

POLICY: Bone Modifiers – Zoledronic Acid IV (Reclast) [Reclast® {zoledronic acid injection}, Novartis, generics]

APPROVAL DATE: 02/27/2019

OVERVIEW

Zoledronic acid (Reclast) is a bisphosphonate given intravenously.¹ Zoledronic acid injection (Reclast) is indicated for the treatment of osteoporosis in postmenopausal women; for the prevention of postmenopausal osteoporosis (PMO) in women; the treatment of Paget's disease of bone in men and women; for the treatment to increase bone mass in men with osteoporosis; and for the treatment and prevention of glucocorticoid-induced osteoporosis (GIO) in patients expected to be on systemic glucocorticoids (daily dosage equivalent to ≥ 7.5 mg of prednisone) for at least 12 months.¹ In PMO, zoledronic acid injection (Reclast) reduces the incidence of fractures (hip, vertebral and non-vertebral osteoporosis-related fractures). Also, for patients at high risk of fracture, defined as a recent low-trauma hip fracture, zoledronic acid injection (Reclast) reduces the incidence of new clinical fractures.¹ Another zoledronic acid injection product, Zometa®, is indicated for hypercalcemia of malignancy; and for multiple myeloma and bone metastases from solid tumors.²

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of zoledronate acid (Reclast). Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist).

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

- 1. Osteoporosis Treatment for a Postmenopausal Patient.** Approve for 1 year if the patient meets 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 or a fragility 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 injection (Reclast); OR
- iv. The patient has had an osteoporotic fracture or a fragility fracture.

Dosing. Approve one 5 mg infusion given IV once every year.

2. Osteoporosis Treatment for Men*. Approve for 1 year if the patient meets 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 of 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.

* Refer to the Policy Statement.

Dosing. Approve one 5 mg infusion given IV once every year.

3. Glucocorticoid-Induced Osteoporosis (GIO) Prevention and Treatment. Approve for 1 year if the patient meets 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 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.

Dosing. Approve one 5 mg infusion given IV once every year.

4. Paget's Disease of Bone. Approve for one dose if the patient meets one of 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).

Dosing. Approve one 5 mg IV infusion.

5. Osteoporosis Prevention in a Postmenopausal Patient. Approve for 1 year if the patient meets the following criteria (A, B and C):

- 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.
- C) If the patient has received Reclast previously, at least 24 months has elapsed since the last dose.

Dosing. Approve one 5 mg infusion given IV once every 2 years.

Other Uses with Supportive Evidence

6. Osteogenesis Imperfecta. Approve for 1 year.

Although not indicated, zoledronic acid injection (Reclast) has been used in patients, mainly children, with osteogenesis imperfecta and benefits were noted, such as increases in bone mineral density.³⁻⁷

Dosing. Dosing information is limited. Approve up to 0.05 mg per kg IV given no more frequently than once every 3 months.

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. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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

REFERENCES

1. Reclast® injection for intravenous infusion [prescribing information]. East Hanover, NJ: Novartis; July 2017.

2. Zometa® injection for intravenous infusion[prescribing information]. East Hanover, NJ: Novartis; December 2018.
3. Biggin A, Munns CF. Long-term bisphosphonate therapy in osteogenesis imperfect. *Curr Osteoporos Rep.* 2017;15(5):412-418.
4. 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. *J Pediatr Endocr Met.* 2012;25(5-6):485-491.
5. Panigrahi I, Das RR, Sharda S, et al. Response to zoledronic acid in children with type III osteogenesis imperfecta. *J Bone Miner Metab.* 2010;28:451-455.
6. Brown JJ, Zacharin MR. Safety and efficacy of intravenous zoledronic acid in paediatric osteoporosis. *J Pediatr Endocrinol Metab.* 2009;22(1):55-63.
7. Dwan K, Phillipi CA, Steiner RD, Basel D. Bisphosphonate therapy for osteogenesis imperfecta. *Cochrane Database Syst Rev.* 2016;10:CD005088.

HISTORY

Type of Revision	Summary of Changes*	Approval Date
Annual revision	--	01/25/2017
Annual revision	<p>Changed the name of the policy to add “Bone Modifiers” – Reclast CC. Regarding osteoporosis treatment for a postmenopausal patient and for the treatment of osteoporosis in men, regarding the T-score it was added to include 33% (one-third) radius (wrist) as a site. Also, a fragility fracture was added as an accepted manner to diagnose osteoporosis, in addition to an osteoporotic fracture. Also, regarding previous criteria that addressed patients with T-score at or below -2.0, the criteria were revised to state low bone mass (T-score 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” (instead of the word “believes”) that the patient is at high risk for fracture (the labs/diagnostic section was altered accordingly). Also, patients who were on oral bisphosphonate therapy and had a fragility fracture (in addition to the previously-cited osteoporotic fracture) are permitted to use either agent (in addition to meeting other criteria). Patients that have had an osteoporotic fracture or a fragility fracture are also granted exceptions as they are at higher risk. For the indication regarding glucocorticoid-induced osteoporosis, patients with a fragility fracture (in addition to the previously-listed an osteoporotic fracture) while receiving oral bisphosphonate therapy are permitted to use zoledronic acid injection (in addition to meeting other criteria). Also, patients with an osteoporotic fracture or a fragility fracture can receive zoledronic acid injection if they are on glucocorticosteroids. For osteoporosis prevention for a postmenopausal patient, the 33% (one third) radius (wrist) was added as a site to assess the T-score (the labs/diagnostic section was changed accordingly). Also, a fragility fracture was added as an accepted manner to diagnose this condition, in addition to an osteoporotic fracture. Also, patients who were on oral bisphosphonate therapy and had a fragility fracture (in addition to the previously-cited osteoporotic fracture) are permitted to use zoledronic acid-injection (in addition to meeting other criteria). Patients that have had an osteoporotic fracture or a fragility fracture are also granted exceptions as they are at higher risk. Evista (raloxifene tablets) was deleted from the list of osteoporosis medications in which Reclast should not be used with concurrently; Tymlos was added to this list.</p>	02/14/2018
Annual revision	<p>The name of the policy was changed from Bone Modifiers - Reclast to Zone Modifiers - Zoledronic Acid IV (Reclast) to reflect availability of the product as a generic. The requirement to check renal function prior to each dose for the cited indications in which it applies was removed. Retreatment based on response for the diagnosis of Paget’s disease of the bone was removed, as well as wording regarding initial and repeat doses. The dose in Paget’s disease was changed from wording stating that “recommended and studied doses have ranged from 0.015 to 0.05 mg per kg intravenously given once every 3 to 12 months to “Approve up to 0.05 mg per kg intravenously once every 3 months.</p>	02/27/2019