

# Surgical Periodontics: Regenerative Procedures

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[➔ Instructions for Use](#)

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## Related Dental Policies

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## Coverage Rationale

### Bone Replacement Grafts for Retained Natural Teeth

Bone Replacement Grafts for retained natural teeth are indicated for the following:

- Infrabony/Intrabony vertical defects
- Class II Furcation involvements

Bone Replacement Grafts for retained natural teeth are not indicated for the following:

- Non-vertical defects
- Individuals with an uncontrolled underlying medical condition
- Individuals who have been non-compliant with previous periodontal therapies
- Individuals with poor oral hygiene
- Teeth with a hopeless prognosis

### Biologic Materials to Aid in Soft and Osseous Tissue Regeneration

The following Biological Materials are indicated to aid in the regeneration of periodontal tissues:

- Biologic growth factors (i.e., Platelet rich fibrin (PRF), platelet rich plasma (PRP) and platelet derived growth factor (PDGF)
- Enamel matrix derivative (Emdogain®)
- Bioactive glass

All other Biological Materials, including, but not limited to bone morphogenic proteins and amniotic membranes are not indicated for periodontal regeneration due to insufficient evidence of efficacy.

### Surgical Revision Procedure (per Tooth)

A surgical revision procedure may be indicated to correct an abnormal healing response that interferes with the therapeutic goals of the original regenerative surgical procedure.

## Exclusions

- Any Dental Procedure performed solely for cosmetic/aesthetic reasons
- Dental Services that are not Necessary
- Procedures that are considered to be Experimental, Investigational or Unproven

## Definitions

**Anatomical Crown:** That portion of tooth normally covered by, and including, enamel. (ADA)

**Biologic Materials/Biologic Response Modifiers:** Agents that alter wound healing or host-tumor interaction. Such materials can include cytokines, growth factor, or vaccines, but do not include any actual hard or soft tissue graft material. These agents are added to graft material or used alone to effect acceleration of healing or regeneration in hard and soft tissue surgical procedures. (ADA)

**Experimental, Investigational or Unproven Services:** Medical, dental, surgical, diagnostic, or other health care services, technologies, supplies, treatments, procedures, drug therapies or devices that, are determined to be:

- Not approved by the U.S. Food and Drug Administration (FDA) to be lawfully marketed for the propose use and not identified in the American Hospital Formulary Service or the United States Pharmacopoeia Dispensing Information as appropriate for the proposed use; or
- Subject to review and approval by any institutional review board for the proposed use; or
- The subject of an ongoing clinical trial that meets the definition of a Phase 1, 2 or 3 clinical trial set forth in the FDA regulations, regardless of whether the trial is actually subject to FDA oversight; or
- Not demonstrated through prevailing peer-reviewed professional literature to be safe and effective for treating or diagnosing the condition or illness for which its use is proposed; or
- Pharmacological regimens not accepted by the American Dental Association (ADA) Council on Dental Therapeutics

**Furcation:** The anatomic area of a multirooted tooth where the roots diverge. A furcation involvement refers to loss of periodontal support in a Furcation (ADA). The Glickman Classification of Tooth Furcation Grading (Sims, 2015):

- Grade I:
  - Incipient
  - Just barely detectable with examination hand instruments
  - No horizontal component of the furcation is evident on probing
- Grade II:
  - Early bone loss
  - Examination hand instrument goes partially into the furcation, but not all the way through
  - Furcation may be grade II on both sides of the tooth, but are not connected
- Grade III:
  - Advanced bone loss
  - Examination hand instrument goes all the way through furcation, to other side of tooth
  - Furcation is through-and-through
- Grade IV:
  - Through-and-through, plus furcation is clinically visible due to gingival recession

**McGuire Classification of Tooth Prognosis:** (Levi 2016)

- Good: Teeth with adequate periodontal support where the etiologic factors can be controlled, including systemic factors
- Fair: No more than 25% attachment loss with Grade 1 Furcation invasion which can be maintained. Plaque control and systemic factors can be maintained
- Poor: As much as 50% bone loss with Grade II Furcation invasions, poor crown: root ratio; Mobility greater than Miller Class I; systemic factors; poor patient participation in treatment
- Questionable: Teeth with greater than 50% attachment loss; Grade II or III Furcation involvements; the tooth is not easily maintained either with professional hygiene or by the patient
- Hopeless: Inadequate attachment to support the tooth; Class III or IV Furcation involvement; Miller Class III Mobility; the tooth cannot be maintained with adequate plaque control by the clinician or by the patient

