Spinal Fusion Enhancement Products (for Ohio Only)

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Instructions for Use

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Related Policies

- Discogenic Pain Treatment (for Ohio Only)
- Prolotherapy and Platelet Rich Plasma Therapies (for Ohio Only)
- Skin and Soft Tissue Substitutes (for Ohio Only)
- Surgical Treatment for Spine Pain (for Ohio Only)

Application

This Medical Policy only applies to the state of Ohio.

Coverage Rationale

The following are proven and medically necessary for the enhancement of spinal fusion:

- Autografts
- Demineralized bone matrix (DBM) without added products listed below as unproven and not medically necessary
- Allograft-based products not listed below as unproven and not medically necessary
- Infuse® Bone Graft (Recombinant human bone morphogenetic protein-2 (rhBMP-2)) of the lumbar spine when the following criteria are met:
  - The approach is anterior or oblique and used in conjunction with an FDA-approved interbody fusion device
  - Skeletally mature individual (18 years of age or older or radiographic evidence of epiphyseal closure) with degenerative disc disease (DDD)
  - The fusion involves vertebral bodies L2-S1, without or with spondylolisthesis of no more than grade 1 (25% displacement) at the involved level
  - The fusion is single-level
- The InFUSE/MASTERGRAFT™ Posterolateral Revision Device System (or InFUSE BMP used with MASTERGRAFT) when used according to U.S. Food and Drug Administration (FDA) indications in individuals who meet all the following criteria:
  - Implanted via a posterolateral approach
  - Presence of symptomatic posterolateral lumbar spine pseudoarthrosis
  - Skeletally mature patient (older than 21 years of age or radiographic evidence of epiphyseal closure)
  - Autologous bone and/or bone marrow harvest is not feasible or is not expected to promote fusion.

The following are unproven and not medically necessary for the enhancement of spinal fusion due to insufficient evidence of efficacy:

- Allograft based products
  - Cell-based [e.g., mesenchymal stem cells (MSC)]

- Ceramic-based products [e.g., beta tricalcium phosphate (b-TCP), calcium phosphate, calcium sulfate and bioactive glass] used alone or in combination with other grafts including bone marrow aspirate
- Human amniotic tissue materials, including amniotic fluid stem cell substitutes for the treatment of spine disease or in spine surgery

- Recombinant human bone morphogenetic protein-2 (e.g., rhBMP-2, InFUSE) and the InFUSE/MASTERGRAFT™ (or InFUSE BMP used with Mastergraft or Mastergraft alone) Posterolateral Revision Device for all other indications not included above
- The OptiMesh® Expandable Interbody Fusion System

Definitions

Allograft: An allograft is obtained from a person other than the surgical candidate. Harvested through a minimally invasive procedure, this allograft provides a population of osteoprogenitor cells and critical growth factors that help cell differentiation, leading to bone healing. It can include cadaveric bone and/or tissue from a bone bank. It may be used alone or in combination with another material. Even when used alone, allograft must be processed to decrease the likelihood of disease transmission and immunogenic response.

More recently, processing methods used for preparation of some allografts have been refined and 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, transforming growth factor-beta, and microglobulin-B, are examples of osteogenic growth factors that are naturally found within the matrix of bone.

Anorganic Bone Graft Materials: Anorganic bone graft materials are 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., anorganic bone material) reducing concerns of disease transmission or immunogenic reactions. Some of the anorganic type xenograft materials may be used as stand-alone graft material to enhance healing.

Autograft: An autograft is taken directly from the patient undergoing surgery. The usual site for an autograft harvest is the posterior iliac crest. When autograft material is of an insufficient volume, of poor quality, or cannot be used for any other reason, another type of material must be used for the bone graft.

Bone Morphogenetic Proteins (BMP) and Recombinant Human Bone Morphogenetic Proteins (rhBMP): RhBMP is a unique subgroup of graft substitutes. Bone morphogenetic proteins are naturally occurring proteins found in human bone and play an active role in bone 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.

Carrier Systems: Function to maintain the concentration of the rhBMP at the treatment site, provide temporary scaffolding for osteogenesis and prevent extraneous bone formation. Carrier systems have included inorganic material, synthetic polymer, natural polymers, and bone allograft. The rhBMP and carrier may be inserted via a delivery system, which may also function to provide mechanical support. The carrier and delivery system are important variables in the clinical use of rhBMPs.

