

Department:	Pharmacy Management	Original Approval:	12/24/2015
Policy #:	PM121	Last Approval:	06/14/2018
Title:	Zoledronic acid (Reclast®)		
Approved By:	UM Committee		

REQUIRED CLINICAL DOCUMENTATION FOR REVIEW

Documentation required to determine medical necessity for Zoledronic acid (Reclast): History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service: -Diagnosis -Labs/diagnostics -Medication list (current and past) to include start and end dates of all osteoporosis therapies -Age -Height -Weight -Renal function (eCrCl) -Dosing and duration requested.

BACKGROUND

Reclast is a bisphosphonate that inhibits osteoclast-mediated bone resorption.¹ Reclast is indicated for the following:

- Treatment of osteoporosis in postmenopausal women;
- Prevention of osteoporosis in postmenopausal women;
- Treatment to increase bone mass in men with osteoporosis;
- Treatment and prevention of glucocorticoid-induced osteoporosis (GIO) in patients expected to be on glucocorticoids for at least 12 months, and;
- Treatment of Paget's disease of bone in men and women.

Zoledronic acid injection is also available as a product called Zometa[®], which is not included in this policy. Zometa is indicated for the treatment of hypercalcemia of malignancy and for patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy.²

DEFINITIONS

None.

INDICATIONS/CRITERIA

Medicaid Members	<i>Continue to criteria for approval below.</i>
Medicare Members	<i>Step-utilization of Part D drugs not required.</i>

FDA-Approved Indications

1. Osteoporosis Treatment for a Postmenopausal Patient.

Criteria. *The patient must meet the following criteria (A AND B):*

- A)** The patient meets ONE of the following conditions (i, ii, or iii):
- i.** The patient has had a T-score (current or at any time in the past) at or below -2.5 at the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius (wrist); OR
 - ii.** The patient has had an osteoporotic fracture or a fragility fracture; OR
 - iii.** The patient has low bone mass (T-score [current or at any time in the past] between -1.0 and -2.5 at the lumbar spine, femoral neck, total hip, and/or 33% [one third] radius [wrist]) and the physician determines that the patient is at high risk for fracture; AND
- B)** The patient meets ONE of the following (i, ii, iii, or iv):
- i.** The patient has tried one oral bisphosphonate or oral bisphosphonate-containing product and meets one of the following (a, b, or c):
 - a)** The patient has had an inadequate response to oral bisphosphonate therapy after a trial duration of 12 months as determined by the prescribing physician (e.g., ongoing and significant loss of bone mineral density [BMD], lack of BMD increase); OR
 - b)** The patient has had an osteoporotic fracture while receiving oral bisphosphonate therapy; OR
 - c)** The patient has experienced intolerability to an oral bisphosphonate (e.g., severe gastrointestinal [GI]-related adverse effects); OR
 - ii.** The patient cannot take an oral bisphosphonate due to one of the following circumstances (a, b, or c):
 - a)** The patient cannot swallow or has difficulty swallowing; OR
 - b)** The patient cannot remain in an upright position post oral bisphosphonate administration; OR
 - c)** The patient has a pre-existing GI medical condition in which IV bisphosphonate therapy may be warranted (e.g., patient with esophageal lesions, esophageal ulcers, or abnormalities of the esophagus that delay esophageal emptying [stricture, achalasia]); OR
 - iii.** The patient has tried ibandronate injection (Boniva IV) or zoledronic acid (Reclast).
 - iv.** The patient has had an osteoporotic fracture or a fragility fracture.

