FEP Medical Policy Manual

FEP 2.02.18 Progenitor Cell Therapy for the Treatment of Damaged Myocardium due to Ischemia

Effective Date: January 15, 2018

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.

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. 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.

Multiple progenitor cell therapies such as MyoCell® (Bioheart, Sunrise, FL), ixmyelocel-T (Vericel, formerly Aastrom Biosciences), Prochymal® (Osiris) and MultiStem® (Athersys) are being commercially developed. Some have received orphan drug designation but none have been approved by 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.

Ixmyelocel-T (Vericel) is an expanded multicellular therapeutic product produced from a patient’s bone marrow by selectively expanding bone marrow mononuclear cells for 2 weeks. The expanded cell product enriched for mesenchymal and macrophage lineages might enhance potency.

MultiStem® is an allogeneic bone marrow–derived adherent adult stem cell product.
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Prochymal® (Osiris) has received FDA orphan drug designation for treatment of acute graft versus host disease and Type I diabetes. Prochymal® is being studied for use in the treatment of dilated cardiomyopathy.

POLICY STATEMENT

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

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).

RATIONALE

Summary of Evidence

For individuals who have acute cardiac ischemia who receive progenitor cell therapy, the evidence includes 2 randomized controlled trials (RCTs) with 200 patients, numerous small 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 that there may be benefits from improving left ventricular ejection fraction, reducing recurrent myocardial infarction, decreasing the need for further revascularization, and perhaps even 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 the effects of the technology on health outcomes.

For individuals who have chronic cardiac ischemia who receive progenitor cell therapy, the evidence includes a nonrandomized comparative trial, 2 RCTs, and systematic reviews of smaller RCTs. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, quality of life, and hospitalizations. The studies included in the meta-analyses have reported on only a small number of clinical outcome events, too few for meaningful analysis. 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. While a single small RCT has demonstrated a statistically significant 37% relative reduction in total clinical events (death, cardiovascular admission to hospital, or unplanned clinic visits for heart failure) with ixmyelocel-T, the other trial failed to meet its primary composite end point that included death, worsening heart failure events, and other multiple events. These findings from early phase 2 trials need to be corroborated in a larger phase 3 trial. The evidence is insufficient to determine the effects of the technology on health outcomes.
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For individuals who have refractory angina who receive progenitor cell therapy, the evidence includes 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 the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements
In 2013, American College of Cardiology Foundation and American Heart Association issued joint guidelines for 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 (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

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


POLICY HISTORY

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<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>December 2011</td>
<td>New Policy</td>
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<tr>
<td>September 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature search, references added and references reordered; policy statements unchanged.</td>
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<tr>
<td>September 2014</td>
<td>Update Policy</td>
<td>Policy updated with literature review. References 13-14, 22, 27, 32-34, and 39-40 added; policy statements unchanged.</td>
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<tr>
<td>September 2015</td>
<td>Update Policy</td>
<td>Policy updated with literature review; references 12, 29-30, and 33-34 added; references 35-36 deleted. Policy statements unchanged.</td>
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<tr>
<td>December 2017</td>
<td>Update Policy</td>
<td>Policy updated with literature review through June 22, 2017; references 10, 19, and 21-22 added; Rationale revised. Policy statements corrected from “not medically necessary” to “investigational” because products are not approved for marketing for cardiac use by the FDA.</td>
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