Medical Coverage Policy

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Bone Graft Substitutes

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will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses bone graft substitutes. For the intent of this policy, many bone graft substitutes that are resorbed into the body, (e.g., allograft materials, bone void fillers with or without antibiotics, synthetic materials, recombinant bone morphogenetic proteins), do not meet the definition of an implant; they are considered surgical supplies. Implants are devices or materials which are placed into a surgically or naturally formed cavity of the human body to continuously assist, restore, or replace the function of an organ system or structure of the human body throughout its useful life. Implants generally include but are not limited to: stents, artificial joints, shunts, plates, screws, anchors and radioactive seeds, in addition to non-soluble, or solid plastic materials used to augment tissues or to fill in areas traumatically or surgically removed. Furthermore, materials defined by the United States Food and Drug Administration (FDA) as being "resorbable" materials (e.g., resorbable calcium salt bone void filler) are not considered to be implants. Over time, these materials are dissolved completely and replaced by bone tissue.

Coverage Policy

See EviCore Spine Surgery Guidelines for spine-related bone graft use.

See Medical Coverage Policy Stem Cell Therapy for Orthopedic Applications (CP 0552) for stem cell therapy (regenerative therapy) for orthopedic and/or musculoskeletal conditions.

See Medical Coverage Policy Autologous Platelet-Derived Growth Factors (Platelet-Rich Plasma [PRP]) (CP 0507) for uses of autologous platelet-derived growth factors (APDGF), for multiple conditions and indications.

Bone Graft Materials/Substitutes
The following bone graft materials and/or substitutes, used alone or in combination, are each considered medically necessary for enhancement of bone healing:

- allograft-based, including demineralized bone matrix (DBM)
- ceramic or polymer-based synthetic bone graft substitutes
- bone graft substitutes containing inorganic bone material (e.g., bovine, coral) when used alone or combined with another covered bone graft substitute

The following bone graft materials and/or substitutes are each considered experimental, investigational, or unproven for the enhancement of bone healing:

- human amniotic membrane bone graft substitute materials, including amniotic fluid stem cell substitutes
- cell-based substitutes (e.g., mesenchymal stem cells used alone, added to other biomaterials for grafting, or seeded onto scaffolds, including allograft materials that undergo enhanced processing to retain and condense inherent cells/growth factors)
- human growth factor substitutes (e.g., fibroblast growth factor, insulin-like growth factor)

- bone marrow aspirate processed to concentrate growth factors, stem cells or mesenchymal cells, (e.g., concentrated bone marrow aspirate, centrifuged bone marrow aspirate), used alone or in combination with other bone graft materials (e.g., allograft
- bone graft substitutes containing inorganic bone material (e.g., bovine, coral) when combined with any non-covered bone graft substitute
- bone graft substitutes used to reduce donor site morbidity (e.g., iliac crest donor site reconstruction)

Recombinant Bone Morphogenetic Protein (rhBMP)
rhBMP-2 (i.e., INFUSE® Bone Graft) is considered medically necessary in surgical repair of an acute, open tibial shaft fractures when BOTH of the following criteria are met:

- fracture is stabilized with intramedullary (IM) nail fixation
- rhBMP–2 is applied within 14 days of the fracture

rhBMP–2 is not medically necessary for ALL other indications, including the following:

- rhBMP–2 (i.e., INFUSE® Bone Graft) as an alternative or adjunct treatment for sinus augmentation and/or localized alveolar ridge augmentation

rhBMP-7 (i.e., OP–1™) is considered experimental, investigational, or unproven for ALL indications.

Dental implants are specifically excluded under many benefit plans. When coverage for dental implants is excluded, the use of bone graft materials in conjunction with a dental implant, including sinus and/or alveolar ridge augmentation, is similarly not covered.

Coding Information

Notes:
1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Most bone graft substitutes used to enhance bone healing do not have a specific CPT or HCPCS code to represent the material. However, there are specific CPT codes to differentiate by type of graft. For all other procedures, coverage will be considered based on the clinical indication and type of material for the procedure requested.

