PART B DRUG MEDICAL/PHARMACY	ASPIRE HEALTH	Effective Date January 1, 2024	
	EVENITY (ROMOSOZUMAB-AQQG)	Policy # Evenity (romosozumab-aqqg)	
		Review Date 09/27/2023	**Applicable to:** ☑ Medicare Advantage ☐ Commercial ☐ Elevance Health HMO ☐ Blue Shield Trio
	Approver's Name & Title QI & UM Drug Subcommittee		

Aspire Health Plan applies medical drug clinical criteria as a reference for medical policy information only. Federal and state laws or requirements, contract language, and Plan benefit may take precedence over the application of these clinical criteria. Please consult the applicable certificate or contract for benefit details. This policy is subject to revision at the discretion of the Plan and is therefore subject to change. Refer to the 'Disclaimer' section below for more information.

POLICY

This policy addresses the coverage of Evenity (romosozumab-aqqg) for the treatment of osteoporosis.

APPLICABLE HCPCS

J3111: Injection, romosozumab-aqqg, 1 mg; 1 billable unit = 1 mg

Available as: 105 mg/1.17 mL solution in a single-use prefilled syringe.

CLINICAL CRITERIA

A. INITIAL CRITERIA

Evenity (romosozumab-aqqg) may be authorized when ALL of the following criteria are met with documentation:

1. Diagnosis of osteoporosis in postmenopausal women who are at a *high risk of fracture

*High risk for fractures include, but are not limited to, one or more of the following:
- Alcohol intake of 3 or more drinks per day
- BMI less than 20 BMI Calculator BMI Calculator
- Current cigarette use
- Glucocorticoid use of 3 months' or greater duration
- Parental hip fracture
- Personal history of fragility or osteoporotic fracture
- Rheumatoid arthritis (confirmed diagnosis)

AND

2. Documentation of **ONE** or more of the following :

    a. Hip/femur DXA (femoral neck or total hip) or lumbar spine T-score ≤ -2.5 and/or forearm DXA at the 33% (one-third) radius site (wrist); **OR**

    b. T-score ≤-1 or low bone mass *and* a history of fragility fracture to the hip or spine; **OR**

    c. T-score between -1 and -2.5 with a FRAX 10-year probability for major fracture ≥ 20% or hip fracture ≥ 3%.

AND

3. Documentation of **ONE** of the following:

    a. Treatment failure with a *bisphosphonate (oral or IV) defined as **ONE** of the following after at least 12 months of compliant therapy:

        i. Progression of bone loss as documented by bone density measurements (BMD); **OR**

        ii. Occurrence of an osteoporotic fracture.

        **Oral bisphosphonate (e.g., alendronate, risedronate, ibandronate); Intravenous bisphosphonate (e.g., ibandronate, zoledronic acid)*

    OR

    b. *Contraindication, hypersensitivity, or intolerance to a bisphosphonate. NOTE: If member has intolerance to oral administration, an intravenous bisphosphonate (e.g., ibandronate, zoledronic acid) will be required.

        **Contraindications to bisphosphonate therapy include: Hypersensitivity to bisphosphonates or any component of the formulations; hypocalcemia (alendronate, ibandronate, risedronate, zoledronic acid [Reclast]); abnormalities of the esophagus that delay esophageal emptying, such as stricture or achalasia (alendronate, etidronate, oral ibandronate, risedronate); increased risk of aspiration (alendronate [effervescent tablet and oral solution]); inability to stand or sit upright for at least 30 minutes (alendronate, risedronate); inability to stand or sit upright for at least 60 minutes (oral ibandronate); clinically overt osteomalacia (etidronate); CrCl less than 35 mL/minute and in those patients with evidence of acute renal impairment due to an increased risk of renal failure (zoledronic acid [Reclast]).(FDA labeling, 2023)*

