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Medical Policy Manual

Topic: Autologous Blood-Derived Growth Factors as a Treatment for Wound Healing and Other Miscellaneous Conditions

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

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 factor. Topically applied autologous platelet-derived growth factors have been most extensively investigated for clinical use in wound healing. For example, platelets are a rich source of PDGFs, transforming growth factors (which function as a mitogen for fibroblasts, smooth muscle cells, and osteoblasts) and vascular endothelial growth factors. Autologous platelet concentrate suspended in plasma, also known as platelet-rich plasma (PRP) or buffy coat, can be prepared from samples of centrifuged autologous blood. Exposure to a solution of thrombin and calcium chloride 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. Activated platelets then degranulate, releasing the various growth factors.

Regulatory Status

There are a number of commercially available centrifugation devices used for the preparation of PRP. For example, 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 AutoloGel™ and SafeBlood® have been specifically marketed for wound healing. Other devices may be used in the operating room setting, such as Medtronic Electromedic, Elmd-500 Autotransfusion system, the Plasma Saver device, or the Smart PreP device. In the operating room setting, PRP has been investigated as an adjunct to a variety of periodontal, reconstructive, and orthopedic procedures. In addition, platelet-rich plasma has also been proposed as a primary treatment of miscellaneous conditions such as epicondylitis, plantar fasciitis and Dupuytren's contracture. The Magellan Autologous Platelet Separator System (Medtronic) includes a disposables 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.

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

Note: This policy is not intended to address Regranex® (becaplermin gel), which is not an autologous platelet-derived growth factor.

MEDICAL POLICY CRITERIA

Autologous blood-derived growth factors (i.e. platelet rich plasma) are considered **investigational** for all indications including but not limited to:

A. Wounds, including but not limited to:

1. Acute traumatic or surgical wounds
2. Chronic non-healing wounds

B. Disorder of joint structures, including but not limited to the following:

1. Achilles tendinopathy
2. Degenerative disorders of the joint, including but not limited to cartilage lesions
3. Dupuytren's contracture
4. Lateral epicondylitis (e.g., tennis elbow, elbow epicondylar tendinosis)
5. Osteoarthritis
6. Patellar tendinosis (jumper's knee)

7. Tendinopathy

8. Traumatic joint injury

C. Plantar fasciitis

D. As an adjunct to surgical procedures, including but not limited to:

1. Spinal fusion

2. Sinus surgery

3. Maxillofacial and periodontal surgery

4. Arthroplasty (e.g., rotator cuff repair, repair of structures of the knee)

E. Injection of ligament tears with any type of blood-derived growth factor, whether from the patient or another source

F. Ophthalmologic conditions or procedures

SCIENTIFIC EVIDENCE

In evaluating the efficacy for use of autologous blood-derived formulas, randomized controlled trials (RCTs) are needed which compare the effects of active and placebo formulas on the healing rates of patients with comparable conditions. Ideally, patients and investigators would be blinded as to group assignment.

The focus of the literature appraisal below is on evidence from randomized controlled trials.

Formula Preparation

Several articles described different methods of preparation of autologous platelet-rich plasma, and noted variability in platelet concentration and viability depending on the preparation.[1-6] The clinical significance of these differences is unclear.

Wound Healing

Acute Wounds

Use of autologous platelet-derived growth factor (PDGF) as a primary treatment of soft tissue injuries is in an early stage, and RCTs are lacking. Evidence is insufficient to permit conclusions concerning the effect of this technology on health outcomes.

Kazakos and colleagues reported a prospective controlled study of the treatment of acute traumatic wounds with platelet gel in 59 consecutive patients (27 PRP and 32 controls).[7] Conventional treatment consisted of topical washing and cleaning of the wounds, removal of the necrotic tissue, and dressing with Vaseline gauze every 2 days. In all patients with open tibial fractures, an external fixation system was applied. PRP gel, prepared with specialized tubes and a bench-top centrifuge, was applied to the

wounds after surgical debridement and placement of the external fixation system. The time needed for preparation and application of the PRP gel was 52 minutes. PRP gel was then applied to the wounds once weekly in the outpatient clinic until there was adequate tissue regeneration (mean of 21 days) to undergo reconstructive plastic surgery. Control patients receiving conventional treatment required a mean of 41 days for adequate tissue regeneration. Pain scores were significantly lower in the PRP-treated patients at 2 and 3 weeks (VAS score of 58 PRP vs. 80 controls). Although these results are encouraging, additional study with a larger number of subjects is needed.

