MASSACHUSETTS

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Medical Policy

Orthopedic Applications of Stem Cell Therapy (Including Allograft and Bone Substitute Products Used with Autologous Bone Marrow)

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Policy Number: 254

BCBSA Reference Number: 8.01.52 (For Plans internal use only)
NCD/LCD: NA

Related Policies

- Autologous Chondrocyte Implantation for Focal Articular Cartilage Lesions, #374
- Orthopedic Applications of Platelet-Rich Plasma, #737
- Prolotherapy, #183

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Mesenchymal stem cell therapy is considered **INVESTIGATIONAL** for all orthopedic applications, including use in repair or regeneration of musculoskeletal tissue.

Allograft bone products containing viable stem cells, including but not limited to demineralized bone matrix (DBM) with stem cells, are considered **INVESTIGATIONAL** for all orthopedic applications, including, but not limited to:

- AlloStem® (AlloSource)
- Map3® (RTI Surgical)
- Osteocel Plus® (NuVasive)
- Trinity Evolution Matrix™ (Orthofix).

Allograft or synthetic bone graft substitutes that must be **combined** with autologous blood or bone marrow are considered **INVESTIGATIONAL** for all orthopedic applications, including, but not limited to:

- Fusion Flex™ (Wright Medical)
- Ignite® (Wright Medical)
- Vitoss® Bioactive Foam Bone Graft Substitute (Stryker)
- NanOss BVF-E (Pioneer Surgical)
- DBX® Putty (DePuy Synthes)
- Integra MOZAIK™ Osteoconductive Scaffold (IsoTis OrthoBiologics)

- Formagraft™ Collagen Bone Graft Matrix (R and L Medical)
- CopiOs® Bone Void Filler (Kensey Nash)
- OrthoBlast® II (Sea Spine)
- DynaGraft® II (Sea Spine)

Supplemental Information
The purpose of the following information is to provide reference material. Inclusion of table 1, Demineralized Bone Matrix Products Cleared by FDA, does not indicate coverage. Orthopedic Applications of Stem Cell Therapy is considered investigational.

Tables 1 and 2 provide a representative sample of these products, differentiated by whether they must be mixed with autologous MSCs.

Table 1. Examples of Demineralized Bone Matrix Products Cleared by FDA that Do Not Require Mixing with Autologous MSCs

Product	Matrix Type	Manufacturer or Sponsor
Vitoss® Bioactive Foam Bone Graft Substitute	Type I bovine collagen	Stryker
NanOss BVF-E	Nanocrystalline hydroxyapatite	Pioneer Surgical
OrthoBlast® II Demineralized bone matrix putty and paste	Human (mixed allograft donor-derived) cancellous bone chips	SeaSpine
DBX® Demineralized bone matrix putty, paste and mix	Processed human (single allograft donor-derived) bone and sodium hyaluronate	Musculoskeletal Transplant Foundation
Formagraft™ Collagen Bone Graft Matrix	Bovine fibrillary collagen	R and L Medical
DynaGraft® II Gel and Putty	Processed human (mixed allograft donor-derived) bone particles	IsoTis Orthobiologics

FDA: U.S. Food and Drug Administration; MSCs: mesenchymal stem cells.

Table 2. Examples of Demineralized Bone Matrix Products Cleared by FDA that Require Mixing with Autologous MSCs

Product	Matrix Type	Manufacturer or Sponsor
CopiOs® Bone Void Filler (sponge and powder disc)	Type I bovine dermal collagen	Kensey Nash
Integra MOZAIK™ Osteoconductive Scaffold-Putty	Collagen matrix with tricalcium phosphate granules	IsoTis OrthoBiologics

FDA: U.S. Food and Drug Administration; MSCs: mesenchymal stem cells.

Prior Authorization Information

Inpatient
- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient
- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is **not** a covered service.
Commercial PPO and Indemnity	This is **not** a covered service.
Medicare HMO Blue℠	This is **not** a covered service.
Medicare PPO Blue℠	This is **not** a covered service.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

According to the policy statement above, the following CPT code is considered investigational for the conditions listed for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
20930	Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure). NOTE: This is a generic graft add on injection code to spine surgery which could be used for stem cells injection.

The following CPT codes are considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
0263T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; complete procedure including unilateral or bilateral bone marrow harvest
0264T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; complete procedure excluding bone marrow harvest
0265T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; unilateral or bilateral bone marrow harvest only for intramuscular autologous bone marrow cell therapy
0489T	Autologous adipose-derived regenerative cell therapy for scleroderma in the hands; adipose tissue harvesting, isolation and preparation of harvested cells including incubation with cell dissociation enzymes, removal of non-viable cells and debris, determination of concentration and dilution of regenerative cells
0490T	Autologous adipose-derived regenerative cell therapy for scleroderma in the hands; multiple injections in one or both hands
0565T	Autologous cellular implant derived from adipose tissue for the treatment of osteoarthritis of the knees; tissue harvesting and cellular implant creation

