Medical Coverage Policy

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Bone Graft Substitutes

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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

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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.

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:

- autografts
- 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
- orthopedic/device/drug matrix/absorbable bone void filler, antimicrobial-eluting

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 when criteria is met for EITHER of the following conditions:

- in combination with a fusion device for a single-level anterior interbody lumbar or lumbosacral fusion* surgery when **ALL** of the following criteria have been met:
  - degenerative disc disease at one level from L2–S1
  - no more than Grade I spondylolisthesis at the involved level
- 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

***Note: For specific medical necessity criteria for lumbar fusion please reference the Cigna Lumbar Fusion for Spinal Instability and Degenerative Disc Conditions Coverage Policy.**

rhBMP–2 is not covered or reimbursable for ALL other indications, including the following:

- rhBMP–2 (i.e., INFUSE® Bone Graft) when used for spinal fusion procedures other than single-level anterior spinal fusion (e.g., posterior lumbar fusion, transforaminal lumbar fusion, more than single-level fusion)
- rhBMP–2 (i.e., INFUSE® Bone Graft) as an alternative or adjunct treatment for sinus augmentation and/or localized alveolar ridge augmentation
- rhBMP–2 (i.e., INFUSE® Bone Graft) for the treatment of cervical spine conditions

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

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 spinal fusion, for enhancement of fracture healing, for 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. Many of the bone graft substitute products are regulated by the United States Food and Drug Administration (FDA). For example, 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 process and upon approval are considered "substantially equivalent" to another marketed device/material used for the same purpose. Other materials, such as those that are considered drug-device combinations require premarket approval (PMA); FDA PMA approval requires an investigational device exemption clinical trial prior to the PMA application (Abjornson, et al., 2018).

Bone Graft Materials

Autografts

Autografts are considered the established standard graft material and are typically retrieved from the patient's tibia, fibula, ileum or iliac crest, by way of a surgical procedure and are then placed at the surgical site. The advantage of autograft is the high probability of success—autograft possesses all of the necessary characteristics such as osteoconductivity, osteogenicity, and osteoinductivity. The disadvantages associated with autografts are that the amount of autogenous bone available for grafting is limited; autografts are associated with increased morbidity; increased anesthesia time and blood loss; and post-operative donor site complications.

The iliac crest is the most common site for autograft harvesting. Once the actual bone graft is obtained the site is allowed to heal independently without backfilling. However, there is often post-operative harvest site pain associated with this procedure. The use of various bone graft substitutes are being investigated for backfilling of iliac crest harvest sites, particularly when used for spinal surgery, as a method of reducing pain and for improving cosmesis. Despite this proposed use there is insufficient data in the peer-reviewed published scientific literature supporting the effectiveness of iliac reconstruction with any type of graft material. Most of the published studies involve small sample populations with inconsistent clinical outcomes for reducing donor site morbidity. The use of bone graft substitutes for this indication is not recommended at this time due to lack of data supporting safety, efficacy and improved clinical outcomes.

Autologous bone marrow aspirate obtained from the iliac crest is also commonly used during orthopedic procedures as an adjunct to other graft materials to enhance bone healing. Freshly harvested bone marrow aspirate contains osteogenic precursor cells (mesenchymal stem cells, growth factors) and once aspirated may be injected directly into defects or mixed with other grafting materials. In theory, combining bone marrow aspirate with an osteoconductive and osteoinductive bone graft material will avoid associated disadvantages of iliac crest graft harvest and improve healing. Although injecting aspirate directly into defects or mixing with other allograft materials is commonly performed, it is considered integral to the surgical procedure.

Another proposed use of bone marrow is aspirate involves various cell retention and processing methods which are now being utilized to increase cell concentration. It has been suggested that stem cell concentration is directly related to overall effectiveness and as a result, in order to increase the concentration of osteoprogenitor cells various cell retention processing methods (e.g., centrifugation) may be employed. Although the amount of aspirate required and proposed indications vary, the process has also been referred to as bone marrow nucleated cell concentrate (BMAC) or autologous bone marrow mononuclear cells (BMMC). The techniques for concentrating bone marrow aspirate vary, as well as the resulting cell concentration and cell viability. Comparative data in the medical literature is insufficient to support clinical effectiveness of

concentrated bone marrow aspirate and strong evidence-based conclusions cannot be made at this time.