AND

4. Prescriber attestation or documentation of the following:

    a. Evenity will not be administered concurrent with other medications for osteoporosis [e.g., a bisphosphonate, denosumab (e.g., Prolia or Xgeva) parathyroid hormone analog [e.g., abloparatide (Tymlos), teriparatide (Forteo)]; **AND**

    b. Hypocalcemia was reviewed and corrected prior to initiation of treatment if applicable; **and**

    member is taking calcium and vitamin D supplements in conjunction if dietary intake is inadequate (documented in medical records or pharmacy claims); **AND**

    c. Member has not had a myocardial infarction or stroke within previous 12 months (Note: in patients with other cardiovascular disease and/or risk factors, consider whether benefits of therapy outweigh the risks.);

B. REAUTHORIZATION / CONTINUATION OF THERAPY CRITERIA

Evenity (romosozumab-aqqg) is limited to a *single course of therapy for 12 months and will not be reauthorized for continuation of treatment.

*NOTE: The anabolic effect of Evenity wanes after 12 monthly doses of therapy. Therefore, the duration of Evenity use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continuing therapy with an antiresorptive agent (e.g., with a bisphosphonate or denosumab) to maintain bone density gains should be considered.

STEP THERAPY

Step therapy criteria do not apply for members who are currently being treated with the requested medications. Step therapy is only applied for members that are new to therapy (have not received the requested drug in the last 365 days.

A. **PREFERRED PRODUCT(S): Bisphosphonates (IV) [Zoledronic acid (first preferred) and ibandronate (second preferred)] -- NO STEP THERAPY REQUIRED**

B. **SECOND-LINE PREFERRED PRODUCT(S): PROLIA (denosumab)**

C. NON-PREFERRED PRODUCT, Evenity (romosozumab-aqqg), may be authorized when ALL of the clinical criteria above are met **AND** the member meets the following with documentation:

1. History of use of bisphosphonates (IV) for osteoporosis (Zoledronic acid [Reclast]; Ibandronate [Boniva]) AND Prolia (denosumab) resulting in minimal clinical response to therapy (defined as a decrease in BMD or a fracture while on therapy);

OR

2. *Contraindication, intolerance, or adverse event(s) to one bisphosphonate (IV) (Zoledronic acid [Reclast]; Ibandronate [Boniva]) AND Prolia (denosumab);

**Contraindications to zoledronic acid: Hypersensitivity to zoledronic acid or any component of the formulation; hypocalcemia (Reclast only); CrCl < 35 mL/minute and in those with evidence of acute renal impairment (Reclast only).*

**Contraindications to Ibandronate: Hypocalcemia; known hypersensitivity to ibandronate or any component of the formulation.*

**Contraindications to Prolia therapy include: hypersensitivity (systemic) to denosumab or any component of the formulation; preexisting hypocalcemia; pregnancy.*

OR

3. Member has previously received Evenity (romosozumab-aqqg) within the past 365 days and therefore not subject to step therapy requirements.

DOSAGE AND AUTHORIZATION TIMEFRAMES

1. Recommended Dose: Administer 210 mg subcutaneously once every month. Each monthly dose consists of two consecutive subcutaneous injections.

2. Maximum Quantity:

    a. 210 mg once every month for 12 months

    b. Monthly dose: Two single-use prefilled syringes (a full dose requires TWO single-use prefilled syringes of 105 mg/1.17 mL per single-use prefilled syringes)

3. Authorization Period: Initial authorization: 12 months: Reauthorization: N/A

DRUG INFORMATION

PHARMACOLOGIC CATEGORY: Ophthalmic Agent; Vascular Endothelial Growth Factor (VEGF) Inhibitor

ROUTE OF ADMINISTRATION: Subcutaneous

FDA-APPROVED INDICATION: **Osteoporosis, postmenopausal, fracture risk reduction**
Treatment of postmenopausal osteoporosis in patients at high risk for fracture, or in patients in whom other available osteoporosis therapy has failed or cannot be taken.

Limitations of use: The anabolic effect of romosozumab wanes after 12 monthly doses of therapy. Therefore, the duration of romosozumab use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an antiresorptive agent should be considered.