0566T	Autologous cellular implant derived from adipose tissue for the treatment of osteoarthritis of the knees; injection of cellular implant into knee joint including ultrasound guidance, unilateral

Description

Mesenchymal Stem Cells

Mesenchymal stem cells (MSCs) are multipotent cells (also called multipotent stromal cells) that can differentiate into various tissues including organs, trabecular bone, tendon, articular cartilage, ligaments, muscle, and fat. MSCs are associated with the blood vessels within the bone marrow, synovium, fat, and muscle, where they can be mobilized for endogenous repair as occurs with the healing of bone fractures. Tissues such as cartilage, tendon, ligaments, and vertebral discs show limited capacity for endogenous repair because of the limited presence of the triad of functional tissue components: vasculature, nerves, and lymphatics. Orthobiologics is a term introduced to describe interventions using cells and biomaterials to support healing and repair. Cell therapy is the application of MSCs directly to a musculoskeletal site. Tissue engineering techniques use MSCs and/or bioactive molecules such as growth factors and scaffold combinations to improve the efficiency of repair or regeneration of damaged musculoskeletal tissues.[1,]

Bone marrow aspirate is considered the most accessible source and, thus, the most common place to isolate MSCs for the treatment of musculoskeletal disease. However, harvesting MSCs from bone marrow requires a procedure that may result in donor-site morbidity. Also, the number of MSCs in bone marrow is low, and the number and differentiation capacity of bone marrow-derived MSCs decreases with age, limiting their efficiency when isolated from older patients.

In vivo, the fate of stem cells is regulated by signals in the local 3-dimensional microenvironment from the extracellular matrix and neighboring cells. It is believed the success of tissue engineering with MSCs will also require an appropriate 3-dimensional scaffold or matrix, culture conditions for tissue-specific induction, and implantation techniques that provide appropriate biomechanical forces and mechanical stimulation. The ability to induce cell division and differentiation without adverse effects, such as the formation of neoplasms, remains a significant concern. Given that each tissue type requires different culture conditions, induction factors (signaling proteins, cytokines, growth factors), and implantation techniques, each preparation must be individually examined.

Summary

Mesenchymal stem cells (MSCs) have the capability to differentiate into a variety of tissue types, including various musculoskeletal tissues. Potential uses of MSCs for orthopedic applications include treatment of damaged bone, cartilage, ligaments, tendons, and intervertebral discs.

For individuals who have cartilage defects, meniscal defects, joint fusion procedures, or osteonecrosis who receive stem cell therapy, the evidence includes randomized controlled trials (RCTs) and nonrandomized comparative trials. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity. Use of mesenchymal stem cells (MSCs) for orthopedic conditions is an active area of research. Despite continued research into the methods of harvesting and delivering treatment, there are uncertainties regarding the optimal source of cells and the delivery method. Studies have included MSCs from bone marrow, adipose tissue, and peripheral blood. Overall, the quality of evidence is low and there is a possibility of publication bias. The strongest evidence to date is on autologous MSCs expanded from bone marrow, which includes several phase 1/2 RCTs and a phase 3 RCT (which also evaluated other cell therapies). The phase 3 trial did not indicate significant improvements with the cell therapy modalities relative to active-control intra-articular corticosteroid injections for patients with knee osteoarthritis after 12 months of follow-up. Another recent phase 3 RCT evaluated autologous MSCs expanded from abdominal adipose tissue for treatment of knee osteoarthritis; this trial indicated autologous adipose-derived MSCs were more effective than matching placebo injections in improving pain, function, and other patient-reported outcomes after 6 months of follow-up. These phase 3 trials' mixed findings may be related to differences in the cell therapy modalities used, baseline cohort characteristics, and/or the use of an active vs placebo control. Alternative methods

of obtaining MSCs have been reported in a smaller number of trials and with mixed results. Additional study with longer follow-up is needed to evaluate the long-term efficacy and safety of these procedures. Also, expanded MSCs for orthopedic applications are not U.S. Food and Drug Administration approved (concentrated autologous MSCs do not require agency approval). Overall, there is a lack of clear evidence that clinical outcomes are improved. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
3/2025	Annual policy review. References updated. Policy statements unchanged.
3/2024	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
9/2023	Policy clarified. Table 1. Demineralized Bone Matrix Products Cleared by FDA added.
5/2023	Clarified coding information
3/2023	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
12/2022	Policy clarified. Allograft and bone substitute products used with autologous bone marrow added. Policy statements unchanged.
2/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
2/2018	Annual policy review. New references added.
8/2017	Annual policy review. New references added.
9/2015	Annual policy review. New investigational indications described; title changed. Clarified coding information. Effective 9/1/2015.
7/2014	Annual policy review. New references added.
10/2013	Annual policy review. New investigational indications described. Effective 10/1/2013.
12/2012	Updated to add new CPT code 38243.
6/2011	Reviewed - Medical Policy Group – Orthopedics, Rehabilitation and Rheumatology, No changes to policy statements.
12/01/2010	New policy, effective 12/01/2010.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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