Molina Clinical Policy
Bone Graft Substitutes for Bone Fusion
Policy No. 218

Last Approval: 04/08/2026
Next Review Due By: April 2027

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OVERVIEW

Recombinant human bone morphogenetic protein (rhBMP) is a bioengineered version of naturally occurring bone morphogenetic proteins, which play a key role in bone healing, regeneration, and function, and can be used as a replacement for or adjunct to autologous bone grafts (autografts). rhBMPs signal mesenchymal stem cells to initiate bone formation. rhBMP is most commonly used in lumbar fusion surgery for degenerative disc disease to promote bone growth that results in fusion. It is also utilized in the treatment of tibial bone fractures and certain oral-maxillofacial procedures. Using recombinant DNA techniques, rhBMP-2 and rhBMP-7 have been developed as alternatives to bone grafts, aiding in the healing of bony defects and fractures when autologous bone harvest, the gold standard, is not feasible or contraindicated (Hayes 2022; Sage & Levin 2024).

P-15 peptide enhanced bone graft substitutes have also been developed for use in spinal fusion surgery. P-15 is a bioactive synthetic peptide that mimics the cell-binding of type I collagen to promote osteogenic cell attachment. These products combine P-15 peptide with a mineral scaffold, such as anorganic bone minerals, to promote bone formation (Spanninga et al. 2022).

Regulatory Status

rhBMP-2: In 2002, INFUSE Bone Graft (Medtronic) received FDA premarket approval (PMA) for single-level anterior fusion of the lumbar spine under product code NEK and PMA number P000058. In 2004, it received FDA-approval for healing of acute, open tibial shaft fractures under product code MPW and PMA number P000054. INFUSE has been subsequently approved for use with multiple interbody devices and surgical approaches as supplements to the original PMA, including FDA-approval in 2026 for transforaminal lumbar fusion at one or two adjacent levels from L2-S1 under PMA number P000058, supplement number S096. While the clinical trial (NCT04073563) met early success criteria, the study is still ongoing. The Infuse Bone Graft/Medtronic Interbody Fusion Device components must be used as a system and cannot be used alone.

rhBMP-7: In 2001, OP-1 Implant and OP-1 Putty (Stryker) received humanitarian device exemption (HDE) as an alternative to autograft in recalcitrant long bone nonunion and lumbar fusion revision under HDE numbers H010002 and H020008 and product codes OKD and OJZ, respectively. The rhBMP-7 products are 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). The safety and effectiveness of INFUSE Bone Graft implanted in the cervical spine has not been established (Medtronic 2025).

P-15 Peptide: In 2015, i-Factor Peptide Enhanced Bone Graft (Cerapedics) received FDA-approval for reconstruction of a cervical disc following anterior cervical discectomy and fusion under product code NOX and PMA number P140019. In 2025, PearlMatrix P-15 Peptide Enhanced Bone Graft (Cerapedics) received FDA-approval for intervertebral body fusion of the lumbar spine (L2-S1) under product code NOX and PMA number P240001.

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COVERAGE POLICY

Medically Necessary

Recombinant human bone morphogenetic protein (rhBMP-2) INFUSE Bone Graft may be **considered medically necessary** when ALL the following criteria are met:

1. Member ≥ 18 years old or documented evidence of skeletal maturity (radiographic evidence of epiphyseal closure)

2. Member meets ONE of the following indications:
   a. For use in conjunction with single-level lumbar spinal fusion procedures when ALL the following are met:
      i. Diagnosis of single-level degenerative disc disease at one level from L2-S1
      ii. No more than Grade 1 spondylolisthesis or retrolisthesis at the involved level
      iii. Used in combination with an FDA-approved interbody fusion cage/device specifically indicated for use with INFUSE
   b. For the treatment of acute, open fracture of the tibial shaft when ALL the following are met:
      i. Fracture is stabilized with intramedullary nail fixation
      ii. Appropriate wound management performed
      iii. INFUSE is applied within 14 days of the initial fracture

