Bone Morphogenetic Protein

Policy Number: 7.01.100  Last Review: 5/2017

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for bone morphogenetic protein when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Use of recombinant human bone morphogenetic protein-2 (rhBMP-2, InFUSE) may be considered medically necessary in skeletally mature patients

- For anterior lumbar interbody fusion procedures when use of autograft is unfeasible
- For instrumented posterolateral intertransverse spinal fusion procedures when use of autograft is unfeasible.
- For the treatment of acute, open fracture of the tibial shaft when use of an autograft is unfeasible.

When Policy Topic is not covered
Bone morphogenetic protein (rhBMP-2) is considered not medically necessary for all other indications, including but not limited to spinal fusion when use of autograft is feasible.

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

There is no specific CPT or HCPCS code for bone morphogenetic protein (BMP). In 2011, CPT code 20930 was revised to include BMP-type materials used in spine surgery:

20930: Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure).

For of spinal fusion, bone morphogenetic proteins may be used primarily as an alternative to autologous bone grafting. Because harvesting of autologous bone
graft is coded separately from the fusion procedure (i.e., CPT codes 20936-20938), when bone morphogenetic protein is used as an alternative to the bone graft, these codes should no longer be reported. In contrast, the CPT code for treating tibial fracture nonunions with autograft (i.e., CPT code 27724) includes the harvesting component and, therefore, when bone morphogenetic protein is used as an alternative in this setting, presumably the associated physician’s work would be decreased, because no autologous harvest is required. Finally, for treatment of acute, open tibial fractures, BMP is not used as an alternative to autologous bone graft, but in addition to standard treatment with an intramedullary nail.

ICD10-PCS procedure codes 3E0U0GB, 3E0U3GB, 3E0V0GB, and 3E0V3GB explicitly identify the use of BMP in open or percutaneous procedures on joints and bones.

**Description of Procedure or Service**

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Individuals:  
- Who are undergoing anterior or posterolateral lumbar spinal fusion and in whom autograft is not feasible | Interventions of interest are:  
- Bone morphogenetic protein | Comparators of interest are:  
- Allograft bone or synthetic bone substitute | Relevant outcomes include:  
- Symptoms  
- Morbid events  
- Functional outcomes  
- Treatment-related morbidity |

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| Individuals:  
- Who are undergoing surgery for acute tibial shaft fracture and in whom autograft is not feasible | Interventions of interest are:  
- Bone morphogenetic protein | Comparators of interest are:  
- Plate or intramedullary nail | Relevant outcomes include:  
- Symptoms  
- Morbid events  
- Functional outcomes  
- Treatment-related morbidity |

Two recombinant human bone morphogenetic proteins (rhBMPs) are now commercially available, rhBMP-2, applied with an absorbable collagen sponge (InFUSE, Medtronic, Memphis, TN) and rhBMP-7, applied in putty (OP-1). These products have been investigated as an alternative 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.

The evidence for rhBMP in individuals who are undergoing anterior or posterolateral lumbar spinal fusion and in whom autograft is not feasible includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, and treatment-related morbidity. In 2013, 2 systematic reviews of rhBMP-2 trials that used manufacturer-provided individual patient data were published. Overall, these systematic 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 rate of adverse events was a low, though concerns remain about increased adverse event rates with rhBMP-2, including cancer. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for rhBMP in individuals who are undergoing surgery for acute tibial shaft fracture and in whom autograft is not feasible 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 the rate of reoperations compared to soft-tissue management with or without intramedullary nailing. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

Use of rhBMP has not been shown to be as beneficial as the established alternative and evidence is insufficient to permit conclusions about the effect of rhBMP for all other indications including:

- Tibial shaft fracture nonunion
- Craniomaxillofacial surgeries.

**Background**

Bone morphogenetic proteins (BMPs) are members of the family of transforming growth factors. At present, some 20 different BMPs have been identified, all with varying degrees of cartilage and/or bone inductive properties. 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, function to 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 polymer, natural polymers, and bone allograft. The rhBMP and carrier may be inserted via a delivery system, which may also function to provide mechanical support.

