MASSACHUSETTS

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Medical Policy

Stem Cell Therapy for Peripheral Arterial Disease

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Policy Number: 348

BCBSA Reference Number: 8.01.55 (For Plans internal use only)
NCD/LCD: NA

Related Policies

- Orthopedic Applications of Stem Cell Therapy, #254
- Progenitor Cell Therapy for the Treatment of Damaged Myocardium due to Ischemia, #652

Policy

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

Treatment of peripheral arterial disease, including critical limb ischemia, with injection or infusion of stem cells from concentrated bone marrow, expanded in vitro, stimulated from peripheral blood, or from an allogeneic source, is considered **INVESTIGATIONAL**.

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.

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.

Description

Peripheral Arterial Disease

Peripheral arterial disease (PAD) is a common atherosclerotic syndrome associated with significant morbidity and mortality.[1,] A less common cause of PAD is Buerger disease (also called thromboangiitis obliterans), which is a nonatherosclerotic segmental inflammatory disease that occurs in younger patients and is associated with tobacco use.[2,] The development of PAD is characterized by narrowing and occlusion of arterial vessels and eventual reduction in distal perfusion. Critical limb ischemia is the end stage of lower-extremity PAD in which severe obstruction of blood flow results in ischemic pain at rest, ulcers, and a significant risk for limb loss.

Physiology

Two endogenous compensating mechanisms may occur with occlusion of arterial vessels: capillary growth (angiogenesis) and development of collateral arterial vessels (arteriogenesis).[3,] Capillary growth is mediated by the hypoxia-induced release of chemokines and cytokines such as vascular endothelial growth factor and occurs by sprouting of small endothelial tubes from preexisting capillary beds. The resulting capillaries are small and cannot sufficiently compensate for a large occluded artery. Arteriogenesis with collateral growth is, in contrast, initiated by increasing shear forces against vessel walls when blood flow is redirected from the occluded transport artery to the small collateral branches, leading to an increase in the diameter of preexisting collateral arterioles.

The mechanism underlying arteriogenesis includes the migration of bone marrow-derived monocytes to the perivascular space. The bone marrow-derived monocytes adhere to and invade the collateral vessel wall. It is not known if the expansion of the collateral arteriole is due to the incorporation of stem cells into the wall of the vessel or to cytokines released by monocytic bone marrow cells that induce the proliferation of resident endothelial cells. It has been proposed that bone marrow-derived monocytic cells may be the putative circulating endothelial progenitor cells. Notably, the same risk factors for advanced

ischemia (diabetes, smoking, hyperlipidemia, advanced age) are also risk factors for a lower number of circulating progenitor cells.

Treatment
Use of autologous stem cells freshly harvested and allogeneic stem cells are reported to have a potential role in the treatment of PAD.[4,] Stem cells can be administered in a variety of routes, derived from different progenitors, and be grouped with different co-factors, many of which are being studied in order to determine the best clinical option for patients. The primary outcome in stem cell therapy trials regulated by the U.S. Food and Drug Administration (FDA) is amputation-free survival, defined as time to major amputation and/or death from any cause. Other outcomes for critical limb ischemia include the Rutherford criteria for limb status, healing of ulcers, the Ankle-Brachial Index (ABI), transcutaneous oxygen pressure, and pain-free walking. The ABI measures arterial segmental pressures on the ankle and brachium and indexes ankle systolic pressure against brachial systolic pressure (normative range, 0.95 to 1.2 mm Hg).

Summary

Peripheral arterial disease (PAD) is a common atherosclerotic syndrome associated with significant morbidity and mortality. Critical limb ischemia (CLI) is the end stage of lower-extremity PAD in which severe obstruction of blood flow results in ischemic pain at rest, ulcers, and a significant risk for limb loss. Use of autologous stem cells freshly harvested and allogeneic stem cells are reported to have a role in the treatment of PAD.

For individuals who have PAD who receive stem cell therapy, the evidence includes small randomized trials and systematic reviews. Relevant outcomes are overall survival, symptoms, change in disease status, morbid events, functional outcomes, quality of life, and treatment-related morbidity. The current literature on stem cells as a treatment for CLI due to PAD consists primarily of phase 2 studies using various cell preparation methods and methods of administration. A meta-analysis of the trials with the lowest risk of bias has shown no significant benefit of stem cell therapy for overall survival, amputation-free survival, or amputation rates. Three randomized controlled trials (RCTs) have been published that used granulocyte-macrophage colony-stimulating factor (GM-CSF)-mobilized peripheral blood mononuclear cells (PBMNC). The route of administration of cell therapy and the primary outcomes differed between studies. In the trial that added cell therapy to guideline-based care, there were no significant differences in progression-free survival and frequency of limb amputation at 1 year of follow-up. There was a substantial rate of subsequent surgical intervention in both arms. Well-designed RCTs with a larger number of subjects and low risk of bias are needed to evaluate the health outcomes of these various procedures. Several are in progress, including multicenter randomized, double-blind, placebo-controlled trials. More data on the safety and durability of these treatments are also needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
3/2024	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2023	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
2/2022	Annual policy review. 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.

3/2018	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
12/2017	Annual policy review. Policy statement updated to describe specific sources of stem cells. Effective 12/1/2017.
3/2016	Annual policy review. New references added.
12/2015	Added coding language.
7/2015	Annual policy review. New references added.
6/2013	Annual policy review. New references added.
5/1/12	New policy describing ongoing non-coverage.

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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