Cell-Based Products: Bone graft substitutes that are cell-based use cells to generate new tissue either alone, with other biomaterials, or seeded onto a support matrix (e.g., in combination with allograft material). One material proposed for use in combination with allograft is mesenchymal stem cells (MSC), obtained from bone marrow aspirate. Potential uses of MSCs for orthopedic applications include treatment of damaged bone, cartilage, ligaments, tendons, and intervertebral discs.

Ceramic-Based Products: 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 combined with collagen to augment healing; collagen composites may include bovine material similar to that used with cell-based products. Several types of calcium phosphates, including tricalcium phosphate, synthetic hydroxyapatite, and coralline hydroxyapatite are available in pastes, putties, solid matrices, and granules.

Combination Bone Graft Substitutes: A newer practice in the use of bone graft substitutes is to combine different materials, with the theory that each different property working together will work in synergy with another in the healing and grafting process.

Concentrated Bone Marrow Aspirate (CBMA): CBMA is produced from native BMA, usually obtained from the iliac crest or local vertebrae. The bone marrow aspirate contains stem cells that have been proposed to help with the healing of some bone and joint conditions.

Demineralized Bone Matrix (DBM): DBM is a type of allograft; it is produced by acid extraction of allograft bone (known as decalcification). Based on manufacturing techniques, DBM may be a freeze-dried powder, granules, gel, putty, or strips. After processing, the material contains 90% type I collagen and 10% noncollagen protein containing a variety of bone growth stimulators such as bone morphogenetic protein (BMPs). The bone growth stimulators induce osteoblast formation (osteoinduction) from the patient's osteogenic stem cells. Added materials provide a three-dimensional substance into which capillaries, osteogenic cells, and other tissue can migrate and produce new bone (osteoconduction). DBM is commonly used as a bone graft extender for posterolateral spinal fusion surgery.

Human Amniotic Tissue Membrane: The innermost layer of the amniotic 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.

InFUSE™ Bone Graft: InFUSE™ Bone Graft is the premium product for autograft replacement due to its high osteoinductivity. Infuse bone graft is recombinant human bone morphogenetic protein-2 (rhBMP-2) applied to an absorbable collagen sponge carrier (ACS). One of the functions of the protein is to stimulate natural bone formation.

OptiMesh Grafting System®: OptiMesh is a conformable, porous, polymeric containment device that is inserted into the evacuated disc space and filled with a mixture of cortico-cancellous allograft with demineralized bone matrix, autograft, and bone marrow aspirate to aid traumatic fracture repair and interbody fusion.

Orthobiologics: Designed to substitute for real bone, but they can also enhance bone-fracture healing or bone fusion by providing substances that are either osteoconductive or osteoinductive (described in further detail below). Some products may have both properties. Orthobiologics require an invasive surgical procedure to place the material in the bone void site or at the site of bone fusion.

- Osteoconductive Matrix Materials: Osteoconductive materials provide a three-dimensional substance into which capillaries, osteogenic cells, and other tissue can migrate and produce new bone. This material acts only as a scaffold into which the new bone cells grow.
- Osteoinductive Bone Graft Substitutes: Osteoinduction means that the product induces osteoblast formation from the patient's own osteogenic stem cells that are already present at the fusion site. The osteoinductive properties of bone tissue are attributed to bone morphogenetic proteins (BMPs).

Bone graft substitutes have overlapping properties and are made of a variety of materials such as polymers (degradable and nondegradable), ceramics and composites (calcium phosphate, calcium sulfate, and bioactive glass), factor-based techniques (recombinant growth factors) and cell-based techniques (mesenchymal stem cells).

Applicable Codes

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

CPT Code	Description
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)
22899	Unlisted procedure, spine

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Description of Services

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. The carrier and delivery system are important variables in the clinical use of rhBMPs, and different clinical applications, such as long bone nonunion, or interbody or intertransverse fusion, may require different dosages of rhBMP along with different carriers and delivery systems.