The carrier and delivery system are important variables in the clinical use of rhBMPs, and different clinical applications, such as long-bone nonunion, or 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; PLF), while rhBMP in a collagen sponge with bone dowels or interbody cages are used for interbody spinal fusion. In addition, interbody fusion of the lumbar spine can be approached from an anterior (anterior lumbar interbody fusion; ALIF), lateral (XLIF), or posterior direction (PLIF or TLIF). Surgical procedures may include decompression of the spinal canal and insertion of pedicle screws and rods to increase stability of the spine.

Posterior approaches (PLIF and TLIF) 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 stabilization of the spine and are differentiated from instrumented or noninstrumented posterolateral intertransverse fusion (PLF), 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.

**Regulatory Status**
At the present time, two rhBMPs and associated carrier/delivery systems have received approval from the U.S. Food and Drug Administration (FDA). The InFUSE system consists of rhBMP-2 on an absorbable collagen sponge carrier. The labeled indications for these devices are summarized here. OP-1 consists of rhBMP-7 and bovine collagen, which is reconstituted with saline to form a paste. The addition of carboxymethylcellulose forms a putty.

Infuse® Bone Graft in conjunction with 1 of 2 interbody fusion devices (ie, either the LT-Cage Lumbar Tapered Fusion Device or the Inter Fix RP Threaded Fusion device) was approved by FDA through the premarket approval process. The device is indicated for spinal fusion procedures in skeletally mature patients with degenerative disc disease (DDD) at 1 level from L2-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history, function deficit, and/or neurologic deficit and radiographic studies. These DDD patients may also have up to grade I spondylolisthesis at the involved level or retrolisthesis. The Infuse® Bone Graft/LT-CAGE™ devices are to be implanted via an anterior open or a laparoscopic approach. The Infuse® Bone Graft/INTER FIX™ Threaded Fusion Device; and Infuse® Bone Graft/INTER FIX™ RP Threaded Fusion Device are to be implanted via an anterior open approach only. Patients receiving the Infuse® Bone Graft/Interbody Fusion Device should have had at least 6 months of nonoperative treatment prior to treatment with the Infuse® Bone Graft/Interbody Fusion Device. (Note: A collagen sponge consists of the carrier, while the interbody fusion device is a delivery system. Use with posterior or transforaminal lumbar interbody fusion is considered off-label.) In 2015, FDA approved the use of Infuse® for oblique lateral interbody fusion (OLIF) from L2-S1. FDA product code: NEK

Infuse® is also indicated:
- For the treatment of acute, open fractures of the tibial shaft
- For sinus augmentations, and for localized alveolar ridge augmentations for defects associated with extraction sockets (P050053, March 2007).

OP-1 (Stryker Biotech, Hopkinton, MA) was approved by FDA through the humanitarian device exemption (HDE) process for 2 indications. HDE is available to devices intended for fewer than 4000 patients per year; as part of this process, the manufacturer is not required to demonstrate unequivocal benefit but only “probable” benefit. OP-1 received the following labeled 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: MPY.

“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 recently sought FDA permission to expand use of OP-1 Putty to include use in uninstrumented posterolateral lumbar spinal fusion for the treatment of lumbar spondylolithesis. In March 2009, an FDA advisory committee voted 6-1 against recommending the expanded approval. Olympus Biotech Corp., a subsidiary of Olympus Corp., acquired OP-1 assets in 2010. In 2014, Olympus Corp. closed Olympus Biotech operations in the United States and discontinued sales of the Olympus Biotech products in this country. rhBMP-7 is no longer marketed in the United States.

Both OP-1 and InFUSE Bone Graft/LT-Cage Lumbar Tapered Fusion device are contraindicated in patients who are pregnant, may be allergic to any of the materials contained in the devices, have an infection near the area of the surgical incision, have had a tumor removed from the area of the implantation site or currently have a tumor in that area, or who are skeletally immature.

In July 2008, the FDA issued a public health notification regarding life-threatening complications associated with recombinant human bone morphogenetic protein in cervical spine fusion. The FDA has received reports of complications with the use of rhBMP in cervical spine fusion. (2) These 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 describe 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 effectiveness of rhBMP in the cervical spine have not been demonstrated, and 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 utilizes a higher dose of rhBMP (2.0 mg/mL) with a compression-resistant carrier.

Rationale

This evidence review was created in 2004 and has been updated periodically using the MEDLINE database. The most recent literature update was performed through February 22, 2016.

