MASSACHUSETTS

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Medical Policy
Bone Morphogenetic Protein

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Policy Number: 097

BCBSA Reference Number: 7.01.100 (For Plan internal use only)
NCD/LCD: N/A

Related Policies

- Ultrasound Accelerated Fracture Healing Device, #497
- Electrical Bone Growth Stimulation of the Appendicular Skeleton, #499
- Electrical Stimulation of the Spine as an Adjunct to Spinal Fusion Procedures, #498

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Use of recombinant human bone morphogenetic protein-2 (rhBMP-2; Infuse®) may be considered **MEDICALLY NECESSARY** in skeletally mature individuals:

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

Use of recombinant human bone morphogenetic protein (rhBMP-2) is considered **INVESTIGATIONAL** for all other indications, **including but not limited** to spinal fusion when the use of autograft is feasible and craniomaxillofacial surgery.

*Use of iliac crest bone graft may be considered not feasible due to situations that may include, but are not limited to, prior harvesting of iliac crest bone graft or need for a greater quantity of iliac crest bone graft than available (eg, for multilevel fusion).

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 (see summary of key approvals in Table 1).

In 2008, the 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 the FDA for this use.

In 2011, Medtronic received a "nonapprovable letter" from the 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 the 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."

FDA product code: MPW.

- "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."

FDA product code: MPY.

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, the 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. Recombinant Human Bone Morphogenetic Protein Products and Associated Carrier and Delivery Systems Approved by U.S. Food and Drug Administration	
INFUSE™ Bone Graft • Alternative to autogenous bone graft for sinus augmentations • For localized alveolar ridge augmentations in extraction socket defects	Medtronic
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	
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 • Implantation via anterior open or anterior laparoscopic approach	Medtronic Sofamor Danek USA[a]
INFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device • Extension of device use from L2 to S1 • May be used with retrolisthesis	
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	
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	
INFUSE™ Bone Graft/Medtronic Interbody Fusion Device • Expanded indication for 2 additional interbody fusion devices • Divergence-L Anterior/Oblique Lumbar Fusion System • Pivox™ Oblique Lateral Spinal System	

ALIF: anterior lumbar interbody fusion; OLIF: 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.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO	Prior authorization is **not required**.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

Requesting Prior Authorization Using Authorization Manager

Providers will need to use Authorization Manager to submit initial authorization requests for services. Authorization Manager, available 24/7, is the quickest way to review authorization requirements, request authorizations, submit clinical documentation, check existing case status, and view/print the decision letter. For commercial members, the requests must meet medical policy guidelines.

To ensure the service request is processed accurately and quickly:

- Enter the facility's NPI or provider ID for where services are being performed.
- Enter the appropriate surgeon's NPI or provider ID as the servicing provider, *not* the billing group.

Authorization Manager Resources

Refer to our Authorization Manager page for tips, guides, and video demonstrations.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
20930	Allograft, morselized, or placement of osteopromotive material, for **spine** surgery **only** (Report in addition to the primary spinal fusion procedure)

Description

Bone Morphogenetic Protein and Carrier and Delivery Systems

Bone morphogenetic proteins are members of the transforming growth factors family. At present, some 20 bone morphogenetic proteins 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 polymers, 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 (eg, long-bone nonunion, 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), while rhBMP in a collagen sponge with bone dowels or interbody cages are used for interbody spinal fusion. Also, interbody fusion of the lumbar spine can be approached from an anterior (anterior lumbar interbody fusion), lateral, or posterior direction (posterior lumbar interbody fusion or transforaminal lumbar interbody fusion; see Appendix). Surgical procedures may include decompression of the spinal canal and insertion of pedicle screws and rods to increase the stability of the spine.

Posterior approaches (eg, posterior lumbar interbody fusion, transforaminal lumbar interbody fusion) allow decompression (via laminotomies and facetectomies) for treatment of spinal canal pathology (eg, spinal stenosis, lateral recess and foraminal stenosis, synovial cysts, hypertrophic ligamentum flavum) along with spine stabilization. Such approaches are differentiated from instrumented or noninstrumented posterolateral 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 (eg, radiculopathies). Increased risk of bone resorption around rhBMP grafts, heterotopic bone formation, epidural cyst formation, and seromas have also been postulated.

