BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

REGRANEX® (becaplermin) gel
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Regranex (becaplermin) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Podiatrist or Wound Care Specialist

2. Individual is 16 years of age or older

3. Individual has a confirmed diagnosis of lower extremity diabetic neuropathic ulcer that extends into the subcutaneous tissue or beyond and has an adequate blood supply

4. Individual has **ALL** of the following:

a. Full thickness ulcer of the lower extremity extending into the subcutaneous tissue (full thickness, e.g., Stage III or IV)
b. Adequate blood/tissue oxygenation supply as measured by a transcutaneous partial pressure of oxygen ($TcPo_2$) of 30 mm Hg or greater on the foot dorsum or at the margin of the ulcer or use of another assessment of lower limb vascular function as a predictor for wound healing
c. Recent (within the last 3months) glycosylated hemoglobin (hemoglobin A1c or HbA1c) is less than or equal to 8, with active treatment of diabetes to improve glycemic control has been initiated if greater than 8

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has participated for at least two months in a wound care program which included **ALL** of the following:
   a. Initial sharp debridement and additional debridement as needed
   b. Pressure relief
   c. Infection control
   d. Dressing care

7. Individual will continue to participate in a wound care program

8. Individual's wound/ulcer is free from infection

9. There are no exposed joints, tendons, ligaments, and bone

10. There are **NO** FDA-label contraindications such as known neoplasm(s) at the site(s) of application

Initial approval duration: 2 months, not to exceed 45 g for the treatment period

- **Criteria for continuation of coverage (renewal request):** Regranex (becaplermin) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Podiatrist or Wound Care Specialist

2. Individual's condition has responded while on therapy with response defined as the following:
   a. No evidence of disease progression
   b. Ulcer size has decreased at least 30% after 8-10 weeks

3. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

4. Individual's condition is being continually reassessed for reduction in ulcer size

5. Individual participates in a wound care program
6. Individual's wound/ulcer is free from infection
7. There are no exposed joints, tendons, ligaments, and bone
8. Individual treatment regimen has not exceeded 45 g or will not exceed 45 g by the end of the treatment period

Renewal duration: 3 months, not to exceed 45 g for the treatment period

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Regranex (becaplermin) is indicated for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond that have an adequate blood supply. Becaplermin is indicated as an adjunct to, and not a substitute for, good ulcer care practices. The efficacy of becaplermin has not been established for the treatment of pressure ulcers and venous stasis ulcers. The effects of becaplermin on exposed joints, tendons, ligaments, and bone have not been established in humans. Becaplermin is not intended to be used in wounds that close by primary intention.

A program of good ulcer care consisting of initial complete sharp debridement, a non-weight-bearing regimen, systemic treatment for wound-related infection if present, moist saline dressings changed twice a day, and additional debridement as necessary.

Growth Factors:
Growth factors are proteins that signal cells to divide and grow. Types include platelet-derived growth factor (PDGF), basic fibroblast growth factor (BFGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), transforming growth factor (TFGF) and recombinant PDGF. Regranex (becaplermin) is a recombinant human platelet-derived growth factor, and it is topically applied.

Autologous Wound Healing Factors:
Blood is drawn from an individual and centrifuged at high speeds to create an autologous concentrated platelet rich plasma (PRP) that contains a biologically active mixture of growth factors without the potential for an immune response. Autologous wound healing factors have been investigated for the treatment of wounds and non-orthopedic conditions.

There are numerous PRP preparation systems that have been cleared for marketing by the FDA through the 510(k) process. The use of different devices and procedures can lead to variable concentrations of active platelets and associated proteins, increasing variability between studies of clinical efficacy.

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Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Wound Definitions: [From the National Pressure Ulcer Advisory Panel]

Stage I:
- Intact skin but with non-blanchable erythema for >1 hour after relief of pressure

Stage II:
- Blister or other break in the dermis with partial thickness skin loss involving epidermis and/or dermis with or without infection

Stage III:
- Full thickness skin loss involving damage or necrosis of subcutaneous tissues that may extend down to, but not through, underlying fascia with or without infection; undermining and tunneling may be present

Stage IV:
- Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone, or supporting structures, with or without infection; often includes undermining and tunneling

Unstageable:
- Full thickness tissue loss in which the base of the ulcer is covered by slough and/or eschar in the wound bed

Suspected deep tissue injury:
- Purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying tissue from pressure and/or shear

Chronic:
- A wound or condition present for at least 30 days despite standard medical and surgical management

Calculation of dosage: (15 g tube size):

To calculate the length of gel applied to the ulcer, measure the greatest length of the ulcer by the greatest width of the ulcer. Tube size and unit of measure will determine the formula used in the calculation. Recalculate amount of gel needed every 1 to 2 weeks, depending on the rate of change in ulcer area.

15 g tube using centimeters: [ulcer length (cm) × width (cm)] divided by 4 = length of gel (cm)
15 g tube using inches: [ulcer length (in) × width (in)] x 0.6 = length of gel (in)

Transcutaneous partial pressure of oxygen:

Transcutaneous partial pressure of oxygen (TcPO2) represents the amount of oxygen diffusing outward across the skin and can be used as a surrogate for arterial perfusion
The predictive value of TcPO2 for wound healing potential is established. In the absence of malignancy, infection, inflammatory disease, or other confounding factors, wounds with a TcPO2 < 20mmHg are unlikely to heal and those with a TcPO2 > 40mmHg generally heal well.

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Ankle brachial index:

The ankle-brachial pressure index (ABPI) or ankle-brachial index (ABI) is the ratio of the blood pressure at the ankle to the blood pressure in the upper arm (brachium). Compared to the arm, lower blood pressure in the leg suggests blocked arteries due to peripheral artery disease (PAD). The ABPI is calculated by dividing the systolic blood pressure at the ankle by the systolic blood pressure in the arm.
An ABPI between and including 0.90 and 1.29 considered normal (free from significant PAD), while a lesser than 0.9 indicates arterial disease

Ankle systolic pressure:

Ankle systolic blood pressure is used to determine presence and severity of PAD, the lower the ankle pressure, the greater the severity of occlusive disease

Toe pressure (TP):

A measure of small arterial function in the periphery. TP is used in addition to the ankle-brachial index when screening for peripheral arterial disease (PAD) of the lower limb in those with diabetes, particularly in the presence of lower limb medial arterial calcification. It may be used as an adjunct assessment of lower limb vascular function and as a predictor of wound healing

Resources:

Regranex (becaplermin) gel product information, revised by Smith & Nephew, Inc. 08-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 26, 2024.

Armstrong DG, de Asla RJ. Management of diabetic foot ulcers. In: UpToDate, Eidt JF, Mills JL, Nathan DM, Collins KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through December 2024. Topic last updated October 30, 2024. Accessed January 03, 2025.

Fukaya E, O'Banion LA, Kiguch M, Judelson DR. Evaluation and management of chronic venous insufficiency including venous leg ulcers. In: UpToDate, Eidt JF, Mills JL, Collins KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Literature current through December 2024. Topic last updated July 13, 2023. Accessed January 03, 2025.