Chronic Wounds

Systematic Reviews

- A 2012 Cochrane review included 9 RCTs (325 participants) on PRP for treating chronic wounds.[8] This review was restricted to studies where PRP was compared with no additional treatment or a placebo. Four RCTs included patients with mixed chronic wounds, 3 included patients with venous leg ulcers, and 2 RCTs included patients with diabetic foot ulcers. Only 1 study was considered to be at low risk of bias. After a median treatment time of 12 weeks, there was no significant difference between the PRP and control groups in complete healing of diabetic foot ulcers, venous leg ulcers, or mixed chronic wounds. There was no significant difference in the area epithelialized in 3 RCTs of mixed chronic wounds. In 2 RCTs of mixed chronic wounds, there was a significant difference favoring PRP in the wound area that was healed. The review concluded that there is no current evidence to suggest that autologous PRP is of value for treating chronic wounds.
- A 2009 systematic review identified 42 controlled trials on PRP; 20 of these were RCTs and included in the systematic review.[9] The 20 RCTs comprised 11 studies on oral and maxillofacial surgery, seven on chronic skin ulcers, and two on surgery wounds. The authors concluded that PRP improved the gingival recession but not the clinical attachment level in chronic periodontitis. Results were inconclusive for the healing of skin ulcers, and there were little safety data. Non-randomized controlled studies were identified but not reviewed for chronic elbow tendinosis, muscle strains, lumbar spinal fusions, and other orthopedic procedures.
- An industry-funded systematic review included 21 studies on PRP gel for cutaneous wound healing, 12 of which were RCTs.[10] There were three main types of wounds, including open chronic wounds, acute surgical wounds with primary closure, and acute surgical wound with secondary closure. Study quality was found to vary considerably, with three studies rated as high quality and six rated as poor quality. Two additional studies could not be rated because they were published only as an abstract and letter. The primary outcome measure for this meta-analysis was complete wound healing. Overall, results from the RCTs were mixed, i.e. some trials reported a benefit but others did not. Of four RCTs that evaluated complete healing of chronic wounds, two reported a statistically significant benefit for PRP, and meta-analysis of the four RCTs showed a significant combined effect of PRP for complete healing of chronic wounds. However, two of the four studies were rated as low quality and the other two could not be rated because they were presented only in abstract or letter form. Meta-analysis could not be conducted for complete healing of acute primary or secondary closure wounds. The meta-analysis of the effect of PRP on complete wound healing of chronic wounds was limited by the inclusion of poor quality studies. There were no high-quality RCTs that showed an improvement in complete healing with PRP.
- A 2012 systematic review included 23 randomized trials and ten prospective cohort studies that compared PRP to placebo, corticosteroid, or a standard procedure.[11] Of 22 RCTs that evaluated functional outcomes, six showed a functional benefit of PRP, 15 showed no difference between PRP and the control, and one showed a significant functional advantage for the control group. For most of the studies the outcome measures differed, but six RCTs (n=358) and three prospective cohort

studies (n=88) reported results of PRP using a visual analog score (VAS) and were combined for analysis. These studies assessed injuries to the acromion, rotator cuff, lateral humeral epicondyle, anterior cruciate ligament (ACL), patella, tibia, and spine. Follow-up ranged from 6 weeks to 24 months. No significant benefit of PRP was found for the six RCTs or the three prospective cohort studies. Interpretation of this systematic review is limited by the combination of a wide variety of conditions, as well as the lack of standardization of platelet-separation techniques and outcome measures in the primary literature.

Randomized Controlled Trials

No new RCTs have been published since the systematic reviews summarized above.

Nonsurgical Treatment for Musculoskeletal Disorders

Miscellaneous Tendinopathy

Systematic Reviews

Three recently published systematic reviews for various tendinopathies found few randomized trials, and no studies of high-quality design.[4,12,13] While uncontrolled trials showed promising results, those studies with a control group reported no significant benefit from use of PRP compared with patients who did not receive PRP. These systematic reviews concluded that well-designed, large, long-term, randomized trials with appropriate control groups are needed to determine the impact of PRP for chronic tendinopathies.

