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Medicare Advantage Policy Manual **Policy ID:** M-MED142

Orthopedic Applications of Stem-Cell Therapy, Including Bone Substitutes Used with Autologous Bone Marrow

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IMPORTANT REMINDER

The Medicare Advantage Medical Policy manual is not intended to override the member Evidence of Coverage (EOC), which defines the insured's benefits, nor is it intended to dictate how providers are to practice medicine. Physicians and other health care providers are expected to exercise their medical judgment in providing the most appropriate care for the individual member.

The Medicare Advantage Medical Policies are designed to provide guidance regarding the decision-making process for the coverage or non-coverage of services or procedures in accordance with the member EOC and the Centers of Medicare and Medicaid Services (CMS) policies, when available. In the event of a conflict, applicable CMS policy or EOC language will take precedence over the Medicare Advantage Medical Policy. In the absence of CMS guidance for a requested service or procedure, the health plan may apply their Medical Policy Manual or MCG™ criteria, both of which are developed with an objective, evidence-based process using scientific evidence, current generally accepted standards of medical practice, and authoritative clinical practice guidelines.

Medicare and EOCs exclude from coverage, among other things, services or procedures considered to be investigational, cosmetic, or not medically necessary, and in some cases, providers may bill members for these non-covered services or procedures. Providers are encouraged to inform members in advance when they may be financially responsible for the cost of non-covered or excluded services.

DESCRIPTION

Mesenchymal stem cells (MSCs) are multipotent cells (also known as "stromal multipotent cells"), which possess the ability to differentiate into various tissues including organs, trabecular bone, tendon, articular cartilage, ligaments, muscle, and fat. Potential uses of MSCs for orthopedic applications include, but may not be limited to, treatment of damaged bone, cartilage, ligaments, tendons, and intervertebral discs.

MEDICARE ADVANTAGE POLICY CRITERIA

Note: Other applications for stem cell therapy are addressed in other Medicare Advantage medical policies (see Cross References).

CMS Coverage Manuals*	None

National Coverage Determinations (NCDs)*	See References[1] NCD guidelines state coverage for all other indications of stem cell transplantation not otherwise noted as covered or non-covered nationally remain at Medicare Administrative Contractor (MAC) discretion. The orthopedic application of stem-cell therapy is not addressed within the stem cell transplantation NCD.
Noridian Healthcare Solutions (Noridian) Local Coverage Determinations (LCDs) and Articles*	None
Medical Policy Manual	*Medicare coverage guidance is not available for stem cell therapy used for orthopedic purposes. Therefore, the health plan's medical policy is applicable.* Orthopedic Applications of Stem-Cell Therapy, Including Bone Substitutes Used with Autologous Bone Marrow, Medicine, Policy No. 142 *(see "NOTE" below)*

NOTE: If a procedure or device lacks scientific evidence regarding safety and efficacy because it is investigational or experimental, the service is noncovered as not reasonable and necessary to treat illness or injury. (*Medicare IOM Pub. No. 100-04, Ch. 23, §30 A*). According to Title XVIII of the Social Security Act, §1862(a)(1)(A), only medically reasonable and necessary services are covered by Medicare. In the absence of a NCD, LCD, or other coverage guideline, CMS guidelines allow a Medicare Advantage Organization (MAO) to make coverage determinations, applying an ***objective, evidence-based process, based on authoritative evidence***. (*Medicare IOM Pub. No. 100-16, Ch. 4, §90.5*). The Medicare Advantage Medical Policy - Medicine Policy No. M-149 - provides further details regarding the plan's evidence-assessment process (see Cross References).

POLICY GUIDELINES

REGULATORY STATUS

The U.S. Food and Drug Administration (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 (CFR) title 21, parts 1270 and 1271. Mesenchymal stem cells (MSCs) are included in these regulations.

