02-10000-09

Original Effective Date: 12/15/02

Reviewed: 04/26/24

Revised: 05/15/24

Subject: Platelet-Derived Growth Factors and Platelet-Rich Plasma

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

A variety of growth factors have been found to play a role in wound healing, including platelet-derived growth factor (PDGF), epidermal growth factor, fibroblast growth factors, transforming growth factors, and insulin-like growth factors. Autologous platelets are a rich source of PDGF, transforming growth factors (that function as a mitogen for fibroblasts, smooth muscle cells, and osteoblasts), and vascular endothelial growth factors. Recombinant PDGF also has been extensively investigated for clinical use in wound healing.

Autologous platelet concentrate suspended in plasma, also known as platelet-rich plasma (PRP), can be prepared from samples of centrifuged autologous blood. Exposure to a solution of thrombin and calcium chloride degranulates platelets, releasing various growth factors, and results in the polymerization of fibrin from fibrinogen, creating a platelet gel. The platelet gel can then be applied to wounds or may be used as an adjunct to surgery to promote hemostasis and accelerate healing. In the operating room setting, PRP has been investigated as an adjunct to a variety of periodontal, reconstructive, and orthopedic procedures. For example, bone morphogenetic proteins are a type of transforming growth factor, and therefore PRP has been used in conjunction with bone-replacement grafting (using either autologous grafts or bovine-derived xenograft) in periodontal and maxillofacial surgeries.

Becaplermin gel (Regranex®), a recombinant (genetic recombination) PDGF product, has been approved by the U.S. Food and Drug Administration (FDA) for the following indications: "Regranex Gel is indicated for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply. When used as an adjunct to, and not a substitute for, good ulcer care practices including initial sharp debridement, pressure relief and infection control, Regranex Gel increases the complete healing of diabetic ulcers. The efficacy of Regranex Gel for the treatment of diabetic neuropathic ulcers that do not extend through the dermis into subcutaneous

tissue or ischemic diabetic ulcers has not been evaluated." In 2008, the manufacturer added the following black box warning to the labeling for Regranex: "An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of Regranex Gel in a postmarketing retrospective cohort study. Regranex Gel should only be used when the benefits can be expected to outweigh the risks. Regranex Gel should be used with caution in patients with known malignancy."

POSITION STATEMENT:

Recombinant platelet-derived growth factor (i.e. becaplermin® gel) **meets the definition of medical necessity** when used as an adjunct to standard wound management for the following indications:

- Neuropathic diabetic ulcers extending into the subcutaneous tissue
- Pressure ulcers extending into the subcutaneous tissue.

Candidates for becaplermin gel for the treatment of neuropathic diabetic ulcers **meet the definition of medical necessity** when **ALL** of the following criteria are met:

- Adequate tissue oxygenation, as measured by a transcutaneous partial pressure of oxygen of 30mm Hg or greater on the foot dorsum or at the margin of the ulcer;
- Full-thickness ulcer (stage III or IV) extending through dermis into subcutaneous tissues; **AND**
- Participation in a wound management program, which includes sharp debridement, pressure relief (ie, non–weight bearing), and infection control.

Candidates for becaplermin gel for the treatment of pressure ulcers **meet the definition of medical necessity** when **ALL** of the following criteria are met:

- Full-thickness ulcer (i.e., Stage III or IV), extending through dermis into subcutaneous tissues;
- Ulcer in an anatomic location that can be offloaded for the duration of treatment;
- Albumin concentration is greater than 2.5 dL;
- Total lymphocyte count is greater than 1,000/μL; **AND**
- Normal values of vitamins A and C.

All other applications of recombinant platelet-derived growth factor (i.e.becaplermin) are considered **experimental or investigational**, including, but not limited to ischemic ulcers, venous stasis ulcers, and ulcers not extending through the dermis into the subcutaneous tissue. The evidence is insufficient to determine the effects of the technology on health outcomes.

The use of platelet-rich plasma (i.e. autologous blood-derived preparations) is considered **experimental or investigational** for the treatment of acute or chronic wounds, including surgical wounds and nonhealing ulcers. The evidence is insufficient to determine the effects of the technology on health outcomes.

Use of platelet-rich plasma is considered **experimental or investigational** for all orthopedic indications. This includes, but is not limited to, use in the following situations:

Primary use (injection) for the following conditions:

- Achilles tendinopathy
- Lateral epicondylitis
- Osteochondral lesions
- Osteoarthritis
- Plantar fasciitis.

Adjunctive use in the following surgical procedures:

- Anterior cruciate ligament reconstruction
- Hip fracture
- Long-bone nonunion
- Patellar tendon repair
- Rotator cuff repair
- Spinal fusion
- Subacromial decompression surgery
- Total knee arthroplasty.

The evidence is insufficient to determine the effects of the technology on health outcomes.