Lateral Epicondylitis

Randomized Controlled Trials

- In 2013, Krogh et al. reported a double-blind placebo-controlled RCT in 60 patients with chronic lateral epicondylitis.[14] Patients were randomized to receive either a blinded injection of PRP, saline, or corticosteroid injection. In order to maintain blinding, a blood sample was taken from all patients, and patients were blindfolded during the blood sampling and injections. At 1 month, corticosteroid injections reduced pain to a greater extent than either PRP or saline. At 3-month follow-up, there was no significant difference between the groups in the primary endpoint of pain reduction. Corticosteroid injection was more effective than saline or PRP in reducing color Doppler activity and tendon thickness.
- A double-blind randomized trial of PRP for lateral epicondylitis was reported by Peerbooms and colleagues in 2010.[15] Two-year follow-up of this RCT was reported in 2011 by Gosens et al.[16] One hundred patients with chronic (longer than 6 months) epicondylitis were randomized to receive corticosteroid injection (n=49) and to receive PRP injection (n=51). Stretching and exercise protocols were followed by each group, and normal sport or recreational activities were allowed as tolerated 4 weeks after injection. Eight patients were lost to follow-up, and their last scores were carried forward. Success was defined as 25% reduction in pain on VAS or Disabilities of the Arm, Shoulder, and hand (DASH) outcomes measure score after 1 year without a re-intervention. Initially, mean VAS was 70.1 in the PRP-treated patients and 65.8 in the corticosteroid group. DASH scores were 161.3 and 131.2, respectively.

At 4 and 8 weeks after injection, outcomes on VAS and DASH scores were significantly better in the corticosteroid group. At 12 weeks, between-group differences were not significant. After 1 year, 73% of PRP and 49% of steroid-treated patients met criteria for success on pain VAS; 73% of the PRP group and 51% the steroid group were successful using DASH outcome measures (P=0.005). At two years, both VAS and DASH scores were significantly better in the PRP group (21.3 and 17.6, respectively) compared with the corticosteroid group (42.4 and 36.5, respectively). Success on the DASH was achieved by 73% of the PRP group and 39% of the corticosteroid group, while more patients in the corticosteroid group (47% vs. 14%) had deteriorated at two years. Additional studies are needed with PRP in this condition.

Achilles Tendinopathy

Randomized Controlled Trials

A single center, randomized, double-blind, placebo-controlled trial of PRP injection in patients with chronic midportion Achilles tendinopathy was reported by de Vos et al. in 2010.[17] Fifty-four patients were randomized to receive PRP or saline injection, and all patients performed eccentric exercises. The Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire evaluating pain score and activity level was completed at baseline and at 6, 12, and 24 weeks. The mean VISA-A score improved significantly after 24 weeks in both groups, and the between-group difference was not statistically significant. There were no significant differences on secondary measures of patient satisfaction and number of patients returning to their desired sport. This lack of significant difference in clinical and ultrasonographic outcomes continued through one-year follow-up, reported in a separate article.[18]

Plantar Fasciitis

The 2012 systematic review by Sheth et al. identified three nonrandomized uncontrolled studies that evaluated the effect of autologous blood injections.[11] No controlled trials have been identified that evaluated the effect of PRP for plantar fasciitis.

Osteochondral Lesions

In 2012, Mei-Dan et al. reported a quasi-randomized trial of 29 patients with 30 osteochondral lesions of the talus assigned to three intra-articular injections of hyaluronate or PRP. (21) At 28-week follow-up, scores on the American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale (AHFS) improved to a greater extent in the PRP group (from 68 to 92) than the hyaluronate group (from 66 to 78). Subjective global function also improved to a greater extent in the PRP group (from 58 to 91) than the hyaluronate group (from 56 to 73). Interpretation of the composite measures of VAS pain and VAS function is limited by differences in the groups at baseline. Neither the patients nor the evaluators were blinded to treatment in this small study.

Osteoarthritis

Randomized Controlled Trials

- A double-blind study from 2012 randomized 109 patients with knee chondropathy or osteoarthritis (Kellgen-Lawrence grades I, II, or III) to 3 weekly injections of PRP (previously frozen aliquot) or HA.[19] (26) At 12 months of follow-up, there was significant improvement on

IKDC [International Knee Documentation Committee], VAS, TEGNER, and KOOS scores in both groups, but no significant difference between the groups.

