romosozumab-aqqg (Evenity™)

Policy # 00686
Original Effective Date: 08/14/2019
Current Effective Date: 09/13/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider romosozumab-aqqg (Evenity™)‡ for the treatment of postmenopausal women at high risk for fracture to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for romosozumab-aqqg (Evenity) will be considered when the following criteria are met:

- Patient is a postmenopausal woman who has a central dual x-ray absorptiometry (DEXA) bone mineral density T-score less than or equal to -2.5, confirming osteoporosis, OR a fragility fracture [defined as a major osteoporotic fracture sustained as a result of a low-level trauma (e.g., a fall from standing height or less) that is associated with low bone mineral density, including vertebral (spine), hip, forearm (wrist/distal radius), and proximal humerus (shoulder) fractures]; AND
- Patient has not received greater than or equal to 12 doses of Evenity; AND
- Patient has or has had ONE of the following:
    - Inability to take bisphosphonates; OR
    - A 12-month trial of bisphosphonates with documentation of new fractures or significant loss of bone mineral density; AND
      *(Note: These specific patient criteria are additional company requirements and will be denied as not medically necessary** if not met).*
- Patient has NOT had a heart attack or stroke within the previous 12 months.

romosozumab-aqqg (Evenity™)

Policy # 00686
Original Effective Date: 08/14/2019
Current Effective Date: 09/13/2021

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of romosozumab-aqqg (Evenity) when the patient is able to take bisphosphonates and has not tried and failed a 12-month trial of bisphosphonates to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of romosozumab-aqqg (Evenity) when patient selection criteria are not met (except those denoted to be **not medically necessary****) to be **investigational.***

Background/Overview

Evenity, a sclerostin inhibitor, is indicated for the treatment of osteoporosis in postmenopausal women who are at high risk for fracture. This population is defined by the Food and Drug Administration (FDA) as patients who have failed or are intolerant to other available osteoporosis therapies or in those with a history of osteoporotic fracture, or multiple risk factors for fracture. The drug works by stimulating new bone formation on trabecular and cortical bone surfaces by stimulating osteoblastic activity, leading to increased trabecular and cortical bone mass which improves bone structure and strength. The recommended dose of Evenity is 210 mg (as two separate 105 mg injections) given by subcutaneous injection once every month for 12 doses. Evenity should be given by a healthcare provider. After 12 monthly doses, the anabolic effect of Evenity wanes, which is the reason for the duration limit. If osteoporosis therapy is still necessary, continued treatment with an antiresorptive agent should be considered (e.g., a bisphosphonate). Evenity also has a black box warning regarding the potential risk of myocardial infarction, stroke, and cardiovascular death.

Osteoporosis is characterized by decreased bone mass and increased fracture risk, most commonly at the spine, hip, and wrist. DXA scans of patients with osteoporosis reveal a T-score less than or equal to -2.5. In addition to those patients with a DXA score representing osteoporosis, treatment should be considered in those patients with a fragility fracture. A fragility fracture is a major

osteoporotic fracture, sustained as a result of a low-level trauma (e.g., a fall from standing height or less) that is associated with low BMD, including vertebral (spine), hip, forearm (wrist/distal radius), and proximal humerus (shoulder) fractures. In healthy humans, bone formation and resorption are closely linked; old bone is resorbed and replaced by newly formed bone. In postmenopausal osteoporosis, bone resorption exceeds bone formation, leading to bone loss and increased risk of fracture. After menopause, the risk of fractures of the spine and hip increases; approximately 40% of 50-year old women will experience an osteoporosis-related fracture during their remaining lifetimes.