Clinical Evidence

Bone Morphogenetic Protein (rhBMP or BMP)

A Hayes (2021) comparative effectiveness review identified a large body of moderate-quality evidence that suggests that, compared with an autograft, the use of rhBMP-2 for lumbar spinal fusion provides more rapid fusion and/or a somewhat greater likelihood of achieving fusion, but this did not consistently result in reduced pain or disability or better QOL. Use of rhBMP-2 also appears reasonably safe for lumbar fusion over the short term. Similar results were seen in studies related to cervical fusion, however the small number and quality of studies as well as varied treatment protocols limits reliability of the findings. There is a lack of studies regarding the use of rhBMP-2 for thoracic fusion and the efficacy and safety cannot be determined. Furthermore, due to the limited duration of follow-up in almost all of the reviewed studies, it has not been possible to determine the clinical significance of more complete fusion with rhBMP-2, and it has not been possible to rule out certain serious long-term risks of rhBMP-2, including a low potential risk of cancer. Additional long-term studies are needed to determine whether the benefits outweigh the potential risks.

Liu et al. (2020) conducted a systematic review and meta- analysis regarding the comparative clinical effectiveness and safety of bone morphogenic protein (rhBMP) versus autologous iliac crest bone graft (ICBG) in lumbar fusion. Twenty randomized controlled trials identified through May 2019, with a total of 2,185 patients met the inclusion criteria of age 18 to 80 years, suffering from lumbar degenerative diseases requiring lumbar fusion, and the RCT compared rhBMP with ICBG (patients with spinal deformities, fractures, tumors or infections, cases demonstrated spondylolisthesis classified higher than Meyerding Grade II, follow-up was < 12 months, and there were incomplete follow-up data were excluded). The primary outcomes assessed included fusion success, improvement on the Oswestry disability index (ODI), improvement on short form 36 (SF-36), improvement on the Numeric Rating Scale (NRS) for back pain and leg pain, adverse events, and reoperation. Secondary outcomes included operation time, intraoperative blood loss, and duration of hospital stay. The overall results showed improvement across all primary outcomes. The fusion success rate for rhBMP-2 was approximately 5.5 times higher than that observed in ICBG, with reoperation rates about 60% of ICBG. Adverse events and complications showed no significant differences. The authors acknowledged that the quality of evidence in this meta-analysis is limited by the low quality of the original studies. Most evaluated studies did not report their randomization or allocation methods. Nearly all studies failed to use independent blinding. The authors concluded that evidence is still lacking to support rhBMP superiority to ICBG, and future research should address using more rigorous methods including accurate reporting of pre- and post-operative scores and follow up of long-term complications.

Faundez et al. (2016) conducted an extensive review of randomized controlled trials (RCTs) and controlled series. Review confirmed that the use of rhBMP-2 following FDA-approved recommendations (i.e., one-level ALIF surgery with an LT-cage) is safe. The rate of complications is low, and the AEs had been identified by the FDA during the pre-marketing clinical trials. The clinical efficiency of rhBMP-2 is equal or superior to that of allogenic or autologous bone graft in respect to fusion rate, low back pain disability, patient satisfaction and rate of re-operations. For all other off-label use, the safety and effectiveness of rhBMP-2 have not been established, and further RCTs with high level of evidence are required.

In 2017, James et al. presented a review article regarding the side effects of rhBMP-2. Since it's FDA approval in 2002, increased use has resulted in a growing and well- documented body of side effects that include postoperative inflammation (and associated adverse effects), ectopic bone formation, osteoclast-mediated bone resorption, and inappropriate adipogenesis. Additionally, several large-scale studies have confirmed the relative frequency of adverse events associated when used for cervical spine fusions, and in 2008, the FDA issued a public health notification regarding the life-threatening complications associated with recombinant human bone morphogenetic protein for this use. The authors stress that the use of rhBMP-2 in appropriately selected patients with impaired fusion capacity can result in better overall long-term outcomes, however there are risks when the product is used off label or for inappropriate indications, and dosing.