**Mobility:** The movement of a tooth in its socket resulting from an applied force. (AAP) Miller Index of Tooth Mobility (Harpenau 2013):

- Class 0: Normal physiologic tooth movement
- Class I: First distinguishable signs of movement beyond normal
- Class II: Tooth movement up to 1mm in any direction
- Class III: Tooth can be moved more than 1mm in any direction and/or the tooth can be depressed into the socket

**Necessary:** Dental Services and supplies which are determined through case-by-case assessments of care based on accepted dental practices to be appropriate; and

- Needed to meet your basic dental needs; and
- Rendered in the most cost-efficient manner and type of setting appropriate for the delivery of the dental service; and
- Consistent in type, frequency and duration of treatment with scientifically based guidelines of national clinical, research, or health care coverage organizations or governmental agencies that are accepted; and
- Consistent with the diagnosis of the condition; and
- Required for reasons other than the convenience of you or your dental provider; and
- Demonstrated through prevailing peer-reviewed dental literature to be either:
  - Safe and effective for treating or diagnosing the condition or sickness for which its use is proposed; or
  - Safe with promising efficacy:
    - For treating a life threatening dental disease or condition; and
    - In a clinically controlled research setting; and
    - Using a specific research protocol that meets standards equivalent to those defined by the National Institutes of Health

**Osseous Surgery:** Procedures to modify bone support altered by periodontal disease, either by reshaping the alveolar process to achieve physiologic form without the removal of alveolar supporting bone, or by the removal of some alveolar bone, thus changing the position of the crestal bone relative to the tooth root. (See: Ostectomy; Osteoplasty)

**Quadrant:** One of the four equal sections into which the dental arches can be divided; begins at the midline of the arch and extends distally to the last tooth. (ADA)

**Tooth Bounded Space:** A space created by one or more missing teeth that has a tooth on each side. (ADA)

## Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CDT Code	Description
D4263	Bone replacement graft – retained natural tooth – first site in quadrant
D4264	Bone replacement graft – retained natural tooth – each additional site in quadrant
D4265	Biologic materials to aid in soft and osseous tissue regeneration
D4268	Surgical revision procedure, per tooth
D4999	Unspecified periodontal procedure, by report

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## Description of Services

The American Academy of Periodontology (AAP) guidelines stress that periodontal health should be achieved in the least invasive and most cost effective manner for each individual. Regenerative procedures involve bone grafting, guided tissue regeneration as well as the use of various biological materials. Success of these procedures is highly dependent on individual

patient considerations such as level of oral hygiene, smoking, and overall health status. The development of various regenerative technologies in medicine and dentistry is rapidly advancing and the technologies outlined in this policy are not all inclusive. For information on guided tissue regeneration using barrier membranes, refer to the Dental Clinical Policy titled [Dental Barrier Membrane Guided Tissue Regeneration](#).

## Clinical Evidence

### Amniotic Membranes

Gulameabasse et al. (2020) performed a systematic review of the clinical applications where chorion membrane (CM) and amnion/chorion membrane (ACM) were used for oral tissue regeneration procedures. Seven clinical applications of CM and ACM in oral and periodontal surgery were identified: gingival recession treatment, intrabony and furcation defect treatment, alveolar ridge preservation, keratinized gum width augmentation around dental implants, maxillary sinus membrane repair, and large bone defect reconstruction. CM and ACM were compared to negative controls (conventional surgeries without membrane) or to the following materials: collagen membranes, dense polytetrafluoroethylene membranes, platelet-rich fibrin membranes, amnion membranes, and to a bone substitute. Several studies support the use of CM and ACM as an efficient alternative to current techniques for periodontal and oral soft tissue regeneration procedures. However, further studies are necessary to increase the level of evidence and especially to demonstrate their role for bone regeneration.

