Reclast (zoledronic acid) Injection

Policy Number: MC/PC 035
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Instructions for Use

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Related Policies

- N/A

Coverage Rationale

Glucocorticoid-induced osteoporosis

For initial coverage of Reclast (zoledronic acid) injection for treatment and prevention of glucocorticoid-induced osteoporosis, the following will be required:

- One of the following:
  - Diagnosis of glucocorticoid-induced osteoporosis **or**
  - Patient is either initiating or continuing to take systemic glucocorticoids in a daily dosage of 7.5 mg or greater of prednisone and who are expected to remain on glucocorticoids for at least 12 months **and**
- Patient is taking calcium and vitamin D

For reauthorization coverage Reclast (zoledronic acid) injection for treatment and prevention of glucocorticoid-induced osteoporosis, the following will be required:

- Patient is benefiting from therapy without significant adverse effects

Osteoporosis

For initial coverage of Reclast (zoledronic acid) injection for treatment to increase bone mass in men with osteoporosis, the following will be required:

- Diagnosis of osteoporosis **and**
- Patient is taking calcium and vitamin D

For initial coverage of Reclast (zoledronic acid) injection for the treatment and prevention of postmenopausal osteoporosis, the following will be required:

- One of the following:
  - Diagnosis of postmenopausal osteoporosis **or**
  - Patient is at risk of developing postmenopausal osteoporosis **and**
- Patient is taking calcium and vitamin D

For reauthorization coverage of Reclast (zoledronic acid) injection for the treatment to increase bone mass in men with osteoporosis and for the treatment and prevention of postmenopausal osteoporosis, the following will be required:

- Patient is benefiting from therapy without significant adverse effects

Paget's disease of bone

For initial coverage of Reclast (zoledronic acid) injection for Paget's Disease, the following will be required:

- Diagnosis of Paget's Disease **and**
- An indication that the patient has one of the following:
    - An elevated serum alkaline phosphatase of two times or higher than the upper limit of the age-specific normal reference range **or**
    - The patient is symptomatic **or**
    - The patient is at risk for complications from the disease, to induce remission (normalization of serum alkaline phosphotase) prior to treatment with Reclast

For reauthorization coverage of Reclast (zoledronic acid) Injection for Paget's Disease, the following will be required:

- Patient is benefiting from therapy without significant adverse effects

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J3489	Injection, zoledronic acid, 1 mg

ICD-10 Code	Description
M80.00XA - M80.88XS	Age-related osteoporosis with current pathological fracture, unspecified site, initial encounter for fracture - Other osteoporosis with current pathological fracture, vertebra(e), sequela
M80.8AXA	Other osteoporosis with current pathological fracture, other site, initial encounter for fracture
M80.8AXD	Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing
M80.8AXG	Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing
M80.8AXK	Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion
M80.8AXP	Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion
M80.8AXS	Other osteoporosis with current pathological fracture, other site, sequela
M81.0	Age-related osteoporosis without current pathological fracture
M81.8	Other osteoporosis without current pathological fracture

ICD-10 Code	Description
M85.9	Disorder of bone density and structure, unspecified
M88	Osteitis deformans [Paget's disease of bone]
M89.9	Disorder of bone, unspecified
Z79.52	Long term current use of systemic steroids
Z87.310	Personal history of healed osteoporosis fracture

Background

Osteoporosis is the most common bone disease and is characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to bone fragility and consequent susceptibility to fracture (LeBoff et al 2022). According to the World Health Organization (WHO), osteoporosis is defined by a bone mineral density (BMD) at the hip or spine that is less than or equal to 2.5 standard deviations below the expected average for a healthy young person. Utilizing a reference population of young healthy individuals is common when measuring BMD and is known as a T-score (WHO 2007). Fractures are the most clinically significant physical manifestation of postmenopausal osteoporosis, and low bone mass is the primary indicator of fracture risk (Camacho et al 2020).

Glucocorticoid therapy is associated with an appreciable risk of bone loss, which is most pronounced in the first few months of use. In addition, glucocorticoids increase fracture risk, and fractures occur at higher bone mineral density (BMD) values than occur in postmenopausal osteoporosis. The increased risk of fracture has been reported with doses of prednisone or its equivalent as low as 2.5 to 7.5 mg daily (van Staa et al 2002). Thus, glucocorticoid-induced bone loss should be treated aggressively, particularly in those already at high risk for fracture (older age, prior fragility fracture).

Paget's disease of bone (PDB) is a metabolic bone disease characterized by increased bone resorption followed by excessive unregulated bone formation. This results in weakened, deformed bones of increased mass in which the collagen fibres assume a haphazard irregular mosaic pattern instead of the normal parallel symmetry. PDB rarely occurs before middle age and its prevalence increases steadily with age (Josse et al 2007). Commonly affected areas include the skull, spine, pelvis, and long bones of the lower extremity but the majority of patients with PDB are asymptomatic. The diagnosis in such patients is usually made incidentally following a routine chemistry screen showing an elevated serum concentration of alkaline phosphatase of bone origin or an imaging study obtained for some other reason that shows pagetic changes in bone.

Reclast is a bisphosphonate and acts primarily on bone. It is an inhibitor of osteoclast-mediated bone resorption. As optimal duration of use has not been determined, patients at low-risk for fracture, discontinuation should be discontinued after 3 to 5 years of use. The most common adverse reactions (greater than 10%) include pyrexia, myalgia, headache, arthralgia, pain in extremity (Reclast Prescribing Information 2022).