Rodgers et al. (2013) investigated published results of industry funded trials of recombinant human bone morphogenetic protein 2 (rhBMP-2) in spinal fusion matching underlying trial data by comparing three different data sources: individual participant data, internal industry reports, and publicly available journal publications and conference abstracts. Outcomes from 11 of the 17 manufacturer-sponsored studies were reported in 32 publications. The authors concluded that the published literature only partially represents the total data known to have been collected on the effects of rhBMP-2. This did not lead to substantially different results for meta-analysis of effectiveness outcomes. In contrast, reporting of adverse event data in trial publications was inadequate and inconsistent to the extent that any systematic review based solely on the publicly available data would not be able to properly evaluate the safety of rhBMP-2. Analysis of individual participant data enabled the most complete, detailed, and in-depth analysis and was not more resource intensive than extracting, collating, and analyzing aggregate data from multiple trial publications and conference abstracts. Confidential internal reports presented considerably more adverse event data than publications, and in the absence of individual participant data access to these reports would support more accurate and reliable investigation, with less time and effort than relying on incomplete published data.

Chrastil et al. (2013) published a systematic review of the spectrum of complications reported in the literature after posterior interbody fusions of the lumbar spine augmented with BMP. Seventeen articles were identified and reviewed that addressed the use and complications of BMP use during PLIF and TLIF procedures. The studies ranged from level I prospective randomized trial to case reports of complications. The authors reported appreciable rates of BMP-specific complications, including heterotopic ossification within the epidural space or neuroforamina, postoperative radiculitis, and endplate osteolysis with interbody device subsidence. They conclude by stating, “High-quality clinical trials should be initiated to develop appropriate paradigms to maximize the safety and efficacy of BMP for posterior interbody fusions.”

In a prospective, longitudinal cohort study of 688 patients from three studies, Burkus et al. (2011) analyzed antibody formation to BMP-2, bovine collagen, and human collagen after three prospective clinical studies investigating rhBMP. Neutralizing antibodies were assessed using a cell bioassay. The incidence of antibodies to bovine and human collagen was determined. Radiographic and clinical outcome data were assessed to determine whether antibodies were correlated to patient outcomes. The authors concluded that formation of anti-BMP-2 antibodies was low and transient. No neutralizing antibodies were observed. Formation of antibodies did not affect fusion success or appear to have clinical sequelae.

A report by Glassman et al. (2011) describes a retrospective case review of 1037 subjects who underwent posterolateral spine fusion using rhBMP-2, with a focus on complication rates. They reported that medical and surgical complications were observed in 190 of 1,037 subjects, with 81 major complications and 110 minor complications. New or more severe postoperative radicular symptoms were noted in seven subjects. Complications directly related to rhBMP-2 were observed in at least one and in a worst-case analysis, in as many as six subjects. The authors concluded that, “there were extremely few complications directly attributed to rhBMP-2/ACS, and the overall complication rates were consistent with established norms.”

A systematic review by Agarwal et al. (2009) compared the efficacy and safety of osteoinductive bone graft substitutes using autografts and allografts in lumbar fusion. Of 732 potential studies, 17 studies met the inclusion criteria (nine examined rhBMP-2, three examined rhBMP-7, three examined demineralized bone matrix, and two examined autologous growth factor). Primary outcome measures were nonunion as defined by failure to fuse as demonstrated on CT scans or plain x-rays. Secondary outcome measures were failure to demonstrate improvement on the Oswestry Low-Back Pain Disability Questionnaire (or Oswestry Disability Index [ODI]). When compared with autologous iliac crest bone graft (AIBG), recombinant human BMP-2 significantly increased union as evidenced by radiographic imaging, while rhBMP-7 showed no difference in radiographic nonunion. Neither rhBMP-2 nor rhBMP-7 demonstrated a significant improvement on the Oswestry Disability Index when compared with (AIBG). The controlled trials of demineralized bone matrix or autologous growth factor in comparison with AIBG showed no significant differences in radiographic nonunion. The authors concluded that rhBMP-2 may be an effective alternative to facilitate lumbar fusion in single-level lumbar DJD compared to AIBG. However, the data is limited for rhBMP-7, demineralized bone matrix, and autologous growth factor. The authors note the following limitations: English only published studies were reviewed; there were no double blinded studies; analyses of the efficacy of bone graft substitutes other than rhBMP-2 was limited by the study size and number; and there is a potential for bias because device manufacturers sponsored several studies and more than one author reported conflicts of interest.