When this evidence review was created, randomized controlled trials (RCTs) supported the use of recombinant human bone morphogenetic protein-2 (rhBMP-
2) in the treatment of anterior interbody spinal fusion when used in conjunction with a tapered cage and in the treatment of open tibial fractures. (2) A randomized study supported the use of rhBMP-7 in the treatment of recalcitrant nonunions of the long bones. (3) It should be noted that most of these trials were designed to show that use of rhBMP was equivalent (not superior) to autologous bone grafting. Although the proposed advantage of rhBMP is the elimination of a separate incision site harvest autologous bone graft and the associated pain and morbidity secondary to this procedure, a 2011 study by Howard et al raised questions about the magnitude of pain observed with iliac crest bone graft (ICBG) harvesting. (4) In this study, 112 patients who had an instrumented posterolateral lumbar fusion at 1 or 2 levels were seen at a tertiary spine center for a routine postoperative visit. ICBG was harvested in 53 (47.3%) patients through the midline incision used for lumbar fusion and rhBMP-2 was used in 59 (52.7%) patients with no graft harvest. An independent investigator not directly involved in patient care and was unaware of the type of bone graft used in the fusion examined each patient for tenderness over the surgical site as well as the left and right posterior iliac crest. At a mean follow-up of 41 months (range, 6-211 months), there was no significant difference between the groups in the proportion of patients complaining of tenderness over either iliac crest (mean pain score, 3.8 vs 3.6 on a 10-point scale). While 54% of patients complained of tenderness over 1 or both iliac crests, only 10 (9%) of 112 patients had pain over the crest from which the graft was harvested (mean pain score, 4.4).

**Spinal Fusion**

In 2013, 2 meta-analyses on the effectiveness and harms of rhBMP-2 in spine fusion were published following a 2011 U.S. Senate investigation of industry influence on the Infuse clinical studies and a systematic review by Carragee et al of emerging safety concerns with rhBMP-2. (5-8) The systematic review by Carragee compared conclusions about safety and efficacy from the 13 published rhBMP-2 industry-sponsored trials to available U.S. Food and Drug Administration (FDA) data summaries, subsequent studies, and databases. Evaluation of the original trials suggested methodologic bias against the control group in the study design (discarding local bone graft and failure to prepare facets for arthrodesis) and potential bias (overestimation of harm) in the reporting of iliac crest donor site pain. Comparison between the published studies and FDA documents revealed internal inconsistencies and adverse events (AEs) not reported in the published articles.

Both 2013 meta-analyses assessed individual patient-level data, both published and unpublished, that was provided by the manufacturer through the Yale University Open Data Access (YODA) Project. One meta-analysis was conducted by Simmonds et al from University of York in the United Kingdom; the other was by Fu et al from the Oregon Health and Science University.

Simmonds et al included patient-level data from 12 RCTs (total N=1408 patients), regardless of spinal level or surgical approach, and AE data from an additional 35 observational studies. (5) Use of rhBMP-2 increased the rate of radiographic fusion by 12% compared with ICBG, with substantial heterogeneity across trials. A small
improvement in the Oswestry Disability Index score (3.5 percentage points) fell below the previously defined threshold for a clinically significant effect. The review also found a small improvement in back pain (1 point on a 20-point scale) and 36-Item Short-Form Health Survey Physical Component Summary score (1.9 percentage points). There was no significant difference between the groups for leg pain. There was a potential for bias in the pain and functional outcomes because outcomes were patient-reported and patients were not blinded to the treatment received. Overall, the increase in successful fusion at up to 24 months did not appear to be associated with a clinically significant reduction in pain.

The meta-analysis by Fu et al included individual-patient data from 13 RCTs (total N=1981 patients) and 31 cohort studies.(6) The review found moderate evidence of no consistent differences between rhBMP-2 and ICBG in overall success, fusion rates, or other effectiveness measures for anterior lumbar interbody fusion or posterolateral fusion. A small RCT and 3 cohort studies revealed no difference in effectiveness outcomes between rhBMP and ICBG for anterior cervical fusion. Reporting in of the original published trials was found to be biased, with journal publications selecting analyses and results that favored rhBMP over ICBG.

