Medical Coverage Policy

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Breast Reconstruction Following Mastectomy or Lumpectomy

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Overview

This Coverage Policy addresses reconstructive breast surgery and external breast prostheses and mastectomy bras following mastectomy or lumpectomy.

- For treatments related to lymphedema, see Cigna Medical Coverage Policies:
  - 0354 Compression Devices
  - 0531 Surgical Treatments for Lymphedema and Lipedema
  - Cobranded Cigna/American Specialty Health Coverage Policy Guideline 157 Complex Lymphedema Therapy (Complete Decongestive Therapy).
- For breast reconstruction related to gender dysphoria treatment, see Cigna Medical Coverage Policy 0266 Gender Dysphoria Treatment.
- For the surgical treatment of gynecomastia, see Cigna Medical Coverage Policy 0195 Gynecomastia Surgery.
- For breast reduction surgery on the non-diseased/contralateral breast following a mastectomy or lumpectomy, see Cigna Medical Coverage Policy 0152 Breast Reduction.
- For surgical procedures for the excision of redundant or excessive skin, see Cigna Medical Coverage Policy 0470 Redundant Skin Surgery.

Coverage Policy

Coverage for breast reconstruction* and breast prostheses following mastectomy or lumpectomy is governed by federal and/or state mandates.

Breast Reconstruction

***Please note: Coverage for breast reconstruction services following mastectomy and lumpectomy is available to both females and males. In addition, a diagnosis of breast cancer is not required for breast reconstruction services to be covered, and the timing of reconstructive services is not a factor in coverage.**

Breast reconstruction following mastectomy or lumpectomy is considered medically necessary for EITHER of the following:

- **breast reconstruction procedures performed on the diseased/affected breast (i.e., breast on which the mastectomy/lumpectomy was performed), including:**

- areolar and nipple reconstruction (e.g., correction of inverted nipple)
- areolar and nipple tattooing
- autologous fat transplant (i.e., liposuction, lipoinjection, lipofilling, lipomodeling)
- breast implant removal and subsequent reimplantation
- capsulectomy
- capsulotomy
- flat closure chest wall reconstruction
- implantation of tissue expander
- implantation of U.S. Food and Drug Administration (FDA)-approved internal breast prosthesis
- oncoplastic reconstruction (e.g., breast reduction, mastopexy)
- reconstructive surgical revisions
- tissue/muscle reconstruction (i.e., flap procedures)

- **breast reconstruction procedures performed on the nondiseased/unaffected/contralateral breast, in order to produce a symmetrical appearance, including:**

  - areolar and nipple reconstruction
  - areolar and nipple tattooing
  - augmentation mammoplasty
  - augmentation with implantation of FDA-approved internal breast prosthesis when the unaffected breast is smaller than the smallest available internal prosthesis
  - autologous fat transplant (i.e., liposuction, lipoinjection, lipofilling, lipomodeling)
  - breast implant removal and subsequent reimplantation when performed to produce a symmetrical appearance
  - breast reduction by mammoplasty or mastopexy
  - capsulectomy
  - capsulotomy
  - reconstructive surgery revisions to produce a symmetrical appearance

Intraoperative assessment of tissue perfusion is considered an integral part of the breast reconstruction procedure and not separately reimbursable.

The following products* are considered medically necessary when used in association with a medically necessary breast reconstruction procedure:

- AlloDerm™
- AlloMax™
- Cortiva™
- DermACELL™
- FlexHD® Acellular Hydrated Dermis
- GalaFLEX® Scaffold
- GalaFLEX 3DR Scaffold (formerly known as GalaFORM™ 3D)
- GalaFLEX 3D Scaffold (formerly known as GalaSHAPE™ 3D)

The following products* when used in association with a breast reconstruction procedure are considered experimental, investigational, or unproven (this list may not be all-inclusive):

- ARTIA™ Reconstructive Tissue Matrix
- Avance® Nerve Graft

- BellaDerm® Acellular Hydrated Dermis
- Biodesign® Nipple Reconstruction Cylinder
- DermaMatrix Acellular Dermis
- DuraSorb® Monofilament Mesh/ Polydioxanone Surgical Scaffold™
- Juvederm®
- OviTex®
- Permacol™
- Phasix™ Mesh
- Radiesse®
- Renuva® Allograft Adipose Matrix
- SERI™ Surgical Scaffold
- SimpliDerm™
- Strattice™ Reconstructive Tissue Matrix
- SurgiMend®
- Veritas Collagen Matrix

***Note: Refer to the table in Appendix A for a list of products and the associated CPT and HCPCS codes.**

The following breast reconstruction procedures are considered experimental, investigational or unproven for this indication:

- the use of adipose-derived stem cells in autologous fat transplantation
- xenograft cartilage grafting

Suction lipectomy, ultrasonically-assisted suction lipectomy (liposuction) or excision of redundant skin for correction of surgically-induced donor site asymmetry (e.g., trunk or extremity) or tissue protruding at the end of a scar (e.g., dog ear, standing cone) that results from one or more flap breast reconstruction procedures is considered cosmetic in nature and not medically necessary.