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, cortical allograft is used primarily to fill large osseous defects, are often used in conjunction with supportive hardware or in interody fusions. 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.

Cell-based: Bone graft substitutes that are cell-based use cells to generate new tissue either alone, with other biomaterials (osteoconductive carriers, for example cancellous bone chips or DBM), or seeded onto a support matrix (e.g., in combination with allograft material). Support matrix materials may include xenograft (i.e., bovine) or human type I collagen. Examples of cell-based substitutes include but are not limited to:

- Mesenchymal stem cells (MSCs): MSCs are multipotent stem cells that express a variety of different cell surface proteins and can differentiate into a variety of cell types, such as osteoblasts, chondrocytes, myocytes, adipocytes, and neuronal cells. Although processing techniques vary, and the optimal number of MSCs to be transplanted/seeded has not been established, following autologous bone marrow collection MSCs are either concentrated for direct injection, or cultured and incubated. Once cultured the MSCs can be mixed with biomaterials, such as gels or pastes; the biomaterials hold the cells in suspension and provide a matrix for filling defects. MSCs can also be seeded on scaffolds, and have been investigated when used with a support matrix for implantation (e.g., tissue engineered). In theory, MSCs are responsive to osteogenic growth factors and aid in the healing of bone. Nevertheless evidence in the published peer-reviewed scientific literature evaluating the use of MSCs to enhance bone healing consists mainly of animal trials and limited human trials. At present the evidence is insufficient to support improved clinical outcomes, when used alone, added to other biomaterials, or as cultured/seeded on a support matrix.
- Trinity® Evolution™ (Orthofix®, Inc., Lewisville, TX) is a viable cell allograft that according to the manufacturer contains active adult mesenchymal stem cells.Trinity Evolution contains osteoprogenitor cells, mesenchymal stem cells, and demineralized cortical bone to promote osteoconduction, osteogenisis, and osteoinduction for successful bone grafting.
- Osteocel® Plus (NuVasive, Inc, San Diego, CA) is an allograft cellular matrix that contains viable stem cells. The manufacturer suggests this material promotes fusion in cervical, thoracic, and lumbar procedures. According to the manufacturer, Osteocel Plus mimics the biologic properties of autograft and contains mesenchymal cells, cancellous bone, and

demineralized bone matrix. Osteocel Plus also provides a scaffold for new bone to grow on, theoretically avoiding limitations of other more traditional bone graft alternatives.
- Amniotic membrane, the innermost layer of the fetal membrane, is considered a source of collagen that acts as a scaffold for the attachment of cells. Recently, amniotic membrane allografts have been investigated for various uses including use as bone void fillers during spinal and other orthopedic surgeries to enhance bone healing. Classifications of these products differ depending on the specific product but are generally classified as human tissue and/or cell-based products. Some are claimed to be non-immunogenic by the manufacturer. Amniotic membrane allografts currently under investigation include NuCel® (Nutech Medical, Birmingham, AL, USA), Ovation® cellular repair matrix (Osiris Therapeutics, Inc., Columbia, MD, USA) derived from placental mesenchyme to name a few. In addition, amniotic fluid stem cells, derived from amniotic fluid, are being investigated to form tissue-engineered bone from scaffolds in animal trials; human trials are ongoing but limited.

The use of mesenchymal and other cell-based bone graft substitutes has been and continues to be investigated for various procedures, including spinal fusion, intervertebral disc regeneration and other orthopedic procedures. Although currently under investigation, data published in the medical literature supporting safety and efficacy for these indications are lacking.

Ceramic-based: Ceramic-based bone graft substitutes include materials such as calcium phosphate, calcium sulfate and bioactive glass, used alone or in combination with other grafts. Some ceramic-based products (e.g., calcium phosphate-collagen composites, beta-tricalcium phosphate) are considered bone graft extenders, and are combined with collagen to augment healing; collagen composites may include bovine material similar to that used with cell-based products. Because these materials lack osteogenic and osteoinductive properties, they cannot be used as stand-alone bone graft. Several types of calcium phosphates, including tricalcium phosphate, synthetic hydroxyapatite, and coralline hydroxyapatite are available in pastes, putties, solid matrices, and granules.

