MASSACHUSETTS

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Medical Policy

Progenitor Cell Therapy for the Treatment of Damaged Myocardium Due to Ischemia

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Policy Number: 652

BCBSA Reference Number: 2.02.18 (For Plan internal use only)
NCD/LCD: NA

Related Policies

- Orthopedic Applications of Stem-Cell Therapy, #254
- Stem-cell Therapy for Peripheral Arterial Disease, #348

Policy

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

Progenitor cell therapy, including but not limited to, skeletal myoblasts or hematopoietic stem cells, is **INVESTIGATIONAL** as a treatment of damaged myocardium.

Infusion of growth factors (i.e., granulocyte colony stimulating factor [GCSF]) is **INVESTIGATIONAL** as a technique to increase the numbers of circulating hematopoietic stem cells as treatment of damaged myocardium.

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.

CPT Codes

There is no specific CPT code for this service.

Description

Ischemia

Ischemia is the most common cause of cardiovascular disease and myocardial damage in the developed world. Despite impressive advances in treatment, ischemic heart disease is still associated with high morbidity and mortality. According to the American Heart Association, coronary heart disease has a prevalence of 5.7% among White people, 5.4% among Black people, 8.6% among American Indian/Alaska Native people, and 4.4% among Asian people.[1] For all age strata, the incidence of myocardial infarction is higher in Black males than in Black females, White males, and White females. Heart failure has the highest prevalence among Black males (3.8%) followed by Black females (3.3%), White males (2.9%), Hispanic males (1.8%), Hispanic and White females (both1.6%), Asian males (1.4%), and Asian females (0.5%). Age-adjusted death rates per 100,000 individuals with coronary heart disease and heart failure are higher for Black males and females than their counterparts of other races.

Treatment

Current treatments for ischemic heart disease seek to revascularize occluded arteries, optimize pump function, and prevent future myocardial damage. However, current treatments do not reverse existing heart muscle damage.[2] Treatment with progenitor cells (ie, stem cells) offers potential benefits beyond those of standard medical care, including the potential for repair and/or regeneration of damaged myocardium. Potential sources of embryonic and adult donor cells include skeletal myoblasts, bone marrow cells, circulating blood-derived progenitor cells, endometrial mesenchymal stem cells, adult testis pluripotent stem cells, mesothelial cells, adipose-derived stromal cells, embryonic cells, induced pluripotent stem cells, and bone marrow mesenchymal stem cells, all of which can differentiate into cardiomyocytes and vascular endothelial cells for regenerative medicine advanced therapy (RMAT).[3]The RMAT designation may be given if: (1) the drug is a regenerative medicine therapy (ie, a cell therapy), therapeutic tissue engineering product, human cell and tissue product, or any combination product; (2) the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs.

Summary

Description

Progenitor cell therapy describes the use of multipotent cells of various cell lineages (autologous or allogeneic) for tissue repair and/or regeneration. Progenitor cell therapy is being investigated for the treatment of damaged myocardium resulting from acute or chronic cardiac ischemia and for refractory angina.

Summary of Evidence

For individuals who have acute cardiac ischemia who receive progenitor cell therapy, the evidence includes 2 phase 3 randomized controlled trials (RCTs), numerous small, early-phase RCTs, and meta-analyses of these RCTs. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, quality

of life, and hospitalizations. Limited evidence on clinical outcomes has suggested there may be benefits from improving left ventricular ejection fracion (LVEF), reducing recurrent myocardial infarction (MI), decreasing the need for further revascularization, and perhaps decreasing mortality, although, a recent, large, individual patient data meta-analysis reported no improvement in these outcomes. No adequately powered trial has reported benefits in clinical outcomes (eg, mortality, adverse cardiac outcomes, exercise capacity, quality of life). Overall, this evidence has suggested that progenitor cell treatment may be a promising intervention, but robust data on clinical outcomes are lacking. High-quality RCTs, powered to detect differences in clinical outcomes, are needed to answer this question. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic cardiac ischemia who receive progenitor cell therapy, the evidence includes 1 phase 3 RCT with more than 100 participants, 3 phase 2 RCTs with more than 100 participants, systematic reviews of smaller, early-phase RCTs, and a nonrandomized comparative trial. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, quality of life, and hospitalizations. The studies included in the meta-analyses have reported only on a small number of clinical outcome events. Two phase 2 RCTs (CONCERT-HF and ixCELL-DCM) found significant benefit on heart failure-related death and other cardiac events with cell therapy compared to placebo. Another phase 2 RCT found that cell therapy was safe, but did not impact left ventricular end-systolic volume or secondary quality of life and cardiac outcomes compared to placebo. A well-conducted phase 3 trial failed to demonstrate superiority of cell therapy for its primary composite outcome that included death, worsening heart failure events, and other multiple events. The nonrandomized STAR-Heart trial showed a mortality benefit as well as favorable hemodynamic effect, but a lack of randomization limits interpretation due to the concern about selection bias and differences in known and unknown prognostic variables at baseline between both arms. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have refractory angina who receive progenitor cell therapy, the evidence includes a systematic review of RCTs, phase 2 trials, and a phase 3 pivotal trial. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, quality of life, and hospitalizations. The only phase 3 trial identified was terminated early and insufficiently powered to evaluate clinical outcomes. Additional larger trials are needed to determine whether progenitor cell therapy improves health outcomes in patients with refractory angina. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
7/2024	Annual policy review. Policy updated with literature review through April 8, 2024; guideline updated, and clinical trial added. Policy statements unchanged.
7/2023	Annual policy review. Reference added. Policy statements unchanged.
6/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
7/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2018	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
9/2017	Annual policy review. New references added.
1/2017	Annual policy review. New references added.
8/2015	Annual policy review. New references added.
9/2014	Annual policy review. New references added.

8/2013	Annual policy review. New references added.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
2/2012	Annual policy review. No changes to policy statements.
4/2011	Reviewed - Medical Policy Group - Cardiology and Pulmonology. No changes to policy statements.
9/2010	Annual policy review. Changes to policy statements.
9/2009	Annual policy review. No changes to policy statements.
4/2009	Reviewed - Medical Policy Group - Cardiology and Pulmonology. No changes to policy statements.
9/2008	Annual policy review. No changes to policy statements.
8/2007	Annual policy review. Changes to policy statements.

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

References

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