Reclast is indicated for the treatment of postmenopausal osteoporosis (PMO).¹ Many oral bisphosphonate products are indicated and have proven efficacy. In the American Association of Clinical Endocrinologists (AACE) guidelines for PMO (2016), osteoporosis is defined as a T-score of -2.5 or below in the lumbar spine, femoral neck or total hip and/or 33% (one-third) radius or as the presence of fragility fractures in the absence of other metabolic bone disorders.³ IV bisphosphonate therapy may be preferred in some instances over oral therapy (e.g., GI intolerance, a pre-existing GI medical condition). Oral bisphosphonates are contraindicated if patients have abnormalities of the esophagus which delay emptying (stricture or achalasia). Patients must also not lie down for at least 30 minutes post-oral bisphosphonate administration. In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in the Treatment of Osteoporosis in a Postmenopausal Patient. Dosing must meet the following: 5 mg infusion given IV once a year.

Initial Approval/Extended Approval.

- A) Initial Approval. Initial approval is for 12 months.
- B) Extended Approval. Extended approval is at 12-month intervals.

Duration of Therapy in the Treatment of Osteoporosis in a Postmenopausal Patient. Therapy is indefinite.

Labs/Diagnostics. Monitor renal function before each dose. The patient should have a creatinine clearance (CrCl) ≥ 35 mL/min. In those without osteoporotic fractures or fragility fractures, patients must have had a T-score (current or at any time in the past) at or below -2.5, or low bone mass (between -1.0 and -2.5) and the physician believes the patient is at high risk of fracture. If the CrCl is not given, an example of how to calculate CrCl is provided in Appendix A (see page 9).

2. Osteoporosis Prevention in a Postmenopausal Patient.

Criteria. The patient must meet the following criteria (A AND B):

- A) The patient meets ONE of the following conditions (i or ii):
 - i. The patient has had a T-score (current or at any time in the past) between -1.0 and -2.5 at the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius (wrist); OR
 - ii. The patient has had an osteoporotic fracture or a fragility fracture; AND
- B) The patient meets ONE of the following (i, ii, iii, or iv):
 - i. The patient has tried one oral bisphosphonate or oral bisphosphonate-containing product and meets one of the following (a, b, or c):
 - a) The patient has had an inadequate response to oral bisphosphonate therapy after a trial duration of 12 months as determined by the prescribing physician (e.g., ongoing and significant loss of BMD, lack of BMD increase); OR
 - b) The patient has had an osteoporotic fracture or a fragility fracture while receiving oral bisphosphonate therapy; OR
 - c) The patient has experienced intolerability to an oral bisphosphonate (e.g., severe GI-related adverse effects); OR
 - ii. The patient cannot take an oral bisphosphonate due to one of the following circumstances (a, b, or c):
 - a) The patient cannot swallow or has difficulty swallowing; OR
 - b) The patient cannot remain in an upright position post oral bisphosphonate administration; OR
 - c) The patient has a pre-existing GI medical condition in which IV bisphosphonate therapy may be warranted (e.g., patient with esophageal lesions, esophageal ulcers, or abnormalities of the esophagus that delay esophageal emptying [stricture, achalasia]); OR
 - iii. The patient has tried zoledronic acid injection (Reclast); OR

- iv. The patient has had an osteoporotic fracture or a fragility fracture.

Reclast is indicated for the treatment of PMO.¹ Other oral bisphosphonates are indicated for this condition. Various guidelines support the use of bisphosphonate therapy first-line in many clinical scenarios.⁹⁻¹¹ IV bisphosphonate therapy may be preferred in some instances over oral therapy (e.g., GI intolerance, a pre-existing GI medical condition). Oral bisphosphonates are contraindicated if patients have abnormalities of the esophagus which delay emptying (stricture or achalasia). Patients must also not lie down for at least 30 minutes post oral bisphosphonate administration. In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in the Prevention of Osteoporosis in a Postmenopausal Patient. Dosing must meet the following: 5 mg infusion given IV once every 2 years.

Initial Approval/Extended Approval.

- A) Initial Approval. Initial approval is for 24 months.
B) Extended Approval. Extended approval is at 24-month intervals.

Duration of Therapy in the Prevention of Osteoporosis in a Postmenopausal Patient. Therapy is indefinite.

