MEDICAL POLICY

Medical Policy Title	**Growth Factors for Wound Healing**
Policy Number	**2.01.24**
Current Effective Date	**January 23, 2025**
Next Review Date	**January 2026**

Our medical policies are based on the assessment of evidence based, peer-reviewed literature, and professional guidelines. Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. (Link to Product Disclaimer)

POLICY STATEMENT(S)

Recombinant Platelet-Derived Growth Factors: Becaplermin gel, Regranex

I. Recombinant human platelet-derived growth factor (Becaplermin gel) for topical administration is considered **medically appropriate** when **ALL** the following criteria are met:
   A. Adjunctive to standard wound management for neuropathic diabetic ulcers
   B. Treatment of full-thickness ulcer (i.e., stage III or IV), extending through dermis into subcutaneous tissues;
   C. Participation in a wound management program (e.g. sharp debridement, pressure relief [i.e., non–weight bearing], and infection control)
   D. Adequate tissue oxygenation, as measured by **ANY** of the following:
      1. a transcutaneous partial pressure of oxygen of 30 mm Hg or greater on the foot dorsum or at the margin of the ulcer;
      2. an ankle-brachial blood pressure index (ABI) greater than 0.70 or ankle systolic pressure greater than 70 mm Hg;

II. Becaplermin gel is considered **investigational** for **ALL** of the following indications:
   A. Ischemic diabetic ulcers;
   B. Venous stasis ulcers;
   C. Pressure ulcers;
   D. Ulcers not extending through the dermis into the subcutaneous tissue;
   E. Surgical wounds;
   F. Ulcerated perineal hemangiomas of infancy.

Autologous Platelet-Derived Preparations

III. Autologous platelet-derived preparations (i.e., Basic Fibroblast Growth Factor (BFGF), Epidermal Growth Factor (EGF), Placental Angiogenic Growth Factors (PGFs), and Platelet-Rich Plasma (PRP) are considered **investigational** for **ALL** conditions, including, but not limited to:
   A. Chronic non-healing wounds;

B. Surgical wounds;

C. Arthritis,

D. Dupuytren's contracture,

E. Epicondylitis,

F. Plantar fasciitis,

G. Tendinopathy.

This policy does not address fibrin sealants.

RELATED POLICIES

Corporate Medical Policy

7.01.35 Bioengineered Tissue Products for Wound Treatment and Surgical Interventions

11.01.03 Experimental or Investigational Services

POLICY GUIDELINE(S)

I. Patients are typically treated with Becaplermin gel once daily for up to 20 weeks. Continuing Becaplermin treatment should be reconsidered if the ulcer is not reduced in size by 30% within 10 weeks of treatment, or complete healing has not occurred in 20 weeks. When expected reduction in ulcer size occurs successfully, the treatment is continued until the ulcer is completely healed. The increase in rate of healing must be balanced with the potential for increased risk of cancer. Application of the gel may be performed by the patient in the home.

II. When purchased at a pharmacy, coverage for Becaplermin gel is dependent upon the member's prescription drug coverage.

DESCRIPTION

Growth factors are polypeptides produced by cells during development and in response to injury. Owing to their effects on cell proliferation, growth factors have undergone extensive analyses, to determine their usefulness as wound healing agents.

A recombinant human platelet-derived growth factor, Becaplermin gel (Regranex), has biological activity similar to that of endogenous platelet-derived growth factor, which includes the promotion of chemotactic recruitment, proliferation of cells involved in wound repair, and enhancement of granulation tissue.

Examples of growth factors used in wound healing are:

I. Basic Fibroblast Growth Factor (BFGF);

II. Epidermal Growth Factor (EGF);

III. Placental Angiogenic Growth Factors (PGFs); and

IV. Platelet-Derived Growth Factor (PDGF).

Autologous PDGF is one of the polypeptides that control growth, differentiation, and activation of cell types essential for wound healing. The growth-promoting activities of PDGF are thought to be deficient in chronic wounds. Autologous PDGF preparations have been proposed as an adjuvant therapy for wound healing and to enhance healing following various types of surgery (e.g., oral and maxillofacial surgery, dental implants, non-union fractures).

Platelet-rich plasma (PRP) preparations, which contain growth factors, have been proposed as a primary treatment of miscellaneous conditions such as arthritis, Dupuytren's contracture, epicondylitis, plantar fasciitis, and tendinopathy.

