Medical Policy

PARAMOUNT

Stem Cell Therapy for Orthopedic Applications

Policy Number: PG0400
Last Review: 07/01/2024

HMO AND PPO
ELITE (MEDICARE ADVANTAGE)
MARKETPLACE

GUIDELINES:

- **This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder terms, conditions, exclusions, and limitations contract. It does not constitute a contract or guarantee regarding coverage or reimbursement/payment. Self-Insured group specific policy will supersede this general policy when group supplementary plan document or individual plan decision directs otherwise.**
- **Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards.**
- **This medical policy is solely for guiding medical necessity and explaining correct procedure reporting used to assist in making coverage decisions and administering benefits.**

SCOPE:

X Professional
_ Facility

DESCRIPTION:

Mesenchymal stem cells (MSCs) are multipotent cells (also called “stromal multipotent cells”) have the capability to differentiate into a variety of tissue types, including organs, trabecular bone, tendon, articular cartilage, ligaments, muscle, and fat. Mesenchymal stem cells have been classically obtained from the bone marrow and have been shown to differentiate into various cell types, including osteoblasts, chondrocytes, myocytes, adipocytes, and neuronal cells. Potential uses of MSCs for orthopedic applications include treatment of damaged bone, cartilage, ligaments, tendons, and intervertebral discs. The proposed benefits of MSC therapy are improved healing and possible avoidance of surgical procedures with protracted recovery times.

Although processing techniques vary, and the optimal number of MSCs to be transplanted/seeded has not been established, following autologous bone marrow collection MSCs are either concentrated for direct injection, or cultured and incubated. Once cultured the MSCs can be mixed with biomaterials, such as gels or pastes; the biomaterials hold the cells in suspension and provide a matrix for filling defects. MSCs can also be seeded on scaffolds and have been investigated when used with a support matrix for implantation (e.g., tissue engineered). In theory, MSCs are responsive to osteogenic growth factors and aid in the healing of bone. Nevertheless, evidence in the published peer-reviewed scientific literature evaluating the use of MSCs to enhance bone healing consists mainly of animal trials and a paucity of human trials. At present, the evidence is insufficient to support improved clinical outcomes, when used alone, added to other biomaterials, or as cultured/seeded on a support matrix.

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, Title 21, parts 1270 and 1271. MSCs are included in these regulations. Concentrated autologous MSCs do not require approval by the U.S. Food and Drug Administration (FDA). Currently there are no allogeneic MSC therapies or devices that are approved for marketing by the FDA. However, there are products containing mesenchymal stem cells that are commercially available for orthopedic indications, which include, not all-inclusive:

- AlloStem® Cellular Bone Allograft (AlloSource, Centennial, CO): Comprised of adipose derived mesenchymal stem cells with partially demineralized allograft bone.
- NuCel® (NuTech Medical, Birmingham, AL): Derived from amniotic membrane.

- Map3™ (rti surgical): Contains cortical cancellous bone chips, DBM, and multipotent adult progenitor cells.
- Osteocel Plus® (NuVasive): DBM combined with viable MSCs that have been isolated from allogeneic bone marrow.
- Trinity Evolution Matrix™ (Orthofix): DBM combined with viable MSCs that have been isolated from allogeneic bone marrow.
- Cellentra™ VCBM (Biomet®): An allograft that is cryopreserved containing MSCs, osteoprogenitor cells, and pre-osteoblasts.
- RegenexxSD® (Same Day Stem Cell Procedure): A procedure involving autologous bone marrow that is concentrated and a super-platelet mix is added, and the final product is injected into the affected site.
- RegenexxAD® (Adipose Derived Stem Cell Procedure): A procedure that combines RegenexxSD with stem cells derived from adipose tissue, the final product is then injected into an affected site.
- VIA® Form and VIA® Graft (Vivex Biomedical)8: This is a family of products referred to as "cellular bone matrices" which are viable allogeneic bone allografts with MSC and bone components. These products are intended for use in bone remodeling in a number of applications including spine, upper extremity, foot/ankle, oral/maxillofacial and orthopedic oncology.
- ViviGen® (DePuy)9: This product is a cellular bone matrix is comprised of cryopreserved viable cortical cancellous bone matrix and demineralized bone. ViviGen® is intended for repair or reconstruction of musculoskeletal defects.