Labs/Diagnostics. Monitor renal function before each dose. The patient should have a CrCl \geq 35 mL/min. Patients without osteoporotic fracture or a fragility fracture should have had a T-score (current or at any time in the past) between -1.0 and -2.5 at the lumbar spine, femoral neck, total hip, , and/or 33% (one-third) radius (wrist). If the CrCl is not given, an example of how to calculate CrCl is provided in Appendix A (see page 9).

3. Osteoporosis Treatment for Men*.

Criteria. The patient must meet the following criteria (A AND B):

- A) The patient meets ONE of the following conditions (i, ii, or iii):
- i. The patient has had a T-score (current or at any time in the past) at or below -2.5 at the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius (wrist); OR
 - ii. The patient has had an osteoporotic fracture or a fragility fracture; OR
- B) The patient has low bone mass (T-score [current or at any time in the past] between -1.0 and -2.5 at the lumbar spine, femoral neck, total hip, and/or 33% [one-third] radius [wrist]) and the physician determines that the patient is at high risk of fracture; AND The patient meets ONE of the following (i, ii, or iii, or iv):
- i. The patient has tried one oral bisphosphonate or oral bisphosphonate-containing product and meets one of the following (a, b, or c):
 - a) The patient has had an inadequate response to oral bisphosphonate therapy after a trial duration of 12 months as determined by the prescribing physician (e.g., ongoing and significant loss of BMD, lack of BMD increase); OR
 - b) The patient has had an osteoporotic fracture or a fragility fracture while receiving oral bisphosphonate therapy; OR
 - c) The patient has experienced intolerability to an oral bisphosphonate (e.g., severe GI-related adverse effects); OR

- ii. The patient cannot take an oral bisphosphonate due to one of the following circumstances (a, b, or c):
 - a) The patient cannot swallow or has difficulty swallowing; OR
 - b) The patient cannot remain in an upright position post oral bisphosphonate administration; OR
 - c) The patient has a pre-existing GI medical condition in which IV bisphosphonate therapy may be warranted (e.g., patient with esophageal lesions, esophageal ulcers, or abnormalities of the esophagus that delay esophageal emptying [stricture, achalasia]); OR
- iii. The patient has tried zoledronic acid injection (Reclast); OR
- iv. The patient has had an osteoporotic fracture or a fragility fracture.

* Refer to the Policy Statement.

Reclast is indicated for this condition and data suggest that an annual infusion of Reclast led to similar changes in lumbar spine BMD as oral weekly bisphosphonate therapy. Of the oral bisphosphonates, alendronate, Fosamax® Plus D (alendronate/cholecalciferol tablets), and risedronate are indicated for use in males.⁵⁻⁷ A multicenter, double-blind, placebo-controlled trial involving 1,199 men with primary or hypogonadism-associated osteoporosis (aged 50 to 85 years) found that men who received Reclast (5 mg IV at baseline and at 12 months) had fewer moderate-to-severe vertebral fractures (P = 0.03) and height loss (P = 0.002) compared with placebo over 24 months.⁸ IV bisphosphonate therapy may be preferred in some instances over oral therapy (e.g., GI intolerance, a pre-existing GI medical condition). Oral bisphosphonates are contraindicated if patients have abnormalities of the esophagus which delay emptying (stricture or achalasia). Patients must also not lie down for at least 30 minutes post oral bisphosphonate administration.⁴ In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in the Treatment of Osteoporosis in Men. Dosing must meet the following: 5 mg infusion given IV once yearly.

Initial Approval/Extended Approval.

- A) Initial Approval. Initial approval is for 12 months.
- B) Extended Approval. Extended approval is at 12-month intervals.

Duration of Therapy in the Treatment of Osteoporosis in Men. Therapy is indefinite.

Labs/Diagnostics. Monitor renal function before each dose. The patient should have a CrCl \geq 35 mL/min. In those without osteoporotic fractures or a fragility fracture, patients must have had a T-score (current or at any time in the past) at or below -2.5, or low bone mass (T-score between -2.0 and -2.5) if the physician believes the patient is at high risk of fracture. If the CrCl is not given, an example of how to calculate CrCl is provided in Appendix A (see page 9).