SUPPORTIVE LITERATURE

The effectiveness of PDGF and PRP use for these conditions has not been demonstrated in the peer-reviewed literature.

Available data are insufficient to permit positive conclusions regarding the use of Becaplermin gel for treatment of ulcers (e.g., ischemic diabetic ulcers, pressure ulcers, and venous ulcers), other than chronic neuropathic diabetic ulcers or other non-healing wounds in the investigational setting.

Evidence is insufficient regarding the use of PDGFs as a treatment of chronic non-healing wounds, surgical wounds, and other conditions, including, but not limited to, arthritis, Dupuytren's contracture, epicondylitis, plantar fasciitis, or tendinopathy.

Published studies provide mixed results regarding the use of PRP: some show benefit of the treatment, while others show no or little benefit. Proof of the efficacy of PRP has not been demonstrated in clinical studies; additional well-designed, randomized, controlled studies are needed before conclusion can be made.

PROFESSIONAL GUIDELINE(S)

Not Applicable

REGULATORY STATUS

Becaplermin gel (Regranex) has been approved by the U.S. Food and Drug Administration (FDA) specifically for use in the treatment of chronic neuropathic diabetic ulcers of the lower extremities. Becaplermin gel, in conjunction with a good wound care program, has been found to improve health outcomes of patients with chronic neuropathic diabetic ulcers, by producing complete wound healing and reducing the time to complete wound healing when compared to a good wound care program alone.

In 2008, the manufacturer of Regranex, Ortho-McNeil Pharmaceutical, added a boxed warning to the labeling, stating that an increased rate of mortality secondary to malignancy was observed in patients treated with three or more tubes of Regranex gel. The boxed warning was removed in November 2018 based on data submitted to the FDA by Smith and Nephew.

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, Title 21, parts 1270 and1271. Under these regulations, certain products including blood products such as PRP are exempt and therefore, do not follow the traditional FDA regulatory pathway. To date, the FDA has not attempted to regulate activated PRP.

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
0232T (E/I)	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed

HCPCS Codes

Code	Description
G0460 (E/I)	Autologous platelet rich plasma (PRP) or other blood-derived product for nondiabetic chronic wounds/ulcers (includes, as applicable: administration, dressings, phlebotomy, centrifugation or mixing, and all other preparatory procedures, per treatment)
G0465 (E/I)	Autologous platelet rich plasma (PRP) or other blood-derived product for diabetic chronic wounds/ulcers, using an FDA-cleared device for this indication, (includes, as applicable: administration, dressings, phlebotomy, centrifugation or mixing, and all other preparatory procedures, per treatment)
P9020 (E/I)	Platelet rich plasma, each unit
S0157	Becaplermin gel 0.01%, 0.5 gm
S9055 (E/I)	Procuren or other growth factor preparation to promote wound healing

NCD Codes

Code	Description
50484-0810-15	Becaplermin

ICD10 Codes

Code	Description
E08.621	Diabetes mellitus due to underlying condition with foot ulcer
E08.622	Diabetes mellitus due to underlying condition with other skin ulcer
E09.621	Drug or chemical induced diabetes mellitus with foot ulcer
E09.622	Drug or chemical induced diabetes mellitus with other skin ulcer
E10.621	Type 1 diabetes mellitus with foot ulcer
E10.622	Type 1 diabetes mellitus with other skin ulcer
E11.621	Type 2 diabetes mellitus with foot ulcer
E11.622	Type 2 diabetes mellitus with other skin ulcer
E13.621	Other specified diabetes mellitus with foot ulcer
E13.622	Other specified diabetes mellitus with other skin ulcer

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CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

NCD - Blood-Derived Products for Chronic Non-Healing Wounds (NCD 270.3) [accessed 2024 December 16].

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.
- If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.

- If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY HISTORY/REVISION	
Committee Approval Dates	
10/18/01, 05/16/02, 04/24/03, 05/19/04, 07/21/05, 03/16/06, 01/18/07, 01/17/08, 01/15/09, 02/18/10, 02/17/11, 02/16/12, 02/21/13, 02/20/14, 01/22/15, 01/21/16, 03/16/17, 02/15/18, 01/16/20, 01/21/21, 01/20/22, 01/19/23, 01/18/24, 01/23/25	
Date	**Summary of Changes**
01/23/25	• Annual update, policy intent unchanged.
01/01/25	• Summary of changes tracking implemented.
10/18/01	• Original effective date