In a 2019 randomized clinical trial, Temraz et al. compared the clinical and radiographic outcomes of amnion chorion membrane (ACM) with demineralized bone matrix (DBM) in a putty form in management of periodontal intrabony defects. Twenty-two participants with severe chronic periodontitis and intrabony defects were randomly assigned in two equal parallel groups. Each group was treated with open flap debridement (OFD) and ACM or OFD and DBM putty. Plaque index, gingival index, pocket depth (PD), clinical attachment level (CAL) and radiographic measurement of bone defect area (BDA) were recorded at baseline, 3 and 6 months postoperatively. Both ACM and DBM putty demonstrated significant improvement in all clinical and radiographic outcomes at 6 months compared to baseline values. However, no significant difference was observed between the two treatment modalities when compared at different time intervals. Six months postoperatively, ACM showed  $3.18 \pm 0.85$  mm PD reduction and  $2.25 \pm 0.75$  mm CAL gain, while DBM putty revealed  $3.45 \pm 1.08$  mm PD reduction and  $2.73 \pm 0.85$  mm CAL gain. Radiographic assessment showed that mean baseline BDA for ACM group was  $10.39 \pm 3.86$  mm<sup>2</sup>, which significantly reduced to  $5.21 \pm 2.38$  after 6 months. Mean BDA mm<sup>2</sup> in DBM putty group also significantly improved after 6 months,  $5.35 \pm 3.63$  mm<sup>2</sup> when compared to baseline values  $9.80 \pm 5.77$  mm<sup>2</sup>. Both ACM barrier and DBM putty allograft provided significant improvement in clinical and radiographic outcomes after 6 months, yet no significant differences were noticed between them. This trial implied that both biomaterials have a potential regenerative capacity in treating periodontal intrabony defects.

Mahajan et al. (2018) conducted a study to clinically compare the efficacy of placental membrane (Amnion) and collagen membrane (Healiguide) for the treatment of gingival recession. Twelve patients having isolated bilateral gingival recession defects were included in the study and were divided into two groups randomly. Group I were treated by coronally positioned flap and amnion membrane and Group II were treated by coronally positioned flap and collagen membrane (Healiguide)™. Clinical parameters, including dental plaque index (PI), gingival index (GI), gingival recession depth, probing pocket depth, clinical attachment level, and gingival biotype, were recorded before surgery at baseline and then reevaluated at 3 and 6 months postoperatively. The results showed statistically no significant difference ( $P > 0.05$ ) in dental PI improvement, GI and probing pocket depth for both groups. Significant reduction in gingival recession defects and gain in clinical attachment level was observed in both the groups. Intergroup comparison of gingival recession defects and clinical attachment level yielded nonsignificant differences. However, a statistically significant increase ( $P < 0.05$ ) in gingival tissue thickness was observed in Group II as compared to Group I. The authors concluded that both membranes are equally efficacious in the treatment of gingival recession, with more gingival tissue thickness (gingival biotype) enhancement observed in sites treated with collagen membrane.

In a 2018 comprehensive systematic review, Fénelon et al. analyzed 17 articles including five areas of potential clinical application for human amniotic membrane (hAM): periodontal surgery, cleft palate and tumor reconstruction, prosthodontics and peri-implant surgery. Overall, periodontal surgery was the only discipline to assess the efficacy of hAM with randomized clinical trials. The wide variability of preservation methods of hAM and the lack of objective measurements were observed in this study. There is weak clinical evidence demonstrating convincingly the benefit of hAM in oral surgery compared to standard surgery. Several studies now suggest the interest of hAM for periodontal tissue repair. Due to its biological and mechanical

properties, hAM seems to be a promising treatment for wound healing in various areas of oral reconstruction. However, further randomized clinical trials are needed to confirm these preliminary results.

## Bioactive Glass

Naqvi et al. (2017) conducted a randomized controlled trial to compare the clinical effectiveness of the combination of PRF and bioactive glass putty and bioactive glass putty alone as regenerative techniques for intrabony defects in humans. Ten pairs of intrabony defects were surgically treated with PRF and bioactive glass putty (Test group) on one side or bioactive glass putty alone (Control group) on other side. The primary outcomes of the study included changes in probing depth; attachment level and bone fill of osseous defect. The clinical parameters were recorded at baseline, 3, 6, and 9 months. Radiographic assessment was done using standardized intraoral periapical radiographs. Differences between baseline and postoperative measurements between the control and test groups were calculated using independent t-test. Comparisons were made within each group between baseline, 3 months, 6 months and 9 months using the ANOVA test followed by Bonferroni test. The mean probing depth reduction was greater in the test group (bioactive glass putty and PRF) i.e., (3.2±2.3 mm) than in the control group (bioactive glass putty alone) i.e., (3.15±1.06 mm). The mean CAL gain was also greater in the test group (4.1±1.73 mm) as compared to the control group (3.15±1.06 mm), (p-value<0.95). Furthermore significantly greater mean bone fill was found in the test group (7.1±1.37 mm) as compared to the control group (5.7 ± 1.64 mm), (p-value<0.043). The results of this study showed both the groups bioactive glass putty alone (Control Group) and the combination of PRF and bioactive glass putty (Test Group) are effective in the treatment of intrabony defects. The bioactive glass putty appears to be a suitable vehicle to administer biologic substances like PRF and growth factors to induce the new bone regeneration.

