Surgical Treatments for Breast Cancer–Related Lymphedema

Policy # 00635
Original Effective Date: 10/17/2018
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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: Bioimpedance Devices for Detection and Management of Lymphedema is addressed separately in medical policy 00780.

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 lymphatic physiologic microsurgery to treat lymphedema (including, but not limited to, lymphatico-lymphatic bypass, lymphovenous bypass, lymphaticovenous anastomosis, autologous lymph node transplantation, and vascularized lymph node transfer) in individuals who have been treated for breast cancer to be investigational.*

Based on review of available data, the Company considers lymphatic physiologic microsurgery performed during nodal dissection or breast reconstruction to prevent lymphedema (including, but not limited to, the Lymphatic Microsurgical Preventing Healing Approach [LYMPHA]) in individuals who are being treated for breast cancer to be investigational.*

Background/Overview
Lymphedema
Lymphedema is an accumulation of fluid due to disruption of lymphatic drainage. Lymphedema can be caused by congenital or inherited abnormalities in the lymphatic system (primary lymphedema) but is most often caused by acquired damage to the lymphatic system (secondary lymphedema).

Diagnosis and Staging
A diagnosis of secondary lymphedema is based on history (eg, cancer treatment, trauma) and physical examination (localized, progressive edema and asymmetric limb measurements) when other causes of edema can be excluded. Imaging, such as magnetic resonance imaging, computed...
Surgical Treatments for Breast Cancer–Related Lymphedema

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tomography, ultrasound, or lymphoscintigraphy, may be used to differentiate lymphedema from other causes of edema in diagnostically challenging cases.

Table 1 lists International Society of Lymphology guidance for staging lymphedema based on "softness" or "firmness" of the limb and the changes with an elevation of the limb.

Table 1. Recommendations for Staging Lymphedema

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0 (subclinical)</td>
<td>Swelling is not evident and most patients are asymptomatic despite impaired lymphatic transport</td>
</tr>
<tr>
<td>Stage I (mild)</td>
<td>Accumulation of fluid that subsides (usually within 24 hours) with limb elevation; soft edema that may pit, without evidence of dermal fibrosis</td>
</tr>
<tr>
<td>Stage II (moderate)</td>
<td>Does not resolve with limb elevation alone; limb may no longer pit on examination</td>
</tr>
<tr>
<td>Stage III (severe)</td>
<td>Lymphostatic elephantiasis; pitting can be absent; skin has trophic changes</td>
</tr>
</tbody>
</table>

Breast Cancer-Related Lymphedema

Breast cancer treatment is one of the most common causes of secondary lymphedema. Both the surgical removal of lymph nodes and radiotherapy are associated with development of lymphedema in patients with breast cancer.

In a systematic review of 72 studies (N=29,612 women), DiSipio et al (2013) reported that approximately 1 in 5 women who survive breast cancer will develop arm lymphedema. Reviewers reported that risk factors for development of lymphedema that had a strong level of evidence were extensive surgery (ie, axillary-lymph-node dissection, greater number of lymph nodes dissected, mastectomy) and being overweight or obese. The incidence of breast cancer-related lymphedema was found by DiSipio et al as well as other authors to be up to 30% at 3 years after treatment.

Management and Treatment

Early and ongoing treatment of lymphedema is necessary. Conservative therapy may consist of several features depending on the severity of the lymphedema. Patients are educated on the
Surgical Treatments for Breast Cancer–Related Lymphedema

Policy #  00635
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The importance of self-care including hygiene practices to prevent infection, maintaining ideal body weight through diet and exercise, and limb elevation. Compression therapy consists of repeatedly applying padding and bandages or compression garments. Manual lymphatic drainage is a light pressure massage performed by trained physical therapists or by patients designed to move fluid from obstructed areas into functioning lymph vessels and lymph nodes. Complete decongestive therapy is a multiphase treatment program involving all of the previously mentioned conservative treatment components at different intensities. Pneumatic compression pumps may also be considered as an adjunct to conservative therapy or as an alternative to self-manual lymphatic drainage in patients who have difficulty performing self-manual lymphatic drainage. In patients with more advanced lymphedema after fat deposition and tissue fibrosis has occurred, palliative surgery using reductive techniques such as liposuction may be performed.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Physiologic microsurgery for lymphedema is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration.

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.

Surgery and radiotherapy for breast cancer can lead to lymphedema and are some of the most common causes of secondary lymphedema. There is no cure for lymphedema. However, physiologic microsurgical techniques such as lymphaticovenular anastomosis or vascularized lymph node transfer have been developed that may improve lymphatic circulation, thereby decreasing symptoms and risk of infection. This review focuses on physiologic microsurgical interventions and will not consider reductive (also known as excisional or ablative) surgical interventions such as liposuction.
Summary of Evidence