Allograft (non rhBMP-2), Synthetic (Ceramic/Polymer), Bone Void Fillers

Considered Medically Necessary when criteria in the applicable policy statements listed above are met and when used to report allograft (non rhBMP-2), synthetic ceramic/polymer) and/or bone void fillers used alone or in combination for the enhancement of bone healing:

CPT®* Codes	Description
20999	Unlisted procedure, musculoskeletal system, general
27899	Unlisted procedure, leg or ankle

HCPCS Codes	Description
C1734††	Orthopedic/device/drug matrix for opposing bone-to-bone or soft tissue-to bone (implantable)
C9359††	Porous purified collagen matrix bone void filler (Integra Mozaik Osteoconductive Scaffold Putty, Integra OS Osteoconductive Scaffold Putty), per 0.5 cc
C9362††	Porous purified collagen matrix bone void filler (Integra Mozaik Osteoconductive Scaffold Strip), per 0.5 cc
L8699††	Prosthetic implant, not otherwise specified

††**Note: May not be separately reimbursed to the facility.**

Considered Experimental/Investigational/Unproven when used to report human amniotic membrane grafts, cell-based substitutes (e.g., mesenchymal stem cells), growth factor substitutes, concentrated bone marrow aspirate, inorganic bone-containing substitutes, or materials intended to reduce donor site morbidity:

CPT®* Codes	Description
20999	Unlisted procedure, musculoskeletal system, general
27299	Unlisted procedure, pelvis or hip joint
27599	Unlisted procedure, femur or knee
29999	Unlisted procedure, arthroscopy
38232	Bone marrow harvesting for transplantation; autologous
38241	Hematopoietic progenitor cell (HPC); autologous transplantation

HCPCS Codes	Description
C1762†	Connective tissue, human (includes fascia lata)
C1889†	Implantable/insertable device, not otherwise classified
L8699†	Prosthetic implant, not otherwise specified

†**Note: May not be separately reimbursed to the facility**

Recombinant Bone Morphogenetic Protein (rhBMP)

Considered Medically Necessary when criteria in the applicable policy statements listed above are met and when used to report rhBMP–2 for surgical repair of acute, open tibial fracture:

CPT®* Codes	Description
20999	Unlisted procedure, musculoskeletal system, general
27899	Unlisted procedure, leg or ankle

HCPCS Codes	Description
C1734†	Orthopedic/device/drug matrix for opposing bone-to-bone or soft tissue-to bone (implantable)
L8699†	Prosthetic implant, not otherwise specified

†**Note: May not be separately reimbursed to the facility**

Not Medically Necessary when used to report rhBMP–2 for ALL other indications including adjunct treatment for sinus augmentation and/or localized alveolar ridge augmentation:

CPT®* Codes	Description
21208	Osteoplasty, facial bones; augmentation (autograft, allograft, or prosthetic implant)
21210	Graft, bone; nasal, maxillary or malar areas (includes obtaining graft)
21499	Unlisted musculoskeletal procedure, head
31299	Unlisted procedure, accessory sinuses

HCPCS Codes	Description
L8699†	Prosthetic implant, not otherwise specified

†**Note: May not be separately reimbursed to the facility**

Considered Experimental/Investigational/Unproven when used to report rhBMP–7 (i.e., OP–1™) for ALL indications:

CPT®* Codes	Description
20999	Unlisted procedure, musculoskeletal system, general
23929	Unlisted procedure, shoulder
24999	Unlisted procedure, humerus or elbow
25999	Unlisted procedure, forearm or wrist
27599	Unlisted procedure, femur or knee
27899	Unlisted procedure, leg or ankle

HCPCS Codes	Description
C1734†	Orthopedic/device/drug matrix for opposing bone-to-bone or soft tissue-to bone (implantable)
L8699†	Prosthetic implant, not otherwise specified

†**Note: May not be separately reimbursed to the facility**

***Current Procedural Terminology (CPT®) © 2025 American Medical Association: Chicago, IL.**

General Background

Bone grafts can be harvested from the patient (autograft), a cadaver (allograft), or they can be synthetic. The composition of allograft and synthetic bone graft substitutes and their mechanism of action can vary widely. Bone graft materials are often combined to extend graft availability and enhance healing. Used alone or in combination, bone graft substitutes may be utilized for many orthopedic applications including fracture healing, filling cavities and defects, bridging joints, establishing the continuity of long bone and providing bone blocks. For most of the indications noted above, there is sufficient evidence to support safety and effectiveness, although for some

indications clinical studies are limited, for others there is no evidence, and for some types of materials, clinical studies are not required.