Removal of either a saline-filled OR silicone gel-filled breast implant when associated with breast reconstruction following mastectomy or lumpectomy for ANY indication, including for the purpose of producing a symmetrical appearance of the nondiseased breast is considered medically necessary. Refer to the Breast Implant Removal Medical Coverage Policy for additional information on breast implant removal.

Following removal of a breast implant, the subsequent surgical implantation of a new U.S. Food and Drug Administration (FDA)-approved breast implant is considered medically necessary for EITHER of the following:

- breast reconstruction of a diseased or affected breast following mastectomy or lumpectomy
- creation of a symmetrical appearance in the contralateral/nondiseased breast following mastectomy or lumpectomy in the opposite breast

<u>External Breast Prostheses and Mastectomy Bras</u>

External breast prostheses and mastectomy bras following mastectomy or lumpectomy are covered under the core medical benefits of the plan.

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

Morrow, et al. (2014) conducted a retrospective analysis of women in Los Angeles and Detroit diagnosed with breast cancer who underwent mastectomy and remained disease free at four years to evaluate for breast reconstruction correlates and possible unmet needs of reconstruction. Women (n=485) aged 20–79 years were included in the study if they: were diagnosed with ductal carcinoma in situ (DCIS) or invasive breast cancer between June 2005-February 2007, reported to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program registries, could complete a questionnaire in English or Spanish, underwent mastectomy and remained disease free at four years. Participants were excluded if they: had stage IV breast cancer, died prior to the initial survey, or were Asian because of enrollment in other studies. In order to ensure sufficient representation of racial/ethnic minorities, Latina and Black women were oversampled. The primary outcome was whether or not a women underwent breast reconstruction at any time post mastectomy. Patient satisfaction with various aspects of the reconstruction decision making process (i.e., satisfaction with their decision to have reconstruction, whether they regret their reconstruction choice, satisfaction about being informed about reconstructive issues) and reasons why a participant did not have reconstruction or delayed reconstruction were secondary outcomes. Patient demographics (i.e., age, education, race/ethnicity, partner status, income, insurance, smoking status), clinical/treatment factors (i.e., staging, comorbidities, breast size, chemotherapy, radiation, timing of reconstruction), and geographic location were independent variables that were considered. Follow-up via patient surveys took place at a mean of nine- and 50-months post cancer diagnosis. Overall, 41.6% of the 485 patients treated with mastectomy who remained disease-free had breast reconstruction; 24.8% (n=146) of the procedures were done at the time of mastectomy, and 16.8% (n=76) were delayed. Surgery with implants or tissue expanders was the most common type of reconstruction (61.9%). Compared with respondents, non-respondents to the follow-up survey were more likely to be Black (35.2% versus 26.7%; $p<0.001$) or Latina (17.2% versus 13.3%; $p=0.002$), more likely to have stage II or III disease (54.9% versus 37.8%; $p<0.001$), and more likely to have received mastectomy (37.5% versus 30.8%; $p<0.001$). Black patients, those with a high school or lower education level, those without private insurance, women with any major co-morbid condition, older women, those residing in Los Angeles County, and those patients who received chemotherapy were significantly less likely to undergo reconstruction than their counterparts. A total of 13.3% of women reported being dissatisfied with the decision-making process and was associated with being Black or Latina ($p=0.032$) but not with lower income or education levels. The most common reasons among all women for not undergoing reconstruction was a desire to avoid additional surgery (48.5%), the opinion that reconstruction was unimportant (33.8%), and fear of implants (36.3%). However, ethnic minority groups were less likely to report the desire to avoid additional surgery (70.0% for non-Black, non-Latina patients versus 39.7% and 34.1% for Blacks and Latinas, respectively; $p<0.001$) or that reconstruction was not important (42.4% for non-Black, non-Latina patients versus 21.6% and 31.3% for Blacks and Latinas, respectively; $p=0.043$). More Latinas reported concerns about cancer detection interference, procedure complications, or not being able to take time off from work or family. More Blacks and Latinas reported not having insurance coverage as a barrier to reconstruction. The study is limited by the small geographic sampling, retrospective study design, and possible errors in patient recall. This study highlights

the need for additional patient level education on factors that negatively impact the breast reconstruction decision making process especially among minority women.