When used, calcium sulfate is less desirable for weight bearing applications due to loss of mechanical properties during degradation. When implanted into living tissue, bioactive glass forms a bond with pre-existing bone, however there are only a few products commercially available and use is primarily in dental applications. 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)

Subchondral injection of calcium phosphate bone substitute, into the area of subchondral bone edema, as part of treatment for osteochondritis dissecans of the knee, and other joints has been reported in the literature (Levy, Cousins, 2020; Bonadio, et al., 2017; Cohen, Sharkey, 2016; Abrams, et al., 2013). Conservative treatment of osteoarthritis-related bone marrow lesions generally includes pain control, reduction in weight bearing, activity modification, and appropriate nutrition including additional calcium and vitamin D during treatment if appropriate. One procedure aimed at treating such defects, the Subchondroplasty® (SCP®) procedure (Zimmer

Holdings, Inc.; Warsaw, IN), is a minimally invasive surgery designed to access and treat bone defects associated with chronic bone marrow lesions by filling them with a biomimetic bone substitute material. This material theoretically acts as a scaffold around which new bone growth may occur.

Nairn et al. (2020) published the results of a systematic review evaluating safety and early results of Subchondroplasty® for the treatment of bone marrow lesions. The authors review included 17 studies, all studies were graded as level 4 evidence except one which was graded level 3. The review included 756 subjects in total, 13 studies investigated use for the knee and four evaluated use for foot and ankle joint pain related to a bone marrow lesion. Mean pain scores using VAS improved postoperatively (7.8 +/- 0.6 to 3.4 +/- 0.7), functional scores improved when reported (IKDC 31.7 ± 1.9-54.0 ± 4.2 and KOOS 38.1 ± 0.6-70.0 ± 4.1) and there were high levels of patient satisfaction postoperatively. Complications occurred in seven cases, most seriously osteomyelitis and avascular necrosis. In addition, the authors reported that the rate at which subjects converted to arthroplasty ranged from 12.5 to 30% with followup ranging from 10 months to seven years. In the author's opinion, low quality studies supported a reduction of pain, improved function, high patient satisfaction and a subsequent delay in more invasive procedures. However additional high quality studies with long term followup are required to determine any impact to clinical practice recommendations.

Evidence in the peer reviewed scientific literature evaluating injection of a calcium phosphate bone substitute into the area of subchondral bone edema, or of the Subchondroplasty® procedure, in the treatment of chronic bone marrow lesions / bone marrow edema is lacking. As a result, evidence-based conclusions regarding safety, efficacy, and impact on health outcomes cannot be firmly established.

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. 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. 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

Antimicrobial-eluting: New 2024 HCPCS code C1602 Orthopedic/device/drug matrix/absorbable bone void filler, antimicrobial-eluting (implantable): Allografts and bone graft substitutes can be impregnanted with antibiotics. A local antibiotic delivery system with biodegradable drug carrier can be considered a therapeutically efficient platform for the treatment of osteomyelitis. Using appropriate carriers, specific amount of the antimicrobial agents and controlling the released rate of the drug can help in the infection control and limit the recurrence rate. Additionally, if the delivery system made osteogenic in nature, they can exert dual function of eradicating the pathogens and assisting the bone regeneration after surgical debridement (Shi et al., 2022; Wassif, et al., 2021; Peeters, et al., 2019; van Vugt, et al., 2016).

An allograft example is OSTEOmycin® Orthopaedic. This product is cancellous bone chips impregnated with tobramycin or vancomycin. Another example is Cerament G. This device-drug

combination product is a resorbable, gentamicin-eluting ceramic bone void filler intended for use as a bone void filler in skeletally mature patients as an adjunct to systemic antibiotic therapy and surgical debridement (standard treatment approach to a bone infection) as part of the surgical treatment of osteomyelitis in defects in the extremities.