Sohrabi et al. (2012) conducted a meta-analysis of randomized controlled clinical trials to evaluate bioactive glass in the treatment of intrabony and furcation defects. Criteria included publication in English, follow-up duration of ≥6 months, baseline and follow-up measures of probing depth (PD) and clinical attachment levels (CAL) with 95% confidence intervals (CIs), and an appropriate control arm. Twenty-five citations were identified, 15 of which were included in the final analysis. Pooled analyses showed that BG was superior to control for both measures. CAL heterogeneity appeared secondary to active controls versus open flap debridement (OFD) alone and to defect-type modifying BG treatment success. Per subgroup analyses, the benefit of BG over control treatment was highly significant only in studies comparing BG to OFD. The authors concluded that treatment of intrabony defects with BG imparts a significant improvement in both PD and CAL compared to both active controls and OFD.

## Bone Morphogenic Proteins

Medikeri et al. (2019) conducted a systematic review to assess the amount of radiographic bone fill, clinical attachment level (CAL) gain, and reduction in pocket depth (PD) in patients with intrabony defects in periodontitis patients following the use of recombinant human bone morphogenetic protein-2 (rhBMP-2). Studies using rhBMP-2 to treat periodontal intrabony defects of the maxillary or mandibular region for the treatment of intrabony defects (1, 2, or 3-walled) for periodontal regeneration was compared to other surgical treatment utilizing growth factors, alloplastic, allogeneic grafts, and xenografts with follow-up period of at least 6 months were included. A total of 48 subjects in 2 studies met the inclusion criteria. The results found that rhBMP-2 showed statistically significant results with respect to radiographic defect resolution, CAL, and PD reduction at 9 months compared to open-flap debridement but showed statistically significant results only with respect to radiographic bone fill when compared with platelet-rich fibrin at 6 months. The authors concluded that rhBMP-2 may provide a promising alternative to traditional grafting procedures therapy that can enhance periodontal regeneration in patients having intrabony defects, however due to limited human studies, no definitive evidence exists to ascertain the effectiveness of rhBMP-2 in the treatment of intrabony defects in periodontal diseases.

In a 2016 systematic review, Kaur et al. reviewed the clinical data currently available on the use of bone morphogenetic proteins (BMPs) in various periodontal applications. BMPs have been shown in preclinical and clinical studies to enhance periodontal regeneration. BMPs have demonstrated beyond doubt their role as a superior alternative of autogenous bone graft. However, much of the data in BMP research has been derived from animal studies which are important as far as providing base line data for further clinical studies. The available data on use of rhBMP-2 and 7 in humans are promising in showing an osteoinductive potential in periodontal regeneration, but not conclusive in the predictability and consistency results to allow clinical use at this stage, other than in well-designed clinical trials. Since many other factors including smoking, age, steroid use, malnutrition, and disease severity play a role in determining the physiology of periodontal regeneration in humans, the true efficacy and safety of these agents for different scenarios must be established in carefully designed prospective randomized clinical trials before they are approved for use. Research should continue to focus on improving the use of BMPs in the current clinical applications.

Sasikumar et al. (2012) conducted a literature review regarding the application of bone morphogenetic proteins to periodontal and peri-implant tissue regeneration. Several studies showed significant regeneration of the periodontal tissues and it is important to understand the biologic processes of periodontal wound healing and the effects of these biologic processes on BMP activity. Further studies are needed for the development of delivery systems that have mechanical and surgical properties appropriate for controlled release of bone morphogenetic proteins and identifying optimal condition for the use of BMPs for periodontal regeneration.

### **Enamel Matrix Derivative (EMD, Emdogain®)**

Matarraso et al. (2015) conducted a systematic review and meta-analysis was to assess the clinical efficacy of regenerative periodontal surgery of intrabony defects using a combination of enamel matrix derivative (EMD) and bone graft compared with that of EMD alone. The primary outcome was gain of clinical attachment (CAL). Weighted means and forest plots were calculated for CAL gain, probing depth (PD), and gingival recession (REC). Twelve studies reporting on 434 patients and 548 intrabony defects were selected for the analysis. Mean CAL gain amounted to  $3.76 \pm 1.07$  mm (median 3.63 95 % CI 3.51-3.75) following treatment with a combination of EMD and bone graft and to  $3.32 \pm 1.04$  mm (median 3.40; 95 % CI 3.28-3.52) following treatment with EMD alone. Mean PD reduction measured  $4.22 \pm 1.20$  mm (median 4.10; 95 % CI 3.96-4.24) at sites treated with EMD and bone graft and yielded  $4.12 \pm 1.07$  mm (median 4.00; 95 % CI 3.88-4.12) at sites treated with EMD alone. Mean REC increase amounted to  $0.76 \pm 0.42$  mm (median 0.63; 95 % CI 0.58-0.68) at sites treated with EMD and bone graft and to  $0.91 \pm 0.26$  mm (median 0.90; 95 % CI 0.87-0.93) at sites treated with EMD alone. The authors concluded results indicate that the combination of EMD and bone grafts may result in additional clinical improvements in terms of CAL gain and PD reduction compared with those obtained with EMD alone.