Autografts are the gold standard for bone grafting, typically harvested from the tibia, fibula, or iliac crest. They offer high success rates due to their osteoconductive, osteogenic, and osteoinductive properties. However, drawbacks include limited supply, increased morbidity, longer anesthesia time, blood loss, and donor site complications—especially pain at the iliac crest, the most common harvest site. Backfilling the iliac crest with graft substitutes has been explored to reduce pain and improve appearance, but current evidence is insufficient to recommend this practice.

Bone marrow aspirate from the iliac crest is often used as an adjunct to enhance healing because it contains osteogenic precursor cells. It can be injected directly into defects or combined with graft materials. Techniques to concentrate stem cells (e.g., centrifugation) aim to improve effectiveness, but clinical evidence supporting concentrated bone marrow aspirate (BMAC/BMMC) remains limited and inconclusive.

U.S Food and Drug Administration (FDA)
FDA classifies a product as a drug, device, biological product, or combination product. A combination product is composed of any combination of a drug and device; a biological product and device; a drug and biological product; or a drug, device, and biological product.

FDA has published guidance documents related to bone grafts. Bone grafts intended to fill bony voids or gaps caused by trauma or surgery that are not intrinsic to the bony structure's stability, or those aiming to fill, augment, or reconstruct periodontal or bony defects of the oral and maxillofacial region are considered Class II devices. Bone grafts containing drugs are considered a therapeutic biologic and are regulated as Class III devices, requiring a PMA. Cultured cells combined with other materials (i.e., bone grafts) are considered combination products and may be regulated as devices or biological products.

Nonstructural allograft and cellular allograft materials are considered human cells, tissues and cellular tissue-based products and as such do not require preclinical or clinical data by the FDA. Synthetic bone grafts and demineralized bone matrices (DBM) are considered Class II materials and fall under the FDA 510(k) regulatory. Other materials, such as those that are considered drug-device combinations require premarket approval (PMA).

Allografts
One alternative to autograft is the use of allografts. Allograft offers the advantage of avoiding additional surgery and potential complications associated with harvesting host bone during the primary procedure. Allograft materials are frequently used during various orthopedic procedures and may also be used alone or in combination with other materials. Cancellous allograft is used primarily to pack and fill bony voids, while cortical allograft is used primarily to fill large osseous defects. Allografts are readily available from bone banks and provide osteoconductive (e.g., structural support) properties, however they lack osteogenic properties. Allografts may give less consistent clinical results, and there may be an increased risk of disease transmission and immunogenic response. When allografts are intensively processed to decrease these risks, the osteoinductive potential is lessened, and the processing removes osteogenic cells and reduces mechanical strength. AlloGro® Demineralized Bone Matrix (Wright Medical, Arlington, TN); Dynagraft-D™ (Citagenix, Laval, Quebec, Canada); Opteform® (Exactech, Inc., Gainesville, FL); Grafton® (Osteotech, Eatontown, NJ); OrthoBlast (IsoTis Orthobiologics, Irvine, CA); TruFuse® (minSURG™ Corp., Clearwater, FL); and NuFix™ (Nutech Medical, Birmingham, AL) are examples of allograft-based bone graft substitutes.

Allografts can be processed to retain higher concentrations of inherent growth factors and/or stem cells. With improved processing methods some allograft products are now available that manufacturers claim retain higher concentrations of naturally occurring growth factors and/or stem cells. Human growth factors such as fibroblast growth factor, insulin-like growth factor, platelet-derived growth factor, transforming growth factor-beta, and microglobulin-B, are examples of osteogenic growth factors that are naturally found within the matrix of bone. Despite availability and current use, clinical superiority has not been demonstrated in the medical literature supporting the use of these materials. How these allograft bone graft materials, processed to retain higher concentrations of inherent growth factors and/or stem cells, improve the rate and quality of bone formation compared to other available allograft bone graft substitutes, has not yet been firmly established.