MSC therapy has been proposed as a treatment option for orthopedic indications that include but are not limited to the following:

- Knee: Arthritis, meniscus tears, tendon and ligament tears, overuse injuries and other conditions
- Hip: Injuries, arthritis, bursitis, and other degenerative conditions
- Shoulder: Arthritis, rotator cuff tears, and other shoulder conditions
- Spine and cervical conditions: Back pain, pain from bulging or herniated discs, degenerated discs, or pain from an extruded or torn disc
- Elbow: Injuries, overuse conditions and arthritis (tendon and ligament issues)
- Hand/Wrist: Arthritis and other conditions
- Foot/Ankle: Ligament tears, sprains and instability of the ankle joint, an alternative to fusion or replacement surgery of the ankle
- Non-union fractures

The evidence for stem cell therapy in individuals who have various orthopedic conditions (cartilage defects, meniscectomy, spinal fusion procedures, osteonecrosis) includes small randomized controlled trials and nonrandomized comparative trials. Relevant outcomes are symptoms, morbid events, functions outcomes, quality of life, and treatment-related morbidity. Use of MSCs for orthopedic conditions is an active area of research. Despite continued research into 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, peripheral blood, and synovial tissue. The largest body of evidence is on the use of autologous MSCs, either concentrated or expanded in culture, for cartilage repair. This evidence includes small randomized and nonrandomized comparative trials with insufficient data to evaluate health outcomes. In addition, expanded MSCs for orthopedic applications are not U.S. Food and Drug Administration (FDA) approved (concentrated autologous MSCs do not require FDA approval). Overall, there is lack of evidence that clinical outcomes are improved. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans
Mesenchymal stem-cell therapy is experimental/investigational and/or unproven and therefore considered Non-Covered for all orthopedic applications, including use in repair or regeneration of musculoskeletal tissue.

Mesenchymal stem cell therapy (including but not limited to Regenexx Procedure) for all orthopedic indications is non-covered. This includes but is not limited to allogeneic or autologous stem cells harvested bone marrow, adipose tissue, peripheral blood, synovial or amniotic fluid.

Allograft bone products containing viable stem cells, including but not limited to demineralized bone matrix (DBM) with stem cells (e.g., BIO4®, OSTEOCEL® Plus, OSTEOCEL® Pro, OsteoVive™, Trinity Evolution®, Trinity ELITE®, VIA® Form, VIA® Graft, ViviGen®) are considered investigational and not covered for all orthopedic applications.

Related Medical Policies:

- **PG0293 Platelet Rich Plasma**
- **PG0365 Bone Graft Substitutes**

COVERAGE CRITERIA:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans

Mesenchymal stem cell therapy is considered experimental/investigational and non-covered for all orthopedic indications. Mesenchymal stem cell therapy (including but not limited to Regenexx® Procedure) including use in repair or regeneration of musculoskeletal tissue is considered investigation and therefore non-covered because the safety and/or effectiveness of this service cannot be established by the available published peer-reviewed literature.

Allograft bone products containing viable stem cells, including but not limited to demineralized bone matrix (DBM) with stem cells, is experimental/investigational and therefore considered non-covered for all orthopedic applications.

Allograft or synthetic bone graft substitutes that must be combined with autologous blood or bone marrow are experimental/investigational and therefore considered non-covered for all orthopedic applications.

Use of stem cells for orthopedic applications is considered experimental/investigational due to the lack of evidence that clinical outcomes are improved and the lack of regulatory approval. In addition, expanded MSCs for orthopedic applications are not Food and Drug Administration (FDA) approved (concentrated autologous MSCs do not require FDA approval).

In 2008, the FDA determined that the mesenchymal stem cells sold by Regenerative Sciences for use in the Regenexx™ procedure would be considered drugs or biological products and thus require submission of a New Drug Application (NDA) or Biologics Licensing Application (BLA) to the FDA. In 2014, a federal appellate court upheld FDA's power to regulate adult stem cells as drugs and biologics and ruled that the Regenexx cell product fell within FDA's authority to regulate human cells, tissues, and cellular and tissue-based products (HCT/Ps) (Section 351).[2] To date, no NDA or BLA has been approved by the FDA for this product. As of 2015, the expanded stem cell procedure is only offered in the Cayman Islands. Regenexx™ network facilities in the U.S. provide same-day stem cell and blood platelet procedures, which do not require FDA approval.

