

Corporate Medical Policy

Bone Morphogenetic Protein

File Name:	bone_morphogenetic_protein
Origination:	10/2014
Last CAP Review:	2/2022
Next CAP Review:	2/2023
Last Review:	2/2022

Description of Procedure or Service

Bone morphogenetic proteins (BMPs) are members of the family of transforming growth factors. At present, some 20 different BMPs have been identified, all with varying degrees of tissue stimulating properties. Recombinant human bone morphogenetic proteins (rhBMPs) are delivered to the bone grafting site as part of a surgical procedure; a variety of carrier and delivery systems have been investigated. Carrier systems, which are absorbed over time, 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, and different clinical applications, such as long-bone nonunion, or interbody or intertransverse fusion, have been evaluated with different carriers and delivery systems. For example, rhBMP putty with pedicle and screw devices are used for instrumented intertransverse fusion (posterolateral fusion; PLF), while rhBMP in a collagen sponge with bone dowels or interbody cages are used for interbody spinal fusion. In addition, interbody fusion of the lumbar spine can be approached from an anterior (anterior lumbar interbody fusion; ALIF), lateral (XLIF), or posterior direction (PLIF or TLIF). Surgical procedures may include decompression of the spinal canal and insertion of pedicle screws and rods to increase stability of the spine.

Posterior approaches (PLIF and TLIF) allow decompression (via laminotomies and facetectomies) for treatment of spinal canal pathology (e.g., spinal stenosis, lateral recess and foraminal stenosis, synovial cysts, hypertrophic ligamentum flavum) along with stabilization of the spine and are differentiated from instrumented or noninstrumented posterolateral intertransverse fusion (PLF), which involves the transverse processes. Due to the proximity of these procedures to the spinal canal, risks associated with ectopic bone formation are increased (e.g., radiculopathies). Increased risk of bone resorption around rhBMP grafts, heterotopic bone formation, epidural cyst formation, and seromas has also been postulated.

Regulatory Status

The INFUSE® Bone Graft product (Medtronic) consists of rhBMP-2 on an absorbable collagen sponge carrier; it is used in conjunction with several carrier and delivery systems. The INFUSE® line of products has been approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process (PMA).

In 2008, FDA issued a public health notification on life-threatening complications associated with rhBMP in cervical spine fusion, based on reports of complications with use of rhBMP in cervical spine fusion. Complications were associated with swelling of neck and throat tissue, which

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resulted in compression of the airway and/or neurologic structures in the neck. Some reports described difficulty swallowing, breathing, or speaking. Severe dysphagia following cervical spine fusion using rhBMP products has also been reported in the literature. As stated in the public health notification, the safety and efficacy of rhBMP in the cervical spine have not been demonstrated. These products are not approved by FDA for this use.

In 2011, Medtronic received a “nonapprovable letter” from FDA for AMPLIFY™. The AMPLIFY™ rhBMP- 2 Matrix uses a higher dose of rhBMP (2.0 mg/mL) with a compression-resistant carrier.

OP-1® Putty (Stryker Biotech), which consists of rhBMP-7 and bovine collagen and carboxymethylcellulose, forms a paste or putty when reconstituted with saline. OP-1® Putty was initially approved by FDA through the humanitarian device exemption process for 2 indications:

“OP-1 Implant is indicated for use as an alternative to autograft in recalcitrant long-bone nonunions where use of autograft is unfeasible and alternative treatments have failed.”

“OP-1 Putty is indicated for use as an alternative to autograft in compromised patients requiring revision posterolateral (intertransverse) lumbar spinal fusion, for whom autologous bone and bone marrow harvest are not feasible or are not expected to promote fusion. Examples of compromising factors include osteoporosis, smoking and diabetes.”

Stryker Biotech sought FDA permission to expand the use of OP-1® Putty to include uninstrumented posterolateral lumbar spinal fusion for the treatment of lumbar spondylolisthesis. In 2009, FDA Advisory Committee voted against the expanded approval. Olympus Biotech (a subsidiary of Olympus Corp.) acquired OP-1® assets in 2010. In 2014, Olympus closed Olympus Biotech operations in the United States and discontinued domestic sales of Olympus Biotech products. The rhBMP-7 product is no longer marketed in the United States.

rhBMP Products and Associated Carrier and Delivery Systems Approved by FDA

INFUSE® Bone Graft (Approval 03/07)

- Alternative to autogenous bone graft for sinus augmentations
- For localized alveolar ridge augmentations in extraction socket defects