General Background

Breast reconstruction is designed to reduce post-mastectomy complications and to establish symmetry between the surgical breast and the contralateral breast. Surgical procedures that are performed to establish symmetry can include: breast reduction; breast augmentation with an FDA-approved breast implant; and/or areola-with-nipple reconstruction and nipple-area tattooing. Breast reconstruction after mastectomy has evolved over the last century to become an integral component of therapy for patients with breast cancer. Reconstruction can occur immediately after a mastectomy or be delayed for weeks or years until a patient undergoes radiation, chemotherapy, or decides whether they want breast reconstruction.

Prosthetic Reconstruction

Breast Implants: Breast implants can be inserted at the same time as the mastectomy (e.g., direct-to-implant breast reconstruction or one-stage immediate breast reconstruction) or in two stages, using an implanted tissue expander in the first stage followed by removal of the expander and insertion of a permanent breast implant (e.g., two-stage reconstruction or two-stage delayed reconstruction). The FDA-approved implant is placed either deep in the breast on the pectoral fascia (submammary) or beneath the pectoralis major. The advantages of tissue expander implant reconstruction are the reliability, simplicity, and avoidance of donor-site morbidity. Complications associated with the use of breast implants can occur in the immediate perioperative period or years later. Such complications include exposure, extrusion, or infection of the implants. Longer term problems also include asymmetry, capsular contracture, malposition of the implant, rupture, and pain. These conditions, when they become clinically significant, may require removal of the implant (American Cancer Society [ACS], 2025; Roehl, et al., 2012; Roostaeian, et al., 2012).

Indications for implant reconstruction include: bilateral reconstruction, individuals requiring augmentation in addition to reconstruction, individuals not suited for long surgery, a lack of abdominal tissue, individual unwilling to have additional scars on either their back or abdomen, and a small breast mound with minimal ptosis. Relative contraindications to implant reconstruction include: young age (i.e., may need implant replaced multiple times), individual unwilling to follow up, or very large or ptotic breast. The contraindications to implant reconstruction include: silicone allergy, fear of implants, previously failed implants, or the need for adjuvant radiation therapy (Roehl, et al., 2012).

Surgical complications associated with breast implantation are like those encountered with other breast surgeries: infection, bleeding, change in nipple sensation (e.g., hypersensitivity or hyposensitivity), malposition, delayed healing, and anesthetic accidents.

Although implantable breast prostheses may be inserted for either reconstructive or cosmetic reasons, clinically significant post-implant complications may occur, necessitating removal of the implants. Local complications associated with implanted breast prostheses include: capsular contracture, persistent infection, silicone implant extrusion, tissue necrosis and silicone implant rupture. These conditions, when they become clinically significant, may require removal of the implant. Additionally, the presence of an implant may interfere with the diagnosis or treatment of breast cancer. Infections that may occur in or around an implant include wound infections, as well as infections within a capsular contracture or because of a ruptured implant. Removal of the implant may be necessary when the infection does not respond to antibiotics. Unstable or weakened tissue and/or interruption in wound healing may result in the implant breaking through

the skin or extrusion. Necrotic tissue may form around the implant, requiring implant removal. Silicone gel-filled implant rupture may cause the contents to leak into the surrounding tissues.

U.S. Food and Drug Administration (FDA): In the FDA labeling for approved breast implants (FDA, 2021c), Mentor Corp., Santa Barbara, CA; Ideal Implant ®, Inc., Dallas, TX; Allergan Corp. (formerly Inamed), Irvine, CA and Sientra, Inc., Santa Barbara, CA are listed as manufacturers of silicone and saline breast implants.

FDA-approved saline-filled implants:

- Allergan Medical RTV Saline-Filled Breast Implant
- Ideal Implant Saline-Filled Breast Implant (PMA Number: P120011)
- Mentor Saline-Filled and Spectrum™ Breast Implants (PMA Number: P990075)

The FDA approved saline-filled breast implants for breast augmentation in women age 18 or older and for breast reconstruction in women of any age. They are also used in revision surgeries, which correct or improve the result of an original surgery.