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 and many published trials support safety and efficacy. 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, and are used commonly with spinal instrumentation devices (i.e., cages) during lumbar fusion and for fracture repair. According to the FDA, (FDA, 2008) safety and effectiveness of rhBMP for the treatment of cervical spine conditions has not been demonstrated.

RhBMP–2 appear to be safe when used appropriately, placed accurately, not allowed to come into contact with decompressed areas (i.e., rhBMP carrier must be protected from compression to avoid the forcing out of implant into surrounding tissues) and contained in the region of surgical fusion. BMPs must be used with caution in the presence of defects in the dura. In spinal fusion surgery, BMP cannot resist compression or shear forces within a vertebral motion segment; thus, they cannot be used as stand-alone devices. RhBMP–2 must be used with a cage or some type of supportive structure within the vertebral interspace.

The benefits of rhBMP versus autogenous iliac crest bone graft (AICBG) are the decreases in operating room time, blood loss, and morbidity due to the avoidance of an additional procedure to harvest AICBG. None of the early studies utilizing rhBMP–2 or rhBMP–7 documented any adverse systemic effects occurring as a result of their use. A small percentage (≤10%) of patients develops antibodies to rhBMPs, although there has been no documented evidence of harm resulting from this. Carreon et al. (2008) studied wound related and anaphylactic related adverse events in a case series of patients (n=90) who were re-exposed to rhBMP-2 and reported that multiple exposures from either a secondary primary surgery or revision (through the same approach or a different approach) does not increase the risk of those adverse events.

Although early evidence supports safety and efficacy when used according to FDA indications, adverse events have been reported which include ectopic bone formation, bone resorption or remodeling at the graft site, hematoma, neck swelling, and painful seroma (Benglis, et al., 2008), arachnoiditis, increased neurologic deficits, and retrograde ejaculation (Watson, 2020). Dural tears, bowel/bladder and sexual dysfunction, failure to fuse and paralysis have also been reported (Epstein, 2011), as well as carcinogenicity and teratogenic effects. Recently there has been concern more specifically safety and efficacy of rhBMP–2 used in spinal fusion surgeries. According to Carragee, et al. (2011), who in a systematic review compared conclusions regarding safety and efficacy published in the original rhBMP–2 industry-sponsored trials when used for spinal fusion, to data published following the FDA approval, the risk of adverse events associated with rhBMP–2 for spinal fusion was found to be "10 to 50 times the original estimates calculated from the industry-sponsored peer-reviewed publications."

As a result of reported complications and the recent concern regarding safety and efficacy, use of RhBMP–2 product should be limited to the FDA-approved labeling indications. Evidence in the peer-reviewed scientific literature is insufficient and does not provide strong support to safety and efficacy of rhBMP–7 to enhance bone healing.

RhBMP–2/ INFUSE® Bone Graft
RhBMP–2 is marketed in the U.S. as INFUSE® Bone Graft in conjunction with specific spinal and non-specific tibial fusion devices, as an alternative to autogenous bone graft for sinus augmentation, and for localized alveolar ridge augmentation for defects associated with extraction sockets.

Anterior Lumbar Spinal Fusion: The FDA gave new device approval to the InFuse™ Bone Graft/LT-CAGE™ (Medtronic Sofamor Danek, Memphis, TN) in July 2002. The InFuse Bone Graft /LT Cage is intended to be implanted via an anterior open or an anterior laparoscopic approach. According to the FDA approval, safety and effectiveness for approaches other than anterior have not been established. In December 2003 the approval was broadened to include additional fusion cages, specifically the INTER FIX™ Threaded Fusion Device and the INTER FIX™ RP Threaded Fusion Device (FDA, 2004). The device is to be used by surgeons experienced in spinal fusion surgery and adequately trained in the use of the device.

