

Protocol

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

(20218)

Medical Benefit		Effective Date: 01/01/11	Next Review Date: 07/21
Preauthorization	No	Review Dates: 09/10, 07/11, 07/12, 07/13, 07/14, 07/15, 07/16, 07/17, 07/18, 07/19, 07/20	

This protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

RELATED PROTOCOLS

Orthopedic Applications of Stem Cell Therapy (Including Allograft and Bone Substitute Products Used With Autologous Bone Marrow)

Stem Cell Therapy for Peripheral Arterial Disease

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none">• With acute cardiac ischemia	Interventions of interest are: <ul style="list-style-type: none">• Progenitor cell therapy	Comparators of interest are: <ul style="list-style-type: none">• Standard therapy	Relevant outcomes include: <ul style="list-style-type: none">• Disease-specific survival• Morbid events• Functional outcomes• Quality of life• Hospitalizations
Individuals: <ul style="list-style-type: none">• With chronic cardiac ischemia	Interventions of interest are: <ul style="list-style-type: none">• Progenitor cell therapy	Comparators of interest are: <ul style="list-style-type: none">• Standard therapy	Relevant outcomes include: <ul style="list-style-type: none">• Disease-specific survival• Morbid events• Functional outcomes• Quality of life• Hospitalizations
Individuals: <ul style="list-style-type: none">• With refractory angina	Interventions of interest are: <ul style="list-style-type: none">• Progenitor cell therapy	Comparators of interest are: <ul style="list-style-type: none">• Standard therapy	Relevant outcomes include: <ul style="list-style-type: none">• Disease-specific survival• Morbid events• Functional outcomes• Quality of life• Hospitalizations

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 two phase three 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 fraction, reducing recurrent myocardial infarction, 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, 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 two phase three 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. These findings from early phase two trials need to be corroborated in larger phase three trials. A well-conducted phase three 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 Stem Cell Transplantation in 191 Patients With Chronic Heart Failure (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 two trials, and a phase three pivotal trial. Relevant outcomes are disease-specific survival, morbid events, functional outcomes, quality of life, and hospitalizations. The only phase three 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.

POLICY

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 (i.e., 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

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.

BACKGROUND**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.

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.¹ Treatment with progenitor cells (i.e., 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).² The RMAT designation may be given if: (1) the drug is a regenerative medicine therapy (i.e., 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.

REGULATORY STATUS

Multiple progenitor cell therapies such as MyoCell® (U.S. Stem Cell, formerly Bioheart), ixmyelocel-T (Vericel, formerly Aastrom Biosciences), MultiStem® (Athersys), and CardiAMP™ (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 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.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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