

Corporate Medical Policy

Growth Factors in Wound Healing

File Name:	growth_factors_in_wound_healing
Origination:	4/1993
Last CAP Review:	11/2018
Next CAP Review:	11/2019
Last Review:	11/2018

Description of Procedure or Service

This policy addresses the use of blood-derived growth factors, including recombinant platelet-derived growth factors and platelet rich plasma, as a treatment of wounds or other musculoskeletal conditions, including but not limited to adjunctive use in surgical procedures and treatment of diabetic ulcers, pressure ulcers, venous stasis ulcers, lateral epicondylitis (i.e., tennis elbow), plantar fasciitis, or Dupuytren's contracture.

A variety of growth factors have been found to play a role in wound healing, including platelet-derived growth factors (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 has also 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 the 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, platelet-rich plasma 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 thus platelet-rich plasma has been used in conjunction with bone-replacement grafting (using either autologous grafts or bovine-derived xenograft) in periodontal and maxillofacial surgeries. Alternatively, platelet-rich plasma may be injected directly into the tissue. Platelet-rich plasma has also been proposed as a primary treatment of miscellaneous conditions, such as epicondylitis, plantar fasciitis, and Dupuytren's contracture. Injection of platelet-rich plasma for tendon and ligament pain is theoretically related to prolotherapy. However, prolotherapy involves injection of chemical irritants that are intended to stimulate inflammatory responses and induce release of endogenous growth factors.

Platelet-rich plasma is distinguished from fibrin glues or sealants, which have been used for many years as a surgical adjunct to promote local hemostasis at incision sites. Fibrin glue is created from platelet-poor plasma, and consists primarily of fibrinogen. Commercial fibrin glues are created from pooled homologous human donors; Tisseel® (Baxter) and Hemaseel® (Haemacure Corp) are examples of commercially available fibrin sealants. Autologous fibrin sealants can be created from platelet-poor plasma. This policy does not address the use of fibrin sealants.

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WOUND CLOSURE OUTCOMES

For the purposes of this review, the primary end points of interest for studies of wound closure are as follows, consistent with guidance from the U.S. Food and Drug Administration for industry in developing products for treatment of chronic cutaneous ulcer and burn wounds:

1. Incidence of complete wound closure.
2. Time to complete wound closure (reflecting accelerated wound closure).
3. Incidence of complete wound closure following surgical wound closure.
4. Pain control

Regranex®

In 1997, becaplermin gel (Regranex®; Smith & Nephew), a recombinant platelet-derived growth factor product, was approved by the U.S. Food and Drug Administration (FDA) for the following labeled indication: "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 this 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 post-marketing 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."

The U.S. Food and Drug Administration (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 (CFR) title 21, parts 1270 and 1271. Blood products such as platelet-rich plasma (PRP) are included in these regulations. 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, FDA has not attempted to regulate activated PRP.

A number of PRP preparation systems are available, many of which were cleared for marketing by FDA through the 510(k) process for producing platelet-rich preparations intended to be mixed with bone graft materials to enhance the bone grafting properties in orthopedic practices. The use of PRP outside of this setting (e.g., an office injection) would be considered off-label. The Aurix™ System (previously AutoloGel™; Cytomedix) and SafeBlood® (SafeBlood Technologies) are two related but distinct autologous blood-derived preparations that can be prepared at the bedside for immediate application. Both Aurix and SafeBlood have been specifically marketed for wound healing. Other devices may be used in the operating room setting, such as Medtronic Electromedics Elmd-500 Autotransfusion system, the Plasma Saver device, or the Smart PreP device. The Magellan Autologous Platelet Separator System® (Medtronic) includes a disposable kit designed for use with the Magellan Autologous Platelet Separator portable tabletop centrifuge. BioMet Biologics received marketing clearance through the FDA's 510(k) process for a gravitational platelet separation system (GPS®II), which uses a disposable separation tube for centrifugation and a dual cannula tip to mix the platelets and thrombin at the surgical site. Filtration or plasmapheresis may also be used to produce platelet-rich concentrates. The use of different devices and procedures can lead to variable concentrations of active platelets and associated proteins, increasing variability between studies of clinical efficacy.