INFUSE® Bone Graft (Approval 10/09)

- Expanded indication for spinal fusion procedures in skeletally mature patients with degenerative disc disease at 1 level from L4 to S1
- Expanded indication for acute, open tibial shaft fractures stabilized with nail fixation

INFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device (Approval 07/02)

- Indicated for spinal fusion procedures in skeletally mature patients with degenerative disc disease at 1 level from L4 to S1
- Up to grade 1 spondylolisthesis at involved level
- Implantation via anterior open or anterior laparoscopic approach

INFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device (Approval 07/04)

- Extension of device use from L2 to S1
- May be used with retrolisthesis

INFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device (Approval 10/09)

- Indicated for acute, open tibial shaft fractures stabilized with nail fixation
- Alternative to autogenous bone graft for sinus augmentations
- For localized alveolar ridge augmentations in extraction socket defects

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INFUSE™ Bone Graft/Medtronic Interbody Fusion Device (Approval 12/15, Marketing name change)

- Expanded indication for 2 additional interbody fusion devices
- Perimeter Interbody Fusion Device implanted via retroperitoneal ALIF L2 to S1 or OLIF L5 to S1
- Clydesdale Spinal System implanted via OLIF at single level from L2-S5

INFUSE™ Bone Graft/Medtronic Interbody Fusion Device (Approval 09/17)

- Expanded indication for 2 additional interbody fusion devices:
 - Divergence-L Anterior/Oblique Lumbar Fusion System
 - Pivox™ Oblique Lateral Spinal System

Medtronic is the manufacturer for all of the INFUSE bone graft and carrier systems.

Bioventus LLC is currently sponsoring a clinical trial (NCT02225444) of its allogeneic morphogenetic protein product OsteoAmp® for use in instrumented posterolateral lumbar fusion. The trial is listed as completed; no results have been posted. OsteoAmp® has not received FDA approval for any indication.

Note: This policy only addresses Bone Morphogenetic Proteins. See the BCBSNC policies titled, “Orthopedic Applications of Stem Cell Therapy” and “Growth Factors in Wound Healing” for information regarding treatments for tissue repair and tissue substitutes. For information regarding spinal fusion procedures, please see the BCBSNC policy titled, “Lumbar Spine Fusion Surgery.”

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSNC will provide coverage for FDA-approved Bone Morphogenetic Proteins when it is determined to be medically necessary because the medical criteria and guidelines show below are met.

BCBSNC will not provide coverage for non FDA-approved BMPs or for non-FDA-approved indications (“off label” use) of BMPs because they are considered investigational. BCBSNC does not cover investigational services.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Bone Morphogenetic Protein is covered

Use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE) may be considered medically necessary in skeletally mature patients undergoing interbody spinal fusion when:

- The fusion is single-level
- The approach is anterior
- The fusion involves vertebral bodies L2 – S1, with or without spondylolisthesis of no more than grade 1 (25% displacement)
- The use of autograft is not feasible.

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Use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE) may be considered medically necessary in skeletally mature patients for the treatment of acute, open fracture of the tibial shaft, when use of autograft is not feasible.

When Bone Morphogenetic Protein is not covered

Bone morphogenetic protein (rhBMP-2) is considered investigational for all other indications, including but not limited to spinal fusion or treatment of acute, open fracture of the tibial shaft when use of autograft is feasible and craniomaxillofacial surgery, or when used for non-FDA-approved indications (i.e., “off label”).

Use of InFUSE for posterior (PLIF), posterolateral or lateral approaches to spinal fusion is not FDA-approved and is considered investigational.

Use of InFUSE for multilevel (more than single level) fusion is not FDA-approved and is considered investigational.

Policy Guidelines

Use of iliac crest bone graft (ICBG) may be considered not feasible due to situations that may include, but are not limited to, the following conditions:

- Prior harvesting of ICBG
- Need for a greater quantity of ICBG than available (e.g., for multi-level fusion)
- Diabetes with anticipated poor healing capacity
- End-stage renal failure
- Extensive osteoporosis
- Current smoking
- Current alcohol abuse
- Current steroid use

Two recombinant human bone morphogenetic proteins (rhBMPs) have been extensively studied: rhBMP-2, applied with an absorbable collagen sponge (Infuse) and rhBMP-7, applied in putty (OP-1). These products have been investigated as alternatives to bone autografting in a variety of clinical situations, including spinal fusions, internal fixation of fractures, treatment of bone defects, and reconstruction of maxillofacial conditions.