Medicare coverage for medical devices and products includes those approved by the FDA through the pre-market approval (PMA) process or the 510(k) process, FDA-approved IDE Category B devices, and hospital institutional review board (IRB) approved IDE devices, and only when used within the context of the FDA-approved clinical trial.[2]

The FDA has stated:

> "A major challenge posed by SC [stem cell] therapy is the need to ensure their efficacy and safety. Cells manufactured in large quantities outside their natural environment in the human body can become ineffective or dangerous and produce significant adverse effects, such as tumors, severe immune reactions, or growth of unwanted tissue. In response to this challenge, FDA scientists are developing laboratory techniques that will enable the agency to carefully evaluate and characterize these products in order to reliably predict whether they will be safe and effective.
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> "Our laboratories use cell cultures and animal models to develop such techniques and to study the biochemical signals that govern cell behavior during manufacturing and after administration to patients. A current research focus is to use mesenchymal stromal cells, or MSCs, (widely called mesenchymal stem cells) to develop strategies that will lead to improved, more predictive ways to characterize stem-cell based cell products.
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> "These studies will help us develop testing methods that are practical and applicable to specific manufacturing steps. This will help CBER to ensure the consistency, safety, and efficacy of stem cell-based products."[3]

Concentrated autologous MSCs do not require approval by FDA. No products using engineered or expanded MSCs have been approved by FDA for orthopedic applications.

The following products are examples of commercialized demineralized bone matrix (DBM) products. They are marketed as containing viable stem cells. In some instances, manufacturers have received communications and inquiries from FDA related to the appropriateness of their marketing products that are dependent on living cells for their function. The following descriptions are from the product literature.

- AlloStem® (AlloSource) is a partially demineralized allograft bone seeded with adipose-derived MSCs.
- Map3™ (rti Surgical) contains cortical cancellous bone chips, DBM, and cryopreserved multipotent adult progenitor cells (MAPC®).
- Osteocel Plus® (NuVasive) is a DBM combined with viable MSCs isolated from allogeneic bone marrow.
- Trinity Evolution Matrix™ (Orthofix) is a DBM combined with viable MSCs isolated from allogeneic bone marrow.
- Other products contain DBM alone and are designed to be mixed with bone marrow aspirate:
    - Fusion Flex™ (Wright Medical) is a dehydrated moldable DBM scaffold (strips and cubes) that will absorb autologous bone marrow aspirate.
    - Ignite® (Wright Medical) is an injectable graft with DBM that can be combined with autologous bone marrow aspirate.

A number of DBM combination products have been cleared for marketing by FDA through the 510(k) process, some of which are specifically labeled for mixing with bone marrow aspirate. Examples include, but may not be limited to: Vitoss® Bioactive Foam Bone Graft Substitute (Stryker), nanOss® BVF-E (Pioneer Surgical), OrthoBlast® II Demineralized bone matrix putty and paste (SeaSpine), CopiOs® Bone Void Filler (sponge and powder disc) (Kensey Nash), DBX® Demineralized bone matrix putty, paste and mix (Musculoskeletal Transplant Foundation), Integra MOZAIK™ Osteoconductive Scaffold-Putty (IsoTis OrthoBiologics), Formagraft™ Collagen Bone Graft Matrix (R and L Medical), Collage™ Putty (Orthofix), and DynaGraft® II Gel and Putty (IsoTis OrthoBiologics).

In 2008, the FDA determined MSCs sold by Regenerative Sciences for use in the Regenexx-C™ procedure would be considered drugs or biologic products and thus require submission of a new drug application or biologic license application to FDA. In 2014, a federal appellate court upheld FDA authority to regulate adult stem cells as drugs and biologics and ruled that the Regenexx cell product fell within FDA's authority to regulate HCT/Ps. To date, no new drug application (NDA) or biologic license application (BLA) has been approved by 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. These procedures are marketed as treatments for arthritis and injuries of the knee, hip, shoulder, spine, hand and wrist, foot and ankle and elbow.[4]

Of note, the fact a service or procedure has been FDA approved for a specific indication does not, in itself, make the procedure medically reasonable and necessary. Medicare contractors evaluate services, procedures, drugs or technology to determine if they may be considered Medicare covered services. The FDA determines safety and effectiveness of a device or drug, but does not establish medical necessity. While Medicare may adopt FDA determinations regarding safety and effectiveness, CMS or Medicare contractors evaluate whether or not the drug or device is reasonable and necessary for the Medicare population under §1862(a)(1)(A).

