



Louisiana

Adipose-Derived Stem Cells in Autologous Fat Grafting to the Breast

Policy # 00493

Original Effective Date: 02/17/2016

Current Effective Date: 03/09/2020

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.

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 the use of adipose-derived stem cells (ADSCs) in autologous fat grafting to the breast to be **investigational**.*

Background/Overview

Fat Grafting to the Breast

Autologous fat grafting to the breast has been proposed for indications that include breast augmentation following oncologic surgery. Grafting would be performed as an adjunct to reconstruction after mastectomy or lumpectomy, and it would be of benefit in the following areas: for contouring purposes, improving breast shape and volume; and for alleviating post mastectomy pain syndrome (neuropathic pain) and irradiated skin (thereby reducing complication and failure rates of implant reconstruction). Variability in long-term results and oncologic concerns have limited application of autologous fat grafting in the breast.

This evidence review does not address the use of autologous fat tissue in aesthetic breast augmentation (ie, cosmesis).

Adipose-Derived Stem Cells

Stem cell biology, and the related field of regenerative medicine involves multipotent stem cells that exist within a variety of tissues, including bone marrow and adipose tissue. A single gram of adipose tissue yields approximately 5000 stem cells; this is 100 to 500 times the number of mesenchymal stem cells found in an equivalent amount of bone marrow. Stem cells, because of their pluripotentiality and unlimited capacity for self-renewal, offer promise for tissue engineering and

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advances in reconstructive procedures. In particular, adipose tissue represents an abundant and easily accessible source of ADSCs, which can differentiate along multiple mesodermal lineages. ADSCs may allow for improved graft survival and generation of new fat tissue after transfer from another site.

The potentially therapeutic properties of ADSC have led to novel techniques of fat grafting in conjunction with ADSC therapy for breast fat grafting. Differentiation of ADSC into adipocytes may provide a reservoir for adipose tissue turnover. Differentiation of ADSC into endothelial cells, with the release of angiogenic growth factors by ADSC, may decrease the rate of graft resorption by increasing blood supply to the grafted fat tissue. Further, ADSC may serve to accelerate wound healing and protect the graft from ischemic reperfusion injury. Current methods for isolating ADSCs can involve various processes, which may include centrifugation and enzymatic techniques that rely on collagenase digestion-which, in turn, is followed by centrifugal separation to isolate the stem cells from primary adipocytes. Isolated ADSCs can be expanded in a monolayer on standard tissue culture plastic surfaces with a basal medium containing 10% fetal bovine serum. Newly developed culture conditions provide an environment in which the study of ADSCs can be done without the interference of animal serum and may also allow rapid expansion of autologous ADSCs in culture for use in human clinical trials. A standard expansion method has not yet been established.

To address the problems of unpredictability and low rates of fat graft survival, Yoshimura et al (2008) developed a technique known as cell-assisted lipotransfer, which produces autogenous fat rich in ADSCs. In cell-assisted lipotransfer, half of the lipoaspirate is centrifuged to obtain a fraction of concentrated ADSCs; meanwhile, the other half is washed, enzymatically digested, filtered, and spun down to an ADSC-rich pellet. The latter is then mixed with the former, converting a relatively ADSC-poor aspirated fat to ADSC-rich fat.

A point-of-care system is available for concentrating ADSC from mature fat. The Celution System is designed to transfer a patient's adipose tissue from one part of the body to another in the same surgical procedure.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In September 2006, Celution™ Cell Concentration System (Cytori Therapeutics; San Diego, CA) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process as a cell saver device. The system is cleared for the collection, concentration, washing, and reinfusion of a patient's cells for applications that may include, but are not limited to, cardiovascular, plastic and reconstructive, orthopedic, vascular, and urologic surgeries and procedures. In 2007, Cytori Therapeutics received the FDA 510(k) clearance to market the Autologous Fat Transfer system, which transfers a patient's own adipose tissue from one part of the patient's body to another. FDA product code: CAC.

In 2017, the Revolve Envi 600 Advanced Adipose System (LifeCell Corporation, Branchburg, NJ) was cleared for marketing by the FDA through the 510(k) process. The system harvests, filters, and transfers autologous adipose tissue for fat grafting. Uses include reconstructive surgery. FDA product code: MUU.

Rationale/Source

Following a mastectomy, patients often experience pain and irradiated skin; as an adjunct to reconstructive breast surgery, surgeons will sometimes graft autologous fat to the breast. Adipose-derived stem cells (ADSCs) have been proposed as a supplement to the fat graft in an attempt to improve graft survival; however, whether ADSCs play a role in tumorigenesis is still relatively unknown.

For individuals who have breast cancer who receive autologous fat grafting to the breast with ADSC enrichment of the graft, the evidence includes small single-arm studies, some of which are prospective. The relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, resource utilization, and treatment-related morbidity. The observational studies were heterogeneous in the patient selection, methods in harvesting stem cells, number of procedures, and outcomes measured. Studies have mainly reported patient and investigator satisfaction and functional and cosmetic results. Limitations of the data include sample sizes, short-term follow-up, and uncertainty about the possible oncologic influence ADSC may have on the fat grafting procedure. In addition, no studies were identified which demonstrated incremental benefits of using

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ADSC enrichment with autologous fat grafting over autologous fat grafting alone. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Practice Guidelines and Position Statements

American Society for Aesthetic Plastic Surgery and American Society of Plastic Surgeons

The American Society for Aesthetic Plastic Surgery and the American Society of Plastic Surgeons (2011) released a joint position statement on the use of stem cells in aesthetic surgery. Based on a systematic review of the peer-reviewed literature, the societies concluded that while there is potential for the future use of stem cells in aesthetic surgical procedures, the scientific evidence and other data are very limited in terms of assessing the safety or efficacy of stem cell therapies in aesthetic medicine.

U.S. Preventive Services Task Force Recommendations

Not applicable.

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

A currently ongoing trial that might influence this review is listed in Table X.

Table X. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			

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NCT02035085	This is a First in Man, Phase I Study Utilizing 19F Magnetic Resonance Imaging to Track Autologous, Adipose Derived Stem Cells	6	Dec 2020
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02/04/2016 Medical Policy Committee review

02/17/2016 Medical Policy Implementation Committee approval. New Policy.

01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes

02/02/2017 Medical Policy Committee review

02/15/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

02/01/2018 Medical Policy Committee review

02/21/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

02/07/2019 Medical Policy Committee review

02/20/2019 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

02/06/2020 Medical Policy Committee review

02/12/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

12/11/2020 Coding update

Next Scheduled Review Date: 02/2021

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 2019 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	19499 Code deleted eff 1/1/2021: 19366
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 the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);

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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: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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