Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 9/1/24**
(See policy history boxes for previous effective dates)

Title: Bone Graft Substitutes

Description/Background

Bone grafts are used to enhance, substitute, or extend bone repairs. Bone graft materials contain osteoconductive (matrix or scaffold upon which the bone is formed), osteoinductive (signal mediated by bioactive molecules to initiate growth and differentiation of bone forming cells), and/or osteogenic (cells necessary to form bone) properties which come from a variety of sources.

- Autograft: Bone taken from the patient either locally from the surgical incision or from a separate surgical site. The most common site for autograft is iliac crest. Promotes bone healing through osteoinduction, osteogenesis and/or osteoconduction. Autograft may be morselized (e.g. bone chips) or a structural piece of bone (e.g. tricortical iliac crest).
- Allograft: Bone is harvested from another person (cadaver). Promotes bone healing primarily through osteoconduction. The degree of osteoconduction depends on method used (fresh, frozen, or freeze-dried) and type of graft (cortical or cancellous).
- Biologics:
  - o Bone morphogenic protein (e.g. rhBMP2, Infuse)
  - o Peptide-based (e.g. P-15, I-factor)
  - o Bone marrow (aspirate or concentrate)
  - o Platelet rich plasma
  - o Human amniotic tissue membrane
- Cell-based grafts: Graft material containing a mixture of osteogenic or precursor cells with an osteo-conductive carrier.
  - o Mesenchymal stem cells (e.g. Orthofix's Trinity Evolution, NuVasive's Osteocel)
- Ceramic-based/Synthetics: Bone graft substitutes used to augment or as an

alternative to autografts and allografts. Promotes bone healing through osteoconduction.
    - o Calcium based: Calcium phosphate, beta-tricalcium phosphate, hydroxyapatite
    - o Silicon-based: Bioactive glass
    - o Synthetic Polymers (e.g. Cortoss (PMMA))
- Combination products: Different bone graft products/substitutes combined to enhance the osteoconductive, osteoinductive, and osteogenic properties.
- Demineralized Bone Matrix (DBM): Produced from cadaveric bone using acid extraction of bone matrix. This process removes the calcium and phosphate while leaving the extracellular matrix (collagen and non-structural proteins, including growth factors such as bone morphogenetic proteins). DBM is often combined with autograft and/or allograft.
- Nano bone graft: Synthetic graft material with altered nano-crystalline surface properties.
- Xenograft: Bone graft substitute made from other than human material (e.g. bovine, coral).

Regulatory Status

Many of the bone graft substitute products are regulated by the United States Food and Drug Administration (FDA). For example, nonstructural allograft and cellular allograft materials are considered human cells, tissues and cellular tissue-based products and as such do not require preclinical or clinical data by the FDA. Synthetic bone grafts and demineralized bone matrices (DBM) are considered Class II materials and fall under the FDA 510(k) regulatory process and upon approval are considered “substantially equivalent” to another marketed device/material used for the same purpose. Other materials, such as those that are considered drug-device combinations require premarket approval (PMA); FDA PMA approval requires an investigational device exemption clinical trial prior to the PMA application (Abjornson, et al., 2018).

Medical Policy Statement

The use of bone grafts/substitutes is considered established for promotion of bone healing when medical criteria is met.

Inclusionary and Exclusionary Guidelines

INCLUSIONS:

A. The use of bone grafts/substitutes that are listed below are considered established for promotion of bone healing when **ALL** of the following are met:

1. Graft is used according to FDA-approved (on-label) indications and contraindications, where applicable.
2. Graft is used alone, or in combination with another acceptable graft (i.e. an

osteoconductive allograft with an osteoinductive allograft). Up to one type of osteoconductive allograft and/or one type of osteoinductive allograft is used per surgical incident.

3. Recognizing that there are clinical scenarios where more product may be necessary, the amount of allograft is determined by the surgeon based on multiple factors including number of levels fused, size of patient, volume and quality of local bone or iliac crest bone harvested, and pseudoarthrosis risk.
4. Bone substitute graft is not being used to backfill or reconstruct donor site.
5. The surgical plan or operative note (whichever is applicable) should identify the graft manufacturer, product name, and amount or size of graft planned/used.

Where applicable, only grafts with FDA approval are considered medically necessary. The following are considered acceptable grafts:

1. Autograft (preferred option: considered gold standard in bone healing enhancement)
2. Allograft – morselized or structural
3. Demineralized bone matrix (DBM)
4. Calcium based synthetics
    a. Beta-tricalcium phosphate
    b. Hydroxyapatite
    c. Calcium Phosphate
    d. Calcium Sulfate
5. Bone marrow aspirate (not concentrated) combined with any other acceptable graft
6. Bone morphogenic protein-rhBMP-2 (Infuse): See JUMP Policy Bone Morphogenetic Protein
7. Peptide-15 (i-Factor), when all of the following are met:
    a. Single level anterior cervical discectomy and fusion between C3 and C7 in a skeletally mature patients who meet criteria for cervical fusion
    b. Must be used in combination with a cortical ring allograft and anterior plate fixation

Note: Processed allograft substitutes must have meaningful human-based studies to be considered for approval.