4. Glucocorticoid-Induced Osteoporosis (GIO) Prevention and Treatment

Criteria. Patient must meet the following criteria (A AND B):

- A)** The patient is either initiating or continuing systemic glucocorticoids (e.g., prednisone); AND
- B)** The patient meets ONE of the following (i, ii, iii, or iv):
 - i.** The patient has tried one oral bisphosphonate or oral bisphosphonate-containing product and meets one of the following (a, b, or c):
 - a)** The patient has had an inadequate response to oral bisphosphonate therapy after a trial duration of 12 months as determined by the prescribing physician (e.g., ongoing and significant loss of BMD, lack of BMD increase); OR
 - b)** The patient has had an osteoporotic fracture or a fragility fracture while receiving oral bisphosphonate therapy; OR
 - c)** The patient has experienced intolerance to an oral bisphosphonate (e.g., severe GI-related adverse effects); OR
 - ii.** The patient cannot take an oral bisphosphonate due to one of the following circumstances (a, b, or c):
 - a)** The patient cannot swallow or has difficulty swallowing; OR
 - b)** The patient cannot remain in an upright position post oral bisphosphonate administration; OR
 - c)** The patient has a pre-existing GI medical condition in which IV bisphosphonate therapy may be warranted (e.g., patient with esophageal lesions, esophageal ulcers, or abnormalities of the esophagus that delay esophageal emptying [stricture, achalasia]); OR
 - iii.** The patient has tried Zoledronic acid (Reclast);OR
 - iv.** The patient has had an osteoporotic fracture or a fragility fracture.

Reclast is indicated for the treatment and prevention of GIO.

Guidelines from the American College of Rheumatology (ACR) for the prevention and treatment of GIO, updated in 2017, recommended use of oral and IV bisphosphonates in various clinical scenarios.⁹ IV bisphosphonate therapy may be preferred in some instances over oral therapy (e.g., GI intolerance, a pre-existing GI medical condition). Oral bisphosphonates are contraindicated if patients have abnormalities of the esophagus which delay emptying (stricture or achalasia). Patients must also not lie down for at least 30 minutes post-oral bisphosphonate administration.⁴ In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis (GIO). Dosing must meet the following: 5 mg infusion given IV once yearly.

Initial Approval/Extended Approval.

- A)** Initial Approval. Initial approval is for 12 months.
- B)** Extended Approval. Extended approval is at 12-month intervals.

Duration of Therapy in the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis.

Therapy is indefinite.

Labs/Diagnostics. Monitor renal function before each dose. The patient should have a CrCl \geq 35 mL/min. If the CrCl is not given, an example of how to calculate CrCl is provided in Appendix A (see page 9).

5. Paget's Disease of Bone.

Criteria. *Patient must meet the following criteria (A, B OR C).*

- A) The patient has elevations in serum alkaline phosphatase of two times higher than the upper limit of the age-specific normal reference range, OR
- B) The patient is symptomatic (e.g., bone pain, hearing loss, osteoarthritis), OR
- C) The patient is at risk for complications from their disease (e.g., immobilization, bone deformity, fractures, nerve compression syndromes).

Reclast is indicated for this condition. A published, randomized, double-blind study involving patients with Paget's disease documented a more rapid and sustained response with zoledronic acid injection (Reclast) as compared with risedronate (Actonel).¹ One dose of zoledronic acid injection (Reclast) is given, and then patients are evaluated after approximately 6 months of therapy.^{1,10-11} Reasons for treatment, or retreatment, include an elevated serum alkaline phosphatase, the patient has symptoms or is at risk of disease complications.^{1,10-11} In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria. A clinical practice guideline regarding Paget's disease of bone from the Endocrine Society states the zoledronic acid injection (Reclast), administered as a single 5-mg IV dose, is the treatment of choice.¹⁷

Dosing in Paget's Disease of Bone. *Dosing must meet the following:* Initial and repeat doses are 5 mg IV infusion over at least 15 minutes at a constant infusion rate.

