



Cigna Medical Coverage Policy

Subject Autologous Platelet-Derived Growth Factors (Platelet-Rich Plasma [PRP])

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Coverage Policy

Cigna does not cover the use of autologous platelet-derived growth factors* (CPT® Code 0232T; HCPCS Code S9055) for ANY condition or indication, including the following, because their use is considered experimental, investigational, or unproven:

- anterior cruciate ligament (ACL) repair
- bone graft supplementation, regeneration, substitution and/or healing (e.g., lumbar fusion, iliac crest bone graft to maxilla)
- degenerative joint disease
- epicondylitis
- epithelial defects of the cornea, persistent

- fractures, including long-bone nonunion
 - joint capsular injuries
 - muscle injuries and disorders
 - osteoarthritis of the knee
 - periodontal disease, gingival recession and dental surgery
 - plantar fasciitis
 - sinus augmentation procedures
 - soft tissue trauma (e.g., tendon and ligament ruptures)
 - total knee arthroplasty
 - tendonitis
 - wound healing (e.g., surgical wounds; chronic wounds; lower extremity ulcers)
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General Background

Autologous platelet-derived growth factors (APDGF) also referred to as platelet-rich plasma (PRP), platelet gel, platelet-rich concentrate, autogenous platelet gel, or platelet releasate, have been proposed for the treatment of multiple conditions to enhance healing. A collection and preparation system is used to collect a small sample of the patient's blood to be used to produce PRP. The plasma is combined with other substances to form a platelet-rich gel that can be applied to the wound. APDGF has been proposed for numerous indications including wound care, orthopedic indications, abdominal surgery and oral/dental procedures.

U.S. Food and Drug Administration (FDA)

The systems used for preparing autologous platelet-derived growth factors are FDA approved under the 510(k) notification process. In general, the systems are approved to be used at the patient's point of care and/or in a clinical laboratory to prepare autologous platelet-rich plasma (PRP)/platelet concentrate from the patient's own blood. Examples of approved devices include:

- AutoloGel (Cytomedix, Inc., Rockville, MD)
- Autologous Platelet Grafting™ (SafeBlood® Technologies, Inc., Little Rock, AR)
- CASCADE® Autologous Platelet System (Musculoskeletal Transplant Foundation [MTF], Edison, NJ)
- Fibrinet® Autologous PRP System (Cascade Medical Enterprises, Wayne, NJ)
- Gravitational Platelet Separation System (GPS®II) (Biomet Biologics, Inc., Warsaw, IN)
- Mini GPSII (Biomet Biologics, Inc., Warsaw, IN)
- SmartPRP® 2 APC⁺ system (Harvest Technologies Corporation, Plymouth, MA)

Literature Review

APDGF has been proposed for the treatment of chronic wounds (e.g., lower extremity wounds, pressure ulcers, graft-versus-host disease [GVHD] ulcers); persistent epithelial defects of the cornea; periodontal disease; bone graft supplementation, regeneration, substitution and/or healing (e.g., lumbar fusion, iliac crest grafted maxilla); ingrown toenails; degenerative cartilage lesions; tendonitis; joint capsular injuries; plantar fasciitis; soft tissue trauma (e.g., tendon and ligament ruptures); fractures; osteoarthritis of the knee; as well as muscle injuries and disorders. Studies have also investigated the use of APDGF to enhance healing in various types of surgical procedures including: blepharoplasty, mammoplasty, cleft lip and palate, maxillofacial surgery, LASIK surgery, dental implantology, mandibular degree II furcation defects, sinus floor augmentation, pediatric tonsillectomy, cystectomy, finger amputation, epithelialization of skin donor sites, skin autografts, saphenectomy, hemithyroidectomy, inguinal hernia repair and other abdominal surgeries, chest surgery and anterior colporrhaphy. However, consensus on the terminology of the platelet products and standardization of the preparation of the platelet-leukocyte gel has not been established (Balbo, et al., 2010; Luaces-Rey, et al., 2010; Mishra, et al., 2009; Everts, et al., 2007). Overall, limitations of the studies include small patient populations, and lack of a control group and/or comparison to standard therapy. Outcomes have been conflicting or reported that the application of APDGF did not make a significant difference in inflammation, closure, healing, bleeding, bone ingrowth, implant stability, reduction in recovery time or postoperative pain. Some studies reported that initial appearing benefits were not maintained. There is insufficient evidence in the published, peer-reviewed scientific literature to support the effectiveness of platelet gel for these indications.

