MEDICAL POLICY

Excellus

SUBJECT: GROWTH FACTORS FOR WOUND HEALING AND OTHER CONDITIONS	**EFFECTIVE DATE: 01/20/00**
	REVISED DATE: 07/19/01, 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
POLICY NUMBER: 2.01.24	
CATEGORY: Technology Assessment	**PAGE: 1 OF: 6**

- ***If the member's subscriber contract excludes coverage for a specific service it is not covered under that contract. In such cases, medical policy criteria are not applied.***
- ***Medical policies apply to commercial and Medicaid products only when a contract benefit for the specific service exists.***
- ***Medical policies only apply to Medicare products when a contract benefit exists and where there are no National or Local Medicare coverage decisions for the specific service.***

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** for the treatment of chronic lower extremity diabetic neuropathic ulcers when:
   1. Used in conjunction with a good wound care program, including patient education on the importance of non-weight bearing and patient understanding on using proper amounts of the gel, initial sharp debridement, maintaining a moist wound environment and infection control measures;
   2. Ulcers extend into the subcutaneous tissue or beyond; and
   3. There is 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.

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; and
   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, and
C. 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. 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.

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) may 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, 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 2007 statement by the American Academy of Orthopedic Surgeons states "available data suggest that PRP may be valuable in enhancing soft-tissue repair and in wound healing. However, the clinical role of PRP in bone repair remains controversial. PRP is not uniformly successful as an adjuvant to bone grafting procedures. PRP may promote or inhibit bone formation, depending on the setting in which it is used and the quality of the PRP. Significant additional research is needed to define the role of PRP and to determine in which settings it might - or might not -be valuable. This may also involve defining a means of ensuring that a given PRP preparation is biologically active, by determining its critical component(s) and developing assays that can provide this information to the surgeon in a timely manner".

CODES:	Number	Description

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.

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

HCPCS:	G0460 **(E/I)**	Autologous platelet rich plasma for chronic wounds/ulcers including phlebotomy, centrifugation, and all other preparatory procedures and administration, 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
ICD9:	707.1	Ulcer of lower limb, except decubitus
	250.8	Diabetes with other specified manifestations
ICD10:	E10.618-E10.628	Type 1 diabetes mellitus (code range)
	E10.65	Type 1 diabetes mellitus with hyperglycemia
	E10.69	Type 1 diabetes mellitus with other specified complication
	E11.618-E11.629	Type 2 diabetes mellitus (code range)
	E11.65	Type 2 diabetes mellitus with hyperglycemia
	E11.69	Type 2 diabetes mellitus with other specified complication
	E13.618-E13.628	Other specified diabetes mellitus (code range)
	E13.69	Other specified diabetes mellitus with other specified complication
	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-I70.449	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-I97.929	Non-pressure chronic ulcer of lower extremity (code range)

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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=gAAAABAAAAAAAA%3d%3d&

According to a Decision Memo issued by CMS in August 2012, CMS covers autologous platelet-rich plasma (PRP) only for patients who have chronic non-healing diabetic, pressure, and/or venous wounds and when the patient is enrolled in a clinical research study that addresses specific questions using validated and reliable methods of evaluation. Please refer to the following website for further information: http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?&NcaName=Autologous%20Blood-Derived%20Products%20for%20Chronic%20Non-Healing%20Wounds&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=New%20York%20-%20Entire%20State&KeyWord=autologous%20blood%20derived%20products&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAABAAEAAA&NCAId=260&.