Molina Clinical Policy
Recombinant Human Bone Morphogenetic Protein (rhBMP) for Bone Fusion: Policy No. 218

Last Approval: 4/13/2022
Next Review Due By: April 2023

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. 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 (e.g., 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 MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Recombinant human bone morphogenetic protein (rhBMP) are key factors necessary for bone healing, regeneration and function used 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 bone growth that results in fusion, as well as in treatment of 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. rhBMPs that have received FDA approval* include:

- *rhBMP-2*: INFUSE® Bone Graft (Medtronic Sofamor Danek) 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 in 2002 (FDA, 2002a; FDA, 2002b). INFUSE® Bone Graft has subsequently been approved for use with multiple associated lumbar fusion carrier and delivery systems by supplements to the original PMA, including devices that can be placed at a single level from L2-S1. The Infuse™ Bone Graft/Medtronic Interbody Fusion Device consists of a spinal fusion cage, the rhBMP solution, and a carrier/scaffold for the rhBMP and resulting bone. Infuse Bone Graft for treatment of tibial shaft fractures consists of two components: the rhBMP and a carrier/scaffold. For each of the indications, the components must be used as a system and cannot be used alone.

- *rhBMP-7:* The OP-1® Implant & Putty (Stryker Biotech) 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 (FDA 2001; FDA 2004). The rhBMP-7 product is no longer marketed in the United States.

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 (FDA, 2008).

* Products and supplemental approvals may be found on the FDA website (here) using the product code NEK.

COVERAGE POLICY

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 the applicable procedure:

   a. For use in conjunction with lumbar spinal fusion procedures when **ALL** of the following are met:
      - Medical necessity criteria for lumbar fusion are met; **AND**
      - Single level degenerative disc disease (DDD) at one level from L2-S1; **AND**
      - No more than Grade 1 spondylolisthesis or retrolisthesis at the involved level; **AND**
      - Used for single-level lumbar fusion in combination with a cage/device approved for use with INFUSE by the FDA; **AND**
      - Skeletally mature (Age 18 years or greater with radiographic evidence of epiphyseal closure); **AND**
      - Absence of contraindications listed below.

   b. For the treatment of acute, open fracture of the tibial shaft **ALL** of the following must be met:
      - Stabilized with intramedullary (IM) nail fixation; **AND**
      - Wound management performed; **AND**
      - Applied within 14 days after the initial fracture; **AND**
      - Skeletally mature (Age 18 years or greater with radiographic evidence of epiphyseal closure).

2. *rhBMP-2 Infuse Bone Graft* **is considered experimental, investigational, and unproven** for cervical spinal fusion, multilevel fusions, 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.

Contraindications

1. Allergy or hypersensitivity to the rhBMP product, collagen, or materials contained in the device.
2. Known or suspected malignancy, or a history of malignancy.
3. Infection near the area of the surgical incision.
4. Not skeletally mature.
5. Pregnant or may become pregnant.
6. Known autoimmune disease or immunodeficiency, including chronic steroid treatment.
7. Should not be used in the vicinity of a resected or extant tumor.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

The **Agency for Healthcare Research and Quality (AHRQ)** published *Bone Morphogenetic Protein: The State of the Evidence of On-Label and Off-Label Use*. The 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 (Ratko et al., 2010).

rhBMP-2 Infuse Bone Graft for Tibial Fracture

There is low to moderate quality of evidence from a very large multinational randomized controlled trial (n=450) by Govender et al. (2002) and a smaller U.S. study by Jones et al. (2006) with 30 participants 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 (Swiontkowski et al., 2006). The small study also demonstrated a benefit of rhBMP-2 for staged reconstruction of tibial shaft fractures (Jones et al., 2006). 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 (Govender et al., 2002).

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 (Garrison et al., 2010).

rhBMP-2 Infuse Bone Graft for Lumbar Spinal Fusion

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.

The key clinical trial of rhBMP-2 as part of the 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 (e.g., lumbar tapered)-Cage with rh-BMP-2 or the same cage filled with iliac crest autograft. 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 (Boden et al., 2002).