Both meta-analyses suggested that cancer risk might be increased with rhBMP-2, although the number of events was low and there was heterogeneity in the types of cancer. In Simmonds, combined analysis revealed a relative risk of 1.84 (95% confidence interval [CI], 0.81 to 4.16) for cancer in the bone morphogenetic protein (BMP) group, but this increased rate was not statistically significant. Fu performed a combined analysis of cancer incidence at 24 and 48 months posttreatment. At 24 months, there was a statistically significant increase in cancer for the BMP group (risk ratio, 3.45; 95% CI, 1.98 to 6.0); at 48 months, the increase was not statistically significant (risk ratio, 1.82; 95% CI, 0.84 to 3.95).

Other AEs were increased for the BMP group. Simmonds et al found a higher incidence of early back and leg pain with rhBMP-2. The individual publications consistently reported increased rates of heterotopic bone formation, leg pain/radiculitis, osteolysis, and dysphagia, but combined analysis for these outcomes was not performed. Fu et al reported that BMP-2 was associated with a statistically nonsignificant increased in the risk for urogenital problems when used for anterior lumbar fusion and an increased in the risk for wound complications and dysphagia when used for anterior cervical spine fusion. Fu et al noted that the data on AEs in the published literature was incomplete compared with the total amount of data available.

Off-label use of BMP can include multiple levels and dosages greater than the FDA-approved dose of rhBMP-2 for single-level fusion. In 2013, Carragee et al assessed cancer risk after high-dose rhBMP-2 (40 mg) using publicly available data from the pivotal, multicenter RCT of AMPLIFY (N=463).(9) The study found an increase in the incidence of cancer, a reduction in the time to first cancer, and a greater number of patients with multiple cancers. For example, at 2 years, there were 15 new cancer events in 11 patients in the rhBMP-2 group compared with 2 new
cancer events in 2 patients treated with autogenous bone graft (incidence rate ratio, 6.75). When calculated in terms of the number of patients with 1 or more cancer events 2 years after surgery, the incidence rate per 100 person-years was 2.54 in the rhBMP-2 group and 0.50 in the control group (incidence rate ratio, 5.04). The mean time to development of cancer was 17.5 months after use of rhBMP-2 and 31.8 months in the controls. Three patients, all in the rhBMP-2 group, developed multiple new cancers.

Long-Bone Fractures and Nonunions
In 2015, Dai et al published a meta-analysis on rhBMP for the healing of acute tibial fractures (4 RCTs; total N=868 patients) and nonunions (4 RCTs; total N=245 patients).(10) For acute tibial fractures, 3 RCTs were conducted with rhBMP-2 and 1 with rhBMP-7. All included studies were conducted over a decade ago. Use of rhBMP was associated with a higher rate of union (relative risk, 1.16) and a lower rate of revision (relative risk, 0.68) than controls (3 trials with soft-tissue management, 1 with intramedullary nail plus autograft). There was no significant difference between the BMP and control groups for hardware failure or infection. For tibial fracture nonunions, 3 trials used rhBMP-7 and the fourth trial did not state which formulation. The relative risk was nearly 1 (0.98), and there was no significant difference between the BMP and intramedullary nail plus autograft groups in the rates of revision or infection. Interpreting these results is difficult given the variations in control groups and formulations of rhBMP used, one of which is no longer marketed in the United States.

A 2010 Cochrane review evaluated the effectiveness and costs of rhBMP for healing of acute fractures and nonunions compared with standard of care.11 The literature search was conducted to October 2008; 11 RCTs (total N=976 participants) and 4 economic evaluations selected for inclusion. The times to fracture healing were comparable between the rhBMP and control groups. There was some evidence for faster healing rates, mainly for open tibial fractures without secondary procedures (risk ratio, 1.19). Three trials indicated that fewer secondary procedures were required for acute fractures treated with rhBMP (risk ratio, 0.65). The authors concluded that limited evidence suggested rhBMP may be more effective than standard of care for acute tibial fracture healing; however, use of rhBMP for treating nonunion remains unclear (risk ratio, 1.02).