3. Absence of ALL the following contraindications:
   a. Allergy or hypersensitivity to the rhBMP-2 product, bovine type I collagen, or any materials contained in the device
   b. Known or suspected malignancy, history of malignancy, or use in the vicinity of a resected/extant tumor
   c. Active infection near the surgical site
   d. Members who are pregnant or planning to become pregnant
   e. Autoimmune disease or immunodeficiency, including chronic steroid treatment
   f. Used in the cervical spine, multilevel fusions, or any other non-FDA-approved indications

Experimental, Investigational, and Unproven

rhBMP-2 Infuse Bone Graft is considered **experimental, investigational, and unproven** for *cervical spinal fusion, multilevel fusion, and any other indication* not listed above due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes

rhBMP-7 OP-1 Implant and OP-1 Putty is considered **experimental, investigational, and unproven** for any indication due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes

P-15 peptide-enhanced bone graft substitutes (e.g., i-Factor, PearlMatrix) are considered **experimental, investigational, and unproven** for any indication due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes

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

rhBMP-2 Infuse Bone Graft for Tibial Fracture

Randomized Controlled Trials

The Major Extremity Trauma Research Consortium (METRC) (2019) conducted a randomized controlled trial (RCT) to

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compare the radiographic union of tibia fractures with bone defects treated using recombinant bone morphogenetic protein-2 (rhBMP-2) with allograft versus autogenous iliac crest bone graft (ICBG). The study included 30 patients with Type II, IIIA, or IIIB open tibia fractures and bone defects, all treatment with an intramedullary nail. Sixteen patients received rhBMP-2, while 14 were treated with ICBG. The primary outcome assessed was radiographic union within 52 weeks, while secondary outcomes included clinical healing, patient-reported function, major complications, and treatment costs. Among the 23 patients with available union data after 52 weeks, 7 of 12 in the rhBMP-2 group achieved radiographic union, compared to 9 of 11 in the ICBG group. Patients treated with rhBMP-2 showed lower clinical healing rates at 52 weeks (27% vs. 54%), higher Short Musculoskeletal Function Assessment scores (indicating greater dysfunction and bother), and a higher number of complications (5 vs. 3). The study concluded that there is insufficient evidence to establish equivalence between ICBG and rhBMP-2 in terms of radiographic union.

Govender et al. (2002) conducted a randomized controlled trial to assess the safety and effectiveness of rhBMP-2 in promoting healing and reducing the need for secondary interventions in open tibial shaft fractures. The study included 450 patients, randomized into three groups: standard care (intramedullary nail fixation and routine soft-tissue management), standard care with a 0.75 mg/mL rhBMP-2 implant, and standard care with a 1.50 mg/mL rhBMP-2 implant. The primary outcome was the rate of secondary interventions due to delayed union or nonunion within 12 months. Among the 421 patients available for follow-up, those treated with 1.50 mg/mL rhBMP-2 experienced a 44% lower risk of requiring secondary intervention ($p = 0.0005$), significantly fewer invasive procedures such as bone grafting and nail exchange ($p = 0.0264$), and faster fracture healing ($p = 0.0022$). This group also demonstrated higher fracture healing rates from 10 weeks to 12 months postoperatively ($p = 0.0008$), fewer hardware failures ($p = 0.0174$), lower infection rates ($p = 0.0219$), and faster wound healing ($p = 0.0010$) compared to the control group. The study concluded that rhBMP-2 is safe, and at a dosage of 1.50 mg/mL, it significantly improves fracture and wound healing, reduces the need for secondary interventions, and lowers infection rates in patients with open tibial fractures.

rhBMP-2 Infuse Bone Graft for Spinal Fusion

Randomized Controlled Trials

Boden et al. (2002) was the key clinical trial of rhBMP-2 as part of the FDA approval process that 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 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. In addition, the rhBMP-2 group had a shorter hospital stay of 3.4 days compared to 5.1 days for the control group.