Koop et al. (2012) conducted a systematic review to give an updated answer to the question of whether the additional use of EMD in periodontal therapy is more effective compared with a control or other regenerative procedures. The use of EMD in treatment of intrabony defects, furcations, and recessions was evaluated. 27 randomized controlled trials (20 for intrabony defects, one for furcation, and six for recession) with  $\geq 1$  year of follow-up were included. The primary outcome variable for intrabony defects was the change in clinical attachment level (CAL), for furcations the change in horizontal furcation depth, and for recession complete root coverage. The primary outcome variable for intrabony defects was the change in clinical attachment level (CAL), for furcations the change in horizontal furcation depth, and for recession complete root coverage. The results showed the treatment of intrabony defects with EMD showed a significant additional gain in CAL of 1.30 mm compared with open-flap debridement, root conditioning, or placebo, but no significant difference compared with resorbable membranes was shown. The use of EMD in combination with a coronally advanced flap compared with a coronally advanced flap alone showed significantly more complete root coverage, but compared with a connective tissue graft, the result was not significantly different. The use of EMD in furcations ( $2.6 \pm 1.8$  mm) gave significantly more improvement in horizontal defect depth compared with resorbable membranes ( $1.9 \pm 1.4$  mm) as shown in one study. The authors concluded the following: for intrabony defects, the use of EMD is superior to control treatments but as effective as resorbable membranes; the additional use of EMD with a coronally advanced flap for recession coverage will give superior results compared with a control but is as effective as a connective tissue graft; and the use of EMD in furcations will give more reduction in horizontal furcation defect depth compared with resorbable membranes.

### **Biologic Growth Factors (Platelet Rich Plasma, Platelet Rich Fibrin and Platelet Derived Growth Factors)**

In a 2019 meta-analysis, Baghele et al. evaluated the actual quantitative mean gain for various clinical (clinical attachment level [CAL], probing pocket depth [PPD] and gingival marginal level [GML]) and radiographic (intrabony defect depth [IBD]) parameters of Platelet Concentrates- PCs (PRP/PRF) as sole grafting material along with open flap debridement (OFD) and OFD alone in the treatment of intrabony defects. The eligibility criteria included human randomized clinical trials, either of a parallel group or a split-mouth design with follow-up period of at least 6 months. Periodontal intrabony defects with radiographic IBD  $\geq 3$  mm with corresponding CAL  $\geq 5$  mm were included. The results showed actual quantitative mean gains for OFD with PRF/PRP - CAL = 1.1 mm, IBD = 1.68 mm, PPD = 0.97 mm and GML = 0.48 mm over and above that of OFD alone. The authors concluded that due to very high heterogeneity of the studies, these results may not be dependable. Apart from gains in radiographic bone fill, all other periodontal clinical parameters showed negligible gains. Using PRF technologies in periodontal intrabony defects may not be of great clinical significance over and above that of OFD alone.

Zhou et al. (2018) conducted a systematic review and meta-analysis to evaluate and compare the clinical outcomes of enamel matrix derivative (EMD), platelet-rich plasma (PRP), platelet rich fibrin (PRF), and amnion membrane (AM) in conjunction with

DFDBA in patients with periodontal intrabony defects. This may also provide some guidance on clinical management strategy for the option of additional bioactive materials. Included were RCTs that compared the performances of DFDBA with or without one of the four bioactive materials (EMD, PRP, PRF, and AM) in patients with periodontal intrabony defects, with follow-up periods of  $\geq 6$  months. The exclusion criteria included retrospective cohort studies, animal studies, in vitro studies, case reports, case series, and reviews. Nine RCTs (four with a parallel design and five with a split-mouth design) published between 2008 and 2017 were selected, and included a total of 259 patients. The follow-up period ranged from 6 to 12 months. The results showed PRF exerts the most significant adjunctive effect on soft tissue healing, while PRP exhibits an impact on hard tissue reconstruction in the treatment of periodontal intrabony defects. EMD and AM demonstrated little additional benefit. PRF/PRP could be a preferred adjunct to promote periodontal regeneration due to proven biological effects, low costs, and ease of preparation. The authors recommend standardization of the protocol for the preparation and application of PRF/PRP is needed to obtain an optimal effect in regenerative procedures.