EXCLUSIONS:

Due to lack of sufficient evidence to establish safety and efficacy, the following are considered investigational and not medically necessary:

1. Cell-based substitute grafts
2. Non-calcium-based synthetics
    a. Bioactive glass
    b. Synthetic Polymers- e.g. Cortoss (PMMA)
3. Concentrated bone marrow aspirate
4. Platelet rich plasma
5. Human amniotic tissue
6. Nano crystalline surface modified synthetics

Note: Exceptions may be made on a case-by-case basis for those who are unable to accept human tissue grafts, due to ethical or religious reasons, and autograft is not a viable option.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

20930	20931	20936	20937	20938	20939
22551	22552	22556	22558	22600	22610
22612	22630	22633	22800	22802	22804
22808	22810	22812			

Other codes (investigational, not medically necessary, etc.):

N/A

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

Autologous Iliac Crest Bone Grafting (ICBG) is considered the gold-standard graft choice for spinal arthrodesis; however, it is associated with donor site morbidity and a limited graft supply. Biological products such as Bone Marrow Aspirate (BMA), recombinant human bone morphogenetic protein-2 (rhBMP-2), and Demineralized Bone Matrix (DBM) may improve spinal fusion success rates and enhance bone healing. Some biological products such as human amniotic membrane derivatives, and cell-based products, as well as synthetics such as ceramic-based products and Bioactive Glass, are being investigated for their ability to improve outcomes.

Demineralized Bone Matrix

Demineralized bone matrix products are a class of commercially available grafting agents that are prepared from allograft bone. There is some evidence for the use of demineralized bone matrix products in spinal fusions as an alternative to allograft. Cammisa, et al. (2004) conducted a prospective equivalency trial of Grafton DBM and iliac crest autograft in spine fusion, with each patient serving as his own control The investigators stated that, while autograft remains the preferred graft material to facilitate spine fusion, the supply is limited and harvesting may have undesirable clinical consequences. A total of 120 patients underwent posterolateral spine fusion with pedicle screw fixation and bone grafting. Iliac crest autograft was implanted on one side of the spine and a Grafton DBM/autograft composite was implanted on the contralateral side in the same patient. An independent, blinded reviewer evaluated anteroposterior and lateral flexion-extension radiographs. The fusion mass lateral to the instrumentation on each side was judged fused or not, and the mineralization of the graft was rated absent, mild, moderate, or extensive. The degree of correspondence in outcomes

between sides was estimated by computing the percentage agreement and kappa statistic. The investigators reported that nearly 70% of patients (81 of 120) provided complete 24-month radiographic studies. The bone graft mass was fused in 42 cases (52%) on the Grafton DBM side and in 44 cases (54%) on the autograft side. The overall percentage agreement for fusion status between sides was approximately 75% (61 of 81), indicating moderately strong statistical correspondence (kappa = 0.51, P < 0.0001). Bone mineralization ratings also were similar between treated sides. Perfect agreement was realized in almost 60% of patients (48 of 81) with moderate statistical correspondence (weighted kappa = 0.54, P < 0.0001). The authors concluded that Grafton DBM can extend a smaller quantity of autograft than is normally required to achieve a solid spinal arthrodesis. Consequently, a reduced amount of harvested autograft may be required, potentially diminishing the risk and severity of donor site complications.

Recombinant Bone Morphogenetic Protein (rhBMP)
Since the introduction of recombinant human bone morphogenetic protein-2 (rhBMP-2) (Infuse) in 2002, surgeons have had an alternative substitute to autograft and its related donor site morbidity. Recently, the prevalence of reported adverse events (AEs) and complications related to the use of rhBMP-2 has raised many ethical and legal concerns for surgeons. As a result of reported complications and the recent concern regarding safety and efficacy, use of RhBMP–2 product should be limited to the FDA-approved labeling indications.

Government Regulations

National:

There are no national coverage determinations specifically related to bone morphogenetic proteins.

Local:

There are no local coverage determinations specifically related to bone morphogenetic proteins.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Bone Morphogenetic Protein
- Orthopedic Applications of Stem-Cell Therapy (Including autologous stem cells used with Allografts and Bone Substitutes)