Initial Approval/Extended Approval.

- A) *Initial Approval.* Approve one initial dose.
- B) *Extended Approval.* Retreatment is based on response (e.g, normalization of serum alkaline phosphatase) and improvement in symptoms (reduced bone pain, etc). Approve retreatment 6 months or longer after the initial dose in those who per the prescribing physician have relapsed (increased serum alkaline phosphatase levels), require further therapy to normalize serum alkaline phosphatase levels, or need therapy to alleviate associated symptoms and complications (e.g., bone pain, hearing loss). Extended approval can be given 6 months or longer after the previous dose.

Duration of Therapy in Paget's Disease of the Bone. A single dose is given initially and then retreatment is based on response and symptoms. Patients may be receiving this therapy long-term.

Labs/Diagnostics. Monitor serum alkaline phosphatase at baseline and subsequently to assess response. Monitor renal function before each dose. The patient must have a calculated CrCl \geq 35 mL/min. If the CrCl is not given, an example of how to calculate CrCl is provided in Appendix A (see page 9).

Other Uses with Supportive Evidence

6. Osteogenesis Imperfecta.

Criteria. Approve.

Zoledronic acid injection (Reclast) is not indicated for use in patients with osteogenesis imperfecta and it is not indicated for use in children.¹ Zoledronic acid injection (Reclast) has been used in patients, mainly children, with osteogenesis imperfecta and benefits were noted, such as increases in BMD.^{1,12-16,18}

Dosing in Osteogenesis Imperfecta. No specific dose has been established. Recommended and studied doses have ranged from 0.015 to 0.05 mg per kg IV given every 3 to 12 months.^{12-16,18}

Initial Approval/Extended Approval.

- A) Initial Approval. Approve at 12-month intervals.
- B) Extended Approval. Approval is at 12-month intervals.

Duration of Therapy in Osteogenesis Imperfecta. Therapy is indefinite.

Labs/Diagnostics required. None required.

Waste Management for All Indications:

- Zoledronic acid injection (Reclast) is available as 5 mg in a 100 mL ready-to-infuse solution (bottle). This dose should be sufficient in most situations.

Conditions Not Recommended for Approval

Zoledronic acid injection (Reclast) has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. **Concurrent Use of zoledronic acid injection (Reclast) with Other Medications for Osteoporosis** (e.g., other bisphosphonates [previously listed], Prolia[®] [denosumab injection for subcutaneous use], Forteo[®] [teriparatide injection for SC use], Tymlos[®] [abaloparatide injection for SC use]), calcitonin nasal spray), except calcium and Vitamin D.

Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

SPECIAL CONSIDERATIONS

None.

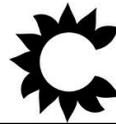
LIMITATIONS/EXCLUSIONS

Please refer to a product line's certificate of coverage for benefit limitations and exclusions for these services:

PRODUCT LINE	LINK TO CERTIFICATE OF COVERAGE
MEDICARE ADVANTAGE	http://healthfirst.chpw.org/for-members/resource-library/handbooks-and-guides
WASHINGTON APPLE HEALTH	http://chpw.org/our-plans/apple-health/
INTEGRATED MANAGED CARE	http://chpw.org/our-plans/apple-health/