Anterior Cruciate Ligament Repair: In a randomized controlled trial (n=100), Nin et al. (2009) evaluated the efficacy of APDGF when used for the treatment of initial anterior cruciate ligament (ACL) reconstruction with bone-patellar tendon-bone allograft. Fifty of the patients were treated with platelet gel and 50 were not (i.e., control group). In the study group during the surgical procedure, the ligament was covered with APDGF and sutured over itself. The gel was also introduced after implantation of the graft prior to closing the wound. Follow-up ranged from 18 to 36 months (mean 24.3 months). Postoperatively, there were no statistically significant differences between the two groups in the perimeters of the kneecap, C-reactive protein levels, magnetic resonance imaging (MRI) appearance of the graft, and clinical evaluation scores including range of knee motion, muscle torque, visual analog scale, International Knee Documentation Committee scores, and KT-1000 arthrometer scores. The pivot shift test was negative in 94% of all patients. There was no discernable clinical or biomechanical effect of APDF for this patient population.

Vogrin et al. (2010) conducted a randomized controlled trial (n=50) to evaluate the effect of APDGF on postoperative knee stability following anterior cruciate ligament reconstruction for ligament rupture. Patients were divided into the study group (n=25) which received APDGF during surgical repair and the control group which was not treated with the platelet gel. The gel was applied locally following hamstring graft placement. Follow-up occurred at three and six months. Clinical evaluations were assessed using the Tegner activity score, Lyshol score and International Knee Documentation Committee (IKDC) score. Anteroposterior knee stability was measured using the KT-2000 arthrometer at 15, 20 and 30 pounds of force with knee flexion at 25 degrees and fixed patella at the same time. There was no significant difference in joint stability of the knee between the two groups at the three-month follow-up. At six months, there was a significant improvement (p=0.011) in the KT-2000 arthrometer scores in the study group compared to the control group. Limitations of the study include the small patient population, short-term follow-up and patients lost to follow-up (n=5).

Blepharoplasty: In 2006, Vick et al. conducted a randomized, controlled trial (n=33) to evaluate the effect of autologous platelet gel on postoperative edema and ecchymosis in one of the two eyes during bilateral blepharoplasty. Of the 33 patients, 28 (85%) completed the study. No significant differences between the treated and untreated sides were noted for discomfort and ecchymosis. A statistically significant difference was noted in photograting of edema on the treated side on day 1 (p=0.03), but the scores were equal on days three and seven. No clinically significant benefits to the use of autologous platelet gel during blepharoplasty were reported.

Breast Surgery: In a randomized controlled trial (n=111), Anzarut et al. (2007) studied the effectiveness of topical application of autologous platelet gel during breast surgery to reduce postoperative wound drainage in patients undergoing bilateral reduction mammoplasty. Each patient had one breast which received the gel and one breast which did not. No statistically significant differences in drainage, pain, size of open areas, clinical appearance, degree of scar pliability, or scar erythema were noted. The data did not support the use of autologous platelet gel to improve outcomes after breast reduction mammoplasty.

Cervical Fusion: Feiz-Erfan et al. (2007) conducted a double-blind randomized study in which platelet gel was used to treat 50 patients who underwent anterior cervical fusion with allograft bone and internal fixation. Altogether, 81 disc levels were treated. Forty-two levels were assigned to the gel group and 39 levels were assigned to the control group. Follow-up evaluations occurred at 6 weeks, 12 weeks, one year and two years. There were no significant differences in fusion rates between the groups at any follow-up evaluation. The data presented did not support the use of platelet gel to improve fusion rates in patients undergoing anterior cervical fusion.

