MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**GROWTH FACTORS FOR WOUND HEALING AND OTHER CONDITIONS**
Policy Number	**2.01.24**
Category	**Technology Assessment**
Effective Date	**10/18/01**
Revised Date	**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, 01/17/19**
Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.* • *If a Medicare 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.*

POLICY STATEMENT

I. Recombinant Platelet-Derived Growth Factors: becaplermin gel, Regranex®

A. Based upon our criteria and assessment of peer-reviewed literature, recombinant human platelet-derived growth factor (becaplermin gel) for topical administration has been medically proven to be effective and therefore **medically appropriate** when used as an adjunct to standard wound management for *neuropathic diabetic ulcers* extending into the subcutaneous tissue. Appropriate candidates should meet **ALL** of the following criteria:

1. Adequate tissue oxygenation, as measured by:
   a. a transcutaneous partial pressure of oxygen of 30 mm Hg or greater on the foot dorsum or at the margin of the ulcer, or
   b. an ankle-brachial blood pressure index (ABI) greater than 0.70 or ankle systolic pressure greater than 70 mm Hg
2. Full-thickness ulcer (ie, stage III or IV), extending through dermis into subcutaneous tissues
3. Participation in a wound management program, which includes sharp debridement, pressure relief (ie, non–weight bearing), and infection control.

B. Based upon our criteria and lack of peer-reviewed literature, becaplermin gel has not been medically proven to be effective and is considered **investigational** for all of the following indications:

1. Ischemic diabetic ulcers
2. Venous stasis ulcers
3. Pressure ulcers
4. Ulcers not extending through the dermis into the subcutaneous tissue
5. Surgical wounds
6. Ulcerated perineal hemangiomas of infancy

II. Autologous Platelet-Derived Preparations: Basic Fibroblast Growth Factor (BFGF), Epidermal Growth Factor (EGF), Placental Angiogenic Growth Factors (PGF's), and Platelet-Rich Plasma (PRP)

Based upon our criteria and lack of peer-reviewed literature, autologous platelet-derived preparations have not been medically proven to be effective and are considered **investigational** in the treatment of:

A. Chronic non-healing wounds
B. Surgical wounds
C. All other conditions including, but not limited to: arthritis, Dupuytren's contracture, epicondylitis, plantar fasciitis, and tendinopathy.

This policy does not address fibrin sealants.

Refer to Corporate Medical Policy #7.01.35 regarding Bioengineered Tissue Products for Wound Treatment and Surgical Interventions.

Refer to Corporate Medical Policy #11.01.03 Experimental and Investigational Services.

POLICY GUIDELINES

I. Patients are typically treated 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 from 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.
III. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

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 that includes promoting chemotactic recruitment and proliferation of cells involved in wound repair and enhancing 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 (PGF's), and
IV. Platelet-Derived Growth Factor (PDGF).

Autologous platelet-derived growth factor is one of the polypeptides that control growth, differentiation, and activation of cell types essential for wound healing. The growth promoting activities of platelet-derived growth factor (PDGF) are thought to be deficient in chronic wounds. Autologous platelet-derived growth factor 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. The effectiveness of PDGF and PRP use, for these conditions, has not been demonstrated in the peer-reviewed literature.

RATIONALE

Becaplermin (Regranex) gel has been approved by the 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 gel, Ortho-McNeil Pharmaceutical, added a black box warning to the labeling stating an increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of Regranex gel in a post-marketing retrospective cohort study, Regranex gel should only be used when the benefits can be expected to outweigh the risks, and Regranex gel should be used with caution in patients with known malignancy**.**
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 platelet-derived growth factors 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.

A 2015 statement by the American Academy of Orthopedic Surgeons states "Biologic therapies are becoming increasingly popular in orthopedics due to their potential to regenerate tissue and enhance bone healing. However, questions still remain about their efficacy and indications for use."
Published studies provide mixed results regarding the use of PRP; with some showing benefit of the treatment while others show no or little benefit. Proof of the efficacy of PRP has not been demonstrated in clinical studies and further well-designed, randomized, controlled studies are needed before conclusion can be made.

The 2017 publication of the American Academy of Orthopedic Surgeons: Management of Osteoarthritis of the Hip Evidence-based Clinical Proactive Guideline they concluded that, "No high quality randomized controlled trials were available comparing the performance of IA injection of stem cells or prolotherapy to placebo. Three studies (Battaglia et al, Dallari et al) compared IA injections of platelet-rich plasma (PRP) versus HA or a combination of PRP and HA. However, *no high quality studies comparing PRP with placebo were available* for inclusion."

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I)*

CPT Codes

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

HCPCS Codes

Code	Description
G0460 **(E/I)**	Autologous platelet rich plasma for chronic wounds/ulcers including phlebotomy, centrifugation, and all other preparatory procedures, administration and dressings, per treatment
P9020 **(E/I)**	Platelet rich plasma, each unit
S0157	Becaplermin gel 0.01%, 0.5 gm
S9055	Procuren or other growth factor preparation to promote wound healing

NDC

Code	Description
50484-0810-15	Becaplermin

ICD10 Codes

Medically Appropriate codes for when criteria is met under Policy Statement IA:

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

Code	Description
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

ICD10 Codes

Investigational codes (See Policy Statement IB):

Code	Description
I70.231-I70.249	Atherosclerosis of native arteries of leg with ulceration (code range)
I70.331-I70.349	Atherosclerosis of unspecified type of bypass graft(s) of leg with ulceration (code range)
I70.431-I70.449	Atherosclerosis of autologous vein bypass graft(s) of the leg with ulceration (code range)
I70.531-I70.549	Atherosclerosis of nonautologous biological bypass graft(s) of the leg with ulceration (code range)
I70.631-I70.649	Atherosclerosis of nonbiological bypass graft(s) of the leg with ulceration (code range)
I70.731-I70.749	Atherosclerosis of other type of bypass graft(s) of the leg with ulceration (code range)
L97.101-L97.929	Non-pressure chronic ulcer of lower extremity (code range)
L89.000-L89.95	Pressure ulcers (code range)

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*Key Article

KEY WORDS

Becaplermin, Growth factors, Regranex, Platelet derived growth factor, PDGF, Platelet-rich plasma.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD) for Blood-Derived Products for Chronic Non-Healing Wounds. Please refer to the following websites for Medicare Members:

http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=217&ncdver=5&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=New+York+-+Entire+State&KeyWord=blood+derived+products&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAABAAAAAAAAAA%3d%3d&