (*see Appendix D);*
2. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
3. Not currently receiving therapy with Reclast®;
4. Dose does not exceed 4 mg.

Approval Duration
Commercial: 6 months
Medicaid: Hypercalcemia of malignancy: 1 week (one infusion); multiple myeloma and bone metastases: 3 months (one infusion every 21 days).

II. Continued Therapy Approval

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

1. Request is for Reclast®;
2. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
3. For osteoporosis-related indications, member is responding positively 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
Commercial: 6 months
Medicaid: Postmenopausal osteoporosis prevention: 24 months (one infusion); **a**ll other indications: 12 months (one infusion)

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

1. Request is for Zometa;
2. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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. If request is for a dose increase, new dose does not exceed 4 mg.

Approval Duration
Commercial: 6 months
Medicaid: Hypercalcemia of malignancy: 1 week (one infusion); multiple myeloma and bone metastases: 12 months (one infusion every 21 days)

III. 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
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
alendronate	Osteoporosis: 10 mg PO once daily or 70 mg PO q week Glucocorticoid-induced osteoporosis: 5 mg PO once daily or 10 mg PO once daily (in postmenopausal women not receiving estrogen) Osteoporosis prophylaxis: 5 mg PO once daily or 35 mg PO q week	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
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 once daily or 35 mg PO q week or for 2 doses/month or 150 mg PO q month. Glucocorticoid-induced osteoporosis: 5 mg PO once daily Paget's disease 30 mg PO once daily for 2 months; may retreat if needed after 2 months	Osteoporosis (including prophylaxis): 5 mg/day or 35 mg/week or 75 mg/day for 2 days per month or 150 mg/month. 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	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 retreat if needed	20mg/kg/day
pamidronate disodium	Paget's disease: 30 mg IV over 4 hours once daily 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.

References

1. Reclast Prescribing Information. East Hanover, NJ: Novartis Pharmaceutical Corporation; April, 2020. Available at http://www.reclast.com. Accessed March 24, 2021.
2. Cosman F, de Beur SJ, LeBoff MS, et al. Position paper: clinician's guide to prevention and treatment of osteoporosis. Osteoporosis Int. 2014; 25(10): 2359-2381. Accessed March 24, 2021.
3. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis – 2016. Endocrin Pract. 2016; 22(Suppl 4). Accessed March 24, 2021.
4. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012; 97(6): 1802-1822. Accessed March 24, 2021.
5. 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. Accessed March 24, 2021.
6. 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. Accessed March 24, 2021.
7. National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Available at: https://cdn.nof.org/wp-content/uploads/2016/01/995.pdf. Accessed March 24, 2021.
8. The North American Menopause Society. Management of osteoporosis in postmenopausal women: 2010 position statement of the North American Menopause Society. Menopause2010;17(1):22-54. Accessed March 24, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated.	06/26/2020	09/14/2020

2. Line of Business Policy Applies to was updated to all lines of business. 3. Updated Initial approval criteria: added closed epiphyses on x-ray in I.A.2 & I.B.2. 4. In Continued therapy criteria II.A.2 & II.B.2 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…" 5. Commercial duration was updated to 6 months and added HIM approval duration. 6. Added "Age ≥ 18 years or documentation of closed epiphyses on x-ray" to initial approval criteria. 7. References were reviewed and updated.		
Policy was reviewed 1. Clinical policy table was updated 2. Zometa removed from policy because it was discontinued in the market. 3. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 4. HIM approval duration is removed from the policy. 5. References were reviewed and updated.	03/24/2021	06/10/2021