Related Policies

Prolotherapy

Bone Morphogenetic Protein

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

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Policy

BCBSNC will provide coverage for Growth Factors in Wound Healing when it is medically necessary because the medical criteria and guidelines below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Growth Factors in Wound Healing are covered

Recombinant platelet-derived growth factor (i.e., becaplermin) may be considered **medically necessary** 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

(See Policy Guidelines section below for further information regarding patient selection criteria.)

When Growth Factors in Wound Healing are not covered

Other applications of recombinant platelet-derived growth factor (i.e., becaplermin) are considered **investigational**, including, but not limited to, ischemic ulcers, venous stasis ulcers, and ulcers not extending through the dermis into the subcutaneous tissue.

Use of autologous blood-derived preparations (i.e., platelet-rich plasma) is considered **investigational**. This includes, but is not limited to, use in the following situations:

- Treatment of acute or chronic wounds including surgical wounds and non-healing ulcers
- Adjunctive use in the following surgical procedures:
 - ACL reconstruction
 - Hip fracture
 - Long-bone nonunion
 - Patellar tendon repair
 - Rotator cuff repair
 - Spinal fusion
 - Subacromial decompression surgery
 - Total knee arthroplasty
- Primary use (injection) for other conditions such as Achilles tendinopathy, lateral epicondylitis (i.e., tennis elbow), osteochondral lesions, plantar fasciitis, osteoarthritis, or Dupuytren's contracture.

Policy Guidelines

Appropriate candidates for becaplermin gel for treatment of neuropathic ulcers should meet ALL of the following criteria:

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

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Appropriate candidates for becaplermin gel for the treatment of pressure ulcers should meet ALL of the following criteria:

1. Full-thickness ulcer (i.e., Stage III or IV), extending through dermis into subcutaneous tissues
2. Ulcer in an anatomic location that can be off-loaded for the duration of treatment
3. Albumin concentration >2.5 dL
4. Total lymphocyte count >1,000 μ L
5. Normal values of vitamins A and C

Patients are typically treated once daily for up to 20 weeks or until complete healing. Application of the gel may be performed by the patient in the home.

Summary

For individuals who have diabetic lower-extremity ulcers or pressure ulcers who receive recombinant PDGF, the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. Results have shown improved rates of healing with use of recombinant PDGF for diabetic neuropathic ulcers and pressure ulcers. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have venous stasis leg ulcers or acute surgical or traumatic wounds who receive recombinant PDGF, the evidence includes small RCTs. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. The level of evidence does not permit conclusions whether recombinant PDGF is effective in treating other wound types, including chronic venous ulcers or acute traumatic wounds. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have chronic wounds or acute traumatic or surgical wounds who receive PRP, the evidence includes a number of small controlled trials. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. Current results of trials using PRP are mixed and the studies are limited in both size and quality. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with tendinopathy who receive PRP injections, the evidence includes multiple RCTs and systematic reviews with meta-analyses. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Findings from meta-analyses of RCTs were mixed and generally found that PRP did not have a statistically and/or clinically significant impact on symptoms (i.e., pain) or functional outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with non-tendon soft tissue injury or inflammation (e.g., plantar fasciitis) who receive PRP injections, the evidence includes three small RCTs, multiple prospective observational studies, and one systematic review. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The systematic review, which identified three RCTs on PRP for plantar fasciitis, did not pool study findings. Results among the three RCTs were inconsistent. The largest RCT showed that treatment with PRP compared to corticosteroid injection resulted in statistically significant but temporary improvements in American Orthopaedic Foot and Ankle Society Ankle-Hindfoot Scale scores, indicating improved outcomes. Confirmation of these results in larger double-blind RCTs is needed to allow greater certainty regarding the efficacy of PRP in plantar fasciitis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with osteochondral lesions who receive PRP injections, the evidence includes an open-labeled quasi-randomized study. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The quasi-randomized study found a statistically significantly greater impact on outcomes in the PRP group than in the

