



Allograft Injection for Degenerative Disc Disease

Policy # 00750

Original Effective Date: 11/01/2021

Current Effective Date: 11/11/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Artificial Intervertebral Disc: Lumbar Spine is addressed separately in medical policy 00145.

Note: Orthopedic Applications of Stem Cell Therapy (Including Allograft and Bone Substitute Products Used With Autologous Bone Marrow) is addressed separately in medical policy 00258.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers injection of allograft (e.g., VIA Disc Matrix) into the intervertebral disc for the treatment of degenerative disc disease to be **investigational**.*

Background/Overview

Degenerative Disc Disease

Back pain is a common condition in adults. Most episodes of back pain are self-limited and will resolve within 1 month, but a small percentage will persist and become chronic. Chronic back pain can arise from a variety of etiologies including musculoskeletal pain, vertebral compression fractures, spinal stenosis, disc herniation, or other degenerative changes to the disc that compress the nerve roots and lead to radiculopathy. Age-related degeneration of the intervertebral discs is common and includes numerous biochemical and morphologic changes; the most common of which is loss of glycosaminoglycan and associated loss in water content. Pro-inflammatory molecules increase, while endplate calcification impairs nutrient flow. Together, these lead to an increase in cell death in the nucleus pulposus. Although degenerative changes to the disc are frequently observed on imaging, their contribution to back pain in the absence of radiculopathy is uncertain. Spine imaging, such as magnetic resonance imaging, computed tomography, or plain radiography, shows that lumbar disc degeneration is widespread, but for most people does not cause symptoms. Because

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many degenerative changes of the disc that are seen on imaging are asymptomatic, identifying the source of the back pain is challenging.

Treatment

Conservative management of back pain is the first-line treatment for most patients. Nonsteroidal anti-inflammatory drugs or other analgesics are used for symptom relief. Duloxetine or tramadol are recommended second-line pharmacologic therapies by the American College of Physicians. Additionally, modification of activity in conjunction with some form of exercise therapy is frequently prescribed early in the course of symptoms. For patients with persistent nonradicular back pain, guidelines recommend interdisciplinary rehabilitation, which is defined as an integrated approach using physical rehabilitation in conjunction with a psychological or psychosocial intervention. Opioids may also be prescribed. Although spinal fusion surgery is frequently performed for non-specific back pain with degenerative changes to the disc, surgery has not been shown to be more effective than comprehensive conservative treatment. Cell therapy is being explored as a method to regenerate the intervertebral disc by rehydration, height restoration, and repopulating native cells.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

VIA Disc Matrix (Vivex Biomedical) is composed of human disc tissue donated from cadavers with viable cells. It consists of a nucleus pulposus allograft suspension that is mixed with a minimum of 6×10^6 cryopreserved cells. The cell source and method of processing has not been disclosed, and it is not clear if VIA Disc Matrix meets the U.S. Food and Drug Administration (FDA) criteria for what is considered minimal manipulation and homologous use for human cells, tissues, and cellular and tissue-based products (HCT/Ps).

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, Title 21, parts 1270 and 1271. In 2017, the FDA published clarification of HCT/Ps, which was then updated in 2020.

HCT/Ps are defined as human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. If an HCT/P does not meet the criteria below and does

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not qualify for any of the stated exceptions, the HCT/P will be regulated as a drug, device, and/or biological product and applicable regulations and premarket review will be required.

An HCT/P is regulated solely under section 361 of the Public Health Service (PHS) Act and Title 21 Code of Federal Regulations (CFR) Part 1271 if it meets all of the following criteria:

1. "The HCT/P is minimally manipulated;
2. The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;
3. The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P; and
4. Either:
 1. The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
 2. The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and:
 1. Is for autologous use
 2. Is for allogeneic use in a first-degree or second-degree blood relative; or
 3. Is for reproductive use"

Rexlemestrocel-L (MPC-06-ID, Mesoblast) is an allogeneic mesenchymal precursor cell (MPC) therapy under investigation for the treatment of chronic low back pain caused by disc degeneration in individuals "who have exhausted conservative treatment options, may have failed epidural steroid injections and have no further treatment option other than invasive and costly surgical intervention." Amirdelfan et al (2021) published results of a multicenter, randomized, controlled study of rexlemestrocel-L in 100 individuals with degenerative disc disease (NCT01290367). Additionally, in July of 2021, Mesoblast completed a larger Phase 3 randomized, double-blind, placebo-controlled trial of rexlemestrocel-L in 404 individuals with degenerative disc disease with 36 months of follow-up (NCT02412735). Although this trial is not yet published, it has been reviewed by FDA's Office of Tissues and Advanced Therapies (OTAT). Based on FDA OTAT feedback, as part of their market approval application, Mesoblast plans to conduct an additional US Phase 3 trial with pain reduction at 12 months as the primary endpoint.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Degeneration of the intervertebral discs is commonly observed in imaging and has been proposed to be a source of back pain. In order to treat the observed changes in the discs, cellular therapies such as mesenchymal stem cells are being studied. One of these cellular therapies involves the intradiscal injection of a mixture of nucleus pulposus allograft and viable cells into the degenerated disc.