Dimar et al. (2009) conducted a multicenter, prospective, randomized study of 463 patients at 29 sites. Patients had symptomatic single-level lumbosacral degenerative disease with no greater than grade-1 spondylolisthesis treated with single-level instrumented posterolateral arthrodesis through an open midline approach. Patients were randomly assigned to receive either the recombinant human bone morphogenetic protein-2 matrix group (239 patients) or the autogenous iliac crest bone-

graft group (224 patients). Outcomes were evaluated with the Oswestry Disability Index, Short Form-36, and back and leg pain scores preoperatively and at 1.5, 3, 6, 12, and 24 months postoperatively. Radiographs and computed tomography scans were made at 6, 12, and 24 months postoperatively to evaluate for fusion. Of the 463 patients who had surgery, 410 (194 iliac crest bone graft group and 216 rhBMP-2 matrix group) were available for assessment at 2 years after surgery. Both groups showed similar improvements in clinical outcomes and reduced pain. Radiographic and computed tomography scans showed a greater incidence of fusion in the rhBMP-2 group. Patients requiring a second surgery was higher in the iliac crest bone graft group (36 patients vs. 20) than the rhBMP-2 group. The authors concluded that the use of recombinant human bone morphogenetic protein-2 in instrumented posterolateral lumbar arthrodesis produces earlier and higher fusion rates than does iliac crest bone graft.

Clinical Practice Guidelines

American Academy of Neurological Surgeons (AANS)

In a 2014 guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine, the AANS makes the following recommendations:

- The use of demineralized bone matrix (DBM) as a bone graft extender is an option for 1- and 2-level instrumented posterolateral fusions.
- The use of b-tricalcium phosphate (b-TCP)/local autograft as a substitute for autologous iliac crest bone (AICB) is an option for single-level instrumented posterolateral fusion due to comparable fusion rates and clinical outcomes.

Hydroxyapatite/Calcium Extenders

- The use of hydroxyapatite (HA) with local autograft/bone marrow aspirate (BMA) as a substitute for AICB in an option for instrumented posterolateral fusion due to comparable fusion rates and clinical outcomes.
- The use of HA can be considered an option as a graft extender when mixed with AICB for instrumented posterolateral fusions
- There is insufficient evidence to recommend for or against the use of a HA-glass/BMA composite as an autograft substitute for posterolateral fusion.
- The use of calcium sulfate preparations mixed with local autograft, as a substitute for autologous iliac crest bone, (AICB), is an option for instrumented posterolateral fusions. (Kaiser 2014)

rhBMP-2

The use of rhBMP-2 as a graft option has been associated with unique complications that the surgeon should be aware of when considering its use.

Interbody Fusion

- As a substitute for AICB for anterior lumbar interbody fusion (ALIF) with threaded interbody cages is an option due to similar fusion rates and clinical outcomes
- As a substitute for AICB for single-level posterior lumbar interbody fusion (PLIF) is an option due to similar fusion rates and clinical outcomes; however, formation of heterotopic bone has been observed
- As a bone graft extender can be considered as an option when performing a transforaminal lumbar interbody fusion (TLIF) procedure with a structural interbody graft
- There is insufficient evidence to make a recommendation regarding the use of rhBMP-2 as a supplement for stand-alone ALIF procedures using femoral ring allograft or with a resorbable spacer when performing TLIF procedures.

Posterolateral Fusion

- Supplemented with 15% HA/85% b-TCP matrix as a substitute for AICB is an option in single-level posterolateral instrumented fusions given the consistent observation of comparable fusion rate and clinical outcomes
- Supplemented with graft extenders as an alternative to AICB is an option for single-level, instrumented posterolateral fusions in patients older than 60 years
- as a graft extender with either AICB or local bone is an option in patients undergoing either instrumented or non-instrumented posterolateral fusions
- There is insufficient evidence to formulate a recommendation regarding the use of rhBMP-2/local bone as a substitute for AICB when performing revision posterolateral fusions or the use of rh- BMP-2/calcium-based extenders for single level posterolateral fusions in patients who smoke and elect to undergo surgery for lumbar spondylosis

North American Spine Society (NASS)

In a 2017 evidence-based coverage policy recommendation for allograft and demineralized bone matrix for spinal fusion, the NASS identified the following scope and clinical indications:

Structural Allograft

Structural cortical or corticocancellous allograft bone (fresh-frozen or freeze-dried), with or without additional autograft, is indicated for use in anterior cervical spinal reconstruction in the following clinical scenarios:

- Anterior Cervical Discectomy and Fusion
  - Uninstrumented single level
  - Instrumented single-level
  - Instrumented multilevel
- One or more level cervical corpectomy

Posterior Cervical Fusion

Structural allograft is indicated for posterior upper cervical and occipitocervical instrumented fusion

- Nonstructural allograft bone
- Demineralized Bone Matrix (DBM) may be indicated for anterior cervical spinal reconstruction and fusion for cervical radiculopathy and/or myelopathy in the following clinical scenarios:
  - Anterior Cervical Discectomy and Fusion
  - Cervical Corpectomy
  - Posterior Cervical Fusion
  - Thoracolumbar Spine Fusion
    - Structural cortical and corticocancellous allograft bone (with or without additional autograft)
      - Interbody Fusion (including transforaminal (TLIF), posterior (PLIF) and anterior (ALIF) lumbar interbody fusion)
      - Anterior Corpectomy and Fusion
    - Nonstructural Allograft (with or without additional autograft)
      - Posterior Instrumentation and Fusion
      - In combination with structural allograft or synthetic cages for thoracolumbar interbody fusion

DBM combined with autograft is indicated for use in posterior instrumented fusion. There is no significant evidence at this time for use as a stand-alone product in non-instrumented posterior fusion or anterior fusions.

Iliac crest bone autograft (ICBG) remains the “gold standard” material for structural and nonstructural bone graft in cervical and thoracolumbar spine fusion, though the morbidity associated with its harvest, including fracture, infection, neurologic injury, and chronic pain at the harvest site, have led to allograft becoming a more frequently used non-autogenous bone graft material in spine surgery

In a 2014 evidence- based coverage policy recommendation for recombinant human bone morphogenic protein (rhBMP-2), the NASS states rhBMP-2 may be considered as an adjunct to spinal fusion for the following diagnoses:

- 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.
- 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
- Posterior Cervical or Thoracic Fusions
  - in pediatric patients at very high risk for fusion failure (e.g., neuromuscular scoliosis, occipitocervical pathology
  - in adult patients at high risk for nonunion, for example, revision surgery
- Anterior cervical fusion in patients at high risk for nonunion

The society also states that rhBMP-2 should not be used for the following:

- Routine anterior and posterior cervical fusion procedures
- Single level posterior/posterolateral fusions in healthy adults
- Routine pediatric spine fusion procedures (e.g., adolescent idiopathic scoliosis)

Ceramic-Based Products

There is insufficient reliable evidence in the form of high-quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes.

Nickoli et al. (2014) performed a systematic view of thirty studies with 1,332 patients. The overall fusion rate for all ceramic products as a bone graft extender in the lumbar spine was 86.4%. Age, gender, method of evaluation (plain radiographs, computed tomography, or combination), or specific ceramic product did not significantly affect fusion rate. Ceramics used in combination with local autograft resulted in significantly higher fusion rates compared with all other adjuncts, and bone marrow aspirate and platelet concentrates resulted in significantly lower fusion rates. The authors concluded that ceramic-based bone grafts represent a promising bone graft extender in lumbar spine fusion when an osteoinductive stimulus, such as local bone graft is available. Although all studies included patients with a degenerative lumbar pathology, critical exclusion criteria were not standardized. As a result, important patient variability could have influenced fusion rates including cigarette smoking, immunosuppression, and medical comorbidities. Also, given the lack of standardization and variability in reporting, the authors were unable to obtain information on other important complications such as infection. In addition, radiographic reporting methods varied among studies, which could certainly affect outcomes. Finally, because volume and technique of ceramic use was so inconsistently reported, recommendations could not be drawn.

Cell-Based Products

The use of cell-based bone graft substitutes has been and continues to be investigated for various procedures, including spinal fusion and for intervertebral disc regeneration. The lack of adequate controls, randomization and blinding and the small sample sizes precludes definitive conclusions regarding the net health benefit of cell-based therapy.