Clinical Evidence

Glucocorticoid-induced Osteoporosis

The efficacy and safety of Reclast to prevent and treat glucocorticoid-induced osteoporosis (GIO) was assessed in a randomized, multicenter, double-blind, stratified, active controlled study of 833 men and women aged 18 to 85 years (mean age of 54.4 years) treated with greater than or equal to 7.5 mg/day oral prednisone (or equivalent) (Reid et al 2009). The duration of the trial was one year. Patients were randomized to either Reclast, which was administered once as a 5 mg dose in 100 mL infused over 15 minutes, or to an oral daily bisphosphonate (active control) for one year. Bone biopsy specimens were obtained from 23 patients (12 in the Reclast treatment group and 11 in the active control treatment group) at Month 12 treated with an annual dose of Reclast or daily oral active control. Qualitative assessments showed bone of normal architecture and quality without mineralization defects.

Men with Osteoporosis
The efficacy and safety of Reclast in men with osteoporosis or significant osteoporosis secondary to hypogonadism, was assessed in a randomized, multicenter, double-blind, active controlled, study of 302 men aged 25 to 86 years (mean age of 64) (Orwoll et al 2010). The duration of the trial was two years. Patients were randomized to either Reclast, which was administered once annually as a 5 mg dose in 100 mL infused over 15 minutes for a total of up to two doses, or to an oral weekly bisphosphonate (active control) for up to two years. An annual infusion of Reclast was non-inferior to the oral weekly bisphosphonate active control based on the percentage change in lumbar spine BMD at Month 24 relative to baseline (Reclast: 6.1% increase; active control: 6.2% increase).

Postmenopausal Osteoporosis
The efficacy and safety of Reclast in the treatment of postmenopausal osteoporosis was demonstrated in a randomized, double-blind, placebo-controlled, multinational study of 7736 women aged 65 to 89 years (mean age of 73) with either: a femoral neck BMD T-score less than or equal to -1.5 and at least two mild or one moderate existing vertebral fracture(s); or a femoral neck BMD T-score less than or equal to -2.5 with or without evidence of an existing vertebral fracture(s) (Black et al 2007). In this trial, Reclast demonstrated superiority to placebo in reducing the incidence of all clinical fractures, clinical (symptomatic) vertebral and non-vertebral fractures (excluding finger, toe, facial, and clinical thoracic and lumbar vertebral fractures). All clinical fractures were verified based on the radiographic and/or clinical evidence.

Paget's Disease
Reclast was studied in male and female patients with moderate to severe Paget's disease of bone, defined as serum alkaline phosphatase level at least twice the upper limit of the age-specific normal reference range at the time of study entry. Diagnosis was confirmed by radiographic evidence. The efficacy of one infusion of 5 mg Reclast vs. oral daily doses of 30 mg risedronate for 2 months was demonstrated in two identically designed 6-month randomized, double-blind trials (Reid et al 2005). Therapeutic response was defined as either normalization of serum alkaline phosphatase (SAP) or a reduction of at least 75% from baseline in total SAP excess at the end of 6 months. SAP excess was defined as the difference between the measured level and midpoint of normal range. In both trials, Reclast demonstrated a superior and more rapid therapeutic response compared with risedronate and returned more patients to normal levels of bone turnover, as evidenced by biochemical markers of formation.

Clinical Guidelines
To prevent and/or treat osteoporosis in postmenopausal women and men, national guidelines recommend adequate calcium and vitamin D intake, weight bearing exercise, cessation of smoking, and limiting alcohol intake (American College of Gynecology and Obstetricians [ACOG] 2022, North American Menopause Society 2021, Adler et al 2016, Camacho et al 2020, Conley et al 2020, Eastell et al 2019, LeBoff et al 2022, Qaseem et al 2023, Watts et al 2012). Within the various osteoporosis treatment guidelines (including postmenopausal osteoporosis, glucocorticoid-induced osteoporosis, and osteoporosis in men), there is general agreement that treatment is indicated for patients > 50 years of age who have experienced a hip or vertebral fracture or have a bone density T-score ≤ -2.5. For most patients with osteoporosis, the majority of guidelines recommend initial or first-line treatment with an oral bisphosphonate (ie, alendronate or risedronate) to reduce fracture risk. For patients who are unable to tolerate oral bisphosphonates or who are nonadherent, an intravenous agent (zoledronic acid or denosumab) is generally recommended. Alendronate, risedronate, zoledronic acid, and denosumab have evidence for "broad spectrum" antifracture efficacy (ie, spine, hip, and nonvertebral fracture risk reduction) (Camacho et al 2020; Qaseem et al 2023).

For patients with osteoporosis at high risk of fracture, treatment with denosumab, zoledronic acid, and the injectable anabolic agents (abaloparatide, romosozumab, and teriparatide) are generally recommended as follows:

• The 2022 ACOG guidelines for postmenopausal osteoporosis recommend bisphosphonates or denosumab as initial therapy for patients at high-fracture risk.
• The 2020 American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) guidelines for postmenopausal osteoporosis recommend initial therapy with abaloparatide, denosumab, romosozumab, teriparatide, or zoledronic acid in patients at very high fracture risk (e.g. older women who have had multiple vertebral fractures or hip fractures or have very low T-scores) or in those who may not be candidates for oral bisphosphonates (Camacho et al 2020).

Zoledronic acid is also the first-choice treatment for Paget disease because of its efficacy and ease of administration. The choice of zoledronic acid as the initial agent for most patients with active Paget disease is consistent with both the 2014 Clinical Practice Guidelines of the Endocrine Society and the 2019 Paget's Association guidelines (Ralston et al 2019, Singer at al 2014).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Reclast is a bisphosphonate indicated for:

- 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

Limitations 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

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Policy History/Revision Information

Date	Summary of Changes
12/13/2023	Approved by OptumRx P&T Committee
11/21/2024	Annual Review. Updated references.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).

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