Degenerative Joint Disease: Kon et al. (2010) conducted a prospective case series (n=100 patients/115 knees) to evaluate the efficacy of APDGF in the treatment of monolateral or bilateral degenerative lesions of articular cartilage of the knee. Patients had experienced at least four months of pain or swelling of the knee and had radiographic findings of degenerative joint changes. Intra-articular injections were administered every 21 days, and follow-up occurred for 12 months. Compared to baseline, statistically significant improvements in the International Knee Documentation Committee (IKDC) objective scores were seen following APDGF injections at the six and 12 month follow-ups (p<0.0005, each). However, a statistically significant worsening of scores was seen between six and twelve months (p<0.0005). The same results were seen with the IKDC subjective scores with significant improvements at six- and 12-month follow-ups (p<0.005, each), but significant worsening at the 12-month follow-up (p=0.02). The Euroqol Visual Analogue Scale (EQ VAS) scores improved significantly at the six- and 12-month follow-ups compared to baseline (p<0.0005, each), but had a tendency to worsen over time (p=0.2), even though not statistically significant. Limitations of the study include the lack of a control group and

randomization, short-term follow-up and the number of patients lost to follow-up or who did not complete the study (n=12).

Epicondylitis: Ahmad et al. (2013) conducted a systematic review to evaluate the evidence for platelet-rich plasma (PRP) for the treatment of lateral epicondylitis. Five randomized controlled trials, one-nonrandomized comparison study and three case series met inclusion criteria. Comparators included blood, bupivacaine, normal saline injections or corticosteroids. Follow-ups ranged from six weeks to three months. Outcomes were conflicting with some studies reporting improvement and other studies reporting no significant differences with PRP. Limitations of the studies included: heterogeneity of outcomes measured; small, heterogeneous patient populations; variations in PRP preparation and post-injection protocol; lack of a non-treatment group; and short-term follow-ups. There is insufficient evidence to support PRP for the treatment of epicondylitis.

Peerbooms et al. (2010) conducted a two-center randomized controlled trial to evaluate the treatment of chronic lateral epicondylitis in patients randomly assigned to receive an APDGF injection (n=51) or a corticosteroid injection (n=49) (control group). Six months prior to onset of the trial, patients had been unresponsive to cast immobilization, corticosteroid injections and/or physiotherapy. Primary outcomes included visual analog scores (VAS) and Disabilities of the Arm, Shoulder, and Hand (DASH) scores. A successful outcome was a more than 25% reduction in VAS or DASH scores without repeat treatment within the first year following injection. Follow-ups occurred for up to 52 weeks. Patients engaged in a stretching protocol and a muscle- tendon- strengthening program following the injections. The VAS and DASH scores were significantly better in the APDGF group compared to the corticosteroid injection group at the six-month ($p<0.001$, $p=0.03$, respectively) and one-year ($p<0.001$, $p=0.001$, respectively) follow-ups. Although the scores were better in the corticosteroid injection group initially, improvement declined. In contrast the APDGF group showed progressive improvement over time. After an average five months, five APDGF-treated patients required reintervention compared to 13 control group patients. Limitations of the study include the small patient populations and patients lost to follow-up or patients with inadequate data sets (n=8).

Foot and Ankle: Vannini et al. (2013) conducted a systematic review of the evidence to determine the clinical effectiveness of PRP for the treatment of foot and ankle pathologies. Four randomized controlled trials, one comparative study and 12 case series met inclusion criteria. Studies included treatment for Achilles tendon, plantar fasciitis, talar osteochondral lesions, total ankle replacement, and foot and ankle fusions. Following review of the evidence the authors concluded that no clear indications for using PRP in foot and ankle pathologies were supported. The studies were of poor methodology with heterogeneous PRP applications and conflicting outcomes.