Hsieh et al. (2019) conducted a systematic comparative review of the evidence regarding the use of allogenic stem cell products for spine fusion when compared with other bone graft materials in patients with degenerative disease of the cervical or thoracolumbar spine. Eleven studies met the inclusion criteria, the majority were retrospective case series and only two retrospective cohort studies were identified, one on lumbar fusion and one on cervical fusion. Both were considered a moderately high risk of bias. No evidence on the impact of patient or intervention characteristics on effectiveness or safety was available for any of the studies included. Across case series, allogenic stem cell products appeared to be associated with improved pain and function, however in the absence of methodologically sound comparative studies, conclusions regarding effectiveness or safety cannot be drawn. While the use is promising, there is a lack of high-quality studies and further research is needed.

Hayes (2018) conducted concentrated bone marrow aspirate (CBMA) for spinal surgery literature review. Overall, a low-quality body of evidence is available to evaluate the use of CBMA for spinal surgeries. The limited evidence suggests that the balance of benefits and harms of concentrated BMA are at least comparable with those of alternative available graft materials. There is a paucity of long-term safety data from the randomized controlled trials. The overall quality of the evidence was assessed taking into consideration the quality of individual studies; the precision, directness, and consistency of data; and the applicability of the data to general practice.

Kerr et al. (2011) conducted a retrospective review to analyze the clinical effectiveness of mesenchymal stem cells allograft (Osteocel") to achieve radiological arthrodesis in adult patients undergoing lumbar interbody fusion surgery for different indications. Fifty-two consecutive patients received lumbar interbody fusion at one (69%) or two contiguous (31%) levels of lumbar spine for various indications. Procedures performed were circumferential fusion (67%), ALIF (17%) and TLIF (16%). Follow-up radiographic data was analyzed to establish arthrodesis versus failure (pseudarthrosis), number of months until achievement of fusion, and possible factors affecting the fusion rate. Follow-up ranged from 8 to 27 (median, 14) months. Solid arthrodesis was achieved in 92.3% of patients at median follow up time of 5 months (95% CI; range, 3 to 11 months). Kaplan-Meier survival curves and Mantle-Cox test were conducted to assess the effect of various factors on the rate of fusion. Statistics showed that increasing age (older than 50 years) and habitual smoking delayed the fusion time and increased the risk of pseudarthrosis. The use of Osteocel allograft is safe and effective in adult patients undergoing lumbar interbody spinal fusion procedure. Increased age and habitual smoking delays fusion but gender, previous surgery at the index level, type of procedure and number of levels do not affect the fusion rates. The study is limited by retrospective study design. Additional studies, preferably long-term randomized controlled trials, are needed to further validate these results.

Human Amniotic Tissue Membrane

A search of the peer-reviewed medical literature databases of amniotic tissues in orthopedic applications show a need for future research. There is limited evidence in human models that amniotic tissue membrane improves health outcomes when used in lumbar spine fusion. Long term safety and efficacy have not been established.

The OptiMesh® Expandable Interbody Fusion System

There is insufficient evidence in the form of high-quality peer-reviewed medical literature to establish the efficacy of the OptiMesh Expandable Interbody Fusion System on spine fusion outcomes.

U.S. Food and Drug Administration (FDA)

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

Allografts are considered tissues for transplantation. FDA: "Minimally manipulated human bone for transplantation: Human cells or tissue intended for implantation, transplantation, infusion, or transfer into a human recipient is regulated as a human cell, tissue, and cellular and tissue-based product or HCT/P." If combined with other materials, the resulting product is considered a device and regulated by the FDA as a medical device.

Products used for bone growth and bone grafts products are extensive. Refer to the following website for more information and search by product name in device name section: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed June 2, 2021)

In July 2002, the FDA granted 510K premarket approval for the InFUSE Bone Graft. It has several supplements. Refer to the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P000058. (Accessed June 29, 2021)

In November 2015, the FDA granted 510 (k) premarket approval for the i-FACTOR® peptide enhanced bone graft. Refer to the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm. (Accessed June 7, 2021)

In October 2008, the FDA granted the InFUSE/MASTERGRAFT Humanitarian Device Exemption. Refer to the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/hde.cfm?id=375525. (Accessed June 1, 2021)

In November 2003 the FDA granted 510(k) premarket approval for the OptiMesh® Expandable Interbody Fusion System for maintaining the relative position of bone graft material within a vertebral body defect that does not impact the stability of the vertebral body and does not include the vertebral endplates. Refer to the following website for more information: https://www.accessdata.fda.gov/cdrh_docs/pdf/K014200.pdf (Accessed June 8, 2021)

In September 2020, the OptiMesh Expandable Interbody Fusion System was granted De Novo classification for expanded indications allowing the use with bone graft and supplemental posterior fixation in lumbar interbody fusion. Refer to the following website for more information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id=DEN200010. Accessed June 16, 2021.