Several systematic reviews and meta-analyses reported that rhBMP-2 was superior to the iliac crest bone graft (ICBG) for achieving fusion success and avoiding reoperation (Chen et al., 2012) and that at 24 months, rhBMP-2 increases fusion rates (Galimberti et al., 2015), reduces pain by a clinically insignificant amount, and increases early postsurgical pain compared with ICBG (Simmonds et al., 2013). Evidence of increased cancer incidence is inconclusive (Simmonds et al., 2013; Vavken et al., 2016a; Dettori et al., 2016). However, the risk of adverse events associated with rhBMP-2 is higher than the original estimates reported in the industry-sponsored peer-reviewed publications (Carragee et al., 2011; Vavken et al., 2016a; Vavken et al., 2016b; Stiel et al., 2016). The clinical efficiency of rhBMP-2 is equal or superior to that of allogenic or autologous bone graft in respect to fusion success rate, low back pain disability, patient satisfaction and rate of re-operations (Fraundez et al., 2016; Liu et al., 2020).

National and Specialty Organizations

The **American Association of Neurological Surgeons (AANS)** and **Congress of Neurological Surgeons (CNS)** published a joint guideline in 2014 stating that the use of rhBMP-2 as a substitute for AICB in lumbar fusion. The guideline also notes that although rhBMP-2 has been shown to have a positive effect on fusion rate, its use is associated with unique complications. Surgeons utilizing rhBMP-2 should be aware of the potential for these complications and be selective in use. Further research on identifying patient populations which would best benefit from rhBMP-2 is warranted (Kaiser et al., 2014).

The North American Spine Society (NASS) published Appropriate Use Criteria for Degenerative Lumbar Spondylolisthesis, citing that BMP is a reasonable option for bone graft in patients who are at higher risk of nonunion due to smoking (NASS, 2020).

For additional sources referenced in the development and review of this policy, please see the *References* section.

SUPPLEMENTAL INFORMATION

None.

CODING & BILLING INFORMATION

CPT Codes

CPT	Description
20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only [when specified as recombinant human bone morphogenetic protein].
20999	Unlisted procedure, musculoskeletal system, general [when specified as placement of recombinant human bone morphogenetic protein for tibial fracture]

HCPCS Codes – N/A

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

04/13/2022	Policy reviewed. Overview, Summary of Evidence and References updated. Coverage criteria for use in lumbar fusion revised to include levels L2-3.
04/05/2021	Policy reviewed, no changes to criteria; literature review did not yield any new applications of the Infuse bone graft.
06/17/2020	Policy reviewed, no changes.
06/19/2019	Policy reviewed, no changes.
07/10/2018	Policy reviewed, no changes, updated references. In the Coding section, changed definition for code 20930; added "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.
09/19/2017	Policy reviewed, no changes.
09/15/2016	Policy reviewed, no changes.
12/16/2015	Policy reviewed, no changes.
12/08/2014	New policy.

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Government Agencies

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3. Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). HDE Approval OP-1 Putty (#H020008) Published April 7, 2004. Available from FDA.
4. Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). PMA Approval INFUSE™ Bone Graft for Tibial Fracture (P000054). Published November 21, 2002b. Available from FDA.
5. Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). PMA approval INFUSE™ Bone Graft/LT-CAGE™ lumbar tapered fusion device (P000058). Published July 2002a. Available from FDA.
6. Food and Drug Administration (FDA). Public health notification: Life-threatening complications associated with recombinant human bone morphogenetic protein in cervical spine fusion. Available from FDA. Published July 2008.

Evidence Based Reviews and Publications

1. Hayes. Recombinant Human bone morphogenetic protein (rhBMP) for use in tibia repair. Available from Hayes. Published September 12, 2011. Updated July 2015. Archived. Registration and login required.
2. Hayes. Comparative effectiveness review: Recombinant human bone morphogenetic protein (rhBMP) for use in spinal fusion. Available from Hayes. Published September 2018. Updated January 2021. Registration and login required.

Peer Reviewed Publications

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2. Boden SD, Kang J, Sandhu H, Heller JG. Use of recombinant human bone morphogenetic protein-2 to achieve posterolateral lumbar spine fusion in humans: a prospective, randomized clinical pilot trial. Spine. 2002; 27(23):2662-2673.
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13. Fuchs T, Stolberg-Stolberg J, Michel PA, et al. Effect of Bone Morphogenetic Protein-2 in the Treatment of Long Bone Non-Unions. J Clin Med. 2021 Oct 6;10(19):4597. doi: 10.3390/jcm10194597.
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National and Specialty Organizations

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Other Peer Reviewed and National Organization Publications (used in the development of this policy)

1. Medtronic. Infuse bone graft. Available from Medtronic. Updated December 2020. Accessed February 25, 2022.

APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*