BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Bone Morphogenetic Protein

Policy #: 189
Category: Surgery

Latest Review Date: April 2020
Policy Grade: A

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Effective for dates of service on or after October 25, 2017:

Blue Advantage will treat **use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE)** as a **covered benefit** for coverage in **skeletally mature patients**:

- For anterior lumbar interbody fusion procedures when use of autograft is not feasible; or
- For instrumented posterolateral intertransverse spinal fusion procedures when use of autograft is not feasible*; or
- For the treatment of acute, open fracture of the tibial shaft, when use of autograft is not feasible.

***As of 2014, rhBMP-7 is no longer marketed in the United States**.

Blue Advantage will treat the **use of bone morphogenetic protein (rhBMP-2)** as a **non-covered benefit** for all other indications, including but not limited to spinal fusion and craniomaxillofacial surgery when use of autograft is feasible.

*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 ICBGH than available (e.g., for multi-level fusion).
**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., 3 months of ultrasound or electrical stimulation).

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;
- Are skeletally immature.

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

Effective for dates of service on or after January 31, 2014 through October 24, 2017:

Blue Advantage will treat **use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE)** as a **covered benefit** for coverage in **skeletally mature patients**:

- For anterior lumbar interbody fusion procedures when use of autograft is not feasible; or
- For instrumented posterolateral intertransverse spinal fusion procedures when use of autograft is not feasible*; or
- For the treatment of acute, open fracture of the tibial shaft, when use of autograft is not feasible.

Blue Advantage will treat **use of recombinant human bone morphogenetic protein-7 (rhBMP-7, OP-1)** as a **covered benefit** for coverage 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.**

As of 2014, rhBMP-7 is no longer marketed in the United States.

*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 ICBGH than available (e.g., for multi-level fusion).
**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., 3 months of ultrasound or electrical stimulation).
***FDA approved under a Humanitarian Device Exemption (HDE). OP-1 is no longer sold in the United States.

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;
- Are skeletally immature.

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

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

One recombinant human bone morphogenetic protein (rhBMP) is commercially available, rhBMP-2 applied with an absorbable collagen sponge (InFUSE®). rhBMP has 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.

Bone Morphogenetic Protein and Carrier and Delivery Systems

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. The 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 has been investigated. Carrier systems, which are absorbed over time, 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 provide mechanical support.

Applications

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 (posterior lumbar interbody fusion [PLIF] or transforaminal lumbar interbody fusion [TLIF]; see Appendix). 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.

KEY POINTS:

This policy has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through January 30, 2020.

Summary of Evidence
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, 2 systematic reviews of rhBMP-2 trials using manufacturer-provided individual patient data were published. Overall, these 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 adverse event rate 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 a meaningful 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 reoperations rates compared with soft-tissue management with or without intramedullary nailing. The evidence is sufficient to determine that the technology results in a meaningful 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, and small case series. Relevant outcomes are symptoms, morbid events, functional outcomes, and treatment-related morbidity. The evidence does not permit conclusions about the effect of rhBMP for craniomaxillofacial surgery or tibial shaft fracture nonunion. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements
American Association of Neurological Surgeons et al
Guidelines on lumbar spinal fusion from the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons were updated in 2014. AANS/CNS gave a Grade B recommendation (multiple level II studies) for the use of rhBMP-2 as a substitute for autologous iliac crest bone for anterior lumbar interbody fusion and single-level posterolateral instrumented fusion. Grade C recommendations were made for rhBMP-2 as an option for PLIF and TLIF, posterolateral fusion in patients older than 60 years, and as a graft extender for either instrumented or noninstrumented posterolateral fusions. AANS/CNS also gave a Grade C recommendation (based on multiple level IV and V studies) that the use of rhBMP-2 as a graft option has been associated with a unique constellation of complications of which the surgeon should be aware when considering the use of this graft extender/substitute.