For individuals who are undergoing anterior or posterolateral lumbar spinal fusion and in whom autograft is not feasible who receive rhBMP, the evidence includes randomized controlled trials (RCTs), systematic reviews, and meta-analyses. Relevant outcomes are symptoms, morbid events, functional outcomes, and treatment-related morbidity. In 2013, two systematic reviews of rhBMP-2 trials that used manufacturer-provided individual patient data were published. Overall, these systematic reviews found little to no benefit of rhBMP-2 over iliac crest bone graft for all patients undergoing spinal fusion, with an uncertain risk of harm. The small benefits reported do not support the widespread use of rhBMP-2 as an alternative to iliac crest autograft. However, the studies do establish that rhBMP-2 has efficacy in promoting bone fusion and will improve outcomes for patients for whom use of iliac crest bone graft is not feasible. The overall rate of adverse events was low, though concerns remain about increased adverse event rates with rhBMP-2, including cancer. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are undergoing surgery for acute tibial shaft fracture and in whom autograft is not feasible who receive rhBMP, the evidence includes RCTs and systematic reviews of the RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, and treatment-related morbidity. Two systematic reviews have concluded that rhBMP can reduce the rate of reoperations

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compared to soft-tissue management with or without intramedullary nailing. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals undergoing other surgical procedures (e.g., oral and maxillofacial, hip arthroplasty, distraction osteogenesis) who receive rhBMP, the evidence includes a health technology assessment, systematic review, clinical trials, and small case series. Relevant outcomes are symptoms, morbid events, functional outcomes, and treatment-related morbidity. The evidence generally shows that rhBMP may not be as effective as a bone graft approach in craniomaxillofacial surgery; however, its use is associated with fewer adverse events. The evidence does not permit conclusions about the effect of rhBMP for tibial shaft fracture nonunion. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: In 2011, CPT code 20930 was revised to include BMP-type materials used in spine surgery.

In the setting of spinal fusion, bone morphogenetic proteins are used primarily as an alternative to autologous bone grafting. Since harvesting of autologous bone graft is coded separately from the fusion procedure, when bone morphogenetic protein is used, these codes should no longer be reported.

In contrast, the CPT code for treating tibial fracture non-unions with autograft includes the harvesting component, and therefore, when bone morphogenetic protein is used as an alternative in this setting, presumably the associated physician work would be decreased since no autologous harvest is required.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Specialty Matched Consultant Advisory Panel review 2/2022

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Policy Implementation/Update Information

- 10/14/04 New policy initiated. Bone Morphogenetic Protein is considered medically necessary when FDA-approved, used for FDA-approved indications, and medical criteria and guidelines are met. References added. Effective 10/14/2004.
- 6/2/2005 Specialty Matched Consultant Advisory Panel review on 5/23/2005. No changes made to the policy statement. References added.
- 7/2/07 Deleted the following statement from the Non Covered section: treatment of multiple levels of spinal fusion, or spinal fusion in the thoracic or cervical vertebrae. Vertebral span changed from L4-S1 to L2-S1 to reflect supplemental FDA approval from 2004. References updated. Specialty Matched Consultant Advisory Panel review 5/18/07. (adn)
- 7/6/09 Added the following to Item 2 in the Description of Procedure section: for sinus augmentations, and for localized alveolar ridge augmentations for defects associated with extraction sockets. Revised the section "When Bone Morphogenetic Protein is covered" to read: Use of recombinant human bone morphogenetic protein (rhBMP-2, InFUSE) may be considered medically necessary for the following indications: As an adjunct to anterior lumbar spinal fusion at one or more levels in skeletally mature patients with degenerative disc disease. Patients should have had at least 6 months of nonoperative treatment prior to treatment with the InFUSE Bone Graft/Interbody Fusion Device; For the treatment of acute, open fracture of the tibial shaft. Use of recombinant human bone morphogenetic protein-7 (rhBMP-7, OP-1) may be considered medically necessary for the following indication: As an alternative to autograft in recalcitrant long bone nonunions where use of autograft is unfeasible and alternative treatments (e.g., electrical bone growth stimulation) have failed. Revised the section "When Bone Morphogenetic Protein is not covered" to read: The use of recombinant human bone morphogenetic protein-2 or recombinant human bone morphogenetic protein-7 is considered investigational for all other indications, including but not limited to: As an alternative to autograft in compromised patients requiring revision posterolateral (intertransverse) lumbar spinal fusion, for whom autologous bone and bone marrow harvest are not feasible or are not expected to promote fusion; As an alternative or adjunct to bone grafting in other locations, including craniomaxillofacial surgeries. Added the FDA's July 2008 public health notification regarding life-threatening complications associated with recombinant human bone morphogenetic protein in cervical spine fusion to the Policy Guidelines section. References updated. Specialty Matched Consultant Advisory Panel review meeting 5/21/09. No change to the policy statement. (adn)
- 8/17/10 Specialty Matched Consultant Advisory Panel review 7/2010. References updated. Removed policy number. (mco)
- 4/12/11 Description section revised. Reference added for the BCBSNC policy "Lumber Spinal Fusion Surgery." Deleted information regarding label indications and interbody fusion devices used in conjunction with InFUSE bone graft. Deleted the following wording from the "When Covered" section: "...with degenerative disc disease. Patients should have had at least 6 months of non-operative treatment prior to treatment with InFUSE Bone Graft."(mco)
- 8/16/11 Specialty Matched Consultant Advisory Panel review. References updated. No changes to policy statements. (mco)
- 3/30/12 Significant revisions to policy. The "When Covered" section revised to state: "A:Use of recombinant human bone morphogenetic protein (rhBMP-2, InFUSE) may be considered medically necessary for the following indications for lumbar fusion in patients where there is a high risk of fusion failure (See Policy Guidelines): and when

