02-38240-02

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Subject: Orthopedic Applications of Stem-Cell Therapy

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

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.

MSCs are multipotent cells (also called stromal multipotent cells) that possess the ability to differentiate into various tissues including organs, trabecular bone, tendon, articular cartilage, ligaments, muscle, and fat. MSCs are associated with the blood vessels within bone marrow, synovium, fat, and muscle, where they can be mobilized for endogenous repair as occurs with healing of bone fractures.

Bone-marrow aspirate is considered to be the most accessible source and, thus, the most common place to isolate MSCs for treatment of musculoskeletal disease. However, harvesting MSCs from bone marrow requires an additional procedure that may result in donor-site morbidity. In addition, 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 efficacy when isolated from older individuals.

Tissues, such as muscle, 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.

Summary and Analysis of Evidence: An UpToDate review "Investigational approaches to the management of osteoarthritis" (Yu, 2023) states "MSCs derived from bone marrow, adipose, synovium, and other tissues have been investigated for their potential role in regenerating chondrocytes, mediating tissue repair, and stimulating growth factors. Published trials have demonstrated that intra-articular injection is well tolerated; small sample size and heterogeneity in selection criteria, MSC tissue source, number of MSCs, and analyzed outcomes limit generalizability and conclusive determination of benefit. In a randomized, placebo-controlled trial of adipose-derived intra-articular MSC injection in 252 patients with moderate knee OA, the treatment group showed improved Visual Analog Scale and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores at six months when compared with placebo and no difference in structural change by magnetic resonance imaging (MRI) evaluation. Given the heterogeneity and small sample size issues with prior studies, this study is notable for its large sample size and inclusion of only patients with moderate OA. Further clinical studies are needed to determine if MSCs are an effective long-term treatment for OA and, if effective, to establish the optimal MSC-harvesting source, MSC cell dose, and number of injections."

POSITION STATEMENT:

Mesenchymal stem-cell therapy is considered **experimental or 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, is considered **experimental or investigational** for all orthopedic applications.

Allograft or synthetic bone graft substitutes that must be combined with autologous blood or bone marrow aspirate are considered **experimental or investigational** for all orthopedic applications.

The use of adipose-derived stem cells is considered **experimental or investigational** for all orthopedic applications.

The use of progenitor cells is considered **experimental or investigational** for all orthopedic applications.

There is insufficient published clinical evidence to support the safety and effectiveness of these therapies for repair or regeneration of musculoskeletal tissue.

BILLING/CODING INFORMATION:

CPT Coding:

20939	Bone marrow aspiration for bone grafting, spine surgery only, through separate skin or fascial incision (List separately in addition to code for primary procedure) (Considered **investigational** **when used to report bone marrow aspirate or bone marrow fluid concentrated or centrifuged for growth factors, stem cell, or mesenchymal cell application)
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous (Considered **investigational** **when used to report bone marrow

	aspirate or bone marrow fluid concentrated or centrifuged for growth factors, stem cell, or mesenchymal cell application)
38230	Bone marrow harvesting for transplantation; allogeneic (Considered **investigational** **when used to report bone marrow aspirate or bone marrow fluid concentrated or centrifuged for growth factors, stem cell, or mesenchymal cell application)
0565T	Autologous cellular implant derived from adipose tissue for the treatment of osteoarthritis of the knees; tissue harvesting and cellular implant creation (**Investigational**)
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 (**Investigational**)
0717T	Autologous adipose-derived regenerative cell (ADRC) therapy for partial thickness rotator cuff tear; adipose tissue harvesting, isolation and preparation of harvested cells, including incubation with cell dissociation enzymes, filtration, washing and concentration of ADRCs (**Investigational**)
0718T	Autologous adipose-derived regenerative cell (ADRC) therapy for partial thickness rotator cuff tear; injection into supraspinatus tendon including ultrasound guidance, unilateral (**Investigational**)

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline reviewed date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

Allogeneic Bone Marrow and Stem Cell Transplantation, 02-38240-01

Autologous Bone Marrow and Stem Cell Transplantation, 02-38241-01

OTHER:

Other names or key words used to report products containing stem cells:

Note: The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Allograft bone products containing viable stem cells

Allogen

AlloStem Stem Cell Bone Growth Substitute

Aminovo

AmnioFix

AmnioPro-A

Arthrex Amnion Matrix & Viscous

Axograft Dual Layer Amniotic Membrane

Bio4 Viable Bone Matrix

BioDfactor

BioDFence

BioDRestore

BioD Dry Flex

Cartistem (not yet available in U.S. as of last review date)

Cellentra VCBM

Cygnus

Fusion Flex

Ignite

MAP3

NuCel

OrthoFlo

Osteocel Plus

Osteocel Pro

OsteoVive

Ovation cellular repair matrix

Ovation OS

PalinGen

PalinGen Flow

Regenexx

ReNu

SXDBM

Trinity Elite

Trinity Evolution

Viaflow

Viaflow C

***When* combined with autologous blood or bone marrow aspirate, products listed below**

CONDUCT Matrix

CopiOs

DBX

Formagraft

Grafton DBM DBF

HEALOS

Ignite

Induce

Integra MOZAIK

MCS Bone Graft

Mastergraft Matrix EXT

Mastergraft Strip

OssiMend

PliaFX Strip

Rybone

ViaSorb

Vitoss

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 02/22/24.

GUIDELINE UPDATE INFORMATION:

09/15/14	New Medical Coverage Guideline.
09/15/15	Scheduled review. Position statement maintained; updated description section, index terms and references.
11/15/16	Scheduled review. Position statement maintained. Updated references.
11/15/17	Scheduled review. Revised description section. Position statement maintained. Updated references.
11/15/18	Scheduled review. Revised description section and CPT coding section. Maintained position statement and updated references.
03/15/19	Revision: deleted codes 0263T, 0264T, and 0265T (refer to MCG 09-A0000-03, Investigational Services).
06/15/19	Unscheduled review. Revised description, maintained position statement and updated references.
10/15/19	Scheduled review. Revised description and index terms. Maintained position statement and update references.
01/01/20	Annual CPT/HCPCS coding update. Added 0565T, 0566T.
05/15/20	Revision: updated OTHER section (products containing stem cells).
11/15/20	Revision. Updated product names and classifications. Updated references.
11/30/20	Revision. Deleted ViviGen from “Allograft bone products containing viable stem cells” section.
05/15/21	Scheduled review. Maintained position statement and updated references.
07/01/22	Quarterly CPT/HCPCS coding update. Added 0717T, 0718T.
11/15/22	Revision: added code 20939.
05/15/23	Scheduled review. Maintained position statement and updated references.
05/25/23	Update to Program Exceptions section.
03/15/24	Scheduled review. Revised description and index terms. Added coverage statement for adipose-derived stem cells. Updated references.