

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;

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- 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).

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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.

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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 and 1271. 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

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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

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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

REFERENCES

Agency for Healthcare Research and Quality. Pressure ulcer treatment strategies: comparative effectiveness. AHRQ Pub [Internet]. 2013 May [accessed 2024 Dec 17] No. 13-EHC003-1-EF. Available from: https://effectivehealthcare.ahrq.gov/sites/default/files/related_files/pressure-ulcer-treatment_executive.pdf

American Academy of Orthopedic Surgeons: Management of Osteoarthritis of the Hip Evidence-based Clinical Practice Guideline [Internet]. 2017 Mar 13 [accessed 2024 Dec 17]. Available from: https://www.aaos.org/globalassets/quality-and-practice-resources/osteoarthritis-of-the-hip/oa-hip-cpg_6-11-19.pdf

Battaglia M, et al. Efficacy of ultrasound-guided intra-articular injections of platelet-rich plasma versus hyaluronic acid for hip osteoarthritis. *Orthopedics*. 2013 Dec;36(12):e1501-8.

Boesen AP, et al. Effect of platelet-rich plasma on nonsurgically treated acute Achilles tendon ruptures: a randomized, double-blinded prospective study. *Am J Sports Med*. 2020 Jul;48(9):2268-2276.

Cardenosa ME, et al. Efficacy and safety of the use of platelet-rich plasma to manage venous ulcers. *J Tissue Viability*. 2017 May;26(2):138-143.

Catapano M, et al. Effectiveness of platelet rich plasma injections for non-surgical management of carpal tunnel syndrome: a systematic review and meta-analysis of randomized controlled trials. *Arch Phys Med Rehabil*. 2020 May;101(5):897-906.

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- Chen X, et al. Use of platelet-rich plasma for the improvement of pain and function in rotator cuff tears: a systematic review and meta-analysis with bias assessment. *Am J Sports Med.* 2020 Jul;48(8):2028-2041.
- Chen Z, et al. Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: a meta-analysis. *Medicine (Baltimore).* 2020 Mar;99(11):e19388.
- Dai J, et al. Autologous platelet-rich plasma treatment for patients with diabetic foot ulcers: a meta-analysis of randomized studies. *Journal of Diabetes and Its Complications.* 2020; 34:1-7.
- Dallari D, et al. Ultrasound-guided injection of platelet-rich plasma and hyaluronic acid, separately and in combination, for hip osteoarthritis: a randomized controlled study. *Am J Sports Med.* 2016 Mar;44(3):664-71.
- Davey MS, et al. Anterior cruciate ligament reconstruction with platelet-rich plasma: a systematic review of randomized control trials. *Arthroscopy.* 2020 Apr;36(4):1204-1210.
- Haunschild ED, et al. Platelet-rich plasma augmentation in meniscal repair surgery: a systematic review of comparative studies. *Arthroscopy.* 2020 Jun;36(6):1765-1774.
- Hossam EM, et al. Autologous platelet rich plasma promotes the healing of non-ischemic diabetic foot ulcers. a randomized controlled trial. *Ann Vasc Surg.* 2022 May;82:165-171.
- Huang K, et al. Platelet-rich plasma versus corticosteroid injections in the management of elbow epicondylitis and plantar fasciitis: an updated systematic review and meta-analysis. *Am J Sports Med.* 2020 Aug;48(10):2572-2585.
- Ji-jun H, et al. Efficacy of using platelet-rich plasma in spinal fusion surgery-a preferred reporting items for systematic reviews and meta-analyses-compliant meta-analysis. *World Neurosurg.* 2020 Jul;139:e517-e525.
- Lawlor DK, et al. The role of platelet-rich plasma in inguinal wound healing in vascular surgery patients. *Vasc Endovascular Surg.* 2011 Apr;45(3):241-5.
- Li F, et al. Effect of platelet-rich plasma injections on pain reduction in patients with temporomandibular joint osteoarthrosis: a meta-analysis of randomized controlled trials. *J Oral Facial Pain Headache.* 2020 Spring;34(2):149-156.
- Luo P, et al. How to choose platelet-rich plasma or hyaluronic acid for the treatment of knee osteoarthritis in overweight or obese patients: a meta-analysis. *Pain Res Manag.* 2020 Mar 10;2020:7587936.
- Martí-Carvajal AJ, et al. Growth factors for treating diabetic foot ulcers. *Cochrane Database of Systematic Reviews.* 2015 Oct;10:CD008548.
- Mohammadi Tofigh A, Tajik M. Comparing the standard surgical dressing with dehydrated amnion and platelet-derived growth factor dressings in the healing rate of diabetic foot ulcer: A randomized clinical trial. *Diabetes Res Clin Pract.* 2022 Mar;185:109775.
- Nolan GS, Smith OJ, Heavey S, Jell G, Mosahebi A. Histological analysis of fat grafting with platelet-rich plasma for diabetic foot ulcers-A randomized controlled trial. *Int Wound J.* 2022 Feb;19(2):389-398.

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Qu W, et al. Platelet-rich plasma for wound care in the Medicare population. Technology assessment program project ID 040-353-492. Rockville, MD: Agency for Healthcare Research and Quality [Internet]. 2020 Sep. [accessed 2024 Dec 17]. Available from: <http://www.ahrq.gov/research/findings/ta/index.html>

Shetty S, et al. Platelet-rich plasma has better long-term results than corticosteroids or placebo for chronic plantar fasciitis: randomized controlled trial. J Foot Ankle Surg. 2019 Jan;58(1):42-46.

Smith ME, et al. Pressure ulcer treatment strategies: a systematic comparative effectiveness review. Ann Intern Med. 2013 Jul 2;159(1):39-50.

Smith OJ, et al., Fat grafting and platelet-rich plasma for the treatment of diabetic foot ulcers: A feasibility-randomized controlled trial. Int Wound J. 2020 Dec; 17(6): 1578-1594.

U.S. Food and Drug Administration. Guidance for Industry: Chronic Cutaneous Ulcer and Burn Wounds -- Developing Products for Treatment [Internet]. 2006 June [accessed 2024 Dec 17]. Available from: <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm071324.pdf>

Wu Q, et al. Platelet-rich plasma versus hyaluronic acid in knee osteoarthritis: a meta-analysis with the consistent ratio of injection. J Orthop Surg (Hong Kong). Jan-Apr 2020;28(1):2309499019887660.

Xie J, et al. Autologous platelet-rich gel for the treatment of diabetic sinus tract wounds: a clinical study. J Surg Res. 2020 Mar;247:271-279.

Yilmaz, G and Tanrikulu, Y. Short-term results of platelet-rich plasma in the treatment of chronic anal fissure: randomized controlled clinical study. Dis Colon Rectum. 2021; 64(6): 714-723.

Zhao Z, et al. Different intra-articular injections as therapy for hip osteoarthritis: a systematic review and network meta-analysis. Arthroscopy. 2020 May;36(5):1452-1464.e2.

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.

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- 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	<ul style="list-style-type: none">• Annual update, policy intent unchanged.
01/01/25	<ul style="list-style-type: none">• Summary of changes tracking implemented.
10/18/01	<ul style="list-style-type: none">• Original effective date