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group that received hyaluronic acid. Limitations of the evidence base include lack of adequately randomized studies, lack of blinding, lack of sham controls and comparison only to an intervention of uncertain efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with knee or hip osteoarthritis (OA) who receive PRP injections, the evidence includes multiple RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Three RCTs have compared PRP with placebo while other trials have compared PRP with hyaluronic acid for knee OA. A meta-analysis of three trials comparing PRP with placebo showed a significant improvement in functional scores. However, only one of the trials was considered at low risk of bias. Comparisons between PRP and hyaluronic acid have shown inconsistent results. A meta-analysis including only low risk of bias trials showed no difference between the two treatments in functional scores. Also, using hyaluronic acid as a comparator is questionable, because the evidence demonstrating the benefit of hyaluronic acid treatment for OA is not robust. The single RCT evaluating hip OA reported statistically significant reductions in visual analog scale scores for pain, with no difference in functional scores. Additional studies comparing PRP to placebo and to alternatives other than hyaluronic acid are needed to determine the efficacy of PRP for knee and hip osteoarthritis. Further studies are also needed to determine the optimal protocol for delivering PRP. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with anterior cruciate ligament reconstruction who receive PRP injections plus orthopedic surgery, the evidence includes two systematic reviews of multiple RCTs and prospective studies. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. Only one of the two systematic reviews conducted a meta-analysis; it showed that adjunctive PRP treatment did not result in significant effect on International Knee Documentation Committee scores, a patient-reported, knee-specific outcome measure that assesses pain and functional activity. Individual trials have shown mixed results. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with hip fracture who receive PRP injections plus orthopedic surgery, the evidence includes one open-labeled RCT. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. The single open-labeled RCT failed to show a statistically significant reduction in the need for surgical revision with the addition of PRP treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with long bone nonunion who receive PRP injections plus orthopedic surgery, the evidence includes three RCTs. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. One trial with substantial risk of bias failed to show significant differences in patient-reported or clinician-assessed functional outcome scores between those who received PRP plus allogenic bone graft and those who received only allogenic bone graft. While the trial showed a statistically significant increase in the proportion of bones that healed in patients receiving PRP in a modified intention-to-treat (ITT) analysis, the results were not different in the ITT analysis. The second RCT, which compared PRP with recombinant human bone morphogenetic protein-7 (rhBMP-7), also failed to show any clinical or radiologic benefits of PRP over rhBMP-7. The third RCT reported no difference in the number of unions or time to union in patients receiving PRP injections compared with no treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with rotator cuff repair who receive PRP injections plus orthopedic surgery, the evidence includes multiple RCTs and systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization,

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and treatment-related morbidity. The systematic reviews and meta-analyses failed to show statistically and/or clinically significant impact on symptoms (i.e., pain) or functional outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with spinal fusion who receive PRP injections, the evidence includes two controlled prospective studies. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. The two studies failed to show any statistically significant differences in fusion rates between the PRP arm and the control arm. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with subacromial decompression surgery who receive PRP injections plus orthopedic surgery, the evidence includes one small RCT. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. A single small RCT failed to show reduced self-assessed or physician-assessed spinal instability scores with PRP injections. However, subjective pain, use of pain medications, and objective measures of range of motion showed clinically significant improvements with PRP. Larger trials are required to confirm these benefits. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with total knee arthroplasty who receive PRP injections plus orthopedic surgery, the evidence includes one small RCT. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, morbid events, resource utilization, and treatment-related morbidity. The RCT showed no significant differences between the PRP and untreated control groups in terms of bleeding, range of motion, swelling around the knee joint, muscle power recovery, pain, or Knee Society Score and Knee Injury and Osteoarthritis Outcome Score. The evidence is insufficient to determine the effects of the technology on health outcomes.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable Codes: G0460, P9020, S0157, S9055, 0232T, 0481T

Code 0232T should not be reported with 20550-20551, 20600, 20604, 20605, 20606, 20610, 20926, 76942, 77002, 77012, 77021, 86965.

