Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: AmeriHealth Caritas Pennsylvania & Keystone First	Submission Date: 7/1/2025
Policy Number: Platelet rich plasma for nonhealing diabetic wounds	Effective Date: 2/2017 Revision Date: 2/2025
Policy Name: ccp.1278	

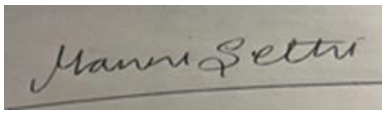
Type of Submission:

☐ New Policy	☒ Prior Authorization Policy
☒ Revised Policy*	☐ Base Policy
☐ Annual Review- no revisions	☐ Experimental/Investigational Policy
	☐ Statewide PDL
	☐ Other:

*All revisions to the policy must be highlighted using track changes throughout the document.

Please provide any clarifying information for the policy below:

Please see track changes below.

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	Signature of Authorized Individual: 

Keystone First
Family of Health Plans

Platelet rich plasma for nonhealing diabetic wounds

Clinical Policy ID: CCP.1278

Recent review date: 2/2025

Next review date: 6/2026

Policy contains: Diabetic wounds; platelet-derived growth factors; platelet rich plasma.

Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First's clinical policies are not guarantees of payment.

Coverage policy

Platelet rich plasma is investigational/not clinically proven and, therefore, not medically necessary for any clinical indication except the following:

- As an adjunct treatment for chronic diabetic wounds, when both criteria are met (Qu, 2020):
  - There is a lack of healing progress with standard wound care (e.g., offloading, infection control, glycemic control, and wound bed preparation including debridement).*
  - Platelet rich plasma is prepared using devices that are U.S. Food and Drug Administration-approved for management of exuding cutaneous wounds, such as diabetic ulcers.

*Note: Generally defined as ulcer reduction of less than 40% after at least four weeks of standard therapy (Wound Healing Society, 2017).

Limitations

Required documentation includes wound history, recurrence, and characteristics (location, staging, size, base, exudates, infection condition of surrounding skin and pain). The rate of wound healing should be evaluated to determine if treatment is optimal (Wound Healing Society, 2017).

The effectiveness of platelet rich plasma for treating chronic non-healing diabetic wounds should be reevaluated at 20 weeks of treatment (Qu, 2020). Continuation of treatment beyond 20 weeks requires secondary medical review.

Alternative covered services

Primary care and specialty physician (including surgical) evaluation and management including:

- Simple analgesics.
- Anti-inflammatory medications.
- Corticosteroid injections.
- Physical or occupational therapy.
- Immobilization.
- Thermal therapy.
- Reducing workload and increasing rest.
- Relaxation and biofeedback techniques.
- Strengthening and conditioning exercises.
- Stretching exercises and therapeutic massage.

Background

Platelets contain hundreds of growth factors important to healing injuries and regenerating tissue (Roffi, 2013). Platelet rich plasma is a blood derivate containing a higher concentration of platelets and a correspondingly higher concentration of growth factors above levels in peripheral blood. Although the mechanism of action is unclear, laboratory studies suggest a correlation between the increased concentration of growth factors in platelet rich plasma and an increase in the native inflammatory healing cascade.

A wide variation of protocols used for standardization and preparation of platelet rich plasma exists (Dhurat, 2014). It may be produced in an autologous manner or homologous manner from blood from multiple donors. The basic protocols involve a two-stage centrifugation process to separate platelets from blood plasma and red blood cells, require intrinsic or exogenous activation of platelet rich plasma to initiate formation of a fibrin network, and ultrasonographic guidance to inject autologous platelet rich plasma into the injured area. Platelet rich plasma may be leukocyte-rich or leukocyte-poor.

The U.S. Food and Drug Administration Center for Biologics Evaluation and Research regulates both the systems used to separate out platelets and the clinical use of platelet rich plasma (21CFR640.34). Nearly all of these systems have received 510(k) clearance for producing platelet rich preparations intended to be mixed with bone graft materials to enhance bone graft handling properties in orthopedic practices to treat bony defects (21CFR864.9245). Uses in other fields such as dermatology (for tissue regeneration and scar revision) and chronic wound care (U.S Food and Drug Administration, 2021) are expanding.

Findings

Platelet rich plasma has been studied in many clinical domains, including orthopedic procedures, dentistry/oral surgery, and chronic wound care. While newer evidence suggests that platelet rich plasma may benefit individuals with chronic diabetic foot ulcers that do not respond to standard care, most other applications continue to be evaluated in relatively small studies with high risk of bias and heterogeneous protocols. Investigators frequently report inconsistent outcome measures and variable participant selection criteria. As a result, despite some encouraging results, the overall evidence for most uses remains inconclusive or conflicting, and there is no clear consensus on clinical utility beyond diabetic foot ulcer management. Guidelines

Guidance documents on platelet-rich plasma are limited. The National Institute for Health and Care Excellence (2019) does not formally recommend platelet-rich plasma for most conditions except diabetic foot ulcers, which is consistent with inconclusive outcomes in broader clinical use. The Wound Healing Society (2017) supports adjunctive therapies for individuals with diabetic foot ulcers who do not respond to conventional methods such as offloading, infection control, glycemic control, and wound bed preparation. The American Academy of Orthopedic Surgeons (2017, 2019, 2021, 2022) includes no formal endorsement of platelet-rich plasma for knee

osteoarthritis, tendinopathies, anterior cruciate ligament injuries, or other orthopedic indications because of insufficient or conflicting data.

