GUIDELINES
This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder contract. Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards. This guideline is solely for explaining correct procedure reporting and does not imply coverage and reimbursement.

DESCRIPTION
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. The proposed benefits of MSC therapy are improved healing and possible avoidance of surgical procedures with protracted recovery times.

MSCs are multipotent stem cells that express a variety of different cell surface proteins and can differentiate into a variety of cell types, such as osteoblasts, chondrocytes, myocytes, adipocytes, and neuronal cells. Although processing techniques vary, and the optimal number of MSCs to be transplanted/seeded has not been established, following autologous bone marrow collection MSCs are either concentrated for direct injection, or cultured and incubated. Once cultured the MSCs can be mixed with biomaterials, such as gels or pastes; the biomaterials hold the cells in suspension and provide a matrix for filling defects. MSCs can also be seeded on scaffolds, and have been investigated when used with a support matrix for implantation (e.g., tissue engineered). In theory, MSCs are responsive to osteogenic growth factors and aid in the healing of bone. Nevertheless evidence in the published peer-reviewed scientific literature evaluating the use of MSCs to enhance bone healing consists mainly of animal trials and a paucity of human trials. At present the evidence is insufficient to support improved clinical outcomes, when used alone, added to other biomaterials, or as cultured/seeded on a support matrix.

The concentrated autologous MSC products are not regulated by the U.S. Food and Drug Administration (FDA). Currently there are no allogeneic MSC therapies or devices that are approved for marketing by the FDA. However, there are products containing mesenchymal stem cells that are commercially available for orthopedic indications, which include:

- **AlloStem® Cellular Bone Allograft (AlloSource, Centennial, CO):** Comprised of adipose derived mesenchymal stem cells with partially demineralized allograft bone.
- **NuCel® (NuTech Medical, Birmingham, AL):** Derived from amniotic membrane.
- **Map3™ (rti surgical):** Contains cortical cancellous bone chips, DBM, and multipotent adult progenitor cells.
- **Osteocell Plus® (NuVasive):** DBM combined with viable MSCs that have been isolated from allogeneic bone marrow.
- **Trinity Evolution Matrix™ (Orthofix):** DBM combined with viable MSCs that have been isolated from allogeneic bone marrow.
- **Cellentra™ VCBM (Biomet®):** An allograft that is cryopreserved containing MSCs, osteoprogenitor cells, and pre-osteoblasts.
- **RegenexxSD® (Same Day Stem Cell Procedure):** A procedure involving autologous bone marrow that is concentrated and a super-platelet mix is added and the final product is injected into the affected site.
- **RegenexxAD® (Adipose Derived Stem Cell Procedure):** A procedure that combines RegenexxSD with stem cells derived from adipose tissue, the final product is then injected into an affected site.

The evidence for stem cell therapy in individuals who have various orthopedic conditions (cartilage defects, meniscectomy, spinal fusion procedures, osteonecrosis) includes small randomized controlled trials and nonrandomized comparative trials. Relevant outcomes are symptoms, morbid events, functions outcomes, quality of life, and treatment-related morbidity. Use of MSCs for orthopedic conditions is an active area of research. Despite continued research into methods of harvesting and delivering treatment, there are uncertainties regarding the optimal source of cells and the delivery method. Studies have included MSCS from bone marrow, adipose tissue, peripheral blood, and synovial tissue. The largest body of evidence is on the use of autologous MSCs, either concentrated or expanded in culture, for cartilage repair. This evidence includes small randomized and nonrandomized comparative trials with insufficient data to evaluate health outcomes. In addition, expanded MSCs for orthopedic applications are not U.S. Food and Drug Administration (FDA) approved (concentrated autologous...
MSCs do not require FDA approval). Overall, there is lack of evidence that clinical outcomes are improved. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

Mesenchymal stem cell therapy (including but not limited to Regenexx Procedure) for all orthopedic indications is non-covered.

Refer to PG0293 Platelet Rich Plasma (0232T, G0460, S9055) for coverage determination.
Refer to PG0365 Bone Graft Substitutes for coverage determination.

HMO, PPO, Individual Marketplace, Elite, Advantage
Mesenchymal stem cell therapy is considered investigational and not medically necessary for all orthopedic indications.

Use of stem cells for orthopedic applications is considered investigational due to the lack of evidence that clinical outcomes are improved and the lack of regulatory approval. In addition, expanded MSCs for orthopedic applications are not Food and Drug Administration (FDA) approved (concentrated autologous MSCs do not require FDA approval).

CODING/BILLING INFORMATION
The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

CPT CODES

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<tr>
<th>Code</th>
<th>Description</th>
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<tr>
<td>38205</td>
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<td>38206</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous</td>
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<td>38212</td>
<td>Transplant preparation of hematopoietic progenitor cells; red blood cell removal</td>
</tr>
<tr>
<td>38215</td>
<td>Transplant preparation of hematopoietic progenitor cells; cell concentration in plasma, mononuclear or buffy coat layer</td>
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<tr>
<td>38230</td>
<td>Bone marrow harvesting for transplantation; allogeneic</td>
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<td>38232</td>
<td>Bone marrow harvesting for transplantation; autologous</td>
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<td>38240</td>
<td>Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor</td>
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<tr>
<td>38241</td>
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TAWG REVIEW DATES: 07/22/2016 (per PG0365 Bone Graft Substitutes), 04/21/2017

REVISION HISTORY EXPLANATION
04/21/17: Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

REFERENCES/RESOURCES
Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services
Ohio Department of Medicaid [http://ifs.ohio.gov/](http://ifs.ohio.gov/)
American Medical Association, Current Procedural Terminology (CPT®) and associated publications and services
Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets
Industry Standard Review
Hayes, Inc.