Subject: Recombinant Human Bone Morphogenetic Protein (rhBMP) for Bone Fusion		Original Effective Date: 12/8/14
Policy Number: MCP-218	**Revision Date(s):**	
Review Date: 12/16/15, 9/15/16, 9/19/17, 7/10/18, 6/19/19, 6/17/20, 4/5/21		
MCPC Approval Date: 7/10/18, 6/19/19, 6/17/20, 4/5/21		

Contents

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina Clinical Policy (MCP) document and provide the directive for all Medicare members.[1]

DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL

Recombinant human bone morphogenetic protein (rhBMP) are key factors necessary for bone healing and regeneration and function as a replacement for or adjunct to autologous bone grafts (autografts). rhBMP is most commonly used in spinal fusion surgery for degenerative disc disease to promote the bone growth that results in fusion and in bone fractures. Recombinant DNA techniques have been used to produce BMP2 and BMP7 as alternatives to bone grafts to improve healing of bony defects and fractures when autograft bone harvest is not possible or contraindicated.

rhBMP's that have received FDA approval* include but are not limited to:

- *rhBMP-2*: Marketed in the U.S. as INFUSE® Bone Graft (Medtronic Sofamor Danek) has received premarket approval for fusion of the lumbar spine in skeletally mature patients with degenerative disc disease (DDD) at one level from L4-S1 and for healing of acute, open tibial shaft fractures stabilized with an intramedullary (IM) nail and treated within 14 days of the initial injury. [3 6]
- *rhBMP-7:* Marketed in the U.S. as OP-1® Implant & Putty (Stryker Biotech) has received humanitarian device exemption approval as an alternative to autograft in recalcitrant long bone nonunions where use of autograft is unfeasible and alternative treatments have failed. It is also approved 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. [4 5]

The FDA released a Public Health Notification in 2008 warning that use of rhBMP for cervical spinal fusion can cause life-threatening complications such as airway compression, compression of neurological structures, and difficulty swallowing, breathing, or speaking. [2]

*Additional products may be found on the FDA website using the product code NEK: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm

POSITION STATEMENT CRITERIA [7-37]

1. **rhBMP-2 Infuse Bone Graft** may be considered medically necessary and may be authorized when all of the following criteria have been met:

   ❑ *For anterior lumbar spinal fusion* procedures: [3 8 13-21 23-37] [ALL]
   - Diagnosis of degenerative disc disease (DDD) defined as: [ALL]
     - ➢ discogenic back pain with degeneration of the disc confirmed by:
       - patient history, and
       - function deficit and/or neurological deficit and
       - radiographic studies
   - DDD involving one level from L4-S1; and
   - Age ≥ 18 years with radiographic evidence of epiphyseal closure; and
   - Failed at least 6 months of non-surgical treatment

   ❑ For the treatment of acute, open fracture of the tibial shaft: [6-7 10-12 22] [ALL]
   - stabilized with intramedullary (IM) nail fixation; and
   - wound management performed; and
   - applied within 14 days after the initial fracture; and
   - age > 18 years with radiographic evidence of epiphyseal closure

2. **rhBMP-2 Infuse Bone Graft** is considered experimental, investigational and unproven for cervical spinal fusion and any other indication not listed above due to insufficient evidence in the peer reviewed medical literature that indicate long term benefit on health outcomes.

3. **rhBMP-7 OP-1® Implant &Putty** is considered experimental, investigational and unproven for any indication due to insufficient evidence in the peer reviewed medical literature that indicate long term benefit on health outcomes.

4. **Contraindications:**
    - Allergy or hypersensitivity to the rhBMP product, collagen, or materials contained in the device
    - Known or suspected malignancy, or a history of malignancy
    - Infection near the area of the surgical incision
    - Not skeletally mature
    - Pregnant or may become pregnant
    - Known autoimmune disease or immunodeficiency, including chronic steroid treatment
    - Should not be used in the vicinity of a resected or extant tumor, in patients with any active malignancy or patients undergoing treatment for a malignancy

SUMMARY OF MEDICAL EVIDENCE

The Agency for Healthcare Research and Quality (AHRQ) published a report in 2010 called Bone Morphogenetic Protein: The State of the Evidence of On-Label and Off-Label Use. This report assessed the available evidence addressing the use of bone morphogenetic protein. Overall, the report concluded that the available data addressing the safety and efficacy of rhBMP2 and rhBMP7 for both on-label and off-label indications is moderate at best, and significant questions still exist regarding the benefits and drawbacks of its use in the clinical setting.[9]

rhBMP-2 Infuse Bone Graft for Tibial Fracture [10 11 12 22]

There is low to moderate quality of evidence from a very large multinational randomized controlled trial (n=450) [10] and a smaller U.S. study (n=30) [11] that suggest recombinant human bone morphogenetic protein (rhBMP)-2 is safe and, when combined with standard fracture treatment, may reduce the need for secondary intervention in patients with fresh open tibial fractures, compared with standard care alone. Subgroup analysis of the study (n=60) results suggests that this benefit may be greatest in patients with severe-grade fractures. [12] The small study also demonstrated a benefit of rhBMP-2 for staged reconstruction of tibial shaft fractures. [11] None of the studies focused on rhBMP-2 for the treatment of fresh closed tibial fractures or nonunion. Follow-up was 1 year.