FDA-approved silicone gel-filled breast implants:

- Allergan Natrelle®
- Allergan Natrelle® 410 Highly Cohesive Anatomically Shaped Silicone-Filled Breast Implant
- Mentor MemoryGel® (PMA Number: P030053)
- Mentor MemoryShape™ Silicone Gel-Filled Breast Implant (PMA Number: P060028)
- Sientra® Silicone Gel Breast Implant (PMA Number: P070004)

The FDA labeling for silicone and saline breast implantation states that breast implant surgery should not be performed in women with: an active infection, existing cancer or precancer of a breast that has not been adequately treated, or who are pregnant or nursing.

In June 2011 (updated 2018), the FDA released a report updating the clinical and scientific information for silicone gel-filled breast implants, including preliminary safety data from studies conducted by the manufacturers as a condition of their November 2006 approval. The conclusion in the report states that, "Based on the totality of the evidence, the FDA believes that silicone gel-filled breast implants have a reasonable assurance of safety and effectiveness when used as labeled. Despite frequent local complications and adverse outcomes, the benefits and risks of breast implants are sufficiently well understood for women to make informed decisions about their use." Manufacturers and physicians should continue to provide balanced and up-to-date information to women considering breast implants to help inform their decisions (FDA, 2018). On July 24, 2019, the FDA requested that Allergan, recall specific models of their textured breast implants from the U.S. market due to the risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). The FDA's analysis was attributed to a new worldwide reported total of 573 unique BIA-ALCL cases including 33 patient deaths. Of the 573 cases of BIA-ALCL, 481 are reported to have Allergan breast implants at the time of diagnosis. (FDA, 2019b; FDA, 2019c).

In September 2022, the FDA issued a safety communication informing the public about emerging and rare reports of squamous cell carcinoma (SCC) and various lymphomas in the scar tissue that forms around smooth and textured and saline and silicone breast implants. Ten medical device reports (MDRs) about SCC and 12 MDRs about various lymphomas related to breast implants have been reported to the FDA as of September 1, 2022 and in some cases, people were diagnosed years after having the breast implants. The following recommendations were provided for people who have or are considering breast implants:

- "If you are considering breast implants or if you have them, learn more about the risks and benefits of breast implants.

- If you have breast implants, you do not need to change your routine medical care or follow-up.
- Be aware that cases of SCC and various lymphomas in the capsule around the breast implant have been reported.
- Monitor your breast implants for as long as you have them. If you notice any abnormal changes in your breasts or implants, promptly talk to your surgeon or health care provider.
- If you do not have symptoms, the FDA does not recommend the removal of breast implants because of this safety communication.
- If you have breast implants and experience a problem, the FDA encourages you to file a report through MedWatch, the FDA Safety Information and Adverse Event Reporting program. Your report, along with information from other sources, can provide information that helps improve patient safety."

The following recommendations were provided for health care providers:

- "Continue to provide routine care and support to your patients with breast implants.
- Be aware that cases of SCC and various lymphomas in the capsule around the breast implant have been reported.
- When examining breast implant specimens (for example, seroma, capsule, devices) for diagnostic evaluation, characterize all findings and potential diagnoses.
- Report cases of SCC, lymphomas, and any other cancers in the capsule around the breast implant to the FDA. Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with medical devices (FDA, 2022a)"

Tissue Expanders

Following mastectomy, some individuals have inadequate elasticity in the remaining tissue to accommodate and support a breast implant. For these individuals, tissue expanders can be inserted under the chest muscle or skin. The expander is an empty balloon-like container that, over time, is injected with saline to cause the tissue to expand. The tissue expander is surgically removed once an adequate pocket has been established, and the permanent implant is then inserted. The most appropriate patients for this type of reconstruction are individuals who do not qualify for autogenous reconstruction, individuals who do not want additional scars from other donor sites, individuals who prefer a typically quicker postoperative recovery period, and individuals who have relatively small breasts. Contraindication for this type of reconstruction are mastectomy flaps that are too thin for adequate implant coverage and the completed or planned use of adjuvant radiation therapy because of higher implant complication rates (Hu, et al., 2007).

Tissue Flap Procedures

Autologous tissue/muscle breast flap reconstruction procedures are safe and effective and are a well-established standard of care. Methods of autologous tissue breast reconstruction include local flaps and distant flaps. Local flaps rely on transposition of muscle, subcutaneous tissue, and skin into the mastectomy defect and remain attached to the native blood supply of the muscle (e.g., latissimus dorsi myocutaneous (LD) flap, pedicled transverse rectus abdominus myocutaneous (TRAM) flap). Distant flap breast reconstruction requires