Gingival Recession: Keceli et al. (2008) conducted a randomized controlled trial to evaluate the effectiveness of platelet gel used for the treatment of 40 patients with gingival recession. Patients were randomized to either connective tissue graft only or to connective tissue graft plus platelet gel. Outcomes were measured in terms of gingival index, plaque index, recession depth, probing depth, keratinized tissue width, recession width, clinical attachment level, and localization of mucogingival junction. Although significant improvements were seen within each group following treatment, no statistically significant differences were seen in outcomes between the two groups at the six-week, six-month and 12-month postoperative follow-up visits. No benefits from application of the platelet gel were identified.

Knee Osteoarthritis: Khoshbin et al. (2013) conducted a systematic review (n=577) to evaluate the use of PRP for the treatment of symptomatic knee osteoarthritis. Four randomized controlled trials and two case series met inclusion criteria. Comparators included injections of hyaluronic acid (HA) or normal saline. Based on the Western Ontario and McMaster Universities Arthritis Index scale, pooled results of four studies showed that PRP was significantly better than HA or NS ($p<0.001$). The International Knee Documentation Committee scores (three studies) favored PRP as a treatment modality ($p<0.001$). There was no difference in the pooled results for visual analog scale score or overall patient satisfaction. There were significantly more adverse events in patients treated with PRP than in those treated with HA or placebo ($p=0.002$). Limitations of the studies included: heterogeneity of study designs, patient populations, treatment regimens and PRP preparation techniques; short-term follow-up (≤ 6 months); and use of various outcome measures. The authors noted that the ideal number, frequency, and timing of treatments; the grade of OA best treated; the concurrent use of nonsteroidal anti-inflammatory agents, corticosteroids, or analgesic agents; the optimal post-treatment rehabilitation protocol; and the most bioavailable delivery method are unknown.

ECRI (2013) conducted a health technology forecast regarding the use of PRP for the treatment of knee osteoarthritis. Current studies were primarily in the form of case series and retrospective reviews with small patient populations (n=50–261). ECRI noted that the available evidence did not demonstrate a significant additional benefit from PRP therapy compared to injections of corticosteroids or hyaluronic acid.

Long-Bone Nonunion: Lenza et al. (2013) conducted a systematic review to evaluate the effectiveness of PRP as an adjunctive therapy for the union of long bones. Two randomized controlled trials (RCT) (n=148) met inclusion criteria. Outcomes included bone regeneration, adverse events, pain, quality of life and cost. One RCT compared PRP to recombinant human morphogenetic bone protein-7 for the treatment of pseudoarthrosis and the second RCT evaluated the effects of platelet-rich plasma, platelet-rich plasma plus bone marrow stromal cells, and no adjuvant treatment. Follow-ups occurred for up to 12 months. Overall, there was no significant difference with the use of PRP.

Periodontal Intraosseous Defects: Kotsovilis et al. (2009) conducted a systematic review of randomized controlled trials (n=10 studies) to evaluate the efficacy of APDGF for the treatment of periodontal intraosseous defects. Seven trials had a parallel group design and three exhibited a split-mouth design. Four studies were conducted by the same research group. Various parameters of APDGF preparations and applications were used (e.g., type of centrifuge, pattern of centrifuge steps, baseline and treatment platelet concentration, growth factor concentration in platelets) and APDGF was combined with various types of bone grafts or substitutes, alloplastic materials, and/or guided tissue regeneration. According to the authors, overall primary and secondary outcomes failed to confer statistically significant additive benefits of APDGF in the therapy of periodontal intraosseous defects. There were no safety issues identified.

Rotator Cuff Repair: Chahal et al. (2012) conducted a systematic review and meta-analysis to determine the efficacy of PRP when used in patients with full thickness rotator cuff tears who underwent arthroscopic repair. Two randomized and three nonrandomized studies met inclusion criteria (n=261). The primary outcome was the rotator cuff retear rate after arthroscopic repair. There was no significant difference in retear rates among patients including those who had large or at-risk tears regardless of PRP treatment status or in patients who underwent a double-row rotator cuff repair. There were no statistically significant differences in the Constant Murley score; Simple Shoulder Test score; American Shoulder and Elbow Surgeons score; University of California, Los Angeles shoulder score; or Single Assessment Numeric Evaluation score. Due to the inclusion of nonrandomized trials, true meta-analysis could not be performed. Limitations of the studies included: the small patient populations; heterogeneity of repair techniques, differences in rotator cuff tear sizes and number of tendons involved, and the use of various PRP products.