BILLING/CODING INFORMATION:

CPT Coding:

0232T	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed (**Investigational**)

HCPCS Coding:

G0460	Autologous platelet rich plasma for non-diabetic chronic wounds/ulcers, including phlebotomy, centrifugation, and all other preparatory procedures, administration and dressings, per treatment **(Investigational)**
G0465	Autologous platelet rich plasma (prp) for diabetic chronic wounds/ulcers, using an fda-cleared device (includes administration, dressings, phlebotomy, centrifugation, and all other preparatory procedures, per treatment) (**Investigational**)
P9020	Platelet rich plasma, each unit **(Investigational)**
S0157	Becaplermin gel 0.01%, 0.5 gm
S9055	Procuren or other growth factor preparation to promote wound healing (**Investigational**)

ICD-10 Diagnosis Codes That Support Medical Necessity for S0157:

E10.40 – E10.49 E10.621- E10.622	Type 1 diabetes mellitus with complications
E11.40 – E11.49	Type 2 diabetes mellitus with complications

E11.621- E11.622	
E13.40 – E13.49 E13.621- E13.622	Other specified diabetes mellitus with complications
L89.000- L89.95	Pressure Ulcer
L97.101-L97.929	Non-pressure chronic ulcer of lower limb, not elsewhere classified
L98.491 – L98.499	Non-pressure chronic ulcer of skin, not elsewhere classified

REIMBURSEMENT INFORMATION:

Refer to sections entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: The following National Coverage Determination (NCD) was reviewed on the last guideline reviewed date: Blood-Derived Products for Chronic Non-Healing Wounds (270.3) located at cms.gov.

The following Local Coverage Determination (LCD) was reviewed on the last guideline reviewed date: Platelet Rich Plasma (L39071) located at fcso.com.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

None applicable.

OTHER:

None applicable

REFERENCES:

1. Agency for Healthcare Research and Quality (AHRQ), Guideline for Management of Wounds in Patients with Lower-Extremity Neuropathic Disease, last updated 12/08, accessed at guideline.gov on 08/06/09.
2. Agency for Healthcare Research and Quality (AHRQ), Treatment of Pressure Ulcers, December 1994 accessed at ncbi.nlm.nih.gov on 09/02/08.

3. American Academy of Orthopaedic Surgeons. Management of Osteoarthritis of the Knee (Non-Arthroplasty). 2021; located at aaos.org.
4. American Academy of Orthopaedic Surgeons A. Management of Osteoarthritis of the Hip - Evidence-Based Clinical Practice Guideline. 2017; located at aaos.org.
5. Association for the Advancement of Wound Care (AAWC). AAWC Guideline: Pressure Ulcer, located at aawconline.org.
6. Association for the Advancement of Wound Care (AAWC). AAWC Venous Ulcer Guideline, located at aawconline.org.
7. Bloomgarden Z, The Diabetic Foot, The American Diabetes Association, Diabetes Care 31: 372-376, 2008 accessed at diabetes.org on 08/03/09.
8. Blue Cross Blue Shield Association Evidence Positioning System®; 2.01.16 Recombinant and Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Conditions; 02/24.
9. Blue Cross Blue Shield Association Evidence Positioning System®; 2.01.98 Orthopedic Applications of Platelet-Rich Plasma, 05/22.
10. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Becaplermin for wound healing. TEC Assessments. 1999;Volume 14:Tab 5.
11. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Growth factors for wound healing. TEC Evaluations. 1992;7:352-377.
12. Centers for Medicare & Medicaid Services (CMS), National Coverage Determination (NCD) for Blood-Derived Products for Chronic Non-Healing Wounds (270.3), accessed at cms.gov.
13. Del Pino-Sedeno T, Trujillo-Martin MM, et al. Platelet-rich Plasma for the Treatment of Diabetic Foot Ulcers: A Meta-Analysis. Wound Repair Regen, 2019 Mar;27(2):170-182.PMID 30575212.
14. Dougherty EJ, An Evidence-Based Model Comparing the Cost-Effectiveness of Platelet-Rich Plasma Gel to Alternative Therapies for Patients with Nonhealing Diabetic Foot Ulcers, Adv Skin Wound Care, 2008 Dec; 21(12): 568-75.
15. First Coast Service Options, Inc. Local Coverage Determination (LCD) Platelet Rich Plasma (L39071), accessed at fcso.com
16. Han SK, Kim DW, Jeong SH, et al, Potential Use of Blood Bank Platelet Concentrates to Accelerate Wound Healing of Diabetic Ulcers, Ann Plast Surg. 2007 Nov; 59(5): 532-7.
17. Hom DB, Linzie BM, Huang TC, The Healing Effects of Autologous Platelet Gel on Acute Human Skin Wounds, Arch Facial Plast Surg. 2007 May-Jun; 9(3): 174-83.
18. Huang Y, Liu X, et al. Intra-articular injections of platelet-rich plasma, hyaluronic acid or corticosteroids for knee osteoarthritis : A prospective randomized controlled study. Orthopade. 2019 Mar;48(3). PMID 30623236.
19. Kazakos K, Lyras DN, Verettas D, et al, The Use of Autologous PRP Gel as an Aid in the Management of Acute Trauma Wounds, Injury, 2008 Aug 12.
20. Kubota G, Kamoda H, et al. Platelet-rich plasma enhances bone union in posterolateral lumbar fusion: A prospective randomized controlled trial. Spine J. 2019 Feb;19(2). PMID 28735763.
21. Lacci KM, Dardik A, Platelet-Rich Plasma: Support for Its Use in Wound Healing, Yale J Biol Med, Mar 2010.
22. Li Y, Gao Y, et al. Autologous Platelet-Rich Gel Treatment for Diabetic Chronic Cutaneous Ulcers: A Meta-Analysis of Randomized Controlled Trials. J Diabetes, 2019 May;11(5):359-369.PMID 30182534.