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Policy History/Revision Information

Date	Summary of Changes
02/01/2023	• Created state-specific policy version
12/01/2021	**Title Change** • Previously titled *Bone or Soft Tissue Healing and Fusion Enhancement Products* **Related Policies** • Added reference link to the Medical Policy titled *Skin and Soft Tissue Substitutes* • Removed reference link to the Medical Policy titled *Ablative Treatment for Spinal Pain* **Coverage Rationale** ***Proven and Medically Necessary*** • Replaced language indicating "the [listed products] are proven and medically necessary for the enhancement of fusion *and/or bone healing*" with "the [listed products] are proven and medically necessary for the enhancement of *spinal* fusion" • Revised list of proven and medically necessary products; replaced: ○ "Allograft-based products" with "Allograft-based products *not listed [in the policy] as unproven and not medically necessary*" ○ "Demineralized Bone Matrix (DBM)" with "Demineralized Bone Matrix (DBM) *without added products listed [in the policy] as unproven and not medically necessary*" ○ "Recombinant human bone morphogenetic protein-2 (*e.g.,* rhBMP-2, Infuse® Bone Graft) of the

Date	Summary of Changes
	lumbar spine" with "Infuse® Bone Graft [recombinant human bone morphogenetic protein-2 (rhBMP-2)] of the lumbar spine" ○ "The InFUSE/MASTERGRAFT™ Posterolateral Revision Device system" with "the InFUSE/MASTERGRAFT™ Posterolateral Revision Device System *(or InFUSE BMP used with MASTERGRAFT)*" ● Revised coverage criteria for: **Infuse® Bone Graft** ○ Replaced criterion requiring "the fusion involves vertebral bodies *L4*-S1, with or without spondylolisthesis of no more than grade 1 (25% displacement) at the involved level" with "the fusion involves vertebral bodies *L2*-S1, without or with spondylolisthesis of no more than grade 1 (25% displacement) at the involved level" ○ Removed criterion requiring failure of at least 6 months of non-operative medical treatment **InFUSE/MASTERGRAFT™ Posterolateral Revision Device System** ○ Removed criterion requiring treatment of 2 or more levels of the lumbar spine ***Unproven and Not Medically Necessary*** ● Replaced language indicating "the [listed products] are unproven and not medically necessary for the enhancement of fusion *and/or bone healing*" with "the [listed products] are unproven and not medically necessary for the enhancement of *spinal* fusion" ● Revised list of unproven and not medically necessary products: ○ Added language to indicate the following are Allograft based products: ▪ Cell-based products ▪ Ceramic-based products ▪ Human amniotic *tissue* materials ○ Removed recombinant human bone morphogenetic protein-7 (rhBMP-7) including but not limited to, Osteogenic Protein-1 (OP-1® Implant & Putty) with or without use of other devices ○ Replaced: ▪ "Recombinant human bone morphogenetic protein-2 (e.g., rhBMP-2, InFUSE) and InFUSE/MASTERGRAFT™ Posterolateral Revision Device for all other indications not included [in the policy as proven and medically necessary]" with "recombinant human bone morphogenetic protein-2 (e.g., rhBMP-2, InFUSE) and InFUSE/MASTERGRAFT™ *(or InFUSE BMP used with MASTERGRAFT or MASTERGRAFT alone)* Posterolateral Revision Device for all other indications not [listed in the policy as proven and medically necessary]" ▪ "The OptiMesh® *deployable grafting system*" with "the OptiMesh® *Expandable Interbody Fusion System*" **Definitions** ● Removed definition of "RhBMP–7/Osteogenic Protein-1 (OP–1® Implant & Putty)" **Applicable Codes** ● Removed CPT codes 20932, 20933, 20934, 22558, and 22585 **Supporting Information** ● Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information ● Archived previous policy version CS009.M

Instructions for Use

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

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