References

1. Abjornson C, Brecevich A, Callanan T, Dowe C, Cammisa F, Lorio M. ISASS Recommendations and Coverage Criteria for Bone Graft Substitutes used in Spinal Surgery. International Journal of Spine Surgery. 2018;12(6):757-771. doi:10.14444/5095.
2. Cammisa Jr FP, Lowery G, Garfin SR, et al. Two-year fusion rate equivalency between Grafton DBM gel and autograft in posterolateral spine fusion: A prospective controlled trial employing a side-by-side comparison in the same patient. Spine. 2004;29(6):660-666
3. Fernandez de Grado G, Keller L, Idoux-Gillet Y, Wagner Q, Musset A, Benkirane-Jessel N, Bornert F, Offner D. Bone substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management. Journal of Tissue Engineering. 2018;9:1-18.
4. Arnold P, Sasso R, Janssen M, Fehlings M, Smucker J, Vaccaro A, Heary R, Patel A, Goulet B, Kalfas I, Kopjar B. Efficacy of i-Factor bone graft versus autograft in anterior cervical discectomy and fusion: Results of the prospective, randomized, single-blinded food and drug administration investigational device exemption study. Spine. 2016;41(13):1075-1083. doi:10.1097/BRS.0000000000001466.
5. Brannigan K, Griffin M. An update into the application of nanotechnology in bone healing. The Open Orthopaedics Journal. 2016;10(Suppl-3, M2):808-823. doi:10.2174/1874325001610010808.
6. Buser Z, Brodke D, Youssef J, Meisel H, Myhre S, Hashimoto R, Park J, Yoon T, Wang J. Synthetic bone graft versus autograft or allograft for spinal fusion: a systematic review. Journal of Neurosug Spine. 2016;25:509-516. doi:10.3171/2016.1.SPINE151005.
7. Campana V, Milano G, Pagano E, et al. Bone substitutes in orthopaedic surgery: from basic science to clinical practice. J Mater Sci Mater Med. 2014;25(10):2445-2461. doi:10.1007/s10856-014-5240-2.
8. Carragee E, Hurwitz E, Weiner B. A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned. The Spine Journal. 2011;11(6):471-491. doi:10.1016/j.spinee.2011.04.023.
9. Dimar J, Glassman S, Burkus K, Carreon L. Clinical outcomes and fusion success at 2 years of single-level instrumented posterolateral fusions with recombinant human bone morphogenetic protein-2/compression resistant matrix versus iliac crest bone graft. Spine. 2006;31(22):2534-2539. doi:10.1097/01.brs.0000240715.78657.81.
10. Fu R, Selph S, McDonagh M, Peterson K, Tiwari A, Chou R, Helfand M. Effectiveness and harms of recombinant human bone morphogenic protein-2 in spine fusion: a systematic review and meta-analysis. Annals of Internal Medicine. 2018;158(12):890-902. doi:10.7326/0003-4819-158-12-201306180-00006.
11. Gupta A, Kukkar N, Sharif K, Main B, Albers C, El-Amin S. Bone graft substitutes for spine fusion: A brief review. World Journal of Orthopedics. 2015;6(6):449-456. doi:10.5312/wjo.v6.i6.449
12. Lauweryns P, Raskin Y. Prospective analysis of a new bone graft in lumbar interbody fusion: results of a 2-year prospective clinical and radiological study. International Journal of Spine Surgery. 2015;9(2). doi:10.14444/2002.
13. Lykissas M, Gkiatas L. Use of recombinant human bone morphogenic protein-2 in spine surgery. World Journal of Orthopedics. 2017;8(7):531-535. doi:10.5312/wjo.v8.i7.531.

14. Roberts T, Rosenbaum A. Bone grafts, bone substitutes and orthobiologics: The bridge between basic science and clinical advancements in fracture healing. Organogenesis. 2012;8(4):114-124. doi:10.4161/org.23306.
15. Simmonds M, Brown J, Heirs M, Higgins J, Mannion R, Rodgers M, Stewart L. Safety and effectiveness of recombinant human bone morphogenetic protein-2 for spinal fusion: a meta-analysis of individual-participant data. Ann Intern Med. 2013;158(12):877-889. doi:10.7326/0003-4819-158-12-201306180-00005.
16. Washington State Health Care Authority. Autologous blood/platelet-rich plasma injections. April 2016. Retrieved from https://www.hca.wa.gov/assets/program/prp_final_findings_decision.pdf.
17. Washington State Health Care Authority. Stem cell therapy for musculoskeletal conditions. July 2020. Retrieved from https://www.hca.wa.gov/assets/program/stem-cell-musculoskeletal-final-findings-decision-20200710.pdf.
18. Zwingenberger S, Nich C, Valladares R, Yao Z, Stiehler M, Goodman S. Recommendations and Considerations for the Use of Biologics in Orthopedic Surgery. BioDrugs. 2012;26(4):245-256.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 5/7/2024, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
9/1/23	6/13/23		Joint policy established Vendor: N/A 8/28/23: When a policy include add-on codes, generally included is a list of appropriate primary procedure codes that it can be billed with. This is because the payability of the service depends on whether the primary procedure is covered. Added the below codes to the policy: 22551, 22552, 22556, 22558, 22600 22610, 22612, 22630, 22633, 22800 22802, 22804, 22808, 22810, 22812 (ky)
9/1/24	6/11/24		• Routine maintenance • No BCBSA policy • Vendor: This JUMP policy is in alignment with TurningPoint (TP) policy OR-1046 Bone Graft Substitutes,1/2023. (ky)

Next Review Date: 2nd Qtr, 2025

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN:	Revised:
BCBSM:	Revised:

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: BONE GRAFT SUBSTITUTES

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered criteria applied.
BCNA (Medicare Advantage)	See government section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.
- Duplicate (back-up) equipment is not a covered benefit.