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there are approved indications for lumbar spine fusion surgery (see medical policy titled, “Lumbar Spine Fusion Surgery”): 1. As an adjunct to anterior lumbar interbody spinal fusion at one or more levels in skeletally mature patients with approved indications for lumbar spine fusion surgery. 2. For instrumented posterolateral intertransverse lumbar spinal fusion procedures, in conjunction with an FDA-approved device, at one or more levels in skeletally mature patients with degenerative disc disease. B: Use of recombinant human bone morphogenetic protein (rhBMP-2, InFUSE) may be considered medically necessary for the treatment of acute, open fracture of the tibial shaft. C: Use of recombinant human bone morphogenetic protein-7 (rhBMP-7, OP-1) may be considered medically necessary for noninstrumented revision posterolateral intertransverse lumbar spinal fusion in patients where there is a high risk of fusion failure (See Policy Guidelines) and when there are approved indications for lumbar spine fusion surgery (see medical policy titled, “Lumbar Spine Fusion Surgery”). D: Use of recombinant human bone morphogenetic protein-7 (rhBMP-7, OP-1) may be considered medically necessary as an alternative to autograft in recalcitrant long bone nonunions where use of autograft is unfeasible and alternative treatments (e.g., electrical bone growth stimulation) have failed.” The “When not Covered” section revised to state: “Bone Morphogenetic Proteins is considered not medically necessary when all of the above criteria are not met. The use of recombinant human bone morphogenetic protein-2 or recombinant human bone morphogenetic protein-7 is considered investigational for all other indications, including but not limited to: Cervical spinal fusion; Posterior or transforaminal lumbar interbody spinal fusion; As initial treatment or revision of noninstrumented posterolateral intertransverse spinal fusion that does not meet the criteria listed above; As an alternative or adjunct to bone grafting in other locations, including craniomaxillofacial surgeries.” Policy Guidelines updated with the following clinical criteria listed as high risk for fusion failure: “one or more previous failed spinal fusion(s); grade III or worse spondylolisthesis; fusion to be performed at more than one level; current tobacco use; diabetes; renal disease; alcoholism; osteoporosis; steroid use; when autologous bone and bone marrow harvest are not feasible or are not expected to promote fusion.” The following statement was removed from the “Billing/Coding” section: “There is no specific CPT code for bone morphogenetic proteins. Services should be submitted in the form of an unlisted code (such as 20999, 22899, or 27899). Medical records for the explanation of the service rendered may be necessary.” Added the following statement to “Billing/Coding” section: “In 2011, CPT code 20930 was revised to include BMP-type materials used in spine surgery.” References updated. Medical Director review 2/2012. Specialty Matched Consultant Advisory panel review 2/2012. Policy noticed 3/30/2012 for effective date 7/1/2012. (mco)