Demineralized bone matrix (DBM) is a type of allograft. It is produced through a process that involves the decalcification of cortical bone (produced by acid extraction of allograft bone); substantially decreasing the structural strength. However, it is more osteoinductive than ordinary allograft. Although the reason for this is not completely understood, it has been speculated that the osteoinductive growth factors contained in the extracellular bone matrix are more easily accessed once the mineral phase of the bone has been removed. Allograft DBM preparations available for use include Osteotech's Grafton®, Regeneration Technology's Osteofil® and Medtronic's Magnifuse to name a few. These preparations differ in shape and size of DBM particles, the amount of inherent growth factors, the amount of residual minerals, and the type of carrier materials. DBM is available in various forms such as freeze-dried powder, granules, gel, putty or strips.

Inorganic Bone Graft Materials
Inorganic bone graft material is a type of xenograft bone graft substitute made from other than human material, such as cow (i.e., bovine) or coral, and is typically used in combination with other types of bone graft materials, for example with collagen or a calcified matrix. The animal bone is processed to remove any organic components (i.e., inorganic bone material) reducing concerns of disease transmission or immunogenic reactions. Some of the inorganic type xenograft materials (e.g., Bio-Oss) may be used as stand-alone graft material to enhance healing, such as when used for dental implants. When used according to U.S. Food and Drug Administration (FDA) approved indications, either alone or combined with other bone graft materials proven effective, inorganic bone graft materials are considered safe and effective for promoting bone formation.

Bone Graft Substitutes
Due to the limitations of autogenous bone and allograft material, and the number of surgeries that require grafting, investigators have developed grafting alternatives, some of which are available for current use and others which are still in developmental stages. Bone graft substitutes have overlapping properties and are often made of a variety of materials such as polymers (degradable and nondegradable), ceramics and composites (calcium phosphate, calcium sulfate, and bioactive glass), factor-based materials (recombinant growth factors) and cell-based materials (mesenchymal stem cells). Some authors classify bone graft substitutes according to these materials. However, these substitutes can also be classified based on their characteristics, such as

- osteoconduction (e.g., calcium sulfate, ceramics, calcium phosphate, cements, collagen), osteoinduction (e.g., DMB, rhBMPs, growth factors),
- osteogenesis (e.g., bone marrow aspirate), or
- combined (composites).

Nonetheless, the ideal bone graft substitute must provide scaffolding for osteoconduction, growth factors for osteoinduction and progenitor cells for osteogenesis. In addition, the bone graft substitute must be able to integrate with the host.

The role of bone graft substitutes is to provide a medium for osteoconduction rather than osteoinduction and can provide variable levels of structural support. These materials appear to be safe when used according to FDA indications; however, each type of product is under varying degrees of regulation and in some cases safety and efficacy of these products remain unproven through human trials. For the intent of this coverage policy, bone graft substitutes are described as those that are cell-based, ceramic-based, polymer-based and factor-based. Synthetic substitutes generally consist of ceramic and polymer based materials.

Human Amniotic Membrane and Amniotic Fluid Stem Cell Substitutes for Bone Healing
Human amniotic membrane and amniotic fluid-derived products have gained attention in regenerative medicine due to their theoretical potential to promote tissue repair. These products contain growth factors, extracellular matrix components, and in some cases, stem cells, which may support osteogenesis and angiogenesis. Their use has been proposed in orthopedic applications, including bone defect repair and enhancement of bone healing.

Despite promising preclinical findings, the clinical evidence supporting the use of human amniotic membrane grafts and amniotic fluid stem cell substitutes for bone healing remain extremely limited. Most published studies are animal-based or involve small human cohorts with heterogeneous methodologies, making it difficult to draw definitive conclusions. A recent review emphasizes that while amniotic products show regenerative potential in laboratory settings, human clinical trials are lacking, and outcomes are inconsistent (Huddleston et al., 2020). No large-scale randomized controlled trials have demonstrated improved safety or efficacy compared to established graft materials such as autografts or allografts.

Cell-based: Cell-based bone graft substitutes employ live cells—most commonly mesenchymal stem/stromal cells (MSCs)either on their own or integrated with carriers such as osteoconductive cancellous bone chips or demineralized bone matrix, sometimes seeded onto support scaffolds composed of xenograft (e.g., bovine bone) or type I human collagen. Although numerous studies, including recent clinical trials and preclinical investigations, explore these MSC-based therapies for bone healing, current data are limited by small sample sizes, study heterogeneity, and preliminary design. Therefore, data published in the medical literature supporting safety and efficacy for these indications are lacking (Rodham et al., 2024).

