MEDICAL POLICY – 7.01.153

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

BCBSA Ref. Policy: 7.01.153

Effective Date: April 1, 2019
Last Revised: March 19, 2019
Replaces: N/A

RELATED MEDICAL POLICIES:
None

Introduction

As part of breast reconstruction, a person’s own fat can be taken from other parts of the body and placed in the breast(s). There are risks of this fat transfer, including death of the fat cells and the chance that some of the transferred fat will migrate away from the breast area. Stem cells concentrated from the fat tissue are known as adipose-derived stem cells or ADSCs. Using ADSCs is proposed as a way to try to increase the success of a fat transfer to the breast. Medical studies have not yet determined whether injecting ADSCs could play a role in creating new tumors. The studies that have been done involve only a few patients who have been followed for a short time. For these reasons, using ADSCs as part of grafting a person’s own fat to the breast is considered investigational (unproven).

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria
Service | Investigational
--- | ---
Adipose-derived stem cells | The use of adipose-derived stem cells in autologous fat grafting to the breast is considered investigational.

**Note:** Autologous fat grafting to the breast without the use of adipose-derived stem cells is not subject to medical review.

## Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>11950</td>
<td>Subcutaneous injection of filling material (eg, collagen); 1 cc or less</td>
</tr>
<tr>
<td>11951</td>
<td>Subcutaneous injection of filling material (eg, collagen); 1.1 to 5.0 cc</td>
</tr>
<tr>
<td>11952</td>
<td>Subcutaneous injection of filling material (eg, collagen); 5.1 to 10.0 cc</td>
</tr>
<tr>
<td>11954</td>
<td>Subcutaneous injection of filling material (eg, collagen); over 10.0 cc</td>
</tr>
<tr>
<td>19366</td>
<td>Breast reconstruction with other technique</td>
</tr>
<tr>
<td>19380</td>
<td>Revision of reconstructed breast</td>
</tr>
<tr>
<td>19499</td>
<td>Unlisted procedure, breast</td>
</tr>
<tr>
<td>20926</td>
<td>Tissue grafts, other (eg, paratenon, fat, dermis)</td>
</tr>
</tbody>
</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

## Related Information

N/A
Evidence Review

Description

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.

Background

*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 policy 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.\(^1\) Stem cells, because of their pluripotentiality and unlimited capacity for self-renewal, offer promise for tissue engineering and 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.\textsuperscript{1,2}

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 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.\textsuperscript{3} 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.\textsuperscript{3} 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.\textsuperscript{4} 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 own adipose tissue from one part of the body to another in the same surgical procedure.

**Summary of Evidence**

For individuals with 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 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.

Ongoing and Unpublished Clinical Trials

A currently ongoing trial that might influence this review is listed in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02035085</td>
<td>This is a First-in-man, Phase I Study Utilizing 19F Magnetic Resonance Imaging to Track Autologous, Adipose Derived Stem Cells</td>
<td>6</td>
<td>Dec 2020</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

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.

Medicare National Coverage

There is no national coverage determination.
Regulatory Status

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.

References

**History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/08/15</td>
<td>New Policy. Policy created with literature review through September 13, 2015; the use of adipose-derived stem cells (ADSC) in autologous fat grafting to the breast is considered investigational. (Note: The former policy addressing both autologous fat grafting and ADSC has been archived. This policy only addresses ADSC. Policy statement regarding ADSC remains investigational.)</td>
</tr>
<tr>
<td>06/01/16</td>
<td>Annual Review, approved May 10, 2016. Policy updated with literature search. Reference added. No change to the policy statement.</td>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2019 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
• Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  • Qualified sign language interpreters
  • Writing information in other formats (large print, audio, accessible electronic formats, other formats)
• Provides free language services to people whose primary language is not English, such as:
  • Qualified interpreters
  • Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592. TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue SW, Room S9FF, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.

Call 800-722-1471 (TTY: 800-842-5357).

Oromoo (Cushite):

Français (French):

Kreyol Ayisyen (Creole):

Deutsche (German):

Hmoob (Hmong):

Illoko (Ilocano):
Daytoy a Pakdaa ket naglaon iti Napateg nga Impomarsion. Daytoy a pakdaa mabalini nga adda ket naglaon iti napateg nga impomarsion maipanggep iti aplikasyonovo wongno coverage babaen iti Premera Blue Cross. Daytoy ket mabalini dagiti importante a pelta iti daytoy a pakdaa. Mabalini nga adda rumbenga nga aramideny nga addang sakbay dagiti partikular a naituding nga aldaw tapno mapagtalaiyado ti coverage ti salun-atyo wongno tulong kadagit gastos. Adda karbenganyo a mangala iti daytoy nga impomarsion ken tulong ti bukodayo a pagasagao nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
Este aviso contém informações importantes. Essas informações foram encontradas em Premera Blue Cross. As informações sobre os prazos para manter sua cobertura de saúde ou ajuda de custos podem não ser completas. Se você tiver dúvidas sobre seu plano de saúde ou ajuda de custos, entre em contato com Premera Blue Cross.

Por favor, tome nota de que este aviso foi escrito em português. É importante que você entenda completamente as informações neste aviso antes de tomar qualquer decisão sobre sua cobertura de saúde.

Estimado cliente,

Este aviso contém informações importantes.

As informações contidas neste aviso foram encontradas em Premera Blue Cross. As informações sobre os prazos para manter sua cobertura de saúde ou ajuda de custos podem não ser completas. Se você tiver dúvidas sobre seu plano de saúde ou ajuda de custos, entre em contato com Premera Blue Cross.

Por favor, tome nota de que este aviso foi escrito em português. É importante que você entenda completamente as informações neste aviso antes de tomar qualquer decisão sobre sua cobertura de saúde.

Atenciosamente,

Premera Blue Cross