The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. **Preauthorization is required; supporting documentation must be submitted to Use Management.** *Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.*

**Description**

Two recombinant human bone morphogenetic proteins (rhBMPs) are now commercially available, rhBMP-2, applied with an absorbable collagen sponge (InFUSE, Medtronic, Memphis, TN) and rhBMP-7, applied in putty (OP-1). These products have been investigated as an alternative 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.

**Background**

Bone morphogenetic proteins (BMPs) are members of the family of transforming growth factors. At present, some 15 different BMPs have been identified, all with varying degrees of cartilage and/or bone inductive properties. RhBMPs are delivered to the bone grafting site as part of a surgical procedure; a variety of carrier and delivery systems has 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, may require different dosages of rhBMP along with different carriers and delivery systems. For example, rhBMP with pedicle and screw devices are commonly used for instrumented intertransverse fusion, while rhBMP with interbody cages are used for interbody spinal fusion. In addition, interbody fusion of the lumbar spine can be approached from an anterior, lateral, or posterior direction. Surgical procedures may include decompression of the spinal canal and insertion of pedicle screws and rods to increase stability of the spine.

- Anterior lumbar interbody fusion (ALIF) provides direct visualization of the disc space through a peritoneal or retroperitoneal approach.
- Extreme lateral interbody fusion (XLIF) and direct lateral interbody fusion (DLIF) use a lateral (retroperitoneal) approach through the psoas.
- An axial approach to lumbar interbody fusion (AxiaLIF) is performed perpendicular to the long axis of the spine with access through the sacrum.
- Posterior lumbar interbody fusion (PLIF) is performed through either a traditional open procedure with a long midline incision and wide muscle retraction, with laminotomy or with a minimally invasive approach using bilateral paramedian incisions.
Transforaminal interbody fusion (TLIF) provides posterior access to the spine with a unilateral approach to the disc space (facetectomy) through the intervertebral foramen. In minimally invasive TLIF, a single incision approximately 2-3 cm in length is made approximately 3 cm lateral to the midline, and a tubular retractor is docked on the facet joint complex to provide a working channel for facetectomy with partial laminectomy.

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, 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**

At the present time, two rhBMPs and associated carrier/delivery systems have received approval from the U.S. Food and Drug Administration (FDA). The InFUSE system consists of rhBMP-2 on an absorbable collagen sponge carrier. The labeled indications for these devices are summarized here. OP-1 consists of rhBMP-7 and bovine collagen, which is reconstituted with saline to form a paste. The addition of carboxymethylcellulose forms a putty.

1. **InFUSE Bone Graft in conjunction with one of two interbody fusion devices, i.e., either the LT-Cage Lumbar Tapered Fusion Device or the Inter Fix RP Threaded Fusion device.** This device received FDA approval through the premarket approval (PMA) process:
   - The device is indicated for spinal fusion procedures in skeletally mature patients with degenerative disc disease (DDD) at one level from L2-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history, function deficit, and/or neurologic deficit and radiographic studies. These DDD patients may also have up to grade I spondylolisthesis at the involved level or retrolisthesis. The InFUSE™ Bone Graft/LT-CAGE™ devices are to be implanted via an anterior open or a laparoscopic approach. The InFUSE™ Bone Graft/INTER FIX™ Threaded Fusion Device; and InFUSE™ Bone Graft/INTER FIX™ RP Threaded Fusion Device are to be implanted via an anterior open approach only. Patients receiving the InFUSE™ Bone Graft/Interbody Fusion Device should have had at least six months of nonoperative treatment prior to treatment with the InFUSE™ Bone Graft/Interbody Fusion Device. (Note: A collagen sponge consists of the carrier, while the interbody fusion device is a delivery system. Use with posterior or transforaminal lumbar interbody fusion is considered off-label.)
   - For the treatment of acute, open fractures of the tibial shaft.
   - For sinus augmentations, and for localized alveolar ridge augmentations for defects associated with extraction sockets (P050053, March 2007).

2. **OP-1 (Stryker Biotech, Hopkinton, MA) has received two FDA approvals through the Humanitarian Device Exemption (HDE) process.** HDE is available to devices intended for fewer than 4,000 patients per year; as part of this process, the manufacturer is not required to demonstrate unequivocal benefit but only “probable” benefit. OP-1 received the following labeled 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 recently sought FDA permission to expand use of OP-1 Putty to include use in uninstrumented posterolateral lumbar spinal fusion for the treatment of lumbar spondylolisthesis. In March 2009, an FDA advisory committee voted six to one against recommending the expanded approval.

Both OP-1 and InFUSE Bone Graft/LT-Cage Lumbar Tapered Fusion device are contraindicated in patients who are pregnant, may be allergic to any of the materials contained in the devices, have an infection near the area of the surgical incision, have had a tumor removed from the area of the implantation site or currently have a tumor in that area, or who are skeletally immature.

In July 2008, the FDA issued a public health notification regarding life-threatening complications associated with recombinant human bone morphogenetic protein in cervical spine fusion. The FDA has received reports of complications with the use of rhBMP in cervical spine fusion. These complications were associated with swelling of neck and throat tissue, which resulted in compression of the airway and/or neurologic structures in the neck. Some reports describe 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 effectiveness of rhBMP in the cervical spine have not been demonstrated, and these products are not approved by the FDA for this use.

On July 27, 2010, the Orthopaedic and Rehabilitation Devices Panel of the Medical Devices Advisory Committee voted to endorse FDA approval of a PMA application for the AMPLIFY rhBMP-2 Matrix, sponsored by Medtronic. The AMPLIFY rhBMP-2 Matrix utilizes a higher dose of rhBMP (2.0 mg/mL) with a compression-resistant carrier and is being evaluated for posterolateral fusion treatment of single level lumbar (L2–S1) degenerative disc disease. The executive summary of the meeting is available online at: [link](http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/OrthopaedicandRehabilitationDevicesPanel/UCM220079.pdf). It has been reported that, in March 2011, Medtronic received a “nonapprovable letter” from the FDA for AMPLIFY.

**Related Protocols:**

- Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Conditions
- Electrical Stimulation of the Spine as an Adjunct to Spinal Fusion Procedures

**Corporate Medical Guideline**

Use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE) may be considered **medically necessary** for the following indications:

- For anterior spinal interbody fusion procedures, in conjunction with an FDA-approved interbody fusion device, at one or more levels in skeletally mature patients with degenerative disc disease from L2-S1. Patients should have failed at least six months of conservative treatment*;
- For instrumented posterolateral intertransverse spinal fusion procedures, in conjunction with an FDA-approved device, at one or more levels in skeletally mature patients with degenerative disc disease from L2-S1. Patients should have failed at least six months of conservative treatment;
- For the treatment of acute, open fracture of the tibial shaft**.

Use of rhBMP should be restricted to cases where there is a high risk of fusion failure. High risk for fusion failure can be defined by the presence of one or more of the following criteria:

- 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;
• steroid use.

Use of recombinant human bone morphogenetic protein-7 (rhBMP-7, OP-1) may be considered medically necessary for the following indications:

• As an alternative to autograft in compromised patients (e.g., osteoporosis, tobacco use, or diabetes) requiring noninstrumented 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 to autograft in recalcitrant long bone nonunions where use of autograft is unfeasible and alternative conservative treatments have failed***.

Bone morphogenetic protein (rhBMP-2 or rhBMP-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.

*FDA approved for one level
**FDA-approved indication
***FDA approved under a Humanitarian Device Exemption (HDE)

Policy Guideline

Because of the differing benefits and risks of iliac crest bone graft harvest and bone morphogenetic protein, patients should make an informed choice between the procedures.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