Systematic Reviews and Meta-Analyses

Fitzgerald et al. (2025) conducted a systematic review to assess existing evidence on bone graft materials used in lumbar interbody fusion procedures for degenerative disc disease (DDD), with a focus on anterior lumbar interbody fusion (ALIF) and oblique lumbar interbody fusion (OLIF). The review included 21 studies, with 18 reporting clinical outcomes and 4 focusing on economic aspects. Nine studies examined Infuse, comprising 3 RCTs, a cohort study, and 4 case series, while 10 studies investigated alternative bone graft materials, such as allografts, vertebral spur combined with apacerum powder, and tricalcium phosphate with autologous bone marrow aspirate. Fusion outcomes from 4 RCTs showed comparable fusion rates between Infuse and iliac crest bone graft (ICBG), with rates ranging from 86.7% to 100% across different graft types. Secondary surgical outcomes, including implant removal and reoperation rates, showed no significant differences between Infuse and ICBG, while artificial disc replacement had higher reoperation rates. Procedural outcomes indicated Infuse led to shorter operative times and reduced blood loss, though differences were not clinically significant. Patient-reported outcomes demonstrated comparable Oswestry Disability Index scores for Infuse and ICBG, but artificial disc replacement showed greater improvements in back pain. Complication rates varied, with perioperative issues more frequent in Infuse recipients compared to artificial disc replacement but not ICBG. Long-term complications were inconsistently reported, with some studies showing no significant differences and others indicating postoperative complications in up to 12% of patients. The review was limited by the scarcity of high-quality comparative trials, making it difficult to establish the superiority of any bone graft. Overall, Infuse provided similar fusion success to ICBG with advantages in surgical efficiency and reduced donor site morbidity, but further research is needed to assess other bone graft options.

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Ambrosio et al. (2025) conducted a systematic review and network meta-analysis to evaluate the safety of efficacy of osteobiologics, including rhBMPs, compared to autologous ICBG. 43 RCTs were included for a total of 3,823 patients. Primary outcomes included radiographic fusion and osteobiologic-related complications. Secondary outcomes included patient-reported measures for pain and disability, and perioperative outcomes (e.g., operative time, blood, loss, length of hospital stay). Follow-up periods ranged from 12 to 60 months. Compared with AICBG, rhBMP-2 demonstrated significantly higher fusion rates, with an odds ratio (OR) of 3.71 (95% CI 2.59-5.32, $p < 0.0001$). No other osteobiologic, including rhBMP-7, platelet-rich plasma, demineralized bone matrix, allografts, synthetic materials, and other graft combinations, demonstrated a statistically significant improvement in fusion compared with autologous ICBG. Subgroup analysis found that rhBMP-2 remained to be associated with significantly higher fusion rates compared with autologous ICBG in both industry-funded and non-industry funded studies. Additionally, rhBMP-2 demonstrated significantly lower complication rates compared with autologous ICBG (OR 0.30, 95% CI 0.13 to 0.68, $p < 0.0001$). There were no significant differences found between any osteobiologic treatment and AICBG for either pain or disability outcomes. Blood loss was significantly lower with rhBMP-2 compared to autologous ICBG (mean difference -72.6 mL, $p = 0.002$). The authors concluded that rhBMP-2 was associated with significantly higher fusion rates and lower complication rates compared with autologous ICBG, as well as decreased operative time and blood loss. While other osteobiologics may offer benefits, supporting evidence is low in quantity and quality.