Citations & References

References	
	<ol style="list-style-type: none"> 1. Reclast[®] injection [prescribing information]. East Hanover, NJ: Novartis; July 2017. 2. Zometa[®] injection [prescribing information]. East Hanover, NJ: Novartis; December 2016. 3. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis. <i>Endocrin Pract.</i> 2016;22(Suppl 4):1-42. Available at: http://journals.aace.com/doi/pdf/10.4158/EP161435.GL. Accessed on February 5, 2018. 4. Cosman F, De Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. <i>Osteoporos Int.</i> 2014;25:2359-2381. 5. Fosamax[®] tablets and oral solution [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc; March 2016. 6. Fosamax[®] Plus D tablets [prescribing information]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2016. 7. Actonel[®] tablets [prescribing information]. Rockaway, NJ and North Norwich, NY: Warner Chilcott Norwich Pharmaceuticals; March 2015. 8. Boonen S, Reginster JY, Kaufman JM, et al. Fracture risk and zoledronic acid therapy in men with osteoporosis. <i>N Engl J Med.</i> 2012;367(18):1714-1723. 9. Buckley L, Guyatt G, Fink HA, et al. 2017 American College of Rheumatology guideline for the prevention and treatment of glucocorticoid-induced osteoporosis. <i>Arthritis Rheumatol.</i> 2017;69(8):1521-1537. Available at: https://www.rheumatology.org/Portals/0/Files/Guideline-for-the-Prevention-and-Treatment-of-GIOP.pdf. Accessed on January 28, 2018. 10. Ralston SH. Paget's disease of bone. <i>N Engl J Med.</i> 2013;368:644-650. 11. Devogelaer JP, Bergmann P, Body JJ, Boutsen Y, Goemaere S, et al. Management of patients with Paget's disease: a consensus document of the Belgian Bone Club. <i>Osteoporos Int.</i> 2008;19:1109-1117.



	<p>12. Cheung MS, Florieux FH. Osteogenesis imperfecta: update on presentation and management. <i>Rev Endocr Metab Disord.</i> 2008;9:153-160.</p> <p>13. Barros ER, Saraiva GL, de Oliveira P, Lazaretti-Castro M. Safety and efficacy of a 1-year treatment with zoledronic acid compared with pamidronate in children with osteogenesis imperfecta. <i>J Pediatr Endocr Met.</i> 2012;25(5-6):485-491.</p> <p>14. Panigrahi I, Das RR, Sharda S, et al. Response to zoledronic acid in children with type III osteogenesis imperfecta. <i>J Bone Miner Metab.</i> 2010;28:451-455.</p> <p>15. Brown JJ, Zacharin MR. Safety and efficacy of intravenous zoledronic acid in paediatric osteoporosis. <i>J Pediatr Endocrinol Metab.</i> 2009;22(1):55-63.</p> <p>16. Reclast. Data on file. Novartis Pharmaceuticals. October 24, 2012.</p> <p>17. Singer FR, Bone HG, Hosking DJ, et al. Paget's disease of bone: an Endocrine Society Clinical Practice Guideline. <i>J Clin Endocrinol Metab.</i> 2014;99:4408-4422.</p> <p>18. Dwan K, Phillipi CA, Steiner RD, Basel D. Bisphosphonate therapy for osteogenesis imperfecta. <i>Cochrane Database Syst Rev.</i> 2016;10:CD005088.</p> <p>19. Qaseem A, Forciea MA, McLean RM, et al. Treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical practice guideline updated from the American College of Physicians. <i>Ann Intern Med.</i> 2017;166:818-839.</p>
CFR	
WAC	WAC 284-43-2050
RCW	
Contract Citation	<input checked="" type="checkbox"/> WAH <input checked="" type="checkbox"/> IMC <input checked="" type="checkbox"/> MA
Other Requirements	
NCQA Elements	

Revision History

Revision Date	Revision Description	Revision Made By
12/23/2015	New	Kelly Force; Yusuf Rashid, RPh
12/24/2015	Approval	MMLT
01/11/2017	No revisions	Fran McGaugh
01/12/2017	Approval	MMLT
07/24/2017	Criteria completely updated and revised	Michael Sporck, Pharmacy Intern Sophia Yun, PharmD
07/25/2017	Approved	MMLT
03/28/2018	Changed from UM313 to PM121	Cindy Bush
04/23/2018	Transferred to new template	Cindy Bush
06/11/2018	Revised	Jennifer Farley, PharmD
06/14/2018	Approval	UM Committee