Summary of Evidence

For individuals with degenerative disc disease who receive a viable allograft injection, the evidence includes 12-month results from an RCT. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Results from the first 12 months of the planned 36 months of follow-up did not find statistically significant differences between the active allograft, placebo allograft, and conservative management groups on the co-primary pain and disability endpoints. However, the proportion of treatment responders was significantly greater in the active allograft group on some, but not all pain and disability response outcomes. Given the various important comparator and outcome relevance, data completeness, and power limitations, evidence from well-conducted trials demonstrating consistent improvements in health outcomes is still needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or the National Institute for Health and Care Excellence (NICE). Priority will be

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given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Physicians

In 2017, the American College of Physicians recommended that "For patients with chronic low back pain, clinicians and patients should initially select nonpharmacologic treatment with exercise, multidisciplinary rehabilitation, acupuncture, mindfulness-based stress reduction (moderate-quality evidence), tai chi, yoga, motor control exercise, progressive relaxation, electromyography biofeedback, low-level laser therapy, operant therapy, cognitive behavioral therapy, or spinal manipulation. (Grade: strong recommendation, low-quality evidence).

In patients with chronic low back pain who have had an inadequate response to nonpharmacologic therapy, clinicians and patients should consider pharmacologic treatment with nonsteroidal anti-inflammatory drugs as first-line therapy, or tramadol or duloxetine as second-line therapy. Clinicians should only consider opioids as an option in patients who have failed the aforementioned treatments and only if the potential benefits outweigh the risks for individual patients and after a discussion of known risks and realistic benefits with patients. (Grade: weak recommendation, moderate-quality evidence)."

North American Spine Society et al

In 2020, the North American Spine Society, along with 9 other societies, published multidisciplinary evidence-based guidelines on the diagnosis and treatment of low back pain. There were 82 clinical questions that were addressed in the comprehensive evidence review. Regarding degenerative disc disease, the guideline gave a grade A recommendation that provocative discography without manometric measurements correlates with both pain reproduction in the presence of moderate to severe disc degeneration on MRI/CT [magnetic resonance imaging/computed tomography] discography and with the presence of endplate abnormalities on MRI imaging. There was insufficient evidence to make a recommendation for or against the use of intradiscal bone marrow concentrate in patients with discogenic low back pain, and no review of intradiscal allograft injection.

U.S. Preventive Services Task Force Recommendations

Not applicable.

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Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Unpublished</i>			
NCT02412735 ^a	A Prospective, Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of a Single Injection of Rexlemestrocel-L Alone or Combined With Hyaluronic Acid (HA) in Subjects With Chronic Low Back Pain	404	Jun 2021

NCT: national clinical trial.
^a Denotes industry-sponsored or cosponsored trial.

References

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2. U.S. Food and Drug Administration. Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use Guidance for Industry and Food and Drug Administration Staff. 2020. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/regulatory-considerations-human-cells-tissues-and-cellular-and-tissue-based-products-minimal>.



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4. Amirdelfan K, Bae H, McJunkin T, et al. Allogeneic mesenchymal precursor cells treatment for chronic low back pain associated with degenerative disc disease: a prospective randomized, placebo-controlled 36-month study of safety and efficacy. *Spine J.* Feb 2021; 21(2): 212-230. PMID 33045417
5. Mesoblast. Single Dose of Mesoblast's Allogeneic Cell Therapy Provides Durable Pain Reduction for At Least Three Years in Patients with Degenerative Disc Disease: Global Newswire. January 11, 2022. <https://www.globenewswire.com/news-release/2022/01/12/2365313/0/en/Single-Dose-of-Mesoblast-s-Allogeneic-Cell-Therapy-Provides-Durable-Pain-Reduction-for-at-Least-Three-Years-in-Patients-With-Degenerative-Disc-Disease.html>
6. Katz NP, Paillard FC, Ekman E. Determining the clinical importance of treatment benefits for interventions for painful orthopedic conditions. *J Orthop Surg Res.* Feb 03 2015; 10: 24. PMID 25645576
7. Parker SL, Mendenhall SK, Shau DN, et al. Minimum clinically important difference in pain, disability, and quality of life after neural decompression and fusion for same-level recurrent lumbar stenosis: understanding clinical versus statistical significance. *J Neurosurg Spine.* May 2012; 16(5): 471-8. PMID 22324801
8. Beall DP, Wilson GL, Bishop R, et al. VAST Clinical Trial: Safely Supplementing Tissue Lost to Degenerative Disc Disease. *Int J Spine Surg.* Apr 2020; 14(2): 239-253. PMID 32355632
9. Beall DP, Davis T, DePalma MJ, et al. Viable Disc Tissue Allograft Supplementation; One- and Two-level Treatment of Degenerated Intervertebral Discs in Patients with Chronic Discogenic Low Back Pain: One Year Results of the VAST Randomized Controlled Trial. *Pain Physician.* Sep 2021; 24(6): 465-477. PMID 34554689
10. North American Spine Society. Evidence-based clinical guidelines for multidisciplinary spine care: Diagnosis and treatment of low back pain. 2020. <https://www.spine.org/Portals/0/assets/downloads/ResearchClinicalCare/Guidelines/LowBackPain.pdf>.

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08/05/2021 Medical Policy Committee review
08/11/2021 Medical Policy Implementation Committee approval. New policy.
10/06/2022 Medical Policy Committee review
10/11/2022 Medical Policy Implementation Committee approval. No change to coverage.
10/05/2023 Medical Policy Committee review
10/11/2023 Medical Policy Implementation Committee approval. No change to coverage.
10/03/2024 Medical Policy Committee review
10/08/2024 Medical Policy Implementation Committee approval. No change to coverage.
Next Scheduled Review Date: 10/2025

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)®, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	0627T, 0628T, 0629T, 0630T
HCPCS	No codes
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

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