In a 2018 Cochrane database systematic review, Del Fabbro et al. sought to assess the effects of autologous platelet concentrates (APC) used as an adjunct to periodontal surgical therapies (open flap debridement (OFD), OFD combined with bone grafting (BG), guided tissue regeneration (GTR), OFD combined with enamel matrix derivative (EMD) for the treatment of infrabony defects. The primary outcomes assessed were: change in probing pocket depth (PD), change in clinical attachment level (CAL), and change in radiographic bone defect filling (RBF). The authors included randomised controlled trials (RCTs) of both parallel and split-mouth design, involving patients with infrabony defects requiring surgical treatment. Studies had to compare treatment outcomes of a specific surgical technique combined with APC, with the same technique when used alone. Data was organized into four groups, each comparing a specific surgical technique when applied with the adjunct of APC or alone: 1. APC + OFD versus OFD, 2. APC + OFD + BG versus OFD + BG, 3. APC + GTR versus GTR, and 4. APC + EMD versus EMD. Based on very low quality evidence, the results showed:

- APC + OFD versus OFD alone: Twelve studies were included in this comparison, with a total of 510 infrabony defects. There is evidence of an advantage in using APC globally from split-mouth and parallel studies for all three primary outcomes.
- APC + OFD + BG versus OFD + BG: Seventeen studies were included in this comparison, with a total of 569 infrabony defects. Considering all follow-ups, as well as 3 to 6 months and 9 to 12 months, there is evidence of an advantage in using APC from both split-mouth and parallel studies for all three primary outcomes.
- APC + GTR versus GTR alone: Seven studies were included in this comparison, with a total of 248 infrabony defects. Considering all follow-ups, there is probably a benefit for APC for both PD and CAL. However, given the wide confidence intervals, there might be a possibility of a slight benefit for the control. When considering a 3 to 6 months and a 9 to 12 months follow-up there were no benefits evidenced, except for CAL at 3 to 6 months. No RBF data were available.
- APC + EMD versus EMD: Two studies were included in this comparison, with a total of 75 infrabony defects. There is insufficient evidence of an overall advantage of using APC for all three primary outcomes.
- All studies in all groups reported a survival rate of 100% for the treated teeth. No complete pocket closure was reported.

The authors concluded that there is very low-quality evidence that the adjunct of APC to OFD or OFD + BG when treating infrabony defects may improve probing pocket depth, clinical attachment level, and radiographic bone defect filling. For GTR or EMD, insufficient evidence of an advantage in using APC was observed.

Patel et al. (2017) conducted a randomized controlled trial to assess the adjunctive use of platelet-rich fibrin (PRF) in regenerative management of intrabony defects in comparison with open flap debridement (OFD). Twenty-six bilateral defects (13 per group) in 13 patients were randomized as either PRF (test group) or OFD alone (control group) sites. Primary outcomes assessed were changes in PD, CAL, and percentages of bone fill at 6, 9, and 12 months. Secondary outcome was assessment of wound healing using a wound healing index (WHI). The PRF group showed significant improvement in clinical parameters compared with the control group at 6, 9, and 12 months. The PRF group showed a bone fill of  $45.18\% \pm 7.57\%$ , which was statistically significant compared with  $21.6\% \pm 9.3\%$  seen in the control group at the end of the study period. The PRF group also showed significant soft tissue healing and reduction in PD. WHI also showed significant advantages for the PRF group. The authors concluded that the adjunctive use of PRF to conventional OFD may be potentially used in the treatment of intrabony defects.

Ravi et al. (2017) completed a split-mouth randomized controlled clinical trial to assess the effect of plasma rich growth factor (PRGF) associated with guided tissue regeneration (GTR) versus GTR only in the treatment of intrabony defects (IBDs) in patients with chronic periodontitis (CP). Patients with CP with 42 contralateral 2- and 3-walled defects were randomly assigned to test (PRGF+GTR) and control (GTR alone) treatment groups. Clinical and radiographic assessments performed at baseline