23. Miller LE, Parrish WR, Roides B, et al. Efficacy of platelet-rich plasma injections for symptomatic tendinopathy: systematic review and meta-analysis of randomised injection-controlled trials. BMJ Open Sport Exerc Med. Nov 6 2017;3(1):e000237.
24. Mishra A, Woodall J, Vieira A, Treatment of Tendon and Muscle Using Platelet-Rich Plasma, Clin Sports Med 28 pg 113-125, 08/07/08.
25. National Institute for Health and Clinical Excellence (NICE). Diabetic foot problems: prevention and management [NG19]. 2016; accessed at nice.org.
26. National Institute for Health and Care Excellence (NICE). Platelet-rich plasma injections for knee osteoarthritis Interventional procedures guidance [IPG637], 2019; accessed at nice.org.
27. Papanas N, Maltezos E, Becaplermin Gel in the Treatment of Diabetic Neuropathic Foot Ulcers, Clin Interv Aging, 2008; 3(2): 233-40.
28. Peerbooms JC, Lodder P, et al. Positive Effect of Platelet-Rich Plasma on Pain in Plantar Fasciitis: A Double-Blind Multicenter Randomized Controlled Trial. Am J Sports Med. 2019 Nov;47(13). PMID 31603721.
29. Qaseem A, Humphrey LL, Forciea MA, et al. Treatment of pressure ulcers: a clinical practice guideline from the American College of Physicians. Ann Intern Med. Mar 03 2015;162(5):370-379.
30. Rabago D, Best TM, Zgierska AE, et al, A Systematic Review of Four Injection Therapies for Lateral Epicondylosis: Prolotherapy, Polidocanol, Whole Blood and Platelet-Rich Plasma, Br J Sports Med, July 2009; 43(7): 471-81.
31. Snow M, Hussain F, et al. The Effect of Delayed Injection of Leukocyte-Rich Platelet-Rich Plasma Following Rotator Cuff Repair on Patient Function: A randomized Double-Blind Controlled Trial. Arthroscopy. 2020 Mar;36(3):648-657. PMID 31784365.
32. U.S. Food and Drug Administration (FDA); accessed at fda.gov.
33. Yeung CY, Hsieh PS, et al. Efficacy of Lyophilised Platelet-Rich Plasma Powder on Healing Rate in Patients With Deep Second Degree Burn Injury: A Prospective Double-Blind Randomized Clinical Trial. Ann Plast Surg. 2018 Feb;80(2S Suppl 1):S66-S69. PMID: 29369904.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 04/26/24.

GUIDELINE UPDATE INFORMATION:

12/15/02	Reformat, review & revision of original Medical Coverage Guideline (11/91).
12/15/03	Scheduled review and revision of guideline; consisting of updated references.
12/15/04	Scheduled review and revision of guideline; consisting of updated references.
01/01/06	Scheduled review; maintain current coverage.
10/15/06	Scheduled review; maintain current coverage.
07/15/07	Scheduled review; current coverage maintained; reformatted guideline, references updated.
10/15/08	Annual review: position statements maintained; description section and references updated.
09/15/09	Annual review: position statements maintained; description section and references updated.

07/01/10	Annual review: position statements maintained; references updated. 3rd quarter HCPCS coding update: added CPT code 0232T.
10/15/10	Revision; related ICD-10 codes added.
01/01/11	Annual HCPCS coding update. Revised 0232T.
08/03/12	Revision; Medicare Program exception updated.
10/15/12	Coding section updated.
07/01/13	Quarterly HCPCS update. Added G0460. Revised Program Exception section.
10/01/15	Revision; ICD9 & ICD10 coding sections updated.
11/01/15	Revision: ICD-9 Codes deleted.
06/15/17	Revision; Guideline title, position statements, coding, and references updated.
07/15/18	Review; title, position statements, coding, and references updated.
06/15/20	Review; Position statements maintained and references updated.
01/01/22	Annual CPT/HCPCS coding update. Code G0465 added; G0460 revised.
06/15/22	Review: Position statements maintained; references updated.
05/23/23	Update to Program Exceptions section.
05/15/24	Position statements maintained; program exception and references updated.