The use of these devices in conjunction with surgical spinal fusion has been approved by the FDA, with numerous supplements to the original PMA, for patients who meet all of the following criteria:

- skeletally mature
- degenerative disc disease at one level from L2–S1
- no more than Grade I spondylolisthesis at the involved level
- failure of at least six months of nonoperative therapy

The device is contraindicated in patients with the following conditions:

- hypersensitivity to rhBMP–2, bovine Type I collagen or to other components of the formulation
- resected or extant tumor at the operative site
- active infection at the operative site
- allergy to titanium or titanium alloy
- possible or confirmed pregnancy

Early evidence published in the peer-reviewed scientific literature consists of case series, randomized control trials, meta-analyses, and systematic reviews, many of which demonstrate safety and efficacy for the use of rhBMP–2 during spinal fusion (Burkus, et al., 2005; Glassman, et al., 2005; Baskin, et al., 2003; Burkus, et al., 2002; Kleeman, et al., 2001). Sample populations in these early studies vary in size from 11 subjects to as many as 279 subjects and follow-up periods range from six to 24 months. Most of the patients had single-level lumbar disc disease; the approach to lumbar fusion and the use of instrumentation varies within these trials. Most of the control groups had standard lumbar fusion using autograft bone from the iliac crest. Clinical outcomes demonstrate patients who received rhBMP–2 during spinal fusion surgery had shorter operating room times, shorter length of stay, and less blood loss compared to patients who received autogenous bone graft. Several studies published since that time have demonstrated similar results; moreover that clinical efficiency of rhBMP-2 is at least equal if not superior to allogenic or autologous bone graft in respect to fusion rate, low back pain disability, patient satisfaction and rate of re-operations (Liu, et al 2020, Faundez, et al, 2016). More recent evidence continues to continue to support safety and efficacy.

Posterior Spinal Fusion: RhBMP-2 has been used as part of posterior fusion techniques for treating both single and multi-level spinal deformity, either alone or combined with other osteoconductive scaffolds, and some authors have reported improved clinical outcomes (e.g., earlier and higher fusion rates) compared to iliac crest bone graft (Dawson, et al., 2009; Dimar, et al., 2009; Mulconrey, et al., 2008; Luhmann, et al., 2005). However, this represents an off-label use as it is not FDA-approved for posterolateral, posterior lumbar interbody fusion or multilevel fusion.

The FDA issued an HDE (Humanitarian Device Exemption) for Infuse/Mastergraft in 2008 for the repair of symptomatic, posterolateral lumbar spine pseudarthrosis. A humanitarian device exemption 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, and is not required to contain the results of scientifically valid clinical investigations supporting effectiveness for its intended purpose. According to the FDA this device is intended for use in a small subset of patients for whom autologous bone and/or bone marrow harvest are not feasible or are not expected to promote fusion, individuals who are diabetics and smokers, and is indicated to treat two or more levels of the lumbar spine. Contraindications include known hypersensitivity, tumor and/or active malignancy, skeletally immature individuals, pregnancy and in the presence of active infection at the site. After review of the information submitted to the FDA the review panel concluded that the probable benefit to health from using the product for the target population outweighs the risk of illness or injury, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment when used as indicated in accordance with the directions for use.

Cervical Spinal Fusion: Although it is an off-label use, rhBMP–2 has also been evaluated for use in fusion of the cervical spine. RhBMP-2 has been associated with increased cervical swelling in comparison to non rhBMP subjects in clinical trials; in some trials results were statistically significant ($p<0.001$) (Smucker, et al., 2006). In 2008, the FDA issued a public health notification on life-threatening complications associated with rhBMP in cervical spine fusion, based on various reports of complications. The reported complications included swelling of neck and throat tissue, which resulted in compression of the airway and/or neurologic structures in the neck. Some reports described difficulty swallowing, breathing, or speaking and some reported severe dysphagia following cervical spine fusion using rhBMP products. Although there is no consensus in the literature authors continue to report concern regarding life threatening complications (James, et al., 2017; Zadegan, et al., 2017; Fu, et al., 2013). As a result further clinical trials are required to support safety and efficacy of rhBMP-2 for treatment for cervical spine conditions, its' use remains off-label.

Fracture Repair: RhBMP–2 has also been studied in patients with tibial fractures; this application received premarket approval from the FDA in April 2004. It is marketed as the INFUSE® Bone Graft device (Wyeth Pharmaceuticals, Inc., Philadelphia, PA) and consists of rhBMP–2 in an absorbable collagen sponge.