- 1/29/13 References updated. No changes to Policy Statements. (mco)
- 3/12/13 Specialty Matched Consultant Advisory Panel review 2/2013. References updated. Policy Guidelines updated. (mco)
- 10/15/13 Policy extensively revised. Description section updated. “When Covered” section revised to state: “Use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE) may be considered medically necessary in skeletally mature patients: •For anterior lumbar interbody fusion procedures when use of autograft is unfeasible. •For instrumented posterolateral intertransverse spinal fusion procedures when use of autograft is unfeasible. For the treatment of acute, open fracture of the tibial shaft, when use of autograft is unfeasible. Use of recombinant human bone morphogenetic protein-7 (rhBMP-7, OP-1) may be considered medically necessary in skeletally mature patients: •For revision posterolateral intertransverse lumbar spinal fusion, when use of autograft is unfeasible. •For recalcitrant long-bone nonunions where use of autograft is unfeasible and alternative conservative treatments have failed.” “When not Covered” section revised to state: “Bone morphogenetic protein (rhBMP-2 or rhBMP-7) is

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considered not medically necessary for all other indications, including but not limited to spinal fusion when use of autograft is feasible.” Policy Guidelines updated. References updated. Medical Director review 10/2013. Policy noticed on 10/15/13 for effective date 12/31/13. (mco)

- 3/11/14 Specialty Matched Consultant Advisory Panel review 2/2014. Medical Director review 2/2014. Policy statement revised as follows: “BCBSNC will provide coverage for FDA-approved Bone Morphogenetic Proteins when it is determined to be medically necessary because the medical criteria and guidelines show below are met. BCBSNC will not provide coverage for non FDA-approved BMPs or for non-FDA-approved indications (“off label” use) of BMP’s because they are considered investigational. BCBSNC does not cover investigational services.” “When Covered” section revised as follows: “Use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE) may be considered medically necessary in skeletally mature patients undergoing interbody spinal fusion when: the fusion is single-level, the approach is anterior, the fusion involves vertebral bodies L4 – S1, with or without spondylolisthesis of no more than grade 1 (25% displacement), and use of autograft is unfeasible. Use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE) may be considered medically necessary in skeletally mature patients for the treatment of acute, open fracture of the tibial shaft, when use of autograft is unfeasible. Use of recombinant human bone morphogenetic protein-7 (rhBMP-7, OP-1) may be considered medically necessary in skeletally mature patients: For revision (i.e., repeat procedure after prior failure) posterolateral intertransverse lumbar spinal fusion, when use of autograft is unfeasible. For recalcitrant long-bone nonunions where use of autograft is unfeasible and alternative conservative treatments have failed.” “When not Covered” section revised to delete “not medically necessary” and replace with “investigational” as follows: “Bone morphogenetic protein (rhBMP-2 or rhBMP-7) is considered investigational for all other indications, including but not limited to spinal fusion or treatment of acute, open fracture of the tibial shaft when use of autograft is feasible, or when used for non-FDA-approved indications (i.e., “off label”). Use of InFUSE for posterior (PLIF), posterolateral (TLIF) or lateral (XLIF) approaches to spinal fusion is not FDA-approved and is considered investigational. Use of InFUSE for multilevel (more than single level) fusion is not FDA-approved and is considered investigational. Use of OP-1 for interbody fusion is not FDA-approved and is considered investigational.” Policy Guidelines updated. References updated. Policy noticed on 3/11/14 for effective date 5/13/14. (mco)
- 3/31/ 15 Reference added. Specialty Matched Consultant Advisory Panel review 2/25/15. Removed medically necessary indications for use of rhBMP-7 and OP-1 from the When Covered section. Added “Use of recombinant human bone morphogenetic protein-7 (rhBMP-7, OP-1*) is considered not medically necessary as these products have been withdrawn from the United States market and are no longer sold” to the When Not Covered section. (sk)
- 4/1/16 Specialty Matched Consultant Advisory Panel review 2/24/2016. (sk)
- 7/26/16 Reference added. Policy Guidelines updated. FDA approval for rhBMP-2 in oblique lateral interbody fusion added; rhBMP-7 removed from policy statements. (sk)
- 3/31/17 Specialty Matched Consultant Advisory Panel review 2/22/17. (sk)
- 1/26/18 Reference added. Changed the word “unfeasible” to “not feasible” in the medically necessary statements in the When Covered section. Added craniomaxillofacial surgery to the list of investigational indications in the When Not Covered section. Added information related to Bioventus’ allogeneic morphogenetic protein product OsteoAmp® to the Regulatory Status section. (sk)

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- 8/24/18 Specialty Matched Consultant Advisory Panel review 2/28/18. Reference added. Regulatory Status section reorganized for better clarity. (sk)
- 3/12/19 Specialty Matched Consultant Advisory Panel review 2/20/2019. (sk)
- 3/10/20 Reference added. Specialty Matched Consultant Advisory Panel review 2/19/2020. (sk)
- 3/9/21 Reference added. Specialty Matched Consultant Advisory Panel review 2/17/2021. (sk)
- 12/30/21 Reference added. Policy Guidelines updated. (sk)
- 3/8/22 Specialty Matched Consultant Advisory Panel review 2/16/2022. (sk)