COMPENDIAL APPROVED (OFF-LABELED) USES: NONE

BOXED WARNING: Potential risk of MI, stroke, and cardiovascular death. Romosozumab should not be initiated in patients who have had an MI or stroke within the preceding year. Consider whether the benefits outweigh the risks in patients with other cardiovascular risk factors.

CONTRAINDICATIONS: Hypersensitivity (e.g., angioedema, erythema multiforme, urticaria) to romosozumab or any component of the formulation; uncorrected hypocalcemia.

OTHER CONSIDERATIONS:

Monitoring Parameters
Signs/symptoms of hypersensitivity; signs/symptoms of adverse cardiovascular events; serum calcium.

BMD (clinical trials assessed at baseline and then at 6 or 12 months [Cosman 2016; Saag 2017]); may consider monitoring biochemical markers of bone turnover (e.g., fasting serum CTX, serum P1NP) at baseline, 3 months, and 6 months to assess treatment response (Cosman 2016; ES [Eastell 2019]; Saag 2017).

CLINICAL SUMMARY / APPENDIX

Osteoporosis, postmenopausal, fracture risk reduction; 210 mg SUBQ once monthly; each monthly dose is given as 2 separate 105-mg injections administered immediately one after the other.

Osteoporosis is a skeletal disorder characterized by decreased bone mass. The most common diagnostic test is the DEXA scan (dual energy X-ray absorptiometry) to measure BMD (bone mineral density). Results are typically reported as a T-score, which compares the BMD of the subject to a standard BMD of a healthy young adult. T-Scores are reported as standard deviations (SD) World Health Organization criteria:

- Normal - T-Score within 1 SD of normal
- Osteopenia- T-Score of -1 to -2.5 SD below normal
- Osteoporosis- T-Score of -2.5 or less SD below normal
- Severe Osteoporosis- T-Score of -2.5 or less SD below normal with fragility fractures

Fracture Risk Assessment Tool (FRAX®) tool: The FRAX® tool (www.shef.ac.uk/FRAX) was developed by the World Health Organization (WHO) to evaluate fracture risk of patients. It integrates clinical risk factors with BMD at the femoral neck. The FRAX® tool provides the 10-year probability of fracture. The output is a 10-year probability of hip fracture and a 10-year probability of major osteoporotic fracture (forearm, shoulder, or clinical vertebral fracture).

The US National Osteoporosis Foundation recommends treatment of osteopenic patients whose FRAX score for hip fracture is 3% or greater, or whose risk for other bone fracture is greater than 20%.

Professional Society Guidelines

The National Osteoporosis Foundation (NOF) states that the diagnosis of osteoporosis (OP) can be established by either measurement of BMD or by the occurrence of adulthood hip or vertebral fracture in the absence of major trauma (such as a motor vehicle accident or multiple story fall). For evaluation, BMD measurement should be taken by central dual-energy X-ray absorptiometry at the lumbar spine and femoral neck (hip). A BMD taken at the one-third (33%) radius site can be used for diagnosing osteoporosis when the hip and lumbar spine cannot be measured or are unusable or uninterpretable. In postmenopausal women and men age 50 and older, WHO diagnostic T-score criteria is applied to the BMD measurement. For those patients that are not postmenopausal women and not men age 50 and older, WHO BMD classification should not be applied, and the diagnosis of osteoporosis should not be made on densitometric criteria alone.

The American College of Endocrinology (AACE/ACE) (2020) osteoporosis treatment guidelines stratify initial treatment based on risk status.

- For individuals at high risk or no prior fractures, initial therapy options include bisphosphonates (alendronate, risedronate, or zoledronic acid) or denosumab.
- The 2020 AACE Guidelines created a ‘very high’ risk category for post-menopausal women with osteoporosis. The following patients are considered to be a very high fracture risk:
    - Patients with a recent fracture (within the past 12 months), fractures while on approved osteoporosis therapy multiple fractures, or fractures while on drugs causing skeletal harm (e.g., long-term glucocorticoids),
    - Patients with a very low T-score (less than -3.0),
    - Patients with a high risk for falls or history of injurious falls, and very high fracture probability by FRAX (e.g., major osteoporosis fracture >30%, hip fracture >4.5%) or other validated fracture risk algorithm.