Sinus Augmentation Procedures: Arora et al. (2010) conducted a systematic review of randomized controlled trials (n=5 trials; 5–39 patients per trial) of at least six months duration to evaluate the efficacy of APDGF when used with bone and bone substitutes in sinus augmentation procedures. Limitations noted by the authors included heterogeneity of the study designs, small patient populations and inconsistent single outcome variables for sinus elevation. A meta-analysis of the data was not possible due to the heterogeneity of the outcome variables. The authors concluded that “the disparity in the study design, surgical techniques, and different outcome assessment variables used makes it difficult to assess the practical benefit of using APDGF in sinus grafting procedures.”

Tendon Repair: de Vos et al. (2010) conducted a single-center, double-blind, randomized controlled trial (n=54) to determine if autologous platelet gel would improve the pain and functional outcomes of patients with chronic midportion Achilles tendinopathy. Randomization was stratified by activity level to the study group (n=27; mean age 49 years) or to the saline injection placebo group (n=27; mean age 50 years). Both groups were also involved in an eccentric exercise program. Stratification into one of two treatment groups was based on the ankle activity score that objectively quantified ankle-related activity into a high activity group or a low activity group. The primary outcome measure was the self-reported Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire, which quantified pain and activity levels. The secondary outcome measures were subjective patient satisfaction, return to sports, and adherence of the eccentric exercises. At the 24-week follow-up, the VISA-A score improved significantly in both groups (study group 21.7 points; placebo group 20.5 points), but the difference between the two groups was not significant, and there were no significant differences in the secondary outcomes. The injection of platelet gel did not result in greater improvements than placebo. Two author-noted limitations of the study were the amount of platelets and the quantity of activated growth factors in the platelet gel injections were unknown and the use of eccentric exercises.

In a technology assessment (2010), the California Technology Assessment Forum (CTAF) conducted a systematic review of the literature to evaluate the evidence on platelet-rich plasma injections for the treatment of Achilles tendinopathy. One randomized controlled trial (deVos, et al., 2010), one case series (n=14) and one case report met inclusion criteria. CTAF concluded that based on the evidence, PRP injection added to standard eccentric exercise therapy was not an effective approach to the treatment of Achilles tendinopathy.

Total Knee Arthroplasty: Peerbooms et al. (2009) conducted a randomized controlled trial (n=102) to evaluate the efficacy of platelet gel in wound healing following total knee arthroplasty. Patients were randomly assigned to a control group who received no platelet gel (n=52) or to the study group treated with platelet gel (n=50). Due to insufficient data, the final analysis included 32 study group patients and 41 control group patients. There were no significant differences in the two groups based on comparison of postoperative wound scores, visual analog scale, Western Ontario MacMaster (WOMAC) questionnaire scores, knee function, use of analgesics, and the pre- and postoperative hemoglobin values. Results of the study indicated that the application of platelet gel “did not promote wound healing” and had “no effect on pain, knee function, or hemoglobin values.”

Wound Healing: The outcomes of systematic reviews, randomized controlled trials, and case series investigating the efficacy of autologous platelet gel in the treatment of wounds including lower extremity ulcers, pressure ulcers, diabetic ulcers, and venous ulcers have been conflicting. In a systematic review and meta-analysis of nine randomized controlled trials (n=325), Martinez-Zapata et al. (2012) assessed the outcomes of autologous platelet-rich plasma (PRP) for the treatment of chronic wounds. The range of participants per study was 10–86 (median 26). Follow-ups ranged from 8–40 weeks (median 12 weeks). Four studies included subjects with mixed chronic wounds (wounds caused by more than one etiology and wounds of several etiologies in the same trial), three studies included subjects with venous leg ulcers and two studies considered patients with diabetic foot ulcers. The two studies that reported percentage of wound area healed, reported a statistically significant improvement with PRP. There were no statistically significant differences reported between PRP and standard of care or placebo in total healing, the total area epithelialized, wound complications and adverse effects. The results of the meta-analyses showed no difference in the rate of wounds completely healed when PRP was compared to standard care, with or without placebo, by ulcer etiology or by the procedure used to obtain the PRP. Limitations of the studies included: the heterogeneous, small patient populations; heterogeneity of PRP preparation; short-term follow-up; and risk of bias.