- In an additional 2012 RCT, 4 intra-articular injections of PRP or hyaluronic acid (HA) were compared in 120 patients with gonarthrosis (early stage knee arthritis, Kellgen-Lawrence grades I, II, or III).[20] At 4 weeks, both groups showed improvement in Western Ontario and McMaster (WOMAC) scores compared to baseline. In this non-blinded study, WOMAC scores for the PRP group continued to improve over 24 weeks (79.6 at baseline, 49.6 at 4 weeks and 36.5 at 24 weeks), whereas WOMAC scores in the HA group declined in the post-treatment period (75.4 at baseline, 49.6 at 4 weeks, and 65.1 at 24 weeks).
- In 2013, Patel et al. reported a double-blind placebo-controlled RCT with 78 patients (156 knees).[21] This study compared a single injection of PRP, 2 injections of PRP, or a single injection of saline. Adverse effects at the time of injection were observed in 22% of patients in the 1 injection PRP group and 44% in the 2 injection PRP group, compared to none in the saline group. At 6 month follow-up WOMAC scores had improved in the 2 PRP groups but not in the control group. VAS pain scores improved from 4.54 to 2.16 after a single injection of PRP and from 4.64 to 2.54 after 2 injections of PRP. VAS scores did not change in the placebo-control group (from 4.57 at baseline to 4.61 at 6-month follow-up).

  A 2009 report from Europe described a prospective study of intra-articular injection of PRP in 100 consecutive patients affected by chronic degenerative cartilage lesions.[22] Patients had a history of pain or swelling of the knee for at least 4 months and imaging findings on radiograph or magnetic resonance imaging (MR) of degenerative changes in the joint; 58 knees presented with a degenerative chondral lesion, 33 with early osteoarthritis, and 24 had advanced osteoarthritis. Exclusion criteria included systemic disorders, axial malalignment, severe cardiovascular diseases, infections, or immunodepression. Three injections were administered at 21-day intervals. Evaluation was conducted in 91 patients (91% follow-up) before and at the end of the 3 treatments and at 6 and 12 months after treatment. The International Knee Documentation Committee (IKDC) objective score improved from 46% (of normal and nearly normal knees) to 78% at the end of therapy, declining to 67% at 12-month follow-up. The IKDC subjective score improved from 41 to 63 after treatment, with a score of 61 at 12-month follow-up. Treatment was less effective in older, heavier, and more advanced osteoarthritis patients than in younger patients with less severe chondral damage.

Adjunct to Surgical Procedures

Spinal Fusion

Randomized Controlled Trials

Only one randomized controlled trial was found for use of autologous growth factor concentrate (AGF), including PRP, as an adjunct to lumbar fusion.[23] In this small trial, outcomes for 40 patients who underwent spinal fusion with (n=20) versus w/o (n=20) AGF. One patient per group was lost to follow-up. No significant between-group differences were found with CT scan at 1 year, which showed osseous healing in all but one patient. The pain and function outcomes at 2 years follow-up also showed no significant between-group differences. The authors concluded that use of PRP as an adjunct to spinal fusion was not justified.

Shoulder Surgery

Randomized Controlled Trials

- Rotator Cuff Repair

  In 2012, Rodeo et al. reported a RCT arthroscopic rotator cuff tendon repair with or without PRP (platelet rich fibrin matrix) in 79 patients.[24] Follow-up at 6 weeks, 3 months, and 12 months postoperatively found no significant differences between the PRP and control groups for tendon healing, tendon vascularity, manual muscle strength, or clinical rating scales. Logistic regression analysis suggested that PRP might have a negative effect on healing.

  Castricini et al randomized 88 patients with a rotator cuff tear to arthroscopic repair without (n=45) or with (n=43) augmentation with platelet-rich fibrin matrix.[25] At average follow-up of 20.2 months (range, 16-30 months), both groups demonstrated statistically significant improvement in the primary endpoint (Constant Scores evaluating pain, activities of daily living, range of movement, and power), but the between-group difference was not significant.

