Medical Coverage Policy | Progenitor Cell Therapy for the Treatment of Damaged Myocardium due to Ischemia

EFFECTIVE DATE: 02|01|2017
POLICY LAST REVIEWED: 07|17|2024

OVERVIEW
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.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
Medicare Advantage Plans
Progenitor cell therapy, including but not limited to skeletal myoblasts or hematopoietic cells, is considered not covered as a treatment of damaged myocardium as the evidence is insufficient to determine the effects of the technology on health outcomes.

Infusion of growth factors (ie, granulocyte colony stimulating factor) is considered not covered as a technique to increase the numbers of circulating hematopoietic cells as treatment of damaged myocardium as the evidence is insufficient to determine the effects of the technology on health outcomes.

Commercial Products
Progenitor cell therapy, including but not limited to skeletal myoblasts or hematopoietic cells, is considered not medically necessary as a treatment of damaged myocardium as the evidence is insufficient to determine the effects of the technology on health outcomes.

Infusion of growth factors (ie, granulocyte colony stimulating factor) is considered not medically necessary as a technique to increase the numbers of circulating hematopoietic cells as treatment of damaged myocardium as the evidence is insufficient to determine the effects of the technology on health outcomes.

COVERAGE
Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable not medically necessity/not covered benefits/coverage.

BACKGROUND
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. 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 (both 1.6%), 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.

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. 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). 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.

For individuals who have acute cardiac ischemia who receive progenitor cell therapy, the evidence includes 2 phase 3 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 maybe benefits from improving LVEF, reducing recurrent 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, exercisecapacity, 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, 2 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. 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.

Regulatory Status

Multiple progenitor cell therapies such as MyoCell® (U.S. Stem Cell, formerly Bioheart), Ixmyelocel-T (Vericel, formerly Aastrom Biosciences), MultiStem® (Athersys), and CardiAMPTM (BioCardia) are being commercially developed, but none has been approved by the U.S. Food and Drug Administration (FDA) so far.

MyoCell comprises patient autologous skeletal myoblasts that are expanded ex vivo and supplied as a cell suspension in a buffered salt solution for injection into the area of damaged myocardium. In 2017, U.S. Stem

Cell reprioritized its efforts away from seeking RMAT designation for MyoCell. The expanded cell product enriched for mesenchymal and macrophage lineages might enhance potency. Vericel has received RMAT designation for Ixmyelocel-T.

MultiStem is an allogeneic bone marrow-derived adherent adult stem cell product that has received RMAT designation.

The CardiAMP Cell Therapy system consists of a proprietary assay to identify patients with a high probability to respond to autologous cell therapy, a proprietary cell processing system to isolate process and concentrate the stem cells from a bone marrow harvest at the point of care, and a proprietary delivery system to percutaneously inject the autologous cells into the myocardium. BioCardia has received an investigational device exemption from the FDA to perform a trial of CardiAMP and is designated as an FDA Breakthrough Device.

CODING

Medicare Advantage Plans and Commercial Products

There are no specific code(s) for this procedure, either describing the laboratory component of processing the harvested autologous cells or for the implantation procedure. Claims should be filed with an unlisted CPT code(s).

RELATED POLICIES

Unlisted Procedures

PUBLISHED

Provider Update, September 2024
Provider Update, August 2023
Provider Update, September 2022
Provider Update, July 2021
Provider Update, January/August 2020

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