and after 6 months were: gingival index (GI), probing depth (PD), clinical attachment level (CAL), radiologic defect depth, and bone fill. The results demonstrated that the parameters measured at baseline and after 6 months showed mean PD reduction of  $3.37 \pm 1.62$  mm in the control group and  $4.13 \pm 1.59$  mm in the test group. There was a significant difference in mean change in CAL in the control group ( $5.42 \pm 1.99$ ) and the test group ( $5.99 \pm 1.77$ ). Mean change in GI was  $1.89 \pm 0.32$  and  $1.68 \pm 0.58$  in the control group and test group, respectively, and the difference was statistically significant. When compared between groups, clinical parameters did not show any statistically significant variations. Mean radiographic bone fill was  $1.06 \pm 0.81$  and  $1.0 \pm 0.97$  in the control group and test group, respectively. However, the difference was not statistically significant. The authors concluded that PRGF with GTR, as well as GTR alone, was effective in improving clinical and radiographic parameters of patients with CP at the 6-month follow-up. There was no additive effect of PRGF when used along with GTR in the treatment of IBDs in patients with CP in terms of both clinical and radiologic outcomes.

Cieplik et al. (2017) completed a 13-year follow-up of a randomized controlled clinical split-mouth study on the influence of autogenous platelet concentrate (APC) on combined guided tissue regeneration (GTR)/graft therapy in intrabony defects. In 25 patients, two deep contra-lateral intrabony defects were treated according to GTR using  $\beta$ -TCP and bio-resorbable membranes. In test defects, APC was applied additionally. After 13 years, clinical healing results were assessed and compared to results at baseline and after 1 year, and a tooth survival analysis completed. After 13 years, 22 patients were available for tooth survival analysis showing 81.8% of test and 86.4% of control teeth still in situ. Based on the 15 patients still available for split-mouth analysis, median CAL was 10.0 mm in test and 12.0 mm in control sites at baseline. After 1 year, both groups revealed significant CAL gains of 5.0 mm, followed by a new CAL loss of 1.0 mm in the following 12 years. There were no significant differences between test and control sites. The authors concluded that within the limits of this study, the data shows that most of the CAL gain following GTR can be maintained over 13 years. The additional use of APC had no positive influence on the long-term stability.

Miron et al. (2017) conducted a systematic review with the goal of gathering the extensive number of articles published to date on platelet rich fibrin (PRF) in the dental field to better understand the clinical procedures where PRF may be utilized to enhance tissue/bone formation. Randomized clinical trials were searched systematically until May 2016 and separated into the following categories: intrabony and furcation defect regeneration, extraction socket management, sinus lifting procedures, gingival recession treatment, and guided bone regeneration (GBR) including horizontal/vertical bone augmentation procedures. In total, 35 articles were selected and divided accordingly. Overall, the use of PRF has been most investigated in periodontology for the treatment of periodontal intrabony defects and gingival recessions where the majority of studies have demonstrated favorable results in soft tissue management and repair. Little to no randomized clinical trials were found for extraction socket management, although PRF has been shown to significantly decrease dry socket complications in third molar sites. Little to no data was available directly investigating the effects of PRF on new bone formation in GBR, horizontal/vertical bone augmentation procedures, treatment of peri-implantitis, and sinus lifting procedures. The authors concluded that investigation supports the use of PRF for periodontal and soft tissue repair. There remains a lack of well-conducted studies demonstrating convincingly the role of PRF during hard tissue bone regeneration. Future human randomized clinical studies evaluating the use of PRF on bone formation are necessary.

Galav et al (2016) conducted a randomized controlled trial to compare the clinical efficacy of platelet-rich fibrin (PRF) with autogenous bone grafting (ABG) for the treatment of intra bony defects (IBD's) in chronic periodontitis. Twenty chronic periodontitis patients with IBDs were randomly treated by PRF or ABG. Probing pocket depth (PPD), relative attachment level (RAL), surgical reentry bone fills, and radiographic bone fill (RBF) were recorded at baseline, 3, 6, and 9 months postsurgery, respectively. Both PRF and ABG sites produced a significant improvement from baseline to 9 months for all the parameters. However, there was no significant difference between the two treatment modalities in the reduction of PPD and RAL gain at 9 months. In addition, ABG showed significantly greater RBF (30.34%) as compared to PRF (20.22%). Similar findings were supported by surgical reentry, where a surgical reentry of 65.31% at ABG sites and 43.64% at PRF sites was seen. The authors concluded that both ABG and PRF can be used predictably to reconstruct lost periodontal structures as indicated by PPD reduction and RAL gain. However, in terms of osseous defect fill, ABG yields more definitive outcome than PRF.