Rodham et al. (2024) conducted a narrative scoping review to describe the applications of cellular therapies for bone repair, including harvest methods, delivery approaches, adjunctive therapies, and clinical results. The review synthesized multiple studies since 2010 involving individuals treated for acute fractures, fracture nonunion, segmental bone defects, and femoral head osteonecrosis. Interventions encompassed autologous or allogeneic mesenchymal stromal/stem cells delivered as bone marrow aspirate concentrate, ex-vivo expanded cells, and cells seeded onto osteoconductive scaffolds; comparators in the included studies varied and included standard fixation, autograft alone, synthetic scaffold alone, and core decompression alone. Inclusion criteria comprised English-language studies published since 2010 assessing progenitor cells or marrow aspirate for augmenting bone healing, while exclusion criteria were not reported. Outcomes measured across studies included radiographic union and consolidation, time to union, pain scores, disability indices, Harris Hip Score, and conversion to total hip arthroplasty. Follow-up durations varied by indication and study design, ranging from months to several years. Attrition was not consistently reported. Reported results included descriptive and inferential statistics at the individual-study level indicating improved pain scores, accelerated union, improved functional outcomes, and reduced conversion to arthroplasty in some cohorts; diagnostic test metrics such as negative predictive value, positive predictive value, sensitivity, and specificity were not reported. Adverse events were infrequent but included deep infections requiring debridement and development of donor-specific anti-HLA antibodies without clinical hypersensitivity in allogeneic cell therapy. The review identified key limitations, including heterogeneity, small sample sizes,

and risk of bias, and recommended further research to standardize protocols, optimize cell processing, and improve scaffold biocompatibility.

Theodosaki et al. (2024) conducted a systematic review of human clinical trials to evaluate the effectiveness and safety of mesenchymal stem cells (MSCs) delivered in scaffolds for bone regeneration. Fourteen studies published in the last 15 years that included individuals with various bone defects (n=138). Interventions consisted of MSCs combined with different scaffold materials, compared to standard care such as autologous bone grafts, xenografts, scaffold alone, or no intervention; some studies lacked a control group. Inclusion criteria were human clinical studies using MSCs in scaffolds for bone defect treatment, with no age or health restrictions, while exclusion criteria included studies not using MSCs or scaffolds in combination, not applied to bone defects, not in humans, published before 2007, in progress, lacking ISCT-defined cell markers, not cultivating stem cells, case reports, or withdrawn results. Primary outcomes measured were bone regeneration assessed by clinical, radiographic, or histological methods, and safety/adverse events; secondary outcomes included functional rehabilitation and quality of life. Follow-up periods ranged from 1 month to 3 years depending on the study. Attrition was not reported. Negative predictive value, positive predictive value, sensitivity, and specificity were not reported; statistical significance was observed in some studies for functional and radiographic outcomes, but most studies did not demonstrate statistically significant differences due to small sample sizes and Phase I/II design. Adverse events were minimal and mostly related to the surgical procedure, with no serious adverse events attributed to the intervention. Limitations included small sample sizes, heterogeneity in study design, defect type, MSC origin, and scaffold type, lack of meta-analysis, and low certainty of evidence. The authors concluded that MSCs in scaffolds appear safe and effective for bone regeneration in humans, with outcomes comparable or superior to standard care, but without statistically significant differences; they recommend larger, standardized clinical trials to validate these findings.

Ceramic-based: Ceramic-based bone graft substitutes include materials such as calcium phosphate, calcium sulfate, and bioactive glass, which may be used alone or in combination with other grafts (Ivanova et al., 2025). Certain ceramic-based products, including calcium phosphate-collagen composites and beta-tricalcium phosphate, function as bone graft extenders and are often combined with collagen—sometimes derived from bovine sources—to enhance healing, similar to composites used in cell-based products (Ivanova et al., 2025). These materials lack osteogenic and osteoinductive properties and therefore cannot serve as stand-alone bone grafts (Ivanova et al., 2025). Available forms of calcium phosphates include tricalcium phosphate, synthetic hydroxyapatite, and coralline hydroxyapatite, which are manufactured as pastes, putties, solid matrices, and granules (Ivanova et al., 2025). Calcium sulfate is less desirable for weight-bearing applications due to its loss of mechanical properties during degradation (Ivanova et al., 2025). Bioactive glass, when implanted into living tissue, forms a bond with pre-existing bone, but there are only a few products commercially available and use is primarily in dental applications (Ivanova et al., 2025). Synthetic hydroxyapatite products are brittle and have little tensile strength, making them suitable for bone defects with internal fixation. Pure beta-tricalcium phosphate scaffolds are intended for small defects in the extremities, pelvis, and spine.

