Related Policies:
8.01.52 Orthopedic Applications of Stem Cell Therapy (Including Allografts and Bone Substitutes Used With Autologous Bone Marrow)
8.01.55 Stem Cell Therapy for Peripheral Arterial Disease

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

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.

OBJECTIVE
The objective of this evidence review is to determine whether the use of progenitor cell therapy for the treatment of damaged myocardium due to ischemia improves the net health outcome.

POLICY STATEMENT
Progenitor cell therapy, including but not limited to skeletal myoblasts or hematopoietic cells, is considered investigational as a treatment of damaged myocardium.

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Infusion of growth factors (ie, granulocyte colony stimulating factor) is considered investigational as a technique to increase the numbers of circulating hematopoietic cells as treatment of damaged myocardium.

**POLICY GUIDELINES**

There are no specific codes for this procedure, either describing the laboratory component of processing the harvested autologous cells or for the implantation procedure. In some situations, the implantation may be an added component of a scheduled coronary artery bypass graft; in other situations, the implantation may be performed as a unique indication for a cardiac catheterization procedure.

**BENEFIT APPLICATION**

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

**FDA 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 title 21, parts 1270 and 1271. Progenitor cells are included in these regulations. The FDA marketing clearance is not required when autologous cells are processed on site with existing laboratory procedures and injected with existing catheter devices. Several cell products are expanded ex vivo and require FDA approval. The 21st Century Cures Act (December 2016) established new expedited product development programs including 1 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.

Multiple progenitor cell therapies such as MyoCell (U.S. Stem Cell, formerly Bioheart), ixmyelocel-T (Vericel, formerly Aastrom Biosciences), MultiStem (Athensys), and CardiAMP™ (BioCardia) are being commercially developed, but none has been approved by the 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.

Ixmyelocel-T is an expanded multicellular therapeutic product produced from a patient’s bone marrow by selectively expanding bone marrow mononuclear cells for two weeks. 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.

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™.

**RATIONALE**

**Summary of Evidence**

For individuals who have acute cardiac ischemia who receive progenitor cell therapy, the evidence includes two phase 3 RCTs, numerous small, early-phase RCTs, and meta-analyses of these RCTs. The relevant outcomes are disease-specific survival, morbid events, functional outcomes, QOL, and hospitalizations. Limited evidence on clinical outcomes has suggested that there may be 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 (e.g., mortality, adverse cardiac outcomes, exercise capacity, QOL). 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 the effects of the technology on health outcomes.

For individuals who have chronic cardiac ischemia who receive progenitor cell therapy, the evidence includes 2 phase 3 RCTs with more than 100 participants, systematic reviews of smaller, early-phase RCTs, and a nonrandomized comparative trial. The relevant outcomes are disease-specific survival, morbid events, functional outcomes, QOL, and hospitalizations. The studies included in the meta-analyses have reported only on a small number of clinical outcome events. These findings from early phase 2 trials need to be corroborated in larger phase 3 trials. A well-conducted, phase 3 RCT 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 the effects of the technology on health outcomes.

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. The relevant outcomes are disease-specific survival, morbid events, functional outcomes, QOL, 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 the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

The American College of Cardiology Foundation and American Heart Association (2013) issued joint guidelines on the management of ST-segment elevation myocardial infarction. Progenitor cell therapy was not recommended.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

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

REFERENCES


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