Nevins et al. (2013) provided results from a 36-month extension study of a multicenter, randomized, controlled clinical trial evaluating the effect and long-term stability of homodimer platelet derived growth factor (PDGF-BB) treatment in patients with localized severe periodontal osseous defects. A total of 135 participants were enrolled from six clinical centers for this trial, and eighty-three individuals completed the study at 36 months and were included in the analysis. The study investigated the local application of  $\beta$ -tricalcium phosphate scaffold matrix with or without two different dose levels of PDGF (0.3 or 1.0 mg/mL PDGF-BB) in patients possessing one localized periodontal osseous defect. Clinical and radiographic evidence of treatment success



was defined as percentage of cases with clinical attachment level (CAL)  $\geq 2.7$  mm and linear bone growth (LBG)  $\geq 1.1$  mm. Although there were no significant increases in CAL and LBG at 36 months among all groups, there were continued increases in CAL gain, LBG, and percentage bone fill over time, suggesting overall stability of the regenerative response. The authors concluded that PDGF-BB in a synthetic scaffold matrix promotes long-term stable clinical and radiographic improvements in patients with localized severe periodontal osseous defects.

Shah et al. (2014) conducted a systematic review and meta-analysis to determine the clinical and radiographic outcomes of using platelet-rich fibrin (PRF) for the treatment of periodontal intra-bony defect (IBD) compared with open flap debridement (OFD). Studies investigating the effect of platelet concentrate in surgical procedure for the treatment of periodontal intra osseous defects compared with the control group in which platelet concentrate was not used were included. A total of 298 sites were treated using PRF either in combination with graft or as a monotherapy in comparison to traditional OFD procedure. The meta-analysis showed a standard mean difference of 0.95 mm in clinical attachment level (CAL) and 2.33 mm in IBD after treatment of IBD with PRF compared with OFD. The authors concluded that clinically significant improvements in periodontal parameters such as CAL, IBD, and reduction in probing depth were achieved when IBDs were treated with PRF alone when compared to OFD.

## U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Products used for bone grafting, bone growth and resorbable and non-resorbable membranes for guided tissue regeneration use in periodontal applications are extensive. See the following websites for more information and search by product name in device name section: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>. (Accessed January 5, 2021)

Connective tissue grafting products from donated human skin are regulated by the (FDA) as human tissue for transplantation. They are processed and marketed in accordance with the FDA's requirements for banked human tissue (21 CFR, Part 1270 and Part 1271) and Standards for Tissue Banking of the American Association of Tissue Banks (AATB). Information is available at: <http://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/default.htm>. (Accessed January 5, 2021)

Currently, there are two biologic products approved by the FDA for regenerative periodontal therapy:

- GEM 21S™ (Osteohealth Company, Division of Luitpold Pharmaceuticals, Inc.); see the following website for more information: [http://www.accessdata.fda.gov/cdrh\\_docs/pdf4/P040013b.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf4/P040013b.pdf). (Accessed January 5, 2021)
- Emdogain™ (Straumann); see the following website for more information: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P930021>. (Accessed January 5, 2021)

There are several devices cleared for marketing by FDA for point-of-care preparation of platelet-rich plasma (PRP) from a sample of a patient's blood (see listings under product code JQC for additional devices). See the following website for more information: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>. (Accessed January 5, 2021)

In April 2003, the FDA approved the use of the GPS™ Platelet Separation Kit. The GPS™ separation kit aids separation of the patient's own blood components by density through the use of the GPS™-Thermo International Equipment Company (IEC) centrifuge. The GPS separation kit permits platelet rich plasma to be rapidly prepared from a small volume of the patient's blood that is drawn at the time of treatment. The GPS Platelet Separation Kit is designed for use in the clinical laboratory or intraoperatively at point of care, for the safe and effective preparation of platelet poor plasma and platelet concentrate from a small sample (50-60 ml) of whole blood. See the following website for more information: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K030555>. (Accessed January 5, 2021)

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## Policy History/Revision Information

Date	Summary of Changes
04/01/2021	<p><b>Coverage Rationale</b></p> <ul style="list-style-type: none"><li>Added language to clarify Bone Replacement Grafts are indicated for/in the listed conditions “for retained natural teeth”</li><li>Removed language addressing coverage limitations; refer to the member specific benefit plan document(s)</li></ul> <p><b>Supporting Information</b></p> <ul style="list-style-type: none"><li>Updated <i>Clinical Evidence, FDA, and References</i> sections to reflect the most current information</li><li>Archived previous policy version DCP014.07</li></ul>

## Instructions for Use

This Dental Clinical Policy provides assistance in interpreting UnitedHealthcare standard dental benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard dental plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Dental Clinical Policy is provided for informational purposes. It does not constitute medical advice.