Appendix

Procedures used for lumbar interbody fusion differ primarily in the direction of approach to the spine, i.e., from the front (anterior), from the back (posterior or transforaminal) or from the side (lateral). An alternative approach to interbody fusion is arthrodesis of the transverse processes alone (posterolateral), which does not fuse the adjoining vertebral bodies. Circumferential fusion fuses both the adjacent vertebral bodies and the transverse processes, typically using both an anterior and posterior approach to the spine.

Open and Minimally Invasive Approaches to Lumbar Interbody Fusion Procedure	Access	Approach	Visualization
Anterior (ALIF)	Open, MI, or laparoscopic	Transperitoneal or retroperitoneal	Direct, endoscopic or laparoscopic with fluoroscopic guidance
Posterior (PLIF)	Open or MI	Incision centered over spine with laminectomy/laminotomy and retraction of nerve	Direct, endoscopic or microscopic, with fluoroscopic guidance
Transforaminal (TLIF)	Open or MI	Offset from spine, through the intervertebral foramen via unilateral facetectomy	Direct, endoscopic or microscopic, with fluoroscopic guidance
Lateral Extreme lateral (XLIF) Direct lateral (DLIF)	MI	Retroperitoneal through trans psoas	Direct, with neurologic monitoring and fluoroscopic guidance

LIF: lumbar interbody fusion; MI: minimally invasive

Anterior Lumbar Interbody Fusion

Bone Morphogenetic Protein

Anterior access provides direct visualization of the disc space, potentially allowing a more complete discectomy and better fusion than lateral or posterior approaches. An anterior approach avoids trauma to the paraspinal musculature, epidural scarring, traction on nerve roots, and dural tears. However, the retraction of the great vessels, peritoneal contents, and superior hypogastric sympathetic plexus with a peritoneal or retroperitoneal approach place these structures at risk of iatrogenic injury. Access to the posterior space for the treatment of nerve compression is also limited. Laparoscopic anterior lumbar interbody fusion has also been investigated.

Posterior Lumbar Interbody Fusion

Posterior lumbar interbody fusion (PLIF) can be performed through either a traditional open procedure with a midline incision or with a minimally invasive approach using bilateral paramedian incisions. In the open procedure, the midline muscle attachments are divided along the central incision to facilitate wide muscle retraction and laminectomy. In minimally invasive PLIF, tubular retractors may be used to open smaller central bilateral working channels to access the pedicles and foramen. Minimally invasive PLIF typically involves partial laminotomies and facetectomies. The decompression allows treatment of spinal canal pathology (eg, spinal stenosis, lateral recess and foraminal stenosis, synovial cysts, hypertrophic ligamentum flavum), as well as stabilization of the spine through interbody fusion.

Transforaminal Lumbar Interbody Fusion

Transforaminal lumbar interbody fusion (TLIF) is differentiated from the more traditional bilateral PLIF by a unilateral approach to the disc space through the intervertebral foramen. In minimally invasive TLIF, a single incision about 2 to 3 cm in length is made approximately 3 cm lateral to the midline. A tubular retractor is docked on the facet joint complex and a facetectomy with partial laminectomy is performed. Less dural retraction is needed with access through the foramen via unilateral facetectomy, and contralateral scar formation is eliminated. TLIF provides access to the posterior elements along with the intervertebral disc space.

Lateral Interbody Fusion

Lateral interbody fusion (eg, extreme lateral interbody fusion or direct lateral interbody fusion) uses specialized retractors in a minimally invasive, lateral approach to the anterior spine through the psoas. In comparison with ALIF, the lateral approach does not risk injury to the peritoneum or great vessels. However, exposure to the spine may be more limited, and dissection of the psoas major places the nerves of the lumbar plexus at risk. Electromyographic monitoring and dissection predominantly within the anterior psoas major may be utilized to reduce the risk of nerve root injury. These various factors decrease the ability to perform a complete discectomy and address pathology of the posterior elements.

Circumferential Fusion

Circumferential fusion is 360° fusion that joins vertebrae by their entire bodies and transverse processes, typically through an anterior and posterior approach.

Posterolateral Fusion

Posterolateral fusion is a procedure where the transverse processes of the involved segments are decorticated and covered with a mixture of bone autograft or allograft.

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