The FDA approval for this device is for the treatment of patients with acute, open tibial shaft fractures when all of 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 granted premarket approval from the FDA for use in oral surgical procedures, (i.e., sinus augmentation and localized alveolar ridge augmentation for defects associated with extraction sockets), as an alternative to autograft. 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™ Putty
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, and OP–1™ Putty for use in spinal fusion. The FDA approved the OP–1 Implant and the OP–1 Putty for use in specifically-defined patients under a humanitarian device exemption (HDE).

Posterolateral Lumbar Spinal Fusion: The FDA granted HDE approval in April 2004 for the use of OP–1™ Putty (Stryker Biotech, Hopkinton, MA) for use as an alternative to autograft in compromised patients requiring revision posterolateral spinal fusion of the lower back. OP–1 Putty is made from a manufactured human protein powder and bovine collagen that is mixed with a saline solution and a thickening agent to form a putty-like material. During surgery, the putty is

placed on each side of the spinal levels to be fused. The FDA approval specifies patient selection criteria as those who meet both of the following:

- failed previous spinal fusion surgery
- not candidates for autograft because of a condition such as osteoporosis, diabetes, or smoking

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

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

The data presented to the FDA for consideration of approval is contained in the FDA Summary of Safety and Probable Benefit (FDA, 2004). Forty-eight patients with single-level degenerative lumbar spondylolisthesis and spinal stenosis received rhBMP–7 alone, rhBMP–7 combined with autograft, or autograft alone. The patients receiving rhBMP–7 alone demonstrated superior success, as evidenced by radiograph and clinical improvement, over those receiving autograft alone.

The FDA decision is based on the clinical data, as well as the following rationale provided in the approval summary: "When revision of a failed fusion is required, most patients are limited to either living with pain and altered function or repeating the original procedure with additional autologous bone, which may result in depletion of the bone stock and further risk to the patient. Allograft bone and bone graft substitutes are not considered feasible alternatives to autograft in revision surgery due to their lack of osteogenic potential. For certain patients, e.g., those with implanted leads, bone growth stimulators would not be considered as feasible options. OP–1 Putty has the potential to eliminate the risk and complications associated with these treatment alternatives while providing a feasible and beneficial alternative treatment."

Some of the outcomes reported for osteoinductive properties and fusion rates are comparable to those of autograft, and the use of rhBMP–7 does avoid the need for autogenous bone graft harvest. Overall, a paucity of studies have assessed rhBMP–7 in spine fusion surgery (Delawi, et al., 2010; Vaccaro, et al., 2008; Kanayama, et al., 2006; Vaccaro, et al., 2004; Vaccaro, et al., 2003; Johnsson, et al., 2002). Limitations to these available studies such as use of combined materials, small sample size and short-term follow-up does not lead to formation of evidence-based conclusions regarding safety, efficacy and improved clinical outcomes. Additionally these trials evaluated primary fusion surgery and not revision surgery as mentioned in the HDE approval, and are therefore not in agreement with FDA limitations. Studies evaluating safety and efficacy of on-label use in the peer-reviewed published scientific literature are lacking. Other variables precluding generalizations include inconsistency with regard to instrumentation; some procedures were instrumented while others were not. Additional studies are needed to assess clinical outcomes.

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

Similar to posterolateral lumbar fusion surgery, 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.