Summary

Description

Two recombinant human bone morphogenetic proteins (rhBMPs) have been extensively studied:

1. recombinant human bone morphogenetic protein-2 (rhBMP-2), applied with an absorbable collagen sponge (Infuse), **and**
2. recombinant human bone morphogenetic protein-7 (rhBMP-7), applied in putty (OP-1; not currently available in the U.S.).

These protein 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.

Summary of Evidence
For individuals who are undergoing anterior or posterolateral lumbar spinal fusion and in whom autograft is not feasible who receive recombinant human bone morphogenetic proteins (rhBMPs), the evidence includes randomzied 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 recombinant human bone morphogenetic protein-2 (rhBMP-2) trials using manufacturer-provided individual patient-level 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 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 reoperations rates compared with 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 (eg, 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.

Policy History

Date	Action
4/2024	Policy revised to remove prior authorization requirements. Clarified coding information. Effective 4/1/2024.
9/2023	Policy clarified to include prior authorization requests using Authorization Manager.
9/2023	Policy clarified. Regulatory Status section added. Table 1 clarified.
4/2023	Annual policy review. Policy statement updated to note that the use of recombinant human bone morphogenetic protein-2 is considered investigational (instead of "not medically necessary") for all other indications, including but not limited to spinal fusion when the use of autograft is feasible and craniomaxillofacial surgery.
4/2023	Policy clarified to include guidelines when the use of autograft is not feasible.
8/2022	Policy clarified. FDA-approved INFUSE™ products added. Policy statements unchanged.
6/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2022	Prior authorization information clarified for PPO Plans. Effective 6/1/2022.
5/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2020	Annual policy review. Description, summary and references updated. Policy statements unchanged.

5/2019	Annual policy review. Description, summary and references updated. Policy statements unchanged.
5/2018	Annual policy review. New references added. Summary clarified.
3/2018	Annual policy review. The term “unfeasible” clarified to “not feasible” in the medically necessary statement. The not medically necessary statement was revised to add craniomaxillofacial surgery. Clarified coding information. Effective 3/1/2018.
9/2016	Annual policy review. FDA approval for rhBMP-2 in oblique lateral interbody fusion added; rhBMP-7 removed from policy statements. Effective 9/1/2016.
9/2015	Added coding language.
12/2014	Annual policy review. New references added.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
4/2014	Annual policy review. One FDA-approved indication that had been omitted re-inserted: treatment of tibial shaft with BMP-2 (when autograft is unfeasible added); return to use of FDA language regarding treatment of noninstrumented revision posterolateral intertransverse lumbar spinal fusion with BMP-7 where use of autograft is unfeasible. Effective 4/1/2014.
3/2014	Annual policy review. New medically and not medically necessary indications described. Effective 3/1/2014.
1/2014	Coding information clarified
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
6/2011	Reviewed - Medical Policy Group – Orthopedics, Rehabilitation and Rheumatology. No changes to policy statements.
1/2011	Reviewed - Medical Policy Group – Neurology and Neurosurgery. No changes to policy statements.
12/2010	Annual policy review. No changes to policy statements.
7/2010	Reviewed - Medical Policy Group – Orthopedics, Rehabilitation Medicine and Rheumatology. No changes to policy statements.
1/2010	Reviewed - Medical Policy Group – Neurology and Neurosurgery. No changes to policy statements.
1/2010 2/01/2010	Annual policy review. Covered indications for bone morphogenetic protein-2 clarified; bone morphogenetic protein-7 is now covered based on the indications in this policy. Effective 2/1/2010.
7/2009	Reviewed - Medical Policy Group - Orthopedics, Rehabilitation Medicine, and Rheumatology. No changes to policy statements.
5/1/ 2009	Medical Policy #097 effective 5/1/2009 created.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

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