For individuals who have breast cancer-related secondary lymphedema who receive physiologic microsurgery to treat lymphedema along with continued conservative therapy, the evidence includes a randomized controlled trial (RCT), observational studies, and systematic reviews. Relevant outcomes are symptoms, morbid events, functional outcomes, health status measures, quality of life, resource utilization, and treatment-related morbidity. Several physiologic microsurgeries have been developed; examples include lymphaticovenular anastomosis and vascularized lymph node transfer. No RCTs of lymphaticovenular anastomosis or similar surgeries involving the venous system were identified. One RCT of vascularized lymph node transfer with 36 participants has been conducted. Systematic reviews have indicated that the preponderance of the available evidence comes from single-arm clinical series from individual institutions. Surgical technique, outcomes metrics, and follow-up time have varied across these studies. These types of studies might be used for preliminary estimates of the amount of volume reduction expected from surgery, the durability of the reduction in volume, and the rates of adverse events. However, these studies are not adequate for determining the comparative efficacy of physiologic microsurgery versus conservative treatment or decongestive therapy, or the comparative efficacy of different microsurgery techniques. Randomized controlled trials are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are undergoing lymphadenectomy for breast cancer who receive physiologic microsurgery to prevent lymphedema, the evidence includes a RCT, observational studies, and systematic reviews. Relevant outcomes are symptoms, change in disease status, morbid events, quality of life, and treatment-related morbidity. Lymphatic Microsurgical Preventing Healing Approach is a preventive lymphaticovenular anastomosis performed during nodal dissection. One RCT including 46 patients has been conducted. The trial reported that lymphedema developed in 4% of women in the Lymphatic Microsurgical Preventing Healing Approach group and 30% in the control group by 18 months of follow-up. However, because the cumulative incidence of lymphedema after breast cancer treatment approximates 30% at 3 years, longer follow-up is needed to assess the durability of the procedure. The trial methods of randomization and allocation concealment were not described and there was no blinding, potentially introducing bias. The remaining evidence consists of 2 controlled observational studies with inadequate description of control selection and uncontrolled studies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.
Surgical Treatments for Breast Cancer–Related Lymphedema

Policy # 00635
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Supplemental Information
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 National Institute for Health and Care Excellence (NICE). Priority will be 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.

National Lymphedema Network
The National Lymphedema Network published a position paper on the diagnosis and treatment of lymphedema in 2011. The paper provided the following statements, although notably, the document has been retracted and the Network is currently in the process of drafting a new position statement:

"Microsurgical and supramicrosurgical (much smaller vessels) techniques have been developed to move lymph vessels to congested areas to try to improve lymphatic drainage. Surgeries involve connecting lymph vessels and veins, lymph nodes and veins, or lymph vessels to lymph vessels. Reductions in limb volume have been reported and a number of preliminary studies have been done, but there are no long-term studies of the effectiveness of these techniques."

International Society of Lymphology
The International Society of Lymphology published a consensus document on the diagnosis and treatment of peripheral lymphedema in 2016. The document stated the following on lymphaticovenous (or lymphovenous) anastomoses (LVA):

"LVA are currently in use at multiple centers around the world. These procedures have undergone confirmation of long-term patency (in some cases more than 20 years) and some demonstration of improved lymphatic transport (by objective physiologic measurements of long-term efficacy)."

American Society of Breast Surgeons
The American Society of Breast Surgeons published recommendations from an expert panel on preventive and therapeutic options for breast cancer-related lymphedema in 2017. The document stated that "the Panel agrees that LVA and VLNT may be effective for early secondary breast cancer-related lymphedema."
Surgical Treatments for Breast Cancer–Related Lymphedema

Policy # 00635
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National Comprehensive Cancer Network
The National Comprehensive Cancer Network (NCCN) published recommendations on management of lymphedema as part of its guideline on survivorship; however, it does not discuss physiologic microsurgical techniques. The guideline states that high-level evidence in support of treatments for lymphedema are lacking. In addition, the NCCN guideline on breast cancer does not give recommendations on use of physiological microsurgical techniques for preventing or treating lymphedema.

American Association of Plastic Surgeons
The American Association of Plastic Surgeons sponsored a conference to create consensus statements and recommendations for surgical treatment and prevention of upper and lower extremity lymphedema. The recommendations were based on the results of a systematic review and meta-analysis. The relevant recommendations include:

"There is evidence to support that lymphovenous anastomosis can be effective in reducing severity of lymphedema (grade 1C). There is evidence to support that vascular lymph node transplantation can be effective in reducing severity of lymphedema (grade 1B). Currently, there is no consensus on which procedure (lymphovenous bypass versus vascular lymph node transplantation) is more effective (grade 2C). A few studies show that prophylactic lymphovenous bypass in patients undergoing extremity lymphadenectomy may reduce the incidence of lymphedema (grade 1B). More studies with longer follow-up are required to confirm this benefit."

U.S. Preventive Services Task Force Recommendations
No U.S. Preventive Services Task Force recommendations for lymphedema have been identified.

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.
Surgical Treatments for Breast Cancer–Related Lymphedema

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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>
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<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02790021</td>
<td>Improving Quality of Survivorship for Breast Cancer-related Lymphedema by Lymphaticovenous Anastomosis: A Randomized Controlled Trial</td>
<td>60</td>
<td>Aug 2022</td>
</tr>
<tr>
<td>NCT03941756</td>
<td>Lymphovenous Bypass Procedure Before Underarm Lymph Node Surgery in Preventing Lymphedema in Patients With Inflammatory or Locally Advanced Non-inflammatory Breast Cancer</td>
<td>50</td>
<td>Dec 2020</td>
</tr>
<tr>
<td>NCT03428581</td>
<td>Preventing Lymphedema in Patients Undergoing Axillary Lymph Node Dissection Via Axillary Reverse Mapping and Lympho-venous Bypass</td>
<td>264</td>
<td>Feb 2023</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

References

Surgical Treatments for Breast Cancer–Related Lymphedema

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Surgical Treatments for Breast Cancer–Related Lymphedema

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10/04/2018 Medical Policy Committee review
10/03/2019 Medical Policy Committee review
10/01/2020 Medical Policy Committee review
10/07/2021 Medical Policy Committee review
10/06/2022 Medical Policy Committee review
Next Scheduled Review Date: 10/20/23

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 2021 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.
Surgical Treatments for Breast Cancer–Related Lymphedema

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

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>38999</td>
</tr>
<tr>
<td>HCPCS</td>
<td>No codes</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>189.0-189.9, 197.2</td>
</tr>
</tbody>
</table>

*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
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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: 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.