In 2013, Lyon et al reported a manufacturer-funded, randomized, double-blinded trial of injectable rhBMP-2 in a calcium phosphate matrix for closed tibial diaphyseal fractures.(12) The study had a target enrollment of 600 patients but was stopped after interim analysis with 387 patients enrolled. Addition of the injectable rhBMP-2 paste to the standard of reamed intramedullary nail fixation did not shorten the time to fracture healing, resulting in study termination due to futility.

Oral and Maxillofacial Procedures
A 2010 Agency for Healthcare Research and Quality technology assessment by the BlueCross BlueShield Association Evidence-Based Practice Center on the state of
the evidence for on-label and off-label use of rhBMP(13) included the following conclusions:

- The strength of the body of evidence on clinical outcomes is moderate that rhBMP-2 does not provide an advantage in prosthesis implantation and functional loading compared with autograft plus allograft bone.
- There is moderate evidence that oral sensory loss associated with autograft bone harvest can be avoided by use of rhBMP-2.

Overall, the evidence does not support a health benefit of rhBMP in oral and maxillofacial procedures.

**Additional Applications**

There has been research interest in the following applications: management of early stages of osteonecrosis of the vascular head as an adjunct to hip arthroplasty to restore bone defects in the acetabulum or femoral shaft and as an adjunct to distraction osteogenesis (ie, Ilizarov procedure). (14,15) The literature on these applications consists of small case series; no controlled trials have been identified.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tr>
<td>NCT01111045a</td>
<td>A Phase 2, Double Blind, Randomized, Placebo-Controlled, Proof of Concept, Dose Finding Study of Intraarticular Bone Morphogenetic Protein (BMP-7) in Subjects With Osteoarthritis (OA) of the Knee</td>
<td>355</td>
<td>Aug 2011 (completed)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
a Denotes industry-sponsored or cosponsored trial.

**Summary of Evidence**

The evidence for recombinant human bone morphogenetic protein (rhBMP) in individuals who are undergoing anterior or posterolateral lumbar spinal fusion and in whom autograft is not feasible includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, and treatment-related morbidity. In 2013, 2 systematic reviews of rhBMP-2 trials that used manufacturer-provided individual patient data were published. Overall, these systematic 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 rate of adverse events was a low, though concerns remain about increased adverse event rates with rhBMP-2, including cancer. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for rhBMP in individuals who are undergoing surgery for acute tibial shaft fracture and in whom autograft is not feasible 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 the rate of reoperations compared to soft-tissue management with or without intramedullary nailing. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Practice Guidelines and Position Statements**

Guidelines on lumbar spinal fusion from the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CNS) were updated in 2014.(16) AANS/CNS gave a grade B recommendation (multiple level II studies) for the use of rhBMP-2 as a substitute for autologous iliac crest bone for anterior lumbar interbody fusion and single-level posterolateral instrumented fusion. Grade C recommendations were made for rhBMP-2 as an option for posterior lumbar interbody fusion and transforaminal lumbar interbody fusion, posterolateral fusion in patients older than 60 years, and as a graft extender for either instrumented or noninstrumented posterolateral fusions. AANS/CNS also gave a grade C recommendation (based on multiple level IV and V studies) that the use of rhBMP-2 as a graft option has been associated with a unique constellation of complications of which the surgeon should be aware when considering this graft extender/substitute.

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

The Centers for Medicare and Medicaid Services (CMS) has established an add-on to the diagnosis-related group (DRG) payment to cover a portion of the cost of new technologies during the 2-year period before charge data for the technologies are incorporated into the DRG weights. To qualify, a technology must be new, must provide verifiable improvement in the treatment or diagnosis of beneficiaries, and the mean standardized charge for treatment using the new technology must be at least 1 SD above the mean standardized charge for treating the same case without the new technology. In 2004, CMS concluded that the Infuse® Bone Graft/LT-CAGE met these criteria and would receive an add-on payment to DRGs 497 or 498. Medtronic, the manufacturer of the Infuse® device, has applied for a new technology add-on payment for the FDA-approved indication of treatment of open acute fractures of the tibial shaft.
References:

Billing Coding/Physician Documentation Information

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
ICD10 Codes

M51.06  Intervertebral disc disorders with myelopathy, lumbar region
M51.07  Intervertebral disc disorders with myelopathy, lumbosacral region
M51.17  Intervertebral disc disorders with radiculopathy, lumbosacral region
M51.36  Other intervertebral disc degeneration, lumbar region
M51.37  Other intervertebral disc degeneration, lumbosacral region
M80.021K; M80.022K; M80.029K; M80.031K; M80.032K; M80.039K; M80.051K; M80.052K; M80.059K; M80.061K; M80.062K; M80.069K; M80.0821K; M80.0822K; M80.0829K; M80.0831K; M80.0832K; M80.0839K; M80.0851K; M80.0852K; M80.0859K; M80.0861K; M80.0862K; M80.0869K
M80.061A; M80.062A; M80.069A; M80.061A; M80.062A; M80.0869A
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M80.061A; M80.062A; M80.069A; M80.061A; M80.062A; M80.0869A
M84.321K; M84.322K; M84.329K; M84.331K; M84.332K; M84.333K; M84.334K; M84.339K; M84.351K; M84.352K; M84.353K; M84.361K; M84.362K; M84.369K
Osteoporosis with current pathological tibia fracture codes with 7th digit “A” for initial encounter for fracture
Stress fracture of long bones with 7th digit “K” for subsequent encounter for fracture with nonunion
M84.362K; M84.363K; M84.364K; M84.369K
M84.361A; Stress fracture of tibia codes with 7th digit “A” for initial encounter for fracture
M84.362A
M84.421K; Long bone other pathological fracture codes with 7th digit “K” for subsequent encounter for fracture with nonunion
M84.422K;
M84.429K;
M84.431K;
M84.432K;
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M84.632K;
M84.633K;
M84.634K;
M84.639K;
M84.651K;
M84.652K;
There is no specific CPT or HCPCS code for bone morphogenetic protein. In 2011, CPT code 20930 was revised to include BMP-type materials used in spine surgery:

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these codes should no longer be reported. In contrast, the CPT code for treating tibial fracture nonunions with autograft (ie, CPT code 27724) includes the harvesting component, and, therefore, when bone morphogenetic protein is used as an alternative in this setting, presumably the associated physician’s work would be decreased, since no autologous harvest is required. Finally, for treatment of acute, open tibial fractures, bone morphogenetic protein is not used as an alternative to autologous bone graft, but in addition to standard treatment with an intramedullary nail.

**Additional Policy Key Words**

DBM
Demineralized bone matrix

**Policy Implementation/Update Information**

<table>
<thead>
<tr>
<th>Date</th>
<th>Changes</th>
</tr>
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<tbody>
<tr>
<td>5/1/06</td>
<td>New policy.</td>
</tr>
<tr>
<td>5/1/07</td>
<td>Policy statement revised revised. Limitation to single level spinal fusion deleted and type of carrier system deleted from policy statement.</td>
</tr>
<tr>
<td>5/1/08</td>
<td>No policy statement changes.</td>
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<td>5/1/09</td>
<td>No policy statement changes.</td>
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<tr>
<td>5/1/10</td>
<td>Policy statements revised; rhBMP-2 considered medically necessary for instrumented posterolateral intertransverse fusion; rhBMP-7 considered medically necessary for non-instrumented posterolateral intertransverse fusion under specified conditions; other policy statements clarified.</td>
</tr>
<tr>
<td>5/1/11</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>5/1/12</td>
<td>Use restricted to cases where there is a high risk of fusion failure. Investigational policy statement clarified to include cervical spinal fusion.</td>
</tr>
<tr>
<td>5/1/13</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>5/1/14</td>
<td>Medically necessary policy statement revised to clarify coverage is for skeletally mature patients. Policy statement regarding non-covered uses changed from investigational to not medically necessary.</td>
</tr>
<tr>
<td>5/1/15</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>5/1/16</td>
<td>No policy statement changes.</td>
</tr>
<tr>
<td>5/1/17</td>
<td>Removed rhBMP-from policy statements.</td>
</tr>
</tbody>
</table>

**APPENDIX**

Procedures used for lumbar interbody fusion differ primarily in the direction of approach to the spine, ie, from the front (anterior), from the back (posterior or transforaminal) or from the side (lateral). An alternative approach to interbody fusion is arthrodesis of the transverse processes alone (posterolateral), which does not fuse the adjoining vertebral bodies. Circumferential fusion fuses both the adjacent vertebral bodies and the transverse processes, typically using both an anterior and posterior approach to the spine.