Carter et al. (2011) conducted a systematic review and meta-analysis to evaluate the use and clinical outcomes of APDGF for the treatment of cutaneous skin wounds compared to standard wound care. A total of 24 studies met inclusion criteria (i.e., three systematic reviews, 12 randomized controlled trials, two prospective cohort studies, three prospective comparative studies and four retrospective reviews). Three main types of wounds were treated: open chronic wounds, acute surgical wounds with primary closure and acute surgical wounds with secondary closure. Follow-ups ranged from 1 week to six months. A meta-analysis including four randomized controlled trials on chronic wound healing showed results in favor of platelet gel compared to saline gauze, saline gel or no treatment. A meta-analysis for acute wound primary closure was not undertaken because there were only two studies and their outcome measures were incompatible. A meta-analysis of infection and pain for acute wounds showed that there was no significant difference in superficial infection rates using platelet gel compared to no topical treatment. There was also no significant difference in postoperative pain using platelet gel compared to saline spray or no topical treatment. Limitations of the studies included the heterogeneous patient populations, short-term follow-ups, heterogeneous outcome measures, conflicting results, various types of APDGF products and regimens, and multiple heterogeneous wound care regimens.

Kazakos et al. (2009) performed a randomized controlled trial to evaluate the benefit of APDGF in the treatment of soft tissue acute wounds (n=59). The wounds included open fracture of the tibia (n=37), closed fracture of the tibia with skin necrosis (n=9), wide friction burns in the femur (n=11), and one each acute injury of the Achilles tendon and open bimalleolar fracture. The study group (n=27) was treated with topical APDGF and the control group (n=32) was treated with conventional dressings. Follow-up ranged from 2.5–21 months (mean six months). The wound healing rate was significantly faster in the study group at weeks 1, 2 and 3 (p=0.003, p<0.001 and p<0.001, respectively). The mean time to plastic reconstruction in the APDGF group was significantly shorter (21.26 days) compared the control group (40.59 days) (p<0.001). The control group reported higher pain scores at the end of the second and third weeks. No adverse events were observed. Limitations of the study include the small, heterogeneous patient population.

In a prospective double-blind randomized controlled trial (n=44), Litmathe et al. (2009) evaluated the efficacy of APDGF for wound healing following cardiac surgery in high-risk patients (e.g., obesity, diabetes, smokers, peripheral vascular disease, heart failure). All patients underwent either isolated coronary artery bypass grafting (CABG) or combined coronary surgery and valve replacement. APDGF was applied to the wound in the study group (n=22) but not in the control group (n=22). There were no statistically significant differences in sternal wound healing or wound healing at the vein harvesting sites. No beneficial effects of APDGF were noted in this study.

Driver et al. (2006) (n=40) reported that 68.4% of patients with nonhealing diabetic foot ulcers randomized to platelet gel healed compared to 42.9% in the control group. Two randomized controlled trials reported no significant difference in outcomes in treatment of chronic venous ulcers (Senet, et al., 2003; Stacey, et al., 2000) (n=15, 42, respectively) using platelet gel. Additional randomized controlled trials with larger sample sizes are indicated to establish the role of platelet gel in the treatment of lower extremity ulcers.

