Protocol

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

(20218)

Medical Benefit		**Effective Date**: 01/01/11	**Next Review Date**: 07/15
Preauthorization	No	**Review Dates**: 09/10, 07/11, 07/12, 07/13, 07/14	

The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. ***Preauthorization is not required but is recommended if, despite this Protocol position, you feel this service is medically necessary.*** *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.*

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.

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. Current treatments for ischemic heart disease seek to revascularize occluded arteries, optimize pump function, and prevent future myocardial damage. However, current treatments are not able to reverse existing damage to heart muscle. (1, 2) 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. The potential sources of embryonic and adult donor cells include skeletal myoblasts, bone marrow cells, circulating blood-derived progenitor cells, endometrial mesenchymal stem cells (MSCs), adult testis pluripotent stem cells, mesothelial cells, adipose-derived stromal cells, embryonic cells, induced pluripotent stem cells, and bone marrow MSCs, all of which are able to differentiate into cardiomyocytes and vascular endothelial cells.

The mechanism of benefit following treatment with progenitor cells is not entirely understood. Differentiation of progenitor cells into mature myocytes and engraftment of progenitor cells into areas of damaged myocardium has been suggested in animal studies using tagged progenitor cells. However, there is controversy concerning whether injected progenitor cells actually engraft and differentiate into mature myocytes in humans to a degree that might result in clinical benefit. It has also been proposed that progenitor cells may improve perfusion to areas of ischemic myocardium. Basic science research also suggests that injected stem cells secrete cytokines with anti-apoptotic and pro-angiogenesis properties. Clinical benefit may result if these paracrine factors are successful at limiting cell death from ischemia or stimulating recovery. For example, myocardial protection can occur through modulation of inflammatory and fibrogenic process. Alternatively, paracrine factors might affect intrinsic repair mechanisms of the heart through neovascularization, cardiac metabolism and contractility, increase in cardiomyocyte proliferation, or activation of resident stem and progenitor cells. The relative importance of these proposed paracrine actions will depend on the age of the infarct, e.g., cytoprotective effects with acute ischemia versus cell proliferation with chronic ischemia. Investigation of the specific factors that are induced by administration of progenitor cells is ongoing.

There are also a variety of potential delivery mechanisms for donor cells, encompassing a wide range of

invasiveness. Donor cells can be delivered via thoracotomy and direct injection into areas of damaged myocardium. Injection of progenitor cells into the coronary circulation can also be done using percutaneous, catheter-based techniques. Finally, progenitor cells can be delivered intravenously via a peripheral vein. With this approach, the cells must be able to target damaged myocardium and concentrate at the site of myocardial damage.

Adverse effects of treatment with progenitor cells include the risk of the delivery procedure (e.g., thoracotomy, percutaneous catheter-based, etc.) and the risks of the donor cells themselves. Donor progenitor cells can differentiate into fibroblasts rather than myocytes. This may create a substrate for malignant ventricular arrhythmias. There is also a theoretical risk that tumors, such as teratomas, can arise from progenitor cells, but the actual risk in humans is currently unknown.

Regulatory Status

U.S. Food and Drug Administration (FDA) approval is not required in situations in which autologous cells are processed on site with existing laboratory procedures and injected with existing catheter devices. However, there are several products that require FDA approval. MyoCell™ (BioHeart, Inc., Sunrise, FL) consists of 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. MyoCell SDF-1 (BioHeart, Inc.) is similar to MyoCell®, but before injection, myoblast cells are genetically modified to release excess stromal-derived factor (SDF)-1. Increased SDF-1 levels at the site of myocardial damage may accelerate recruitment of native stem cells to increase tissue repair and neovascularization. For both products, myoblast isolation and expansion occurs at a single reference laboratory (BioHeart), both products are therefore subject to FDA approval. Currently, neither product is FDA-cleared. Implantation may require the use of a unique catheter delivery system (MyoCath™) that is FDA-cleared.

An allogeneic human mesenchymal stem cell (hMSC) product (Prochymal®) is being developed by Osiris Therapeutics, Inc. (Baltimore, MD) for treatment of acute myocardial infarction (MI). (3) Prochymal (also referred to as Provacel®) is a highly purified preparation of ex vivo cultured adult hMSCs isolated from the bone marrow of healthy young adult donors. Prochymal has been granted “fast track” status by the FDA for Crohn’s disease and graft-versus-host disease (GVHD), and has orphan drug status for GVHD from the FDA and the European Medicines Agency. Prochymal is being studied in Phase II trials for the treatment of acute MI (AMI), pulmonary disease, and type 1 diabetes.

MultiStem® (Athersys) is an allogeneic bone marrow-derived adherent adult stem-cell product. MultiStem has received orphan drug status from the FDA for GVHD and has received authorization from the FDA for a Phase II trial for treatment of acute myocardial infarction with an adventitial delivery system.

Related Protocols

Orthopedic Applications of Stem-Cell Therapy

Stem-cell Therapy for Peripheral Arterial Disease

Policy (Formerly Corporate Medical Guideline)

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

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

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