



MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an independent licensee of the Blue Cross and Blue Shield Association

Medical Policy Bone Morphogenetic Protein

Table of Contents

- [Policy: Commercial](#)
- [Policy: Medicare](#)
- [Authorization Information](#)
- [Coding Information](#)
- [Description](#)
- [Policy History](#)
- [Information Pertaining to All Policies](#)
- [References](#)

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 BlueSM and Medicare PPO BlueSM 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 **NOT MEDICALLY NECESSARY** for all other indications, including but not limited to spinal fusion when the use of autograft is feasible and craniomaxillofacial surgery.

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 required .

Commercial PPO	Prior authorization is required .
Medicare HMO BlueSM	Prior authorization is required .
Medicare PPO BlueSM	Prior authorization is required .

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)

ICD-10 Procedure Codes

ICD-10-PCS procedure codes:	Code Description
3E0V0GB	Introduction of Recombinant Bone Morphogenetic Protein into Bones, Open Approach

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 recombinant human bone morphogenetic protein (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 recombinant human bone morphogenetic protein (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 (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 has also been postulated.

Summary

Two recombinant human bone morphogenetic proteins (rhBMPs) have been extensively studied: recombinant human bone morphogenetic protein-2 (rhBMP-2), applied with an absorbable collagen sponge (Infuse), and 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.

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-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 reoperation 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
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

1. Schultz DG, Center for Devices and Radiological Health, Food and Drug Administration (FDA). FDA Public Health Notification: Life-threatening Complications Associated with Recombinant Human Bone Morphogenetic Protein in Cervical Spine Fusion [letter]. 2008 July 1; <https://wayback.archive-it.org/7993/20170111190511/http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm062000.htm>. Accessed February 19, 2022.

2. U.S. Food and Drug Administration (FDA). Summary of Safety and Effectiveness: InFUSE Bone Graft/LT-Cage Lumbar Tapered Fusion Device [P000058]. 2002; https://www.accessdata.fda.gov/cdrh_docs/pdf/P000058b.pdf. Accessed February 22, 2022.
3. Govender S, Csimma C, Genant HK, et al. Recombinant human bone morphogenetic protein-2 for treatment of open tibial fractures: a prospective, controlled, randomized study of four hundred and fifty patients. *J Bone Joint Surg Am*. Dec 2002; 84(12): 2123-34. PMID 12473698
4. Howard JM, Glassman SD, Carreon LY. Posterior iliac crest pain after posterolateral fusion with or without iliac crest graft harvest. *Spine J*. Jun 2011; 11(6): 534-7. PMID 20947439
5. 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*. Jun 18 2013; 158(12): 877-89. PMID 23778905
6. Fu R, Selph S, McDonagh M, et al. Effectiveness and harms of recombinant human bone morphogenetic protein-2 in spine fusion: a systematic review and meta-analysis. *Ann Intern Med*. Jun 18 2013; 158(12): 890-902. PMID 23778906
7. United States Senate Finance Committee. Staff report on Medtronic's influence on INFUSE clinical studies. *Int J Occup Environ Health*. Apr-Jun 2013; 19(2): 67-76. PMID 23684264
8. Carragee EJ, Hurwitz EL, Weiner BK. A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned. *Spine J*. Jun 2011; 11(6): 471-91. PMID 21729796
9. Feng JT, Yang XG, Wang F, et al. Efficacy and safety of bone substitutes in lumbar spinal fusion: a systematic review and network meta-analysis of randomized controlled trials. *Eur Spine J*. Jun 2020; 29(6): 1261-1276. PMID 31872300
10. Liu S, Wang Y, Liang Z, et al. Comparative Clinical Effectiveness and Safety of Bone Morphogenetic Protein Versus Autologous Iliac Crest Bone Graft in Lumbar Fusion: A Meta-analysis and Systematic Review. *Spine (Phila Pa 1976)*. Jun 15 2020; 45(12): E729-E741. PMID 31923133
11. Mariscal G, Nunez JH, Barrios C, et al. A meta-analysis of bone morphogenetic protein-2 versus iliac crest bone graft for the posterolateral fusion of the lumbar spine. *J Bone Miner Metab*. Jan 2020; 38(1): 54-62. PMID 31292724
12. Wu Z, Zhou B, Chen L, et al. Bone morphogenetic protein-2 against iliac crest bone graft for the posterolateral fusion of the lumbar spine: A meta-analysis. *Int J Clin Pract*. Apr 2021; 75(4): e13911. PMID 33277737
13. Carragee EJ, Chu G, Rohatgi R, et al. Cancer risk after use of recombinant bone morphogenetic protein-2 for spinal arthrodesis. *J Bone Joint Surg Am*. Sep 04 2013; 95(17): 1537-45. PMID 24005193
14. Zadegan SA, Abedi A, Jazayeri SB, et al. Bone Morphogenetic Proteins in Anterior Cervical Fusion: A Systematic Review and Meta-Analysis. *World Neurosurg*. Aug 2017; 104: 752-787. PMID 28315798
15. Khan TR, Pearce KR, McAnany SJ, et al. Comparison of transforaminal lumbar interbody fusion outcomes in patients receiving rhBMP-2 versus autograft. *Spine J*. Mar 2018; 18(3): 439-446. PMID 28822825
16. Cooper GS, Kou TD. Risk of cancer after lumbar fusion surgery with recombinant human bone morphogenetic protein-2 (rh-BMP-2). *Spine (Phila Pa 1976)*. Oct 01 2013; 38(21): 1862-8. PMID 23883824
17. Cooper GS, Kou TD. Risk of Cancer Following Lumbar Fusion Surgery With Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2): An Analysis Using a Commercially Insured Patient Population. *Int J Spine Surg*. Apr 2018; 12(2): 260-268. PMID 30276083
18. Dettori JR, Chapman JR, DeVine JG, et al. Longer follow-up continues to reveal no increased risk of cancer with the use of recombinant human bone morphogenetic protein in spine fusion. *Spine J*. Oct 2019; 19(10): 1640-1647. PMID 31108234
19. Dai J, Li L, Jiang C, et al. Bone Morphogenetic Protein for the Healing of Tibial Fracture: A Meta-Analysis of Randomized Controlled Trials. *PLoS One*. 2015; 10(10): e0141670. PMID 26509264
20. Garrison KR, Shemilt I, Donell S, et al. Bone morphogenetic protein (BMP) for fracture healing in adults. *Cochrane Database Syst Rev*. Jun 16 2010; (6): CD006950. PMID 20556771
21. Lyon T, Scheele W, Bhandari M, et al. Efficacy and safety of recombinant human bone morphogenetic protein-2/calcium phosphate matrix for closed tibial diaphyseal fracture: a double-blind, randomized, controlled phase-II/III trial. *J Bone Joint Surg Am*. Dec 04 2013; 95(23): 2088-96. PMID 24306695