Code 20926 should not be billed for application of recombinant or autologous platelet-derived growth factors.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual - 3/96

Medical Policy Advisory Group - 1/99

BCBSA Medical Policy Reference Manual - 7/99

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USPDI, 1999, Volume 1, 19th Edition, p. 550-551

Medical Policy Advisory Group - 12/99

Specialty Matched Consultant Advisory Panel - 10/2000

Medical Policy Advisory Group - 10/2000

BCBSA Medical Policy Reference Manual; Policy 2.01.16; Review date 7/12/02

Specialty Matched Consultant Advisory Panel - 8/2002

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 7/17/03.

ECRI. Platelet Gel for Chronic, Nonhealing Wounds [Hotline Request]. 2003/11/05 retrieved on 7/2/04 from

http://www.ta.ecri.org/Hotline/Prod/summarydetail.aspx?doc_id=7793&q=%22Growth+Factors&nm
Specialty Matched Consultant Advisory Panel - 8/2004

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 11/9/04

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 9/27/05

Specialty Matched Consultant Advisory Panel - 8/2006

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 4/17/07

FDA Update of Safety Review. Follow-up to the March 27, 2008, Communication about the Ongoing Safety Review of Regranex (becaplermin). June 6, 2008. Retrieved on July 11, 2008 from

http://www.fda.gov/cder/drug/early_comm/becaplermin_update_200806.htm

FDA Updated labeling for Regranex. Retrieved on July 11, 2008

from http://www.fda.gov/cder/drug/infopage/becaplermin/regranex_cbe_lbl.pdf

Specialty Matched Consultant Advisory Panel - 9/4/08

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 11/12/2009

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 4/14/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 4/12/2012

Specialty Matched Consultant Advisory Panel - 12/2012

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 4/11/13

Specialty Matched Consultant Advisory Panel – 11/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 5/22/14

Specialty Matched Consultant Advisory Panel – 11/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 5/21/15

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.98, 5/21/15

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Specialty Matched Consultant Advisory Panel – 11/2015

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 1/14/16

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.98, 4/14/16

Specialty Matched Consultant Advisory Panel – 11/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 1/12/17

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.98, 4/13/17

Specialty Matched Consultant Advisory Panel – 11/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 1/11/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.98, 4/12/2018

Specialty Matched Consultant Advisory Panel – 11/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.16, 1/17/2019

Policy Implementation/Update Information

12/92	Evaluated: Investigational
7/96	Reaffirmed: National Association reviewed 3/96. No changes.
1/99	Reaffirmed: Medical Policy Advisory Group
8/99	Reformatted, Medical Term Definitions added
12/99	Medical Policy Advisory Group
10/00	Specialty Matched Consultant Advisory Panel review. No change recommended in criteria. System coding changes. Medical Policy Advisory Group review. No change in criteria. Approve. See Also: Keratinocyte Allografts
11/01	Coding format change.
0/02	Specialty Matched Consultant Advisory Panel review 8/15/02. New policy statement on becaplermin gel for treatment of pressure ulcers under "When Growth Factors for Wound Healing are Covered". Under when not covered, removed "pressure ulcers" from third bullet. Added codes S0157 and S9055. System coding changes. See Also: Bioengineered Skin for Treatment of Skin Ulcers (Name of Keratinocyte Allografts policy changed)
4/04	Benefits Application and Billing/Coding sections updated for consistency. Corrected references to match file name in policy.
9/9/04	Specialty Matched Consultant Advisory Panel review. No changes to criteria. Description section updated to add information regarding Autologel, Safeblood and chronic non-

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healing ulcers. Added "See Also: Bioengineered Skin for Treatment of Skin Ulcers (Name of Keratinocyte Allografts policy changed)" to Policy Implementation/Update Information section following 10/02 entry.