Biddau et al. (2024) conducted a systematic review to explore fusion rates and postoperative complications associated with bone graft substitutes in ALIF. rhBMP-2 had the highest fusion rates, ranging from 71% to 100% when assessed by computed tomography (CT) at 12 months. Synthetic grafts exhibited a wide range of fusion rates across different imaging methods, while allografts and peptide-based grafts had fewer CT-based data. However, fusion rates varied significantly due to differences in imaging modalities and postoperative assessment methods. The review's limitations include significant variability in the imaging techniques used to assess spinal fusion, with only one-third of studies using CT at 12 months. Additionally, the inconsistency in diagnosing and reporting postoperative complications across studies, along with differences in surgical protocols, made it difficult to accurately compare complication rates and fusion outcomes between graft materials. The authors concluded that rhBMP-2 demonstrates high efficacy for fusion in ALIF but its potential association with increased postoperative complications remains uncertain, underscoring the need for further studies with standardized fusion criteria and consistent complication reporting to better assess its safety and effectiveness.

Liu et al. (2020) conducted a meta-analysis and systematic review to assess the efficacy and safety of recombinant human bone morphogenetic proteins (rhBMP) compared with autologous ICBG in lumbar fusion. The analysis included 20 randomized controlled trials with 2,185 patients. Results showed that rhBMP was associated with a higher fusion success rate ($p = 0.0002$), improved Oswestry Disability Index (ODI) ($p = 0.03$), and a lower reoperation rate ($p = 0.0007$) compared to ICBG. Subgroup analysis revealed that rhBMP-2 had significant advantages in fusion success and ODI improvement, as well as a reduced reoperation rate ($p < 0.01$), while rhBMP-7 showed no significant differences. There were no notable differences between rhBMP and ICBG in postoperative outcomes, including back pain, leg pain, adverse events, blood loss, or hospital stay. The study's limitations included the low quality of included studies, incomplete data, and inconsistent reporting methods. Additionally, a cost-benefit analysis was not conducted, limiting the ability to assess the economic feasibility of rhBMP. In conclusion, rhBMP-2 shows potential as an effective substitute for ICBG in lumbar fusion. However, rhBMP-7 did not demonstrate significant benefits and is not recommended. Further research, including cost-effectiveness analysis and direct comparison between rhBMP-2 and rhBMP-7, is needed to confirm these findings.

Vavken et al. (2016) performed a meta-analysis to evaluate the effectiveness and safety of recombinant human bone morphogenetic protein-7 (rhBMP-7) in spinal fusion, comparing it with ICBG, local bone, or tricalcium phosphate in spinal fusion. The analysis included six studies with a total of 442 patients (328 experimental, 114 control), with a mean age of 59 years. No significant differences were found between rhBMP-7 and the other treatments in terms of union rates ($p = 0.247$), complications ($p = 0.545$), postoperative pain ($p = 0.941$), or revision rates ($p = 0.449$). The study had limitations, including reliance on data from the included trials, clinical heterogeneity (e.g., cervical vs. lumbar fusion), and off-label use of rhBMP-7 across all studies. The analysis did not provide evidence to support the use of rhBMP-7 for spine fusion, as there were no improvements in union rates and no increase in complications or revisions. Although a mathematical indication of increased tumor rates was noted, it was based on a single case and is unlikely to have clinical significance.

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Non-Randomized Studies, Retrospective Reviews, and Other Evidence

Hayes (2022) published a health technology assessment analyzing 19 studies that evaluated rhRMP-2 for spinal fusion. Thirteen randomized controlled trials, 4 retrospective registry analyses, a prospective trial, and a retrospective comparative cohort study were included. When compared with an autograft, evidence suggests that rhBMP-2 lumbar spinal fusions lead to quicker fusion and a greater likelihood of achieving fusion. However, rhBMP-2 does not seem to offer significant improvements in pain, disability, or quality of life over autografts. Few statistically significant differences were found between rhBMP-2 and bone autographs regarding complication rates. In lumbar spinal fusions, rhBMP-2 was associated with increased postoperative pain but insignificant long-term pain reduction. For cervical fusion, rhBMP-2 was linked to higher rates of wound complications and dysphagia. Another analysis on cervical fusion procedures revealed that rhBMP-2 was correlated with increased risks of dysphagia, dysphonia, neurological complications, and hematoma or seroma formation, but also with a decreased need for tracheostomy tube insertion. The quality of evidence for rhBMP-2 in lumbar spinal fusion was deemed moderate, while for cervical fusion, it was considered low. Consequently, the health technology assessment suggests the necessity for additional studies with extended follow-up periods to ascertain whether the benefits of rhBMP-2 outweigh its associated risks.