In 2024, the Italian Guidelines for the Treatment of Diabetic Foot Syndrome (Monami, 2024) concluded that adjuvant therapies, including platelet-rich plasma or fibrin can significantly increase ulcer healing odds. In a meta-analysis they performed of eight randomized (n = 605) controlled trials focused on platelet-rich plasma or fibrin dressings for diabetic foot ulcers, participants receiving platelet-rich plasma or fibrin achieved higher complete ulcer healing rates relative to standard care. The analysis found significantly higher rates of complete ulcer healing in the treatment group (Mantel-Haenzel odds ratio 2.32, 95% confidence interval 1.41 to 3.83, P = .001), a shorter mean healing time by 10.53 days (95% confidence interval −18.10 to −2.95, P < .001), and fewer major amputations (Mantel-Haenzel odds ratio 0.32, 95% confidence interval 0.11 to 0.93, P = .04), albeit with a higher frequency of serious adverse events (Mantel-Haenzel odds ratio 2.32, 95% confidence interval 1.41 to 3.83, P = .001) (Monami, 2024).

Systematic reviews and meta-analyses through 2020

In 2018, new analyses by Andriolo (2018, updated 2019), Bousnaki (2018), Ye (2018), and Zhang (2018a, 2018b) evaluated patellar tendinopathy, temporomandibular joint disorders, hip osteoarthritis, knee osteoarthritis, and chronic Achilles tendinopathy. Results were inconclusive, reflecting low-quality evidence and heterogeneous study characteristics. In 2019, multiple systematic reviews (Al-Boloushi, 2019; Chen, 2018; Del Pino-Sedeno, 2019; Dragonas, 2019; Gupta, 2018; Li, 2019a; Ling, 2018; Liu, 2019; Scott, 2019; Strauss, 2018; Vannabouathong, 2018; Wang, 2019; Yao, 2018) addressed platelet-rich plasma for bony defects, intraoral bone applications, Achilles tendonitis, erectile dysfunction, androgenic alopecia, diabetic foot ulcers, and plantar fasciitis, again noting insufficient evidence. In 2020, investigators cited by Catapano (2020), Chen (2019b, 2020), Cruciani (2019), Hsieh (2019), Li (2019b, 2020), Mao (2019), Marchitto (2019), Sundaram (2019), and Xia (2019) observed persistent study limitations and inconclusive outcomes.

Coverage change in 2022

In 2022, coverage of platelet-rich plasma became medically necessary as an adjunct treatment for chronic diabetic wounds. This decision was based on moderate-strength findings from a systematic review by Qu (2020) under the Agency for Healthcare Research and Quality, confirming that platelet-rich plasma improved wound closure in certain individuals with chronic diabetic ulcers.

Additional reviews in 2023 and 2024

In 2023, more than 150 systematic reviews evaluated platelet-rich plasma for orthopedic and non-orthopedic indications (American Academy of Orthopaedic Surgeons, 2022). These works reiterated a pattern of minimal or conflicting data regarding efficacy outside of diabetic wounds. In 2024, Deng (2023) analyzed 22 studies (n = 1,559) and concluded that platelet-rich plasma offers improved healing rates, faster healing, and fewer amputations for diabetic foot ulcers. Peng (2023) included 10 randomized clinical trials (n = 550), reporting a 38% boost in healing rates and a 23-day reduction in healing time compared to controls.

In 2025, we condensed and reorganized the findings section and removed several older references. No policy changes warranted.

We also found three additional systematic reviews and meta-analysis. Ruiz-Muñoz (2024) pooled 11 randomized controlled trials (n = 828) comparing autologous platelet-rich plasma with conventional wound care for diabetic foot ulcers. Most studies observed participants for about 12 weeks, although follow-up ranged from three weeks to 24 months. Platelet-rich plasma markedly improved complete ulcer healing (odds ratio 3.69, 95% confidence interval 2.62 to 5.20, statistical heterogeneity 0%). Fang (2024) included 15 randomized controlled trials (n = 1,242), finding significant advantages with platelet-rich plasma, including higher rates of complete wound closure (odds ratio 3.23, 95% confidence interval 2.42 to 4.31, P < 0.0001), reduced infections (odds ratio 0.46, 95% confidence interval 0.21 to 0.99, P = 0.05), and fewer amputations (odds ratio 0.50, 95% confidence interval 0.30 to 0.84, P = 0.009). OuYang (2023) evaluated 20 studies (n = 1,131) and observed significantly faster healing (mean difference –3.21 days, 95% confidence interval –3.83 to –2.59, P < 0.001), although changes in ulcer size were not statistically meaningful (P = 0.08). Gong (2023) assessed 19 studies (n = 1,435), noting significant wound closure benefits for both autologous platelet-rich plasma (odds ratio 1.95, 95% confidence interval 1.49 to 2.56, P < 0.001) and allogeneic platelet-rich plasma (odds ratio 6.19, 95% confidence interval 2.32 to 16.56, P < 0.001), despite moderate heterogeneity.

References

On July 10, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Platelet-derived growth factor” (MeSH), “platelet rich plasma” (MeSH), and “platelet-rich plasma.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

10/2016: initial review date and clinical policy effective date: 2/2017

12/2018: Policy references updated. Policy ID changed.

12/2019: Policy references updated.

12/2020: Policy references updated.

2/2022: Policy references updated. Coverage modified.

2/2023: Policy references updated.

2/2024: Policy references updated.

2/2025: Policy references updated.