



MEDICAL COVERAGE GUIDELINES
SECTION: MEDICINE

ORIGINAL EFFECTIVE DATE: 06/23/15
LAST REVIEW DATE: 01/22/19
LAST CRITERIA REVISION DATE: 02/20/18
ARCHIVE DATE:

RECOMBINANT AND AUTOLOGOUS PLATELET-DERIVED GROWTH FACTORS AS A TREATMENT OF WOUND HEALING AND OTHER NON-ORTHOPEDIC CONDITIONS

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

Growth Factors:

Growth factors are proteins that signal cells to divide and grow. Types include platelet-derived growth factor (PDGF), basic fibroblast growth factor (BFGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), transforming growth factor (TGF) and recombinant PDGF.

Regranex® is a recombinant human platelet-derived growth factor. It contains becaplermin and is topically applied. Regranex is FDA approved for treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond that have an adequate blood supply.

Autologous Wound Healing Factors:

Blood is drawn from an individual and centrifuged at high speeds to create an autologous concentrated platelet rich plasma (PRP) that contains a biologically active mixture of growth factors without the potential for an immune response. Autologous wound healing factors have been investigated for the treatment of wounds and non-orthopedic conditions.

There are numerous PRP preparation systems that have been cleared for marketing by the FDA through the 510(k) process. These devices are intended to concentrate an individual's plasma at the point of care during bone grafting procedures. 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.

Wound Definitions:

Stage I: Nonblanchable erythema of intact skin

Stage II: Partial thickness skin loss involving epidermis and/or dermis

Stage III: Full thickness skin loss involving damage or necrosis of subcutaneous tissues that may extend down to, but not through, underlying fascia

Stage IV: Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone, or supporting structures

Chronic: A wound or condition present for at least 30 days despite standard medical and surgical management



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Criteria:

For orthopedic applications of platelet-rich plasma, see BCBSAZ Medical Coverage Guideline #O956, "Orthopedic Applications of Platelet-Rich Plasma".

- Recombinant platelet-derived growth factor (i.e., Regranex) is considered **medically necessary** as an adjunct to standard wound care management with documentation of **ALL** of the following:
 1. **ONE** of the following:
 - Chronic neuropathic diabetic ulcers of the lower extremity extending into the subcutaneous tissue (full thickness, e.g., Stage III or IV)
 - Pressure ulcers extending into the subcutaneous tissue (full thickness, e.g., Stage III or IV)
 2. Adequate blood/tissue oxygenation supply
 3. Participation in a wound care program, which includes initial sharp debridement, pressure relief and infection control
- Recombinant platelet-derived growth factor (i.e., Regranex) for all other indications not previously listed or if above criteria not met is considered **experimental or investigational** based upon:
 1. Lack of final approval from the Food and Drug Administration, and
 2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
 3. Insufficient evidence to support improvement of the net health outcome, and
 4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

These indications include, *but are not limited to*:

- Ischemic ulcers
- Venous stasis ulcers
- Ulcers not extending through the dermis into the subcutaneous tissue



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Criteria: (cont.)

- Use of autologous wound healing factors (i.e., platelet rich plasma) for all indications is considered **experimental or investigational** based upon:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

These indications include, *but are not limited to*:

- Treatment of acute or chronic wounds
 - Treatment of surgical wounds
 - Treatment of nonhealing ulcers
- Platelet rich plasma (PRP) preparation systems used to prepare autologous wound healing factors are considered **experimental or investigational** based upon:
 1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
 2. Insufficient evidence to support improvement of the net health outcome, and
 3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.



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Resources:

Literature reviewed 02/20/18. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.

1. 2.01.16 BCBS Association Medical Policy Reference Manual. Recombinant and Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Conditions. Re-issue date 01/11/2018, issue date 03/31/96.
2. BCBS Association Technology Assessment Program. Growth Factors for Wound Healing. 11-12/1992 1992.
3. BCBS Association Technology Assessment Program. Becaplermin for Wound Healing. 06/1999 1999;14(5).
4. Bello YM, Phillips TJ. Recent advances in wound healing. *JAMA*. 2000 Feb 9 2000;283(6):716-718.
5. California Technology Assessment Forum. Platelet-rich Plasma Injection for Achilles Tendinopathy. 10/13/2010.
6. Glover JL, Weingarten MS, Buchbinder DS, Poucher RL, Deitrick GAR, Fylling CP. A 4-year outcome-based retrospective study of wound healing and limb salvage in patients with chronic wounds. *Adv Wound Care*. 1997 Jan-Feb 1997;10(1):33-38.
7. Koob TJ, Lim JJ, Masee M, et al. Angiogenic properties of dehydrated human amnion/chorion allografts: therapeutic potential for soft tissue repair and regeneration. *Vasc Cell*. 2014;6:10.
8. Leitner GC, Gruber R, Neumuller J, et al. Platelet content and growth factor release in platelet-rich plasma: a comparison of four different systems. *Vox Sang*. 2006 Aug 2006;91(2):135-139.



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Resources: (cont.)

9. Rees RS, Robson MC, Smiell JM, Perry BH. Becaplermin gel in the treatment of pressure ulcers: a phase II randomized, double-blind, placebo-controlled study. *Wound Repair Regen.* 1999 May-Jun 1999;7(3):141-147.
10. Roukis TS, Zgonis T, Tiernan B. Autologous platelet-rich plasma for wound and osseous healing: a review of the literature and commercially available products. *Adv Ther.* 2006 Mar-Apr 2006;23(2):218-237.
11. Zavadil DP, Satterlee CC, Costigan JM, Holt DW, Shostrom VK. Autologous platelet gel and platelet-poor plasma reduce pain with total shoulder arthroplasty. *J Extra Corpor Technol.* 2007 Sep 2007;39(3):177-182.



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Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1-800-368-1019, 800-537-7697 (TDD). Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nilinígíí Blue Cross Blue Shield of Arizona haada yit'éego bina'idíłkígo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yina'idíłkígo beehaz'áanii hólo díí t'áa hazaadk'ehjí háká a'doowołgo bee haz'ą doo baqah ilinígóó. Ata' halne'ígíí kojį' bich'į' hodíłnih 877-475-4799.

Chinese: 如果您, 或是您正在協助的對象, 有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題, 您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員, 請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون أية تكلفة. للتحدث مع مترجم اتصل بـ 877-475-4799.



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Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulangan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799 로 전화하십시오.

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d'obtenir de l'aide et l'information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizona についてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:

اگر شما، یا کسی که شما به او کمک میکنید، سوال در مورد Blue Cross Blue Shield of Arizona، داشته باشید حق این را دارید که کمک و اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799 [تماس حاصل نمایید.]

Assyrian:

Blue Cross Blue Shield of Arizona، ئه سەن وێرێتێt

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคน หรือคนที่คุณกำลังช่วยเหลือถามเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณสามารถโทรขอความช่วยเหลือและข้อมูลในภาษา ของคุณได้โดยไม่มีค่าใช้จ่าย โปรดยกหมายเลข โทร 877-475-4799