Vincentelli et al. (2019) published a phase IV, national, multicenter, retrospective study to assess the utilization of rhBMP-2 in spine fusion surgery. Analysis encompassed four hundred patients exhibiting a spectrum of primary diagnostic indications, including degenerative disc disease (32.3%), spondylolisthesis (29.8%), deformity (14.8%), and pseudoarthrosis (7.3%). Fusion, the primary outcome, exhibited success rates in 48.4% of patients, with 13.7% experiencing fusion failure. Fusion status remained undetermined in 12.4% of cases, and 25.4% of patients did not undergo fusion assessment. Notably, 12.4% lacked a determinable fusion status, and 25.4% lacked fusion assessments. At the 12-month mark, fusion success reached 94.5% among the assessed subset of 127 patients. Secondary outcomes included adverse events of interest (AEI) and secondary spine interventions, with 31 AEIs observed in 27 patients, only one of which was deemed related to rhBMP-2. Common AEIs comprised device displacement (7 patients) and fluid collection at the implant site (5 patients), necessitating unplanned secondary spine interventions in 4 patients. Limitations arose from the retrospective design and variations in patient follow-up protocols, resulting in over half lost to follow-up at 12 months. Despite limitations, this study offers valuable insights into the safety and efficacy of rhBMP-2 as a treatment option for spine fusion surgery, underlining its potential in clinical practice.

P-15 Peptide Bone Graft Substitutes for Spinal Fusion

Current evidence for p-15 peptide-enhanced bone graft substitutes for spinal fusion is limited to single industry-sponsored RCTs. For cervical fusion, the i-Factor pivotal RCT demonstrated noninferiority to autograft over 6 years, with similar fusion rates, functional outcomes, neurological success, and safety profiles. While the study authors report advantages in overall success rates, this is based on predefined composite endpoints. Superiority in individual clinical outcomes has not been established. For lumbar fusion, the PearlMatrix pivotal RCT demonstrated noninferiority and statistical superiority to autograft based on predefined composite clinical success endpoints at 24 months. This was mostly driven by higher fusion rates, while other clinical outcomes like functional improvement and neurological success were not significantly different between groups. PearlMatrix had higher device and procedure related adverse events and serious adverse events compared to autograft. Follow-up for PearlMatrix is currently limited to 24 months, and therefore conclusions on long-term safety, efficacy, and durability remain limited. Further high-quality, independent studies are needed to establish meaningful clinical benefit over existing standard of care options.

Randomized Controlled Trial

Harrop et al. (2026) conducted a multicenter, single-blind, investigational device exemption RCT to evaluate the safety and effectiveness of a P-15L peptide-enhanced bone graft (PearlMatrix) compared to autograft in single-level transforaminal lumbar interbody fusion. A total of 290 participants with degenerative disc disease and up to Grade I spondylolisthesis were enrolled between 33 centers and randomized 1:1 to P-15L (n = 141) or autograft (n = 149). Participants were also required to have an ODI score $\geq$ 35 and failure of $\geq$ 6 months of conservative therapy. The primary endpoint was composite clinical success at 24 months, defined as meeting five criteria: absence of secondary surgeries, radiographic fusion, a $\geq$ 15-point improvement in ODI, no new or worsening neurological deficit, and absence of any device-related serious adverse events. At 24 months, 55.5% of P-15L participants achieved clinical success compared with 37.5% for autograft, demonstrating non-inferiority ($p < 0.0001$) and superiority ($p = 0.002$) at 24 months. At 24 months, radiographic fusion rates were 84.3% in the P-15L group versus 58.5% for autograft. ODI improvement was similar, but inferior to autograft, with a $\geq$ 15-point improvement of 78.2% of participants for P-15L and 81.1% for autograft. Device-related adverse events occurred in 15.6% of P-15L participants and 13.4% of autograft, while serious adverse events occurred in 5.7% of P-15L participants and 4.7% of autograft. The investigational group also had higher