U.S. Food and Drug Administration (FDA)-Ceramic-based bone graft substitutes
Ceramic-based bone graft substitutes are generally classified as Class II medical devices and are primarily regulated by the FDA through the 510(k)-clearance pathway. However, certain products fall under Class III designation and require FDA review through the Premarket Approval (PMA) pathway. Ceramic-based bone graft substitutes are indicated for filling bone voids or gaps in the skeletal system (such as the extremities, pelvis, and spine) that are not intrinsic to the stability of the bony structure and may be used to augment bone healing in orthopedic, craniofacial, and dental procedures. They are not intended for load-bearing applications unless used with internal fixation.

Synthetic hydroxyapatite (e.g., ProOsteon® Implant 500 [Interpore Cross, Int., Irvine, CA]) is brittle, has little tensile strength and is typically used for bone defects with internal fixation. A pure beta-tricalcium phosphate scaffold, Vitoss® Synthetic Cancellous Bone Filler (Orthovita, Inc., Malvern, PA) is intended for use in small defects in the extremities, pelvis, and spine. Other ceramic-based materials include but are not limited to:

- Osteograf® (Ceramed, Lakewood, CO)
- Norian SRS (Skeletal Repair System) (Synthes, Inc., West Chester, PA)
- Osteoset® (Wright Medical, Arlington, TN)
- Actifuse™ (ApaTech Limited, Elstree, Hertfordshire, UK)
- Integra MOZAIK™ Osteoconductive Scaffold (Integra LifeSciences, Plainsboro, NJ)
- PRO-DENSE® Bone Graft Substitute paste (Wright Medical Technology, Inc., Arlington, TN)

Polymer-based: Polymer-based substitutes are polymers that are either degradable or nondegradable and may be used alone or in combination with other materials. Degradable polymers are resorbed by the body allowing it to heal itself without foreign bodies remaining (Whittle, 2021). Types of polymer-based substitutes include but are not limited to:

- Cortoss® (Orthovita, Inc., Malvern, PA [Stryker])
- OPLA (TMH Biomedical, Inc., Duluth, MN)
- Immix (OsteoBiologics, Smith and Nephew, Memphis, TN).

Factor-based: Factor-based bone graft substitutes consist of human growth factors and recombinant growth factors used alone or in combination with other materials (Whittle, 2021). Factor-based osteogenic bone graft substitutes include but are not limited to:

- human growth factors (e.g., fibroblast growth factor, insulin-like growth factor, transforming growth factor-beta), used alone or in combination with other materials
- recombinant bone morphogenetic proteins (rhBMP), used as an adjunct to autografts

Human growth factors: Fibroblast growth factor (FGF), insulin-like growth factor (ILGF), transforming growth factor-beta (TGF-beta) and bone morphogenetic protein (BMP) are human growth factors found in the matrix of bone. Some of these factors have been isolated in research settings for use alone or in combination with other materials; however, evidence in the published, peer-reviewed scientific literature is insufficient to support safety and efficacy at this time.

Recombinant Bone Morphogenetic Proteins (rhBMP)
RhBMP is a unique subgroup of graft substitutes. The function of BMP is to promote differentiation of mesenchymal cells into chondrocytes and osteoblasts, to promote differentiation of osteoprogenitors into osteoblasts, and to influence skeletal pattern formation. Recombinant human bone morphogenetic proteins act as an adjunct to autogenous bone grafts.