North American Spine Society
In 2014, the North American Spine Society (NASS) issued coverage policy recommendations outlining the clinical indications for the adjunct use of rhBMP-2 in spinal fusion surgeries based on the strength of the available evidence (level I to level IV). NASS recommends adjunct use of rhBMP-2 in spinal fusion surgeries for the following clinical scenarios and qualifying criteria, as appropriate:

1. "Stand-Alone Anterior Lumbar Interbody Fusion (ALIF): in all patient groups except males with a strong reproductive priority"
2. "Posterolateral Lumbar Fusion: in all patients at high risk for nonunion with autogenous bone graft or in those with inadequate or poor quality autogenous bone available"
3. "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"
4. "Posterior Cervical or Thoracic Fusions"
    a. "in pediatric patients at very high risk for fusion failure (eg, neuromuscular scoliosis, occipitocervical pathology)"
    b. "in adult patients at high risk for nonunion, for example, revision surgery"
5. "Anterior Cervical Fusion: in patients at high risk for nonunion, for example, revision surgery"

The NASS emphasizes that rhBMP-2 is not indicated in the following scenarios:
1. "Routine anterior and posterior cervical fusion procedures"
2. "Single level posterior/posterolateral fusions in healthy adults"
3. "Routine pediatric spine fusion procedures (eg, adolescent idiopathic scoliosis)"

U.S. Preventive Services Task Force Recommendations
Not applicable.

KEY WORDS:
Bone morphogenetic protein, BMP, InFUSE®, OP-1, bone morphogenetic protein-2, rhBMP-2, bone morphogenetic protein-7, rhBMP-7, InFUSE™ Bone Graft/LT-CAGE™, InFUSE™ Bone Graft/INTER FIX™ Threaded Fusion Device, OP-1 Implant, OP-1 Putty, osteobiologics, BMP-7, BMP, Recombinant human bone morphogenetic protein

APPROVED BY GOVERNING BODIES:
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) (see summary of key approvals in Table 1).

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.1 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 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 (H020008) 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.

Table 1. rhBMP Products and Associated Carrier and Delivery Systems Approved by FDA

Systems	Manufacturer	Approved	PMA No.
INFUSE® Bone Graft • Alternative to autogenous bone graft for sinus augmentations • For localized alveolar ridge augmentations in extraction socket defects	Medtronic	03/07	P050053
INFUSE® Bone Graft • 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		10/09	P050053/S012
INFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device • 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	Medtronic Sofamor Danek USA[a]	07/02	P000058

• Implantation via anterior open or anterior laparoscopic approach		
INFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device • Extension of device use from L2 to S1 • May be used with retrolisthesis	07/04	P000058/S002
INFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device • 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	10/09	P000058/S033
INFUSE™ Bone Graft/Medtronic Interbody Fusion Device (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	12/15	P000058/S059
INFUSE™ Bone Graft/Medtronic Interbody Fusion Device • Expanded indication for 2 additional interbody fusion devices: o Divergence-L Anterior/Oblique Lumbar Fusion System o Pivox™ Oblique Lateral Spinal System	09/17	P000058/S065

ALIF: anterior lumbar interbody fusion; FDA: Food and Drug Administration; OLI: oblique lateral interbody fusion; rhBMP: recombinant human bone morphogenetic protein; S: supplement.
[a] Medtronic is the manufacturer for all of the INFUSE bone graft and carrier systems.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:

There is not CPT or HCPCS code for bone morphogenic protein. In 2011, CPT code 20930 was revised to include BMP-type materials used in spine surgery.

CPT Code:

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

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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

Procedures	Access	Approach	Visualization
Anterior (ALIF)	Open, MI, or laparoscopic	Transperitoneal or retroperitoneal	Direct, endoscopic or laparoscopic with fluoroscopic guidance Direct, endoscopic or microscopic, 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 (DLIV)	MI	Retroperitoneal through transpsoas	Direct, with neurologic monitoring and fluoroscopic guidance

LIF: lumbar interbody fusion; MI: minimally invasive

Anterior Lumbar Interbody Fusion

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 (e.g., 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 (e.g., 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.