Corporate Medical Policy

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

File Name: progenitor_cell_therapy_for_the_treatment_of_damaged_myocardium_due_to_ischemia
Origination: 11/2004
Last Review: 10/2023

Description of Procedure or Service

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. 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 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.

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 have been approved by the FDA so far.

MyoCell® 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. 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® (Athersys) is an allogeneic bone marrow-derived adherent adult stem cell product that has received RMAT designation.

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.

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

Related Policies:
Orthopedic Applications of Stem Cell Therapy
Stem Cell Therapy for Peripheral Arterial Disease

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Progenitor cell therapy (including but not limited to skeletal myoblasts or hematopoietic stem cells) for the treatment of damaged myocardium is considered investigational. BCBSNC does not provide coverage for investigational services.

Infusion of growth factors (i.e., granulocyte colony stimulating factor) is considered investigational as a technique to increase the numbers of circulating hematopoietic stem cells as treatment of damaged myocardium. BCBSNC does not provide coverage for investigational services.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Progenitor Cell Therapy for the Treatment of Damaged Myocardium is covered

Not Applicable

When Progenitor Cell Therapy for the Treatment of Damaged Myocardium is not covered

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Policy Guidelines

For individuals who have acute cardiac ischemia who receive progenitor cell therapy, the evidence includes 2 phase 3 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 suggests that there may be benefits in improving left ventricular ejection fraction, reducing recurrent MI, 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 outcome, such as mortality, adverse cardiac outcomes, exercise capacity, or 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 with 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. Studies included in the meta-analyses reported only 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 and receive progenitor cell therapy, evidence includes a systemic 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 not sufficiently powered to evaluate clinical outcomes. Additional larger trials are needed to determine whether progenitor cell therapy improved 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.

In 2015, the American College of Cardiology Foundation, American Heart Association, and the Society for Cardiovascular Angiography and Interventions issued a Focused Update on Primary Percutaneous Coronary Interventions for Patients With ST-Elevation Myocardial Infarction. This guideline was an update of the 2011 guideline for percutaneous coronary intervention, and the 2013 guideline on managing ST-elevation myocardial infarction. In 2021, these same organizations published a guideline on coronary artery revascularization. Progenitor cell therapy was not mentioned in any of these guidelines.

The most recent guidelines on treatment of heart failure with reduced ejection fraction from the American College of Cardiology (2021) and American Heart Association/American College of Cardiology/Heart Failure Society of America (2022) do not mention progenitor cell therapy.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: *There is currently no specific CPT code for either 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 (CABG). In other situations, the implantation may be performed as a unique indication for a cardiac catheterization procedure. Services should be submitted in the form of an appropriate unlisted code. Medical records for the explanation of the service rendered may be necessary.*

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BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

For Policy titled Autologous Cell Therapy for the Treatment of Damaged Myocardium

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.02.18, 4/16/04.

Specialty Matched Consultant Advisory Panel - 11/05.

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Pagani FD, DerSimonian H, Zawadska A, Wetzel K, Edge AS, Jacoby DB, et al. Autologous Skeletal Myoblasts Transplanted to Ischemia-Damaged Myocardium in Humans. J Am Coll Cardiol. 2003; 41: 879-88.

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Fisher SA, Brunskill SJ, Doree C et al. Stem cell therapy for chronic ischaemic heart disease and congestive heart failure. Cochrane Database Syst Rev 2014; 4:CD007888.

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Specialty Matched Consultant Advisory Panel review 11/2014.

Senior Medical Director review 11/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.02.18, 6/11/15

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Specialty Matched Consultant Advisory Panel review 10/2022

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Specialty Matched Consultant Advisory Panel review 10/2023

Medical Director review 10/2023

Policy Implementation/Update Information

For Policy titled Autologous Cell Therapy for the Treatment of Damaged Myocardium

11/11/04 New policy issued. Autologous cell therapy for the treatment of damaged myocardium is considered investigational. References added. Notification 11/11/04. Effective 01/20/05.

11/17/05 Specialty Matched Consultant Advisory Panel review 11/7/05.

11/19/07 Information regarding MyoCell and MyoCath deleted from the Description section. Revised information in Policy Guidelines section to support continued investigational status. References updated. Specialty Matched Consultant Advisory Panel review meeting 10/29/07. No change in policy statement. (adn)

12/7/09 Description section extensively revised. Policy Guidelines section updated to reflect findings from BCBSA TEC Assessment. References updated. Specialty Matched

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Consultant Advisory Panel review 10/30/09. Policy status changed to Active Archive, no longer scheduled for routine literature review. (adn)

6/22/10 Policy Number(s) removed. (amw)

Policy re-titled to Progenitor Cell Therapy for the Treatment of Damaged Myocardium Due to Ischemia

5/1/12 Policy status changed to active and will undergo routine literature review. Policy re-titled from "Autologous Cell Therapy for the Treatment of Damaged Myocardium" to "Progenitor Cell Therapy for the Treatment of Damaged Myocardium Due to Ischemia." Description section updated. Policy Guidelines updated. References updated. Medical Director review 4/2012.

8/21/12 Policy Guidelines updated. References updated. Medical Director review 7/2012. No changes to Policy Statements. (mco)

11/13/12 Specialty Matched Consultant Advisory Panel review 10/2012. No changes to Policy Statements. (mco)

7/30/13 Description section updated. References updated. No changes to Policy Statements. (mco)

11/12/13 Specialty Matched Consultant Advisory Panel review 10/2013. No changes to Policy Statements. (mco)

8/12/14 References updated. Policy Guidelines and Description section updated. No changes to Policy Statements. (mco)

1/13/15 References updated. Specialty Matched Consultant Advisory Panel review 11/2014. Senior Medical Director review 11/2014. No change to Policy statements. (td)

7/28/15 Policy Guidelines updated. References updated. Policy Statement remains unchanged. (td)

12/30/15 References updated. Specialty Matched Consultant Advisory Panel review 10/29/2015. Medical Director review 10/2015. (td)

11/22/16 Specialty Matched Consultant Advisory Panel review 10/2016. Medical Director review 10/2016. (jd)

1/27/17 Regulatory Status section added to distinguish FDA regulations. Policy Guidelines and references updated. Medical Director review 12/2016. (jd)

9/15/17 Description section and Policy Guidelines updated. No change to policy intent. References updated. Medical Director review 8/2017. (jd)

11/10/17 Specialty Matched Consultant Advisory Panel review 10/2017. Medical Director review 10/2017. (jd)

6/8/18 Regulatory status updated with the 21st Century Cures Act and CardiAMP Cell Therapy system. Policy guidelines and references updated. Medical Director review 5/2018. (jd)

11/9/18 Specialty Advisory Consultant Advisory Panel review 10/2018. Medical Director review 10/2018. (jd)

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10/29/19 References updated. Specialty Advisory Consultant Advisory Panel review 10/2019. Medical Director review 10/2019. (jd)

11/10/20 Description section and regulatory status extensively revised. No change to policy intent. References updated. Specialty Advisory Consultant Advisory Panel review 10/2020. Medical Director review 10/2020. (jd)

11/2//21 References updated. Specialty Advisory Consultant Advisory Panel review 10/2021. Medical Director review 10/2021. (jd)

11/1/22 Description section, Policy Guidelines and References updated. No change to policy statement. Specialty Advisory Consultant Advisory Panel review 10/2022. Medical Director review 10/2022. (tm)

11/7/23 Policy Guidelines and References updated. Specialty Advisory Consultant Advisory Panel review 10/2023. Medical Director review 10/2023. (tm)

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