  A double-blind quasi-randomized trial from 2013 assigned 60 patients in alternating order to receive rotator cuff surgery with or without PRP (platelet rich fibrin matrix).[26] Mean surgery time was increased by about 10 minutes in the PRP group. At 1-year follow-up, there was no significant difference between the groups in VAS pain scores, narcotic use, recovery of motion, simple shoulder test (SST), and American Shoulder and Elbow Surgeons (ASES) shoulder scores. Mean University of California-Los Angeles (UCLA) scores were slightly lower in the PRP group (27.94 vs. 29.59). There were no significant differences between the groups on MRI scans at 3 to 5 month follow-up.

  In 2012, Gumina et al. reported a RCT of platelet-leukocyte membrane in 80 patients with full thickness rotator cuff tear randomized to arthroscopic repair with or without PRP.[27] Both age and Constant score were significantly different at baseline. At a mean 13-month follow-up, the SST and the change in Constant score did not differ significantly between the 2 groups. Independent evaluation with MRI found that rotator cuff retears occurred only in the control group, and that the use of the PRP membrane resulted in significantly better repair integrity.

  Randelli et al. randomized 53 patients in a double-blind study to activated PRP or to no treatment after arthroscopic rotator cuff repair.[28] VAS pain scores in the PRP group were lower than controls at baseline (4.8 vs. 6.4) through 30 days after surgery (1.1 vs. 2.4). At 3 months after surgery, the PRP group had higher scores on Constant scores (65.0 vs. 57.8) and the Simple Shoulder Test (8.9 vs. 7.1), University of California (UCLA, 26.9 vs. 24.2) and strength in external rotation (3.0 vs. 2.1). There was no difference in functional outcomes between the groups at 6, 12, and 24 months after surgery and no difference in the healing rate measured by magnetic resonance imaging (MRI) at one year or more after surgery. This study was limited by the difference in VAS between the groups at baseline.

  A small double-blind RCT of PRP for rotator cuff healing without surgical repair was reported by Rha et al. in 2012.[29] In this study, 39 patients with tendinosis or a partial tear were randomized to 2 sessions of dry needling or 2 PRP injections. For dry needling, a needle was passed through the lesion of the tendon approximately 40-50 times. PRP was injected into or around the lesion under ultrasound guidance. Both groups showed an improvement in the Shoulder Pain and Disability Index (SPDI) over the 6 months of the study. At 2 weeks, 3 months and 6 months after the treatment, the mean SPDI score was significantly better in the PRP group (17.7 vs. 29.5). Range of motion was generally not different between the groups.

In a small 2013 RCT study, Kesikburun et al. investigated the effect of PRP injections on pain and shoulder function in 40 patients with chronic rotator cuff tendinopathy following a 6-week standard exercise program. Patients were randomized into a PRP group (n=20) or placebo group (n=20). At one-year follow-up, the authors reported the PRP injections were no more effective in improving quality of life, pain, disability, and shoulder range of motion than patients that received placebo.[30]

- Subacromial Decompression Surgery
  Everts and colleagues reported a rigorously conducted, small (n=40) double-blinded RCT of platelet and leukocyte-rich plasma (PLRP) gel following open subacromial decompression surgery in a carefully selected patient population.[31] Blood was drawn from all patients after induction of anesthesia to maintain blinding. PLRP with autologous thrombin was injected into both the subacromial intracapsular space and the subcutaneous layer covering the incision during wound closure. Postoperative examinations at 1, 2, 4, and 6 weeks were performed by independent evaluators; unique patient identifier codes were used to maintain patient and investigator blinding. Neither self-assessed nor physician-assessed instability were improved. Both subjective pain and use of pain medication were significantly lower in the PRP group across the 6 weeks of measurements. For example, at 2 weeks after surgery VAS scores for pain were lower by about 50% in the PLRP group (close to 4 in the control group and close to 2 in the PLRP group) and only 1 patient (5%) was taking pain medication compared with 10 (50%) control patients. Objective measures of range of motion showed clinically significant improvement in the PLRP group across the 6-week assessment period. Significantly more patients in the PLRP group reported improvements in activities of daily living such as ability to sleep on the operated shoulder at 4 weeks after surgery and earlier return to work.

Knee Surgeries

Randomized controlled trials

- In 2012, de Almeida et al. reported a small (n=27) randomized trial of the effect of PRP gel on the harvest site of the patellar tendon during anterior cruciate ligament (ACL) reconstruction.[32] VAS for pain in the postoperative period was significantly lower in the PRP group compared to the control group (3.8 vs. 5.1). At 6 months, assessment by MRI showed a smaller gap in the patellar tendon in the PRP group (4.9 mm vs. 9.4 mm), but there was no significant difference between groups for the Tegner questionnaire or isokinetic testing.

