

FEP 8.01.55 Stem Cell Therapy for Peripheral Arterial Disease

Effective Date: July 15, 2018

Related Policies:

2.02.18 Progenitor Cell Therapy for the Treatment of Damaged Myocardium Due to Ischemia
8.01.52 Orthopedic Applications of Stem-Cell Therapy (Including Allograft and Bone Substitute Products Used with Autologous Bone Marrow)

Stem Cell Therapy for Peripheral Arterial Disease

Description

Critical limb ischemia due to peripheral arterial disease results in pain at rest, ulcers, and significant risk for limb loss. Injection or infusion of stem cells, either concentrated from bone marrow, expanded in vitro, stimulated from peripheral blood, or from an allogeneic source, is being evaluated for the treatment of critical limb ischemia.

FDA REGULATORY STATUS

At least 2 devices that provide a point-of-care concentration of bone marrow aspirate have been cleared for marketing by the FDA through the 510(k) process:

- The SmartPreP2® Bone Marrow Aspirate Concentrate System, SmartPreP Platelet Concentration System (Harvest Technologies)
- The MarrowStim™ Concentration Kit and Marrow Stim™ Mini Concentration Kit (Biomet Biologics).

FDA product code: JQC.

Ixmyelocel-T (Aastrom Biosciences now Vericel Corp.) is an expanded stem cell product where bone marrow aspirate is sent to a processing facility to be cultured in a bioreactor and expanded over a 2-week period. The expanded cell population is enriched with mesenchymal precursor cells and alternatively activated macrophages. This product is currently being evaluated in a pivotal phase 3 trial regulated by FDA.

Pluristem Therapeutics is developing allogeneic cell therapy derived from full-term placenta (PLX-PAD cells). This product has been tested in a phase 1 trial in patients with critical limb ischemia.

POLICY STATEMENT

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**.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

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RATIONALE

Summary of Evidence

For individuals who have peripheral arterial disease who receive stem cell therapy, the evidence includes small randomized trials, systematic reviews, and case series. 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 critical limb ischemia due to peripheral arterial disease 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. Well-designed randomized controlled trials 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 the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American Heart Association and American College of Cardiology

The 2016 guidelines from the American Heart Association and American College of Cardiology provided recommendations on the management of patients with lower-extremity peripheral arterial disease (PAD), including surgical and endovascular revascularization for critical limb ischemia (CLI).^{14,15} Stem cell therapy for PAD was not addressed.

European Society of Cardiology

The 2011 European Society of Cardiology guidelines on the diagnosis and treatment of PAD did not recommend for or against stem cell therapy for PAD.¹⁶ However, in 2017, updated guidelines, published in collaboration with the European Society of Vascular Surgery, stated: "Angiogenic gene and stem cell therapy are still being investigated with insufficient evidence in favour of these treatments." The current recommendation is that stem cell/gene therapy is not indicated in patients with chronic limb-threatening ischemia (class of recommendation: III; level of evidence: B).¹⁷

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY

Date	Action	Description
March 2013	New Policy	Treatment of peripheral arterial disease, including critical limb ischemia,

The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.

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September 2013	Update Policy	Policy updated with literature review. References 3, 4, 6, 10, 12, 13, and 15 added, Some reordered. Policy statement unchanged.
September 2014	Update Policy	Policy updated with literature review, references 5, 14 added; policy statement unchanged.
September 2015	Update Policy	Policy updated with literature review, references 4, 9, and 23 added; policy statement unchanged.
June 2018	Update Policy	Policy updated with literature review through November 7, 2017; references 3, 4, 7, 9, 14, 15 and 17 added. Policy statement unchanged.

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