Platelet Rich Plasma (PRP) for Bone Healing
Platelet rich plasma (plasma having a platelet concentration above baseline) is an approach being investigated for the treatment of bone healing. PRP is also referred to as autologous platelet derived growth factor, platelet enriched plasma, platelet-rich concentrate, and autogenous platelet gel or platelet releasate. When activated in the body, platelets release growth factors which accelerate healing, including platelet-derived growth factor, transforming growth factor beta (TGF-β) and insulin-like growth. It is hypothesized that a concentrated preparation of platelets, which contain higher concentrations of growth factors, may promote more rapid healing. Platelet concentrates are not osteoinductive since they do not include BMPs (Marx, 2004), although in theory they promote osteoblast proliferation and differentiation (Veillette, McKee, 2007). During the procedure, a small amount of the patient's blood is drawn and centrifuged to separate red blood cells from the platelet rich plasma. The platelet rich plasma is then mixed with the patient's bone graft material. Theoretically, the growth factors signal the local mesenchymal and epithelial cells to migrate, divide, and increase collagen and matrix synthesis increasing bone regeneration. Overexposure of cells to PRP yields many cells but limited differentiation of those cells into appropriate cell lines. It has been suggested that the inability to control differentiation is a reason to not use PRP for healing of tissue (Mehta, Watson, 2008).

Platelet concentration devices are approved by the FDA as part of the 510(k) approval process for preparation of platelet rich plasma. Examples of devices that are FDA approved include PCCS(TM) Platelet Concentrate Separation Kit (3i [Implant Innovations Inc.] and Magellan(TM) Autologous Platelet Separator System (Medtronic Perfusion Systems).

The Washington State Health Care Authority (HCA) director selected platelet-rich plasma (PRP) for rereview for osteoarthritis treatment based on published evidence that could change the original coverage determination. Hyaluronic acid (HA)/platelet-rich plasma (PRP) for knee or hip osteoarthritis was reviewed. Following rereview, the committee decided that the current evidence on HA and PRP for knee and hip osteoarthritis was sufficient to determine coverage. The committee considered the evidence, public comment and expert input, and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable. Based on these findings, the committee voted to not cover HA/PRP for knee or hip osteoarthritis (Final adoption: November 17, 2023).

Currently, whether or not platelet rich plasma facilitates osteoinduction and improves clinical outcomes remains unproven in the published scientific literature. (Please refer to CIGNA Coverage Policy: Autologous Platelet-Derived Growth Factors [Platelet Rich Plasma] for further detail regarding autologous platelet derived growth factor).

U.S Food and Drug Administration (FDA)
The FDA classifies most orthobiologicals (e.g., rhBMP–2, Osteoset, Grafton) as Class II devices. Many of the bone graft substitutes are approved through the 510(k) process and are based on a predicate device clearance although some require premarket approval (i.e., Class III devices). In addition, some of the bone graft materials are regulated as human tissue and do not require clinical trials or FDA approval for marketing, such as some of the DBM products and cell-based materials.

Humanitarian Device Exemption (HDE) was granted by the FDA for the OP-1 Implant and the OP-1 Putty, also referred to as rhBMP–7, for use in specifically defined patients (FDA, H010002, H020008). According to the FDA, a humanitarian use device (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.

Professional Societies/Organizations
In a 2014 the North American Spine Society published evidence based recommendations for recombinant human bone morphogenic protein (rhBMP-2). NASS recommends rhBMP-2 may be considered as an adjunct to spinal fusion for the following conditions:

- for stand-alone anterior lumbar interbody fusion (ALIF) in all patient groups (except males with a strong reproductive priority)
- posterolateral lumbar fusion in patients at high risk for nonunion with autogenous bone graft or in those with inadequate or poor quality autogenous bone available
- for posterior lumbar interbody fusion (PLIF and TLIF) in patients at high risk for nonunion with autogenous bone graft or in those with inadequate or poor quality autogenous bone available
- for posterior cervical or thoracic fusions in pediatric patients at very high risk for fusion failure (eg, neuromuscular scoliosis, occipitocervical pathology) or in adult patients at high risk for nonunion (eg., revision surgery)
- for anterior cervical fusion in patients at high risk for nonunion (eg., revision)

NASS recommendations support that due to the potential for life-threatening complications, they emphasize within the document that rhBMP-2 should be used in the anterior cervical spine only in occasional, high-risk patients. Additionall, according to the recommendations rhBMP 2 should not be considered for routine anterior and posterior cervical fusion procedures, single level posterior/posterolateral fusions in healthy adults, or for routine pediatric spine fusion procedrues (NASS, 2014).