There are many treatment options available for postmenopausal osteoporosis. Clinical practice guidelines published in 2016 by the American Association of Clinical Endocrinologists and the American College of Endocrinology suggest that bisphosphonates or denosumab (Prolia®)‡ should be considered as initial therapy. Options for patients unable to tolerate oral therapy or at especially high fracture risk include the anabolic agents, teriparatide (Forteo®)‡ and abaloparatide (Tymlos™)‡, as well as Prolia. These guidelines were published prior to the availability of Evenity.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Evenity was approved in 2019 for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Evenity for the treatment of osteoporosis was established in two phase III pivotal trials in women with postmenopausal osteoporosis, FRAME and ARCH.

romosozumab-aqqg (Evenity™)

Policy # 00686
Original Effective Date: 08/14/2019
Current Effective Date: 09/13/2021

FRAME was a randomized, double-blind, placebo-controlled study of postmenopausal women aged 55 to 90 years (mean age of 71 years) with BMD T-scores less than or equal to -2.5 at the total hip or femoral neck. Women were randomized to receive subcutaneous injections of either Evenity (n=3589) or placebo (n=3591) for 12 months. At baseline, 18% of women had a vertebral fracture. After the 12-month treatment period, women in both arms transitioned to open-label anti-resorptive therapy (denosumab) for 12 months while remaining blinded to their initial treatment. The coprimary efficacy endpoints were new vertebral fracture at month 12 and month 24. At month 12, Evenity significantly reduced the incidence of new vertebral fractures through month 12 compared to placebo (0.5% in Evenity group vs 1.8% in placebo group experienced a new vertebral fracture [p<0.001]). In addition, this reduction persisted through the second year in women who received Evenity during the first year and transitioned to Prolia vs those who transitioned from placebo to Prolia (0.6% in the Evenity group vs 2.5% in the placebo group [p<0.001]).

ARCH was a randomized, double-blind, alendronate-controlled study of postmenopausal women aged 55 to 90 years (mean age of 74 years) with BMD T-score less than or equal to -2.5 at the total hip or femoral neck and either one moderate or severe vertebral fracture or two mild vertebral fractures, or BMD T-score less than or equal to -2.0 at the total hip or femoral neck and either two moderate or severe vertebral fractures or a history of a proximal femur fracture. Women were randomized 1:1 to receive either monthly subcutaneous injections of Evenity (n=2046) or oral alendronate 70 mg weekly (n=2047) for 12 months. After the 12-month treatment period, women in both arms transitioned to open-label alendronate 70 mg weekly while remaining blinded to their initial treatment. The coprimary efficacy endpoints were the incidence of morphometric vertebral fracture at 24 months and time to the first clinical fracture through the primary analysis period, which ended when at least 330 subjects had a clinical fracture and all subjects had completed the 24-month visit. Evenity significantly reduced the incidence of new vertebral fracture at 24 months with 8% in the alendronate alone experiencing new vertebral fracture vs 4.1% in the Evenity group (p<0.001). Evenity also significantly reduced the risk of clinical fracture through the end of the primary analysis period with 13% of women in the alendronate alone group experiencing a fracture vs 9.7% in the Evenity group (p<0.001).

References

1. Evenity [package insert]. Amgen Inc. Thousand Oaks, CA. Updated April 2019
2. Evenity Drug Evaluation. Express Scripts. Updated April 2019.

romosozumab-aqqg (Evenity™)

Policy # 00686
Original Effective Date: 08/14/2019
Current Effective Date: 09/13/2021

Policy History

Original Effective Date: 08/14/2019
Current Effective Date: 09/13/2021
08/01/2019 Medical Policy Committee review
08/14/2019 Medical Policy Implementation Committee approval. New policy.
08/06/2020 Medical Policy Committee review
08/12/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/05/2021 Medical Policy Committee review
08/11/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 08/2022

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2020 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

romosozumab-aqqg (Evenity™)

Policy # 00686
Original Effective Date: 08/14/2019
Current Effective Date: 09/13/2021

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3111, J3490
ICD-10 Diagnosis	M80.00-M80.88, M81.0-M81.8 Added codes eff 10/1/2020: M80.0AXA- M80.0AXS, M80.8AXA-M80.8AXS

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment,

would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.