CROSS REFERENCES

Autologous Blood-Derived Growth Factors as a Treatment for Wound Healing and Other Miscellaneous Conditions, Medicine, Policy No. M-77

Progenitor Cell Therapy for the Treatment of Damaged Myocardium Due to Ischemia, Medicine, Policy No. M-100

Cell Therapy for Peripheral Arterial Disease, Medicine, Policy No. M-141

Investigational (Experimental) Services, New and Emerging Medical Technologies and Procedures, and Other Non-Covered Services, Medicine, Policy No. M-149

REFERENCES

1. National Coverage Determination (NCD) for Stem Cell Transplantation (Formerly 110.8.1) (110.23) [Last Cited 12/13/2024] *(This reference can be found on the Medicare Coverage Database website)*
2. Medicare Benefit Policy Manual, Chapter 14 – Medical Devices, §10 – Coverage of Medical Devices
3. U.S. Food and Drug Administration. Development of strategies to improve cell therapy product characterization. [Last Cited 12/03/2024]; Available from: https://www.fda.gov/vaccines-blood-biologics/biologics-research-projects/development-strategies-improve-cell-therapy-product-characterization
4. FDA Information on Regenexx Procedures. [Last Cited 12/03/2024]; Available from: https://regenexxcorporate.com/fda-information/

CODING

NOTE: There are no specific codes for orthopedic applications of stem cell therapy. The appropriate CPT code for reporting this procedure is 20999, or the code for an unlisted procedure of the body area on which the procedure is performed.

Codes	Number	Description
CPT	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 procedure, musculoskeletal system, general
	21899	Unlisted procedure, neck or thorax
	22899	Unlisted procedure, spine
	23929	Unlisted procedure, shoulder
	24999	Unlisted procedure, humerus or elbow
	25999	Unlisted procedure, forearm or wrist
	26989	Unlisted procedure, hands or fingers
	27299	Unlisted procedure, pelvis or hip joint
	27599	Unlisted procedure, femur or knee
	27899	Unlisted procedure, leg or ankle
	28899	Unlisted procedure, foot or toes
	29999	Unlisted procedure, arthroscopy
	38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
	38230	Bone marrow harvesting for transplantation; allogeneic
	38232	Bone marrow harvesting for transplantation; autologous
	38241	Bone Marrow or blood-derived peripheral stem cell transplantation; autologous

Codes	Number	Description
	0565T	Autologous cellular implant derived from adipose tissue for the treatment of osteoarthritis of the knees; tissue harvesting and cellular implant creation
	0566T	;injection of cellular implant into knee joint using ultrasound guidance, unilateral
	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
	0718T	Autologous adipose-derived regenerative cell (ADRC) therapy for partial thickness rotator cuff tear; injection into supraspinatus tendon including ultrasound guidance, unilateral
	0737T	Xenograft implantation into the articular surface
HCPCS	C9782	Blinded procedure for new york heart association (nyha) class ii or iii heart failure, or canadian cardiovascular society (ccs) class iii or iv chronic refractory angina; transcatheter intramyocardial transplantation of autologous bone marrow cells (e.g., mononuclear) or placebo control, autologous bone marrow harvesting and preparation for transplantation, left heart catheterization including ventriculography, all laboratory services, and all imaging with or without guidance (e.g., transthoracic echocardiography, ultrasound, fluoroscopy), performed in an approved investigational device exemption (ide) study

***IMPORTANT NOTE:** Medicare Advantage medical policies use the most current Medicare references available at the time the policy was developed. Links to Medicare references will take viewers to external websites outside of the health plan's web control as these sites are not maintained by the health plan.*