CODING/BILLING INFORMATION:

The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

CPT CODES	
NOTE: There are no specific codes for orthopedic applications of stem cell therapy. The following codes, not all-inclusive, are considered experimental/investigational and noncovered when performed and billed related to Stem Cell and Cellular Bone Matrix Therapy for Orthopedic Applications as identified above.	
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)
20999	Unlisted musculoskeletal procedure
38205	Blood derived hematopoietic progenitor cell harvesting for transplantation, per collection allogeneic
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
38212	Transplant preparation of hematopoietic progenitor cells; red blood cell removal

38215	Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear or buffy coat layer
38230	Bone marrow harvesting for transplantation; allogeneic
38232	Bone marrow harvesting for transplantation; autologous
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation
38999	Unlisted procedure, hemic or lymphatic system [when specified as bone marrow cell therapy or stem cell therapy such as IM, IV or IA for peripheral vascular disease]
64999	Unlisted procedure, nervous system
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 unilateral or bilateral 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
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
0627T	Percutaneous injection of allogeneic cellular and/or tissue-based product, intervertebral disc, unilateral or bilateral injection, with fluoroscopic guidance, lumbar; first level
0628T	Percutaneous injection of allogeneic cellular and/or tissue-based product, intervertebral disc, unilateral or bilateral injection, with fluoroscopic guidance, lumbar; each additional level (List separately in addition to code for primary procedure)
0629T	Percutaneous injection of allogeneic cellular and/or tissue-based product, intervertebral disc, unilateral or bilateral injection, with CT guidance, lumbar; first level
0630T	Percutaneous injection of allogeneic cellular and/or tissue-based product, intervertebral disc, unilateral or bilateral injection, with CT guidance, lumbar; each additional level (List separately in addition to code for primary procedure)
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 (new 07/01/2022)
0718T	Autologous adipose-derived regenerative cell (ADRC) therapy for partial thickness rotator cuff tear; injection into supraspinatus tendon including ultrasound guidance, unilateral (new 07/01/2022)

REVISION HISTORY EXPLANATION: ORIGINAL EFFECTIVE DATE: 04/21/2017

Date	Explanation & Changes
04/21/17	• Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
07/11/17	• Code 20930 removed • Policy reviewed and updated to reflect most current clinical evidence per Medical Policy Steering Committee
12/28/2020	• Medical policy placed on the new Paramount Medical policy format
04/28/2021	• Policy updated to reflect most current clinical evidence, updated coverage rationale • Clarified; there are no specific codes for orthopedic applications of stem cell therapy. The following codes, not all-inclusive, are considered investigational and noncovered when performed and billed related to Stem Cell and Cellular Bone Matrix Therapy for Orthopedic Applications as identified above • Updated CODING/BILLING INFORMATION section to add procedure codes 20939, 38999, 64999, 0263T, 0264T, 0265T, 0565T, 0566T, 0627T, 0628T, 0629T, 0630T • No change in noncoverage criteria

05/02/2022	• Removed the listing of procedures 0232T, G0460, S9055 from the documentation indicating - Refer to PG0293 Platelet Rich Plasma.
03/01/2023	• Medical Policy updated to reflect Medicaid coverage to Anthem as of 02/01/2023
07/01/2024	• Medical Policy reviewed and updated to reflect the most current clinical evidence • Added non-covered procedure codes 0717T, 0718T

Paramount reserves the right to review and revise our policies periodically when necessary. When there is an update, we will publish the most current policy to https://www.paramounthealthcare.com/providers/medical-policies/policy-library

REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals-IOMs

NCDs https://www.cms.gov/medicare-coverage-database/searchresults.aspx?keyword=&keywordType=starts&areaId=s29&docType=NCD&contractOption=all

LCDs https://www.cms.gov/medicare-coverage-database/searchresults.aspx?keyword=&keywordType=starts&areaId=s29&docType=F,P&contractOption=all

American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services https://www.ama-assn.org/amaone/cpt-current-procedural-terminology

Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets https://www.cms.gov/Medicare/Coding/HCPCSReleaseCodeSets/HCPCS-Quarterly-Update

U.S. Preventive Services Task Force, https://www.uspreventiveservicestaskforce.org/uspstf/
Industry Standard Review

Hayes, Inc., Lansdale, PA: Author. Health Technology Assessments. https://www.hayesinc.com/

Industry Standard Review