22. Cannada LK, Tornetta P, Obrebsky WT, et al. A Randomized Controlled Trial Comparing rhBMP-2/Absorbable Collagen Sponge Versus Autograft for the Treatment of Tibia Fractures With Critical Size Defects. *J Orthop Trauma*. Aug 2019; 33(8): 384-391. PMID 31022069
23. Ratko TA, Belinson SE, Samson DJ, et al. Bone Morphogenetic Protein: The State of the Evidence of On-Label and Off-Label Use (AHRQ Technology Assessment Report). Rockville, MD: Agency for Healthcare Research and Quality; 2010.
24. Ramly EP, Alfonso AR, Kantar RS, et al. Safety and Efficacy of Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) in Craniofacial Surgery. *Plast Reconstr Surg Glob Open*. Aug 2019; 7(8): e2347. PMID 31592029
25. U.S. Food and Drug Administration. Infuse Bone Graft. Summary of safety and effectiveness data. March 2007. https://www.accessdata.fda.gov/cdrh_docs/pdf5/P050053B.pdf. Accessed February 21, 2022.
26. Valentin-Opran A, Wozney J, Csimma C, et al. Clinical evaluation of recombinant human bone morphogenetic protein-2. *Clin Orthop Relat Res*. Feb 2002; (395): 110-20. PMID 11937870
27. 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. PMID 12925614
28. Kaiser MG, Groff MW, Watters WC, et al. Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 16: bone graft extenders and substitutes as an adjunct for lumbar fusion. *J Neurosurg Spine*. Jul 2014; 21(1): 106-32. PMID 24980593
29. North American Spine Society (NASS). NASS Coverage Policy Recommendations: Recombinant Human Bone Morphogenetic Protein (rhBMP-2). 2014. <https://www.spine.org/Product-Details?productid=%7B9567DDCC-4EC7-E411-9CA5-005056AF031E%7D>. Accessed February 22, 2022.