In 2013 the American Orthopaedic Foot and Ankle Society (AOFAS, 2013) published a position statement regarding osteochondral transplantation for the treatment of osteochondral lesions of the talus. According to this position statement the AOFAS does not consider the procedure, using either autograft or allograft, experimental when the individual has failed non-operative management, particularly for large diameter lesions (>15 mm in diameter) and cystic lesions (i.e., cyst in subchondral bone).

The American College of Rheumatology (ACR) Recommendations for the Medical Management of Osteoarthritis of the Hip and Knee (ACR, 2000) has noted that significant advances such as

autologous chondrocyte transplantation, cartilage repair using mesenchymal stem cells, and autologous osteochondral plugs are being investigated; however, they do not recommend those procedures for the treatment of patients with osteoarthritis. There has been no update to the recommendations since the initial publication in 2000.

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)

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.

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

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
20900	Bone graft, any donor area; minor or small (eg, dowel or button)
20902	Bone graft, any donor area; major or large
20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure)
20931	Allograft, structural, for spine surgery only (List separately in addition to code for primary procedure)
20936	Autograft for spine surgery only (includes harvesting the graft); local (eg, ribs, spinous process, or laminar fragments) obtained from same incision (List separately in addition to code for primary procedure)
20937	Autograft for spine surgery only (includes harvesting the graft); morselized (through separate skin or fascial incision) (List separately in addition to code for primary procedure)
20938	Autograft for spine surgery only (includes harvesting the graft); structural, bicortical or tricortical (through separate skin or fascial incision) (List separately in addition to code for primary procedure)

CPT®* Codes	Description
20939†	Bone marrow aspiration for bone grafting, spine surgery only, through separate skin or fascial incision (List separately in addition to code for primary procedure)
20999	Unlisted procedure, musculoskeletal system, general
27899	Unlisted procedure, leg or ankle

†Note: Considered Medically Necessary when used to report bone marrow aspiration WITHOUT processing to concentrate growth factors.

HCPCS Codes	Description
C1602††	Orthopedic/device/drug matrix/absorbable bone void filler, antimicrobial-eluting (implantable)
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.

Factor-based (rhBMP-2)

Considered Medically Necessary when criteria in the applicable policy statements listed above are met and when used to report rhBMP–2 utilized in combination with a fusion device for single-level anterior interbody lumbar fusion surgery or for surgical repair of acute, open tibial fracture:

CPT®* Codes	Description
20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure)
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 covered or reimbursable when used to report rhBMP–2 for ALL other indications including spinal fusions other than single-level anterior spinal fusions, as an alternative or adjunct treatment for sinus augmentation and/or localized alveolar ridge augmentation, or for the treatment of cervical spinal conditions:

CPT®* Codes	Description
20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure)
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

CPT®** Codes	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, per site
D7950	Osseous, osteoperiosteal, or cartilage graft of the mandible or maxilla—autogenous or nonautogenous, by report
D7951	Sinus augmentation with bone or bone substitutes, via a lateral open approach
D7953	Bone replacement graft for ridge preservation– per site

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
20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure)
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

Considered Experimental/Investigational/Unproven when used to report human amniotic membrane bone graft substitute, cell-based/mesenchymal stem cell used as bone graft substitute, factor-based, synthetic or allograft substitute following autograft harvest for iliac crest reconstruction (i.e., back fill grafting of an iliac crest donor site):

CPT®* Codes	Description
20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure)
20999	Unlisted procedure, musculoskeletal system, general
27299	Unlisted procedure, pelvis or hip joint
27599	Unlisted procedure, femur or knee
29999	Unlisted procedure, arthroscopy

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**

Considered Experimental/Investigational/Unproven when used to report bone marrow aspirate or bone marrow fluid concentrated or centrifuged for growth factors, stem cell, or mesenchymal cell application:

CPT®* Codes	Description
20939	Bone marrow aspiration for bone grafting, spine surgery only, through separate skin or fascial incision (List separately in addition to code for primary procedure)
38232	Bone marrow harvesting for transplantation; autologous
38241	Hematopoietic progenitor cell (HPC); autologous transplantation

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• Revised policy statement for bone graft materials and/or substitutes	2/15/2024