Patients who have been diagnosed with osteoporosis but do not meet the above definition of very high fracture risk are to be considered to be at high risk (AACE, 2020).
The AACE recommends alendronate, denosumab, risedronate, and zoledronate as appropriate initial therapy for most osteoporotic patients with high fracture risk. Abaloparatide, denosumab, romosozumab, teriparatide,

and zoledronate should be considered for patients unable to use oral therapy and as initial therapy for patients at very high fracture risk (AACE, 2020).

The Endocrine Society osteoporosis guideline update (2020) recommends initial therapy with bisphosphonates (alendronate, risedronate, zoledronic acid, or ibandronate) or alternatively denosumab for those at high risk.

According to UpToDate (2023), "There are currently no head-to-head trials comparing the anti-fracture efficacy of denosumab with other available osteoporosis therapies (e.g., oral and intravenous bisphosphonates, teriparatide). The reduction in vertebral fracture noted with denosumab is similar to the reductions reported for subcutaneous teriparatide and intravenous zoledronic acid and greater than that reported for oral alendronate. However, these data are based upon clinical trials in different patient populations, not head-to-head comparison trials." (Rosen 2023)

Monitoring Parameters: For osteoporosis, it is recommended that serial bone mineral density (BMD) should be evaluated at baseline and every 1 to 3 years (usually at ~2 years following initiation of therapy, then more or less frequently depending on patient-specific factors and stability of BMD) (AACE/ACE [Camacho 2020]; ES [Eastell 2019]; NOF [Cosman 2014]); may consider monitoring biochemical markers of bone turnover (eg, fasting serum CTX or urinary NTX) at baseline, 3 months, and 6 months, to assess treatment response (ES [Eastell 2019]).

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IMPORTANT REMINDER

This Medicare Part B Step Therapy Medical Necessity Guideline is provided for informational purposes only and neither constitutes nor replaces professional medical advice. Physicians, hospitals, and other providers are expected to administer or use drugs/biologicals in the most effective and clinically appropriate manner. Treating physicians and other health care providers are solely responsible for all medical care decisions. In accordance with the member's Evidence of Coverage (EOC), every benefit plan has its own coverage provisions, limitations, and exclusions. In the event of a conflict between this policy and the member's EOC, the member's EOC provisions will take precedence.

Aspire Health Plan (AHP) adheres to Medicare guidelines, including National Coverage Determination (NCD), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and other relevant Medicare manuals established by CMS. Compliance with these guidelines is required when applicable. Refer to the CMS website at http://www.cms.hhs.gov. For the most up-to-date Medicare policies and coverage, please search the Medicare Coverage Database. All LCDS are the same for each state within a Jurisdiction. Medicare Part B Administrative Contractor (MAC) for CA [Jurisdiction E (1)]: Active LCDs - JE Part B – Noridian (noridianmedicare.com). In the event of a discrepancy between this policy and the Medicare NCD or LCD, the Medicare NCD/LCD will govern.

This policy is utilized by AHP to determine coverage in the absence of applicable CMS Medicare guidelines. Please refer to the links provided in the References section below to access the Medicare source materials that were used for developing this resource document. This document does not serve as a substitute for the official Medicare source materials that provide detailed information on Medicare coverage requirements. In the event of a conflict between this document and Medicare source materials, the Medicare source materials will take precedence.

The inclusion of a code in this policy does not imply that the health service it describes is covered or not covered. Benefit coverage for health services is determined by the member-specific plan document and applicable laws that may mandate coverage for a particular service. Inclusion of a code does not imply or guarantee reimbursement or payment of a claim. Other Policies and Standards may also apply. Providers are expected to retain or have access to the necessary documentation when requested in order to support coverage.

POLICY HISTORY

Version	Date	Summary of Changes
1	9/27/2023	New Policy