**Open and Minimally Invasive Approaches to Lumbar Interbody Fusion**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Access</th>
<th>Approach</th>
<th>Visualization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior (ALIF)</td>
<td>Open, MI, or</td>
<td>Transperitoneal or</td>
<td>Direct, endoscopic or</td>
</tr>
<tr>
<td>Procedure</td>
<td>Access Type</td>
<td>Incision/Approach</td>
<td>Technique</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td><strong>Posterior (PLIF)</strong></td>
<td>Open or MI</td>
<td>Incision centered over spine with laminectomy/laminotomy and retraction of nerve</td>
<td>Direct, endoscopic or microscopic, with fluoroscopic guidance</td>
</tr>
<tr>
<td><strong>Transforaminal (TLIF)</strong></td>
<td>Open or MI</td>
<td>Offset from spine, through the intervertebral foramen via unilateral facetectomy</td>
<td>Direct, endoscopic or microscopic, with fluoroscopic guidance</td>
</tr>
<tr>
<td><strong>Lateral</strong></td>
<td>MI</td>
<td>Retroperitoneal through transpsoas</td>
<td>Direct, with neurologic monitoring and fluoroscopic guidance</td>
</tr>
</tbody>
</table>

LIF: lumbar interbody fusion; MI: minimally invasive.

**Anterior Lumbar Interbody Fusion**

Anterior access provides direct visualization of the disc space, potentially allowing a more complete discectomy and better fusion than lateral or posterior approaches. An anterior approach avoids trauma to the paraspinal musculature, epidural scarring, traction on nerve roots, and dural tears. However, the retraction of the great vessels, peritoneal contents, and superior hypogastric sympathetic plexus with a peritoneal or retroperitoneal approach place these structures at risk of iatrogenic injury. Access to the posterior space for the treatment of nerve compression is also limited. Laparoscopic anterior lumbar interbody fusion has also been investigated.

**Posterior Lumbar Interbody Fusion**

Posterior lumbar interbody fusion (PLIF) can be performed through either a traditional open procedure with a midline incision or with a minimally invasive approach using bilateral paramedian incisions. In the open procedure, the midline muscle attachments are divided along the central incision to facilitate wide muscle retraction and laminectomy. In minimally invasive PLIF, tubular retractors may be used to open smaller central bilateral working channels to access the pedicles and foramen. Minimally invasive PLIF typically involves partial laminotomies and facetectomies. The decompression allows treatment of spinal canal pathology (eg, spinal stenosis, lateral recess and foraminal stenosis, synovial cysts, hypertrophic ligamentum flavum), as well as stabilization of the spine through interbody fusion.

**Transforaminal Lumbar Interbody Fusion**

Transforaminal lumbar interbody fusion (TLIF) is differentiated from the more traditional bilateral PLIF by a unilateral approach to the disc space through the intervertebral foramen. In minimally invasive TLIF, a single incision about 2 to 3 cm in length is made approximately 3 cm lateral to the midline. A tubular retractor is docked on the facet joint complex and a facetectomy with partial laminectomy is performed. Less dural retraction is needed with access through the foramen via unilateral facetectomy, and contralateral scar formation is eliminated. TLIF provides access to the posterior elements along with the intervertebral disc space.

**Lateral Interbody Fusion**

Lateral interbody fusion (eg, extreme lateral interbody fusion or direct lateral interbody fusion) uses specialized retractors in a minimally invasive, lateral...
approach to the anterior spine through the psoas. In comparison with anterior lumbar interbody fusion, the lateral approach does not risk injury to the peritoneum or great vessels. However, exposure to the spine may be more limited, and dissection of the psoas major places the nerves of the lumbar plexus at risk. Electromyographic monitoring and dissection predominantly within the anterior psoas major may be utilized to reduce the risk of nerve root injury. These various factors decrease the ability to perform a complete discectomy and address pathology of the posterior elements.

**Circumferential Fusion**
Circumferential fusion is 360° fusion that joins vertebrae by their entire bodies and transverse processes, typically through an anterior and posterior approach.

**Posterolateral Fusion**
Posterolateral fusion is a procedure where the transverse processes of the involved segments are decorticated and covered with a mixture of bone autograft or allograft.

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