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rates of procedure-related adverse events (56.7% vs. 39.6%) and serious adverse events (26.2% vs. 13.4%). There were three deaths during the study, 2 in the P-15L group and 1 in the autograft group, but none were related to the bone graft devices. The authors concluded that the P-15L peptide-enhanced bone graft achieved significantly higher composite clinical success and higher fusion rates than autograft at 24 months while maintaining a similar safety profile. The trial was funded by Cerapedics Inc., the investigational device manufacturer. (ClinicalTrials.gov NCT03438747).

Arnold et al. (2016) conducted a prospective, randomized, controlled, parallel, single-blinded FDA Investigational Device Exemption trial to evaluate the safety and efficacy of i-Factor Bone Graft compared to local autograft for single-level anterior cervical discectomy and fusion (ACDF) in patients with cervical radiculopathy. The trial included 319 patients, with 154 receiving autograft and 165 receiving i-Factor in a cortical ring allograft. The primary outcomes assessed were fusion rates, Neck Disability Index (NDI) scores, and neurological success rates. Secondary outcomes included VAS pain, SF-36v2 quality of life assessments, and Odom outcomes. At the 12-month mark, fusion rates were 88.97% in the i-Factor group and 85.82% in the autograft group (noninferiority $p = 0.0004$). Both groups showed significant improvements in NDI scores, with a change of 28.75 points for i-Factor and 27.40 points for autograft (noninferiority $p < 0.0001$). Neurological success rates were high for both groups (noninferiority $p < 0.0001$), with no significant difference in adverse event rates ($p = 0.8814$). Both VAS pain and SF-36v2 scores demonstrated similar improvements in both groups. A substantial proportion of patients reported good or excellent Odom outcomes, with 81.4% in both groups. i-Factor met all four FDA-mandated noninferiority success criteria, confirming its safety and efficacy in single-level ACDF for cervical radiculopathy. Both the i-Factor and autograft groups showed significant post-surgery improvements and high fusion success rates.

Arnold et al. (2018) compared the two-year outcomes of patients who received i-Factor versus those who underwent autograft procedures. Fusion rates were similar between the two groups, with i-Factor achieving 97.30% and autograft 94.44% ($p = 0.2513$), as were neurological success rates (94.87% for i-Factor and 93.79% for autograft, $p = 0.7869$). Both groups showed improvements in the Neck Disability Index ($p = 0.1448$), VAS scores for arm ($p = 0.2763$) and neck ($p = 0.1652$) pain, and Short Form-36 (SF-36v2) scores, with no significant differences between the groups. However, the composite endpoint of overall success, which included fusion, Neck Disability Index improvement, neurological success, and absence of re-operations, was higher in the i-Factor group (69.83%) compared to the autograft group (56.35%, $p = 0.0302$). Reoperation rates were similar between the i-Factor (7.45%) and autograft (10.53%) groups ($p = 0.3411$), and no allergic reactions were reported in the i-Factor group. The study concluded, two-year post-surgery, i-Factor used in anterior cervical discectomy and fusion is both safe and effective, with outcomes comparable to those achieved with autograft bone.