Multiple Indications: Martinez-Zapata et al. (2009) conducted a systematic review of the literature to evaluate the safety and efficacy of autologous platelet gel in tissue regeneration reported in randomized controlled trials (n=20). The trials that met inclusion criteria included oral and maxillofacial surgery (n=11), chronic skin ulcers (n=7), and surgical wounds (n=2). In four oral and maxillofacial surgery studies (n=153), which included patients suffering from chronic periodontitis, a meta-analysis was completed. A significant improvement was seen in the depth reduction of gingival recession following the use of platelet gel. The clinical attachment level of a subgroup of patients with more severe disease was better than the results in patients with incipient illness. Meta-analysis revealed no significant differences in patients treated with platelet gel for chronic skin ulcers or surgical wounds. Because of the poor quality of the studies (e.g., small patient populations, large confidence intervals, lack of reporting of adverse events, and heterogeneous outcome measures), well-designed large randomized controlled trials are needed to validate the finding of this analysis.

Systematic Review of Multiple Indications/Products:

Sheth et al. (2012) conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) (n=23) and prospective cohort series (n=10) to assess outcomes regarding decrease in pain and improved healing and function of autologous blood concentrates compared with control therapy in the treatment of orthopedic injuries (e.g., anterior cruciate ligament [ACL] reconstruction, spinal fusion, total knee arthroplasty, humeral epicondylitis, and Achilles tendinopathy). Patient populations ranged from 10–165 subjects per study with follow-ups ranging from two days to two years. Primary outcome measures to define healing and patient-reported quality of life measures included functional parameters (e.g., knee stability, tenderness threshold, visual analog scale [VAS], and Disabilities of the Arm, Shoulder and Hand [DASH] score) and radiographic imaging parameters (e.g., computed tomography, magnetic resonance imaging). Regarding functional outcome measures, six RCTs showed that platelet-rich plasma (PRP) provided a significant functional benefit, fifteen studies demonstrated no difference between PRP and the control, and one study reported a significant benefit from the control. Three prospective cohort studies showed a significant functional benefit with PRP, six reported no difference and one study reported significant benefit with the control. There were no significant differences in VAS scores between the PRP groups and the control groups (p=0.10). Regarding imaging outcomes, there were no significant differences with regard to solid fusion (p=0.33) or the number of patients with low MRI signal intensity of the autograft used in ACL reconstruction between the platelet-rich plasma and control groups (p=0.19). Limitations of the studies included heterogeneity of the preparation (e.g., number of centrifugations, or use of anticoagulation or activating agents) and dosage (volume and number of applications) of the blood concentrates, study protocol, outcome measures and orthopedic indications. Additional limitations included the variability across all pooled outcomes in terms of follow-up due to a lack of consistent study time lines, and the potential for bias in the observational, nonrandomized data.

Professional Societies/Organizations

In the 2013 evidence-based guidelines on osteoarthritis of the knee, the American Academy of Orthopedic Surgeons (AAOS) stated that they are unable to recommend for or against growth factor injections and/or platelet-rich plasma for the treatment of symptomatic osteoarthritis of the knee. AAOS stated that there is a lack of compelling evidence that has resulted in an unclear balance between benefits and potential harm.

Use Outside of the US

According to the overall body of literature, the use of APDGR is being investigated worldwide (e.g., UK, Japan, Asia, Europe). Recommendations in a 2011 guidance document by the National Institute for Health and Clinical

Excellence (NICE) (United Kingdom) stated that autologous platelet-rich plasma gel should not be offered as part of the management of diabetic foot problems unless it is part of a clinical trial.

Summary

Evidence in the published peer-reviewed literature does not support the safety and effectiveness of autologous platelet-derived growth factors (APDGF) for any indication. Studies primarily included small patient populations and short-term follow-ups. In some cases, retreatment was required after the use of platelet-rich plasma (PRP) and more adverse events were reported. In studies reporting initially appearing benefit following the use of APDGF, the benefit was not typically maintained. Overall, data from systematic reviews and randomized controlled trials have reported that there were no significant differences in outcomes (e.g., healing, pain relief, activity) with APDGF.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.

2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Experimental/Investigational/Unproven/Not Covered:

CPT ^{®*} Codes	Description
0232T	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed

HCPCS Codes	Description
S9055	Procuren or other growth factor preparation to promote wound healing

*Current Procedural Terminology (CPT[®]) © 2013 American Medical Association: Chicago, IL.

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