

Corporate Medical Policy

Orthopedic Applications of Stem Cell Therapy

File Name: orthopedic_applications_of_stem_cell_therapy
Origination: 7/2010
Last CAP Review: 2/2012
Next CAP Review: 2/2013
Last Review: 2/2012

Description of Procedure or Service

Mesenchymal stem cells (MSCs) have the capability to differentiate into a variety of tissue types, including various musculoskeletal tissues. Potential uses of MSCs for orthopedic applications include treatment of damaged bone, cartilage, ligaments, tendons and intervertebral discs.

Background

MSCs are multipotent cells (also called stromal multipotent cells) that possess the ability to differentiate into various tissues including organs, trabecular bone, tendon, articular cartilage, ligaments, muscle and fat. MSCs are associated with the blood vessels within bone marrow, synovium, fat and muscle, where they can be mobilized for endogenous repair as occurs with healing of bone fractures.

Stimulation of endogenous MSCs is the basis of procedures such as bone marrow stimulation (e.g., microfracture) and harvesting/grafting of autologous bone for fusion. Bone marrow aspirate is considered to be the most accessible source and thus the most common place to isolate MSCs for treatment of musculoskeletal disease. However, harvesting MSCs from bone marrow requires an additional procedure that may result in donor site morbidity. In addition, the number of MSCs in bone marrow is low, and the number and differentiation capacity of bone marrow derived MSCs decreases with age, limiting their efficiency when isolated from older patients.

Tissues such as muscle, cartilage, tendon, ligaments and vertebral discs show limited capacity for endogenous repair. Therefore, tissue engineering techniques are being developed to improve the efficiency of repair or regeneration of damaged musculoskeletal tissues. Tissue engineering focuses on the integration of biomaterials with MSCs and/or bioactive molecules such as growth factors. In vivo, the fate of stem cells is regulated by signals in the local 3-dimensional microenvironment from the extracellular matrix and neighboring cells. It is believed that the success of tissue engineering with MSCs will also require an appropriate 3-dimensional scaffold or matrix, culture conditions for tissue specific induction and implantation techniques that provide appropriate biomechanical forces and mechanical stimulation.

The ability to induce cell division and differentiation without adverse effects, such as the formation of neoplasms, remains a significant concern. Given that each tissue type requires different culture conditions, induction factors (signaling proteins, cytokines, growth factors, etc.) and implantation techniques, each preparation must be individually examined.

The U.S. Food and Drug Administration (FDA) has stated that cell-based therapies are one of the most rapidly advancing approaches intended to repair, replace, restore, or regenerate cells, tissues and organs. They can be applied to damage caused by disease, injury, or aging. Many cell-based therapies use immature cells (stem cells) that are expanded outside of the body. The expanded cells

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are sometimes used in their immature state, but they are often manufactured into more mature cells before they are given to a patient. The resulting cells are intended to repair cell or tissue damage without unintended serious consequences such as tumors, severe immune reactions, or unwanted tissue development. Manufacturing of large numbers of cells outside the natural environment of the human body may lead to ineffective or dangerous cells, so it is important to understand and carefully control the production process and to define measures that reliably predict safety and efficacy of the cellbased products.

No products using engineered MSCs have been approved by the FDA for orthopedic applications.

******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

Mesenchymal stem cell therapy is considered investigational for all orthopedic applications, including use in repair or regeneration of musculoskeletal tissue. BCBSNC does not cover investigational services or procedures.

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 Orthopedic Applications of Stem Cell Therapy is covered

Not Applicable

When Orthopedic Applications of Stem Cell Therapy is not covered

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Policy Guidelines

In a literature search of the MEDLINE database through January 2012, use of cultured MSCs in humans was identified in only a few centers (U.S. and Asia). At this time, the literature consists almost entirely of review articles describing the potential of stem cell therapy for orthopedic applications in humans, along with basic science experiments on sources of mesenchymal stem cells (MSCs), regulation of cell growth and differentiation and development of scaffolds.

Overall, the literature suggests a technology that is at a very early stage of development, with the vast majority of studies focused on development of methods for tissue engineering along with preliminary testing in animal models. Current evidence on procedures using autologous bone marrow derived MSCs is insufficient to evaluate health outcomes. In addition, MSCs for orthopedic applications are not FDA approved.

There are on-going clinical trials to evaluate this technology including Trinity® Evolution, Cartistem®, Chondrogen™, AlloStem Stem Cell Bone Growth Substitute, and Regenexx™.

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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 codes: 38206, 38230, 38241

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

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.52, 4/08/10

U.S. Food and Drug Administration (FDA), Assuring Safety and Efficacy of Stem Cell Based Products, Retrieved 5/03/10 from <http://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/BiologicsResearchAreas/ucm127182.htm>

Centeno CJ, Schultz JR, et al., Safety and complications reporting on the re-implantation of culture-expanded mesenchymal stem cells using autologous platelet lysate technique, Current Stem Cell Research and Therapy, 2010 (5) Retrieved on 5/03/10 from <http://www.ingentaconnect.com/content/ben/cscr/2010/00000005/00000001/art00011>

Wakitani S, Nawata , et al., Repair of articular cartilage defects in the patello-femoral joint with autologous bone marrow mesenchymal cell transplantation: three case reports involving nine defects in five knees. J Tissue Eng Regen Med 2007; 1(1):74-9. Abstract Retrieved on 5/03/10 from <http://www.ncbi.nlm.nih.gov/pubmed/18038395>

American Academy of Orthopaedic Surgeons. Stem cells and orthopaedics. Your Orthopaedic Connection 2007; Reviewed on February 1, 2012 from <http://orthoinfo.aaos.org/topic.cfm?topic=A00501>

Senior Medical Director review 5/2010

National Institute of Health (NIH). Trinity® Evolution in Anterior Cervical Disectomy and Fusion. NCT00951938. Reviewed on February 1, 2012 from <http://clinicaltrials.gov/ct2/show/NCT00951938>

National Institute of Health (NIH). Evaluation of Trinity® Evolution in Patients Undergoing Ankle Fusion. NCT00988338. Reviewed on February 1, 2012 from <http://clinicaltrials.gov/ct2/show/NCT00988338>

Specialty Matched Consultant Advisory Panel review 2/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.52, 4/14/11

National Institute of Health (NIH). Follow-up Study of Chondrogen® Delivered by Intra-Articular Injection Following Meniscectomy. NCT 00702741. Reviewed February 1, 2012 from

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<http://clinicaltrials.gov/ct2/show/NCT00702741>

National Institute of Health (NIH). Study to Compare the Efficacy and Safety of Cartistem® and Microfracture in Patients With Knee Articular Cartilage Injury or Defect. NCT 01041001. Reviewed February 1, 2012 from <http://clinicaltrials.gov/ct2/show/NCT01041001>

Medical Director review 6/2011

Specialty Matched Consultant Advisory Panel review 2/2012

Policy Implementation/Update Information

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| 7/6/10 | New Medical Policy implemented. Mesenchymal stem cell therapy is considered investigational for all orthopedic applications, including use in repair or regeneration of musculoskeletal tissue. (mco) |
| 8/31/10 | Policy Guideline section updated with clinical trial and product information. References updated. (mco) |
| 3/15/11 | Specialty Matched Consultant Advisory Panel review 2/2011. Added new product titled, “AlloStem Stem Cell Bone Growth Substitute” in the Policy Guidelines section. (mco) |
| 6/21/11 | Medical Director review 6/2011. References updated. No changes to policy statements. (mco) |
| 3/20/12 | Specialty Matched Consultant Advisory Panel review 2/2012. References update. Policy Guidelines updated. (mco) |

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.