RhBMP–2
In 2004, INFUSE® Bone Graft was approved for open tibial fractures with an intermedullary (IM) nail fixation. In March 2007, INFUSE Bone Graft was approved as an alternative to autogenous bone grafts for sinus augmentations, and for localized alveolar ridge augmentations for defects associated with extraction sockets.The use of RhBMP–2 product should be limited to the FDA-approved labeling indications.

Fracture Repair: In 2004, INFUSE® Bone Graft was approved for open tibial fractures with an intermedullary (IM) nail fixation. The use of RhBMP–2 product should be limited to the FDA-approved labeling indications.

is for the treatment of patients with acute, open tibial shaft fractures when all the following criteria are met:

- The fracture must be stabilized with intramedullary (IM) nail fixation after appropriate wound management.
- The rhBMP–2 must be applied within 14 days after the initial fracture.
- The prospective patient should be skeletally mature.

The FDA notes the following contraindications to use of the product:

- possible or confirmed pregnancy
- sensitivity to titanium, titanium alloy, cow (bovine) Type I collagen, or rhBMP–2
- infection near the area of the surgical incision
- previous or current tumor at the site of use
- high risk of amputation of the affected leg
- compartment syndrome of the affected leg

Published clinical studies evaluating the use of rhBMP–2 in patients with tibial fractures support safety and efficacy (Swiontkowski, et al., 2006; Jones, et al., 2006; Govender, yet al., 2002).

Sinus Augmentation/Alveolar Ridge Augmentation: In March 2007 the INFUSE® Bone Graft (Medtronic Sofamor Danek, Memphis, TN) was approved as an alternative to autogenous bone grafts for sinus augmentations, and for localized alveolar ridge augmentations for defects associated with extraction sockets. The use of RhBMP–2 product should be limited to the FDA-approved labeling indications.

According to the FDA, INFUSE Bone Graft is used to fill space where bone is needed in order to place endosseous dental implants. Dental implants should be placed if there is sufficient bone to stabilize them. When the sinus wall is thin, there is not enough bone to place dental implants. In a procedure known as sinus augmentation, a sinus graft is inserted into the floor of the sinus (i.e., the roof of the upper jaw). Dental implants can then be inserted and stabilized in the new sinus bone. The alveolar ridge of the jaw is the bone that surrounds the roots of the teeth. When a tooth is extracted, a socket remains which later heals; however, typically, previous height and width are not restored. Alveolar ridge augmentation is a procedure performed to increase bone volume, making treatment with dental implants possible.

The FDA notes the following contraindications to use for oral surgical procedures:

- in patients with an active infection at the operative site
- in patients who are pregnant
- in patients who are hypersensitive to rhBMP–2 or bovine type I collagen
- in an area where there was a tumor

Evidence in the published scientific literature evaluating rhBMP–2 for oral maxillofacial surgery consists of few published clinical trials (Esposito, et al., 2007; Boyne, et al., 2005; Fiorellini, et al., 2005; Jung, et l., 2003). Although the study results suggest that this technique may be a promising treatment option, the evidence in the published, peer-reviewed, scientific literature is insufficient to allow strong conclusions regarding the long-term effectiveness of rhBMP–2 for sinus augmentation and alveolar ridge augmentation. Published studies have been small in sample size, and data on long-term outcomes are lacking. Patient selection criteria are not well-defined. Some studies have indicated that rhBMP–2 is safe and enhances bone maturation. However, additional well-designed clinical trials assessing long-term health outcomes are needed to validate these results.

RhBMP–7/ OP–1™ Implant
A second type of human bone morphogenetic protein is rhBMP–7, marketed in the United States as OP–1™ Implant for use in healing fractures of the long bones. The FDA approved the OP–1 Implant for use in specifically-defined patients under a humanitarian device exemption (HDE) (H010002).

A HUD is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose.

NOTE: Per Gillman et al. (2021), rhBMP-7 has been withdrawn from the market and is no longer available for clinical use.

Fracture Repair: The FDA gave HDE approval for the use of rhBMP–7 to treat nonunion of long bones. It is a powder that is mixed with normal saline to form a paste which is applied during surgery. The substance is marketed in the U.S. as OP–1™ Implant (Stryker Biotech, Hopkinton, MA).

