

(701100)

Medical Benefit		Effective Date: 04/01/14	Next Review Date: 01/15
Preauthorization	Yes	Review Dates: 03/12, 03/13, 01/14	

*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.** 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 20 different BMPs have been identified, all with varying degrees of tissue stimulating 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, 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

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.”

StrykerBiotech 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. (1) 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.

In 2011, Medtronic received a “nonapprovable letter” from the FDA for AMPLIFY. 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 of single level lumbar (L2–S1) degenerative disc disease.

Related Protocols

Ultrasound Accelerated Fracture Healing Device

Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Conditions

Electrical Bone Growth Stimulation of the Appendicular Skeleton

Electrical Stimulation of the Spine as an Adjunct to Spinal Fusion Procedures

Policy (Formerly Corporate Medical Guideline)

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:

- 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.*
- For 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 **not medically necessary** for all other indications, including but not limited to spinal fusion when use of autograft is feasible.

*FDA approved under a Humanitarian Device Exemption (HDE)

Policy Guideline

Use of iliac crest bone graft (ICBG) may be considered unfeasible due to situations that may include, but are not limited to, prior harvesting of ICBG or need for a greater quantity of ICBG than available (e.g., for multi-level fusion).

There is not a consensus for the definition of nonunions. One proposed definition is failure of progression of fracture-healing for at least three consecutive months (and at least six months following the fracture) accompanied by clinical symptoms of delayed/nonunion (pain, difficulty weight bearing). (2)

The following patient selection criteria are used in the treatment of nonunions (for ultrasound and electrical bone growth stimulators):

- At least three months have passed since the date of the fracture, AND
- serial radiographs have confirmed that no progressive signs of healing have occurred, AND
- the fracture gap is 1 cm or less, AND
- the patient can be adequately immobilized and is of an age when he/she is likely to comply with non-weight bearing.

A recalcitrant nonunion would thus be considered to be a non-union with a larger fracture gap (e.g., greater than 1 cm) or a non-union that has persisted for a longer duration of time with no response to conservative treatment (e.g., three months of ultrasound or electrical stimulation).

In the setting of spinal fusion, bone morphogenetic proteins may be used primarily as an alternative to autologous bone grafting. Also for treatment of acute, open tibial fractures, bone morphogenetic protein is not used as an alternative to autologous bone graft, but in addition to standard treatment with an intramedullary nail.

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.

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6. Simmonds MC, Brown JV, Heirs MK et al. Safety and Effectiveness of Recombinant Human Bone Morphogenetic Protein-2 for Spinal Fusion: A Meta-analysis of Individual-Participant Data. *Ann Intern Med* 2013; 158(12):877-89.

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12. Woo EJ. Adverse events reported after the use of recombinant human bone morphogenetic protein 2. *J Oral Maxillofac Surg* 2012; 70(4):765-7.
13. Valentin-Opran A, Wozney J, Csimma C et al. Clinical evaluation of recombinant human bone morphogenetic protein-2. *Clin Orthop Relat Res* 2002; 395:110-20.
14. Einhorn TA. Clinical applications of recombinant human BMPs: early experience and future development. *J Bone Joint Surg Am* 2003; 85-A(Suppl 3):82-8.