- 11/27/06 Description section revised. Under When Covered #1-adequate tissue oxygenation may be determined by transcutaneous partial pressure of oxygen or "an ankle-brachial index (ABI) of 0.7 or greater, or if an ABI is not obtainable, then a toe pressure of 40 or greater". Under When Not Covered added "Autologous blood-derived preparations (i.e., platelet-rich plasma) are considered investigational as a primary procedure for other miscellaneous conditions including, but not limited to, epicondylitis (i.e., tennis elbow), plantar fasciitis, or Dupuytren's contracture." Medical Terms and Reference sources added. (pmo)
- 10/6/08 Description section updated to include FDA indications for Regranex Gel and recently added Black Box Warning. Reference sources added. Specialty Matched Consultant Advisory Panel review 9/4/08. No changes to criteria. (pmo)
- 4/13/2010 Description section revised. Revised section "When not covered" to include "Autologous blood-derived preparations (i.e., platelet-rich plasma) are considered investigational as a primary procedure for other miscellaneous conditions including, but not limited to: Treatment of acute or chronic wounds including non-healing ulcers, Adjunctive use in surgical procedures, Primary use (injection) for other conditions such as epicondylitis (i.e., tennis elbow), plantar fasciitis, or Dupuytren's contracture" Policy Guidelines updated. Resource added. (mco)
- 6/22/2010 Policy Number(s) removed (amw)
- 8/31/2010 Coding update. CPT 0232T added to Billing/Coding section. (adn)
- 12/21/10 Description section extensively revised. Specific criteria in the Covered/Not Covered sections and in the Policy Guidelines were rearranged for clarity. Intent of policy is unchanged. Specialty Matched Consultant Advisory Panel review 11/29/10. Policy accepted as drafted. (adn)
- 12/20/11 Added coding instructions to Billing/Coding section. No change to policy statement or coverage criteria. Specialty Matched Consultant Advisory Panel review 11/30/10. (adn)
- 1/1/13 Reference added. Specialty Matched Consultant Advisory Panel review 12/4/12. No change to policy statement. (sk)
- 7/1/13 Medical Director review. Reference added. Summary statement added. Codes G0460 and P9020 added to Billing/Coding section. No change to policy statement. (sk)
- 1/14/14 Specialty Matched Consultant Advisory Panel review 11/20/13. No change to Policy statement. (sk)
- 7/29/14 Reference added. Information on Augment Bone Graft added to Description section. No change to Policy statement. (sk)
- 12/9/14 Specialty Matched Consultant Advisory Panel review 11/24/14. No change to Policy statement. (sk)
- 12/30/14 Replaced 20600-20610 in Billing/Coding section with codes 20604, 20605, 20606, 20610, and 20611. Codes 20604, 20606, and 20611 effective date 1/1/2015. (sk)

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- 7/1/15 References added. Section titled, “When Growth Factors in Wound Healing are not Covered”, updated for clarity. No change to Policy intent. (sk)
- 12/30/15 Surgical wounds, total knee arthroplasty, and osteoarthritis added to list of investigational uses. Specialty Matched Consultant Advisory Panel review 11/18/2015. (sk)
- 4/1/16 Reference added. Policy Guidelines updated. (sk)
- 12/30/16 Reference added. Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 11/30/2016. (sk)
- 3/31/17 Reference added. Wound Closure Outcomes added to Description section. (sk)
- 6/30/17 Reference added. Policy Guidelines extensively revised. No change to coverage criteria. (sk)
- 12/15/17 Specialty Matched Consultant Advisory Panel review 11/29/2017. (sk)
- 12/29/17 Code 0481T added to Billing/Coding section for effective date 1/1/2018. (sk)
- 3/9/18 Reference added. (sk)
- 9/7/18 Reference added. Policy Guidelines updated. (sk)
- 12/14/18 Specialty Matched Consultant Advisory Panel review 11/28/2018. (sk)
- 2/26/19 Reference added. (sk)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.