- Nin and colleagues randomized 100 patients undergoing arthroscopic patellar tendon allograft anterior cruciate ligament reconstruction; platelet-enriched gel was used in one group (n=50), and a non-gel group (n=50) served as control.[33] The use of platelet-derived growth factors (PDGF), on the graft and inside the tibial tunnel in patients treated with bone-patellar tendon-bone allografts has no discernible clinical or biomechanical effect at 2-year follow-up.

- Cervellin et al randomized 40 young athletes undergoing anterior cruciate ligament (ACL) reconstruction to either a control group (n=20) or a PRP group (n=20).[34] The PRP group received PRP gel to both the patellar and tendon bone plug harvest site. At 1-year follow-up, the PRP group reported significantly less pain during activities involving the knee. There was no significant difference between the two groups for Visual Analog Scale or for bone defect filling per MRI.

Long Bone Nonunion

Systematic Review

A 2012 Cochrane review found only one small (n=21) RCT of PRP for long bone healing.[35] However, only studies where PRP was compared with no additional treatment or a placebo were included in the review; therefore the authors did not include the larger RCT by Calori et al. described below.

Randomized Controlled Trial

Calori et al. compared application of PRP or recombinant human bone morphogenetic protein-7 (rhBMP-7) for the treatment of long bone nonunions in an RCT with 120 patients and ten surgeons.[36] Inclusion criteria were post-traumatic atrophic nonunion for at least nine months, with no signs of healing over the last three months, and considered as treatable only by means of fixation revision. Autologous bone graft had been used in a prior surgery in 23 cases in the rhBMP-7 group and in 21 cases in the PRP group. Computer-generated randomization was developed to create two homogeneous groups; there were generally similar numbers of tibial, femoral, humeral, ulnar, and radial nonunions in the two groups. Following randomization, the patients underwent surgery for nonunion, including bone grafts according to the surgeon's choice (66.6% of rhBMP-7 and 80% of PRP patients). Clinical and radiologic evaluations by one radiologist and two surgeons trained in the study protocol revealed fewer unions in the PRP group (68%) compared with the rhBMP-7 group (87%). Clinical and radiographic healing times were also found to be slower by 13–14% with PRP.

Other Surgical Procedures

No difference was found between the treatment and control groups in studies of PRP use in the following surgical procedures:

- Sinus surgery[37]
- Periodontal surgery[38]
- Incision site wound closure in vascular surgeries[39-41]
- Blepharoplasty[42]
- Tonsillectomy in children[43]

Ophthalmologic Conditions and Procedures

Use of PRP has been studied as a treatment of persistent corneal defects[44], symptomatic dry eye[45], chemical burns[46], post-LASIK ocular surface syndrome[47]. Studies are limited to small pilot studies with no control group for comparison. No randomized trials were identified.

Clinical Practice Guidelines

A 2009 practice guideline from the National Pressure Ulcer Advisory Panel and the European Pressure Ulcer Advisory Panel concluded, "The combined clinical evidence on platelet-derived growth factor (PDGF) suggests that PDGF-BB may improve healing of pressure ulcers. However, the evidence is not sufficient to recommend this treatment for routine use." [48]

No other clinical practice guidelines from U.S. professional associations were found that address the use of platelet-derived growth factor for any condition.

Summary

The current evidence is insufficient to permit conclusions about the benefits of autologous platelet-derived growth factors (PDGF) in the treatment of any condition. In addition, there are no clinical practice guidelines from U.S. professional associations that recommend the use of PDGF. Therefore, the use of PDGF for any condition is considered investigational.

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Orthopedic Applications of Stem-Cell Therapy, Medicine, Policy No. 142

CODES	NUMBER	DESCRIPTION
CPT	0232T	Injection(s) platelet rich plasma, any tissue including image guidance, harvesting and preparation when performed.
HCPCS	G0460	Autologous platelet rich plasma for chronic wounds/ulcers, including phlebotomy, centrifugation, and all other preparatory procedures and administration, per treatment
	P9020	Platelet rich plasma, each unit
	S9055	Procuren or other growth factor preparation to promote wound healing