Systematic Reviews and Meta-Analyses

Spanninga et al. (2025) conducted a systematic review to evaluate the safety and efficacy of P-15 peptide-enhanced bone graft substitutes in surgical bone regenerative procedures in adult maxillofacial, spinal, and trauma patients. The review included 28 studies, including 20 RCTs and the remaining being observational studies or case series. Of the 28 studies, 18 were maxillofacial, 9 were spinal (n = 710), and 1 was trauma (n = 22). Of the spinal studies, participants underwent cervical or lumbar fusion procedures using anorganic bone minerals (ABM) combined with P-15 bone graft substitutes, allograft, rhBMP-2, or demineralized bone matrix. Fusion success was measured using radiographic criteria, including trabecular bone bridging between vertebral segments. In a 2016 Investigation Device Exemption RCT for cervical fusion, at 24 months, fusion rates were 97% for ABM/P-15 (i-Factor) versus 94% for autograft, meeting non inferiority criteria. For lumbar fusion, studies overall showed comparable or superior fusion outcomes with ABM/P-15. For example, a 2015 prospective clinical study found that at 24 months there was no significant difference in fusion rates between ABM/P-15 (96%) and autograft (93%). However, fusion rates were superior for ABM/P-15 at 6 and 12 months (98% versus 59% and 98% versus 82%, respectively), indicating that ABM/P-15 fuses faster than autograft. In posterior lumbar interbody fusion surgeries, graft migration posteriorly to the cage occurred significantly more in the ABM/P-15 group (48%) compared to autograft (14%), but this reportedly had no clinical consequences. Overall, adverse events were similar between groups, but included axial pain, dysphagia, radiculopathy, infection, cage subsidence, and graft migration. The authors noted potential publication bias, as many studies were at least partially funded by industries associated with the ABM/P-15 product. The authors concluded that the evidence suggests ABM/P-15 is safe and effective to use in multiple surgical contexts as a bone graft substitute.

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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 could be a substitute for AICB in lumbar interbody or posterolateral fusion due to similar fusion rates and clinical outcomes, based on Grade C to Grade B evidence (multiple level II studies). The guideline also notes that while rhBMP-2 has been shown to have a positive effect on fusion rate, its use is associated with unique complications, such as heterotopic bone formation. Surgeons utilizing rhBMP-2 should be aware of the potential for these complications and be selective in its use. Further research on identifying patient populations that 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 rhBMP-2 is appropriate for bone graft in patients who are at higher risk of nonunion due to smoking (NASS 2020).

The **International Society for the Advancement of Spine Surgery (ISASS)** published *Recommendations and Coverage Criteria for Bone Graft Substitutes used in Spinal Surgery*. The recommendations conclude that rhBMP-2 (INFUSE) and P-15 peptide (i-Factor) are FDA-approved based on level I clinical trials showing them to be safe and effective as autograft replacements (Abjornson et al. 2018).

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure)
20999	Unlisted procedure, musculoskeletal system, general [when specified as placement of recombinant human bone morphogenetic protein for tibial fracture]

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

04/08/2026	Policy reviewed. No change to coverage criteria. Added PearlMatrix P-15 peptide-enhanced bone graft substitute to policy. IRO peer reviewed on March 23, 2026 by a practicing physician board certified in orthopaedic surgery.
04/09/2025	Policy reviewed. Removed "Medical necessity criteria for lumbar fusion are met" from lumbar fusion criteria. Updated Summary of Medical Evidence and References.
04/10/2024	Policy reviewed. Changed name to 'Bone Graft Substitutes for Bone Fusion.' Updated coverage criteria to include i-Factor protein. Updated Summary of Medical Evidence and References.
04/13/2023	Policy reviewed. No changes in criteria. Updated references.
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 to coverage criteria.
06/19/2019	Policy reviewed, no changes to coverage criteria.
07/10/2018	Policy reviewed, no changes to coverage criteria.
09/19/2017	Policy reviewed, no changes to coverage criteria.
09/15/2016	Policy reviewed, no changes to coverage criteria.
12/16/2015	Policy reviewed, no changes to coverage criteria.
12/08/2014	New policy.

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