The largest study (BESTT Trial) randomized 450 individuals with open tibial shaft fractures to receive initial irrigation and debridement followed by treatment with a locked intramedullary nail either alone or with additional rhBMP-2 on an absorbable collagen sponge placed over the fracture at the time of definitive wound

closure. The primary outcome measure was the proportion of individuals requiring secondary intervention due to delayed union or nonunion at 12 months. A total of 58% of individuals treated with rhBMP-2 were healed compared with only 38% in the control group. The rhBMP-2 group also had fewer hardware failures, fewer infections and showed faster wound healing. [10]

A Cochrane review highlights a paucity of data on the use of BMP in fracture healing as well as considerable industry involvement in currently available evidence. There is limited evidence to suggest that BMP may be more effective than controls for acute tibial fracture healing, however, the use of BMP for treating nonunion remains unclear. The limited available economic evidence indicates that BMP treatment for acute open tibial fractures may be more favorable economically when used in patients with the most severe fractures. [22]

rhBMP-2 Infuse Bone Graft for Spinal Fusion [13-37]

There is moderate quality of evidence from randomized controlled trials evaluating rhBMP-2 for lumbar spinal fusion that suggest when compared with autograft, rhBMP-2 increases the rate or overall incidence of solid fusion and provides short term benefits such as shorter operative time and less estimated blood loss. Sample size ranged from 19 to 463 patients and follow-up was1 year to 4 years. [13-34]

The key clinical trial of rhBMP-2 as part of the U.S. Food and Drug Administration (FDA) approval process consisted of 279 individuals undergoing single level lumbar fusion via an open anterior approach, who were randomized to receive either the LT (i.e., lumbar tapered)-Cage with rh-BMP-2 or the same cage filled with iliac crest autograft (Bowden, 2002). In a non- randomized portion of the trial, an additional 136 individuals underwent a single level laparoscopic lumbar interbody fusion with rhBMP-2. There were no differences in fusion success rates, Oswestry Disability Index (ODI) scores or back pain between the randomized groups. The group treated laparoscopically also had similar fusion rates. The operative time and blood loss were significantly lower in those receiving the rh-BMP-2, and obviously these individuals did not experience the pain and morbidity associated with the harvesting of autologous bone from the iliac crest. The results were similar in a similarly designed trial of posterior lumbar interbody fusion (PLIF). In addition, the group receiving rhBMP-2 had a hospital stay of 3.4 days compared to 5.1 days for the control group. [21]

Several systematic reviews and meta-analysis reported that RhBMP-2 was superior to the ICBG for achieving fusion success and avoiding reoperation [25] and that at 24 months, rhBMP-2 increases fusion rates [34], reduces pain by a clinically insignificant amount, and increases early postsurgical pain compared with ICBG. [24] Evidence of increased cancer incidence is inconclusive. [24 28 30] However, the risk of adverse events associated with rhBMP-2 is higher than the original estimates reported in the industry-sponsored peer-reviewed publications. [23 27 -29] The clinical efficiency of rhBMP-2 is equal or superior to that of allogenic or autologous bone graft in respect to fusion rate, low back pain disability, patient satisfaction and rate of re-operations. [31]

CODING INFORMATION: THE CODES LISTED IN THIS POLICY ARE FOR REFERENCE PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE.

CPT	Description

20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only [when specified as recombinant human bone morphogenetic protein]. List separately in addition to code for primary procedure. According to 2018 Encoder Pro the following must be coded first: 22319, 22532-22533, 22548-22558, 22590-22612, 22630, 22633-22634, 22800-22812
20999	Unlisted procedure, musculoskeletal system, general [when specified as placement of recombinant human bone morphogenetic protein for tibial fracture]

HCPCS	Description
	N/A

ICD-10	Description (Procedure): [For dates of service on or after 10/01/2015]
3E0U0GB	Introduction of recombinant bone morphogenetic protein into joints, open approach
3E0U3GB	Introduction of recombinant bone morphogenetic protein into joints, percutaneous approach
3E0V0GB	Introduction of recombinant bone morphogenetic protein into bones, open approach
3E0V3GB	Introduction of recombinant bone morphogenetic protein into bones, percutaneous approach
	Diagnosis Codes: [For dates of service on or after 10/01/2015]
M51.36	Other intervertebral disc degeneration, lumbar region
S82.1-S82.49	Fracture of tibia (range of codes)

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Other Resources: Hayes a TractManager Company. Winifred Hayes Inc. Lansdale, PA.

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REVIEW/REVISION HISTORY:

12/8/14: New Policy
12/16/15, 9/15/16, 9/19/17: Policy reviewed, no changes to criteria.
7/10/18: Policy reviewed, no changes to criteria. Changed definition for code 20930 per Encoder Pro 2018: Added the following language: List separately in addition to code for primary procedure. According to 2018 Encoder Pro the following must be coded first: 22319, 22532-22533, 22548-22558, 22590-22612, 22630, 22633-22634, 22800-22812. Updated references.
6/19/19 & 6/17/20: Policy reviewed, no changes to criteria.:
4/5/21: Policy reviewed, no changes to criteria. Evaluation of the literature indicates that no new applications of the Infuse bone graft have been identified.