The FDA approval indicates that the substance is appropriate for use in the surgical repair of long bone nonunion when both of the following patient selection criteria are met:

- autograft is not feasible
- alternative treatments have failed

The use of the product is contraindicated in patients with the following conditions:

- allergy to OP–1 or collagen
- existing tumor or tumor removed at or near the fracture or history of malignancy
- previous history of cancer
- skeletal immaturity
- pregnancy

Studies evaluating the use of rhBMP–7 for nonunion of long bones are limited by small sample size and short term follow-up. Although there is some evidence of successful clinical outcomes resulting from the use of rhBMP-7 for the treatment of nonunion in the published scientific literature (Ronga, et al., 2006; Maniscalco, et al., 2002; Friedlaender, et al., 2001; Geesink, et al., 1999) evidence is insufficient to draw strong conclusions regarding safety and efficacy.

Professional Societies/Organizations

American Association of Orthopaedic Surgeons (AAOS): The AAOS 2022 Evidence-Based Clinical Practice Guideline on Management of Anterior Cruciate Ligament (ACL) Injuries states:

> Autograft vs. Allograft
> When performing an ACL reconstruction, surgeons should consider autograft over allograft to improve patient outcomes and decrease ACL graft failure rate, particularly in young and/or active patients. Quality of Evidence: High; Strength of Recommendation: Strong (Evidence from two or more "High" quality studies with consistent findings for recommending for or against the intervention.)
>
> Autograft Source

When performing an ACL reconstruction with autograft for skeletally mature patients, surgeons may favor BTB to reduce the risk of graft failure or infection, or hamstring to reduce the risk of anterior or kneeling pain. Quality of Evidence: High; Strength of Recommendation: Moderate (Evidence from two or more "High" quality studies with consistent findings for recommending for or against the intervention) (AAOS, 2022).

American Orthopaedic Foot & Ankle Society (AOFAS): The AOFAS 2022 Position Statement on The Use of Osteochondral Transplantation for the Treatment of Osteochondral Lesions of the Talus states:

> The American Orthopaedic Foot & Ankle Society (AOFAS) endorses the use of osteochondral autograft and allograft transplantation for the treatment of osteochondral lesion of the talus, especially large diameter lesions, cystic lesions, and those that have failed previous surgical treatment. AOFAS does not consider these procedures to be experimental in a patient population that has failed nonoperative management.

American Academy of Periodontology (AAP): An AAP 2022 published a Best Evidence systematic review (Suarez-Lopez, et al., 2022) on the efficacy of biologics for alveolar ridge preservation/reconstruction and implant site development. Clinical recommendations regarding rhBMP-2 included:

Alveolar ridge augmentation (ARA)

1. Level of certainty: Low for rhBMP-2
2. Net benefit rating (benefit-harm estimation): Modest or uncertain additional clinical benefits outweigh potential harms or benefits balanced with potential harms.
3. Adverse events and complications: No relevant adverse events and/or complications related to the use of rhBMP-2 were reported in the selected studies. Patient reported outcome measures (PROMS) were assessed in one study reporting slight superiority for the test group using rhBMP-2.
4. Strength of clinical recommendation: Expert opinion supports the use of rhBMP-2 for alveolar ridge augmentation (ARA). Evidence is lacking; the level of certainty is low and, consequently, expert opinion guides the recommendation of this intervention.

Maxillary sinus floor augmentation (MSFA)

1. Level of certainty: Low for rhBMP-2.
2. Net benefit rating (benefit-harm estimation): Modest or uncertain additional clinical benefits outweigh potential harms or benefits balanced with potential harms.
3. Adverse events and complications: No relevant adverse events and/or complications related to the use of rhBMP-2 were reported in the selected studies.
4. Strength of clinical recommendation: Expert opinion supports the use of rhBMP-2 for MSFA. Evidence is lacking; the level of certainty is low and, consequently, expert opinion guides the recommendation of this intervention (Suarez-Lopez, et al., 2022)

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job

opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No Determination found	
LCD		No Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• Revised policy statement for the medically necessary statement bone graft materials and/or substitutes, used alone or in combination	2/15/2026
Annual Review	• No clinical policy statement changes.	2/15/2025
Focused Review	• Removed policy statements for spine-related content, which is delegated to EviCore as of 11/01/2024.	11/01/2024
Annual Review	• Revised policy statement for bone graft materials and/or substitutes	2/15/2024

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