BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**1/18/2018**
LAST REVIEW DATE:	**2/17/2022**
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REGRANEX® (becaplermin) gel

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Regranex (becaplermin) is considered ***medically necessary*** as an adjunct to standard wound care management and will be approved when **ALL** of 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. A confirmed diagnosis of **ONE** of the following:
    a. Chronic neuropathic diabetic ulcer

    b. Pressure ulcer

4. **ONE** of the following:
    a. **For neuropathic diabetic ulcers**:
        i. Full thickness ulcer of the lower extremity extending into the subcutaneous tissue (full thickness, e.g., Stage III or IV)
        ii. There is adequate blood/tissue oxygenation supply as measured by a transcutaneous partial pressure of oxygen ($TcPo_2$) greater than or equal to 30 mm Hg or other assessment of lower limb vascular function as a predictor for wound healing
        iii. Recent (within the last 3months) glycosylated hemoglobin (hemoglobin A1c or HbA1c) is less than or equal to 8, with active treatment to improve glycemic control has been initiated if greater than 8

    b. **For pressure ulcer**:
        i. Full thickness ulcer extending into the subcutaneous tissue (full thickness, e.g., Stage III or IV)
        ii. Ulcer is in an anatomic location that can be offloaded for the duration of treatment
        iii. Albumin concentration >2.5 dL
        iv. Total lymphocyte count >1000/µL

5. The 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

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

7. The wound/ulcer is free from infection

8. There are **NO** FDA-label contraindications, such as:

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a. 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) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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 responded while on therapy
    a. Response is defined as:
        i. No evidence of disease progression
        ii. Ulcer size has decreased at least 30% after 8-10 weeks
3. Individual's condition has been reassessed for reduction in ulcer size
4. Individual participates in a wound care program
5. The wound/ulcer is free from infection
6. 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.

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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.

Definitions:

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

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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.

Centimeters
15 g tube
[ulcer length (cm) × width (cm)] divided by 4 = length of gel (cm)

Inches
15 g tube
[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.

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

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Resources:

Regranex (becaplermin) product information, revised by Smith & Nephew, Inc. 08-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 15, 2021.

Armstrong DG, Meyr A. Basic principles of wound management. In: UpToDate, Eidt JF, Mills JL, Bruera E, Berman RS, Collins KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Topic last updated June 08, 2021. Accessed December 15, 2021.

Berlowitz D. Clinical staging and management of pressure-induced skin and soft tissue injury. In: UpToDate, Berman RS, Schmader KE, Collins KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Topic last updated August 24, 2020. Accessed December 15, 2021.

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Mathes BM, Kabnik LS, Alguire PC. Medical management of lower extremity chronic venous disease. In: UpToDate, Eidt JF, Mills JL, Collins KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Topic last updated August 03, 2021. Accessed December 15, 2021.

2.01.16 BCBS Association Medical Policy Reference Manual. Recombinant and Autologous Platelet-Derived Growth Factors Wound Healing and Other Non-Orthopedic Conditions. Review date February 2021. Accessed December 15, 2021.