White Paper: The Use of Bone Morphogenetic Proteins (BMPs) in Lumbar Fusion: When is the Use of BMP Medically Necessary?

For Health Plans, Medical Management Organizations and TPAs

Overview of Bone Morphogenetic Proteins (BMPs)

Bone morphogenetic proteins (BMPs) are naturally occurring proteins that stimulate bone formation. When applied in the spine, BMPs are capable of inducing bone formation and spinal fusion without any bone graft harvesting, eliminating the need for a second surgery to harvest autogenous bone for placement at the surgery site. Autogenous bone harvest has been associated with increased risk for pain, complications, longer surgical time, and increased anesthesia. Fifteen different BMPs have been identified to date, all with varying degrees of cartilage and/or bone inductive properties.

Currently, there are two commercially available recombinant BMPs: rhBMP-2 and rhBMP-7. These are delivered to the bone grafting site as part of a surgical procedure, using a variety of carrier and delivery systems. Carrier systems function to maintain the concentration of the rhBMP at the treatment site while providing temporary scaffolding for osteogenesis and preventing extraneous bone formation. These systems may be composed of inorganic material, synthetic polymer, natural polymers, and bone allograft, and are absorbed over time. The rhBMP and carrier may be inserted via a delivery system, which may also function to provide mechanical support. For interbody spinal fusion, delivery systems have included interbody fusion cages. The carrier and delivery system are important variables in the clinical use of rhBMP because different clinical applications will require different dosages of rhBMP with different carriers and delivery systems. Therefore, the results of one clinical application cannot be extrapolated to others.

There are a number of alternatives to using BMP, including cast immobilization or other nonoperative approach, internal or external fixation, revision of a previous fixation, autograft, cadaver allograft, compression, dynamization, and use of bone growth stimulators.

Increased Use of BMPs for Spinal Fusion: Not Without Controversy

The use of BMPs for spinal fusion has risen sharply during the last decade, with BMPs now used in nearly 30% of spinal fusion cases. Patients who are more likely to receive BMPs include individuals who have had previous surgery and those undergoing more complex spinal fusion procedures. Unfortunately, BMPs add substantial cost to fusion procedures and their use may not reduce the need for repeat surgery. In addition, recent study results have associated BMPs with increasing safety concerns.

Frequent and life-threatening complications associated with the use of rhBMP-2 are being published. Although original industry-sponsored rhBMP-2 publications regarding safety and efficacy reported no rhBMP-2-associated adverse events (0%), systematic review of U.S. Food and Drug Administration (FDA) documents and subsequent publications have revealed originally unpublished adverse events and internal inconsistencies for on- and off-label indications. In addition, study designs were found to have potential methodological bias against the control group (bone graft). Estimates indicate that risk of adverse events may be 10 to 50 times the original data reported.
Complications Associated With BMPs

Numerous adverse events have been reported for BMPs, including ectopic bone formation, bone resorption, remodeling at the graft site, hematoma, neck swelling, painful seroma, dural tears, bowel/bladder and sexual dysfunction, failure to fuse, paralysis, carcinogenicity, and teratogenic effects. The risk for complications increases when BMPs are used off-label. The use of BMPs for anterior cervical spine fusion has been linked to swelling of neck and throat tissue, resulting in compression of the airway and/or neurological structures of the neck, as well as difficulty swallowing (dysphagia), breathing, or speaking. When used for posterior lumbar interbody fusion, BMPs have been associated with radiculitis, ectopic bone formation, and osteolysis, as well as poorer global outcomes.

Practice Parameters and Guidelines

There are several FDA-approved indications for InFUSE (rhBMP-2 and Absorbable Collagen Sponge Carrier). InFUSE Bone Graft, in conjunction with an interbody fusion device, is indicated for: spinal fusion procedures in mature patients with degenerative disc disease at one level from L4-S1 (anterior open approach only); treatment of acute, open fractures of the tibial shaft; sinus augmentations; and for localized alveolar ridge augmentations for defects associated with extraction sockets.

OP-1 (rhBMP-7 and Bovine Collagen) has received two FDA approvals through the Humanitarian Device Exemption process. The Humanitarian Device Exemption is available to devices intended for fewer than 4,000 patients per year. As part of this process, the manufacturer is not required to demonstrate unequivocal benefit but only “probable” benefit. OP-1 implant is indicated as an alternative to autograft in recalcitrant long-bone nonunions in which the use of autograft is unfeasible and alternative treatments have failed. OP-1 Putty is indicated 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. Compromising factors include osteoporosis, smoking, and diabetes.

Contraindications for using rhBMP include pregnancy, allergy to titanium, allergy to bovine type I collagen, infection, tumor, liver or kidney disease, immunosuppression (for example, lupus or HIV/AIDS), chemotherapy, and use of steroids.

According to the American Academy of Orthopaedic Surgeons Guidelines for off-label BMP use: “The off-label promotion of medical devices is expected to have increased scrutiny from federal authorities.” However, the guidelines also state that off-label use is acceptable as long as it is in the patient’s best interest and based on sound medical evidence.

Determining Medical Necessity for BMPs

Many health plans cover the use of BMPs, as long as patients meet very specific criteria. Examples of plan language include:

• Use of recombinant human bone morphogenetic protein (rhBMP-2) may be considered medically necessary for the following indications:
  o As an adjunct to anterior lumbar spinal fusion at one or more levels in skeletally mature recipients with degenerative disc disease (recipients should have had at least six months of nonoperative treatment)
  o For the treatment of acute, open fracture of the tibial shaft

• Use of recombinant human bone morphogenetic protein-7 (rhBMP-7) may be considered medically necessary for the following indication:
  o As an alternative to autograft in recalcitrant long bone nonunions where use of autograft is unfeasible and alternative treatments (e.g., electrical bone growth stimulation) have failed

• The use of recombinant human bone morphogenetic protein-2 or recombinant human bone morphogenetic protein-7 is considered investigational for all other indications including:
As an alternative to autograft in compromised recipients 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

- As an alternative or adjunct to bone grafting in other locations, including craniomaxillofacial surgeries

- Use of a non-FDA-approved BMP or use of an FDA-approved BMP for an off-label indication is considered investigational

The Role of External Independent Review in Determining Medical Necessity for BMPs

Practice guidelines are continually changing to reflect the advances in understanding the use of BMPs for spinal fusion, which often complicates the process of establishing evidence-based criteria for practice guidelines and reimbursement for new procedures and treatments. An independent medical review, which is normally used by healthcare payers, looks at whether a specific procedure was medically necessary.

The specialty match that an independent review organization (IRO) provides is especially important because results from ongoing clinical trials of BMPs lead to the continual emergence of new data regarding safety and efficacy. The board-certified physician specialists who work with IROs keep up-to-date with the latest medical research literature and with the latest standard of care. Physicians who review cases for IROs stay on top of continually evolving technology and treatments as they are studied more extensively and potentially accepted into clinical guidelines.

Independent medical reviews also avoid conflicts of interest, which can relate to economics, lack of specialists to review cases, or having the same doctor who denied a case review an appeal.

Conclusions

Spinal fusions are under more scrutiny than ever, as the use of BMPs for lumbar fusion has increased significantly in recent years. While indicated in specific patient populations for lumbar fusion, BMPs are often used off-label in surgeries for fusion of the cervical spine, which has been associated with numerous side effects and potentially life-threatening complications. The appropriate use of BMP requires careful consideration, taking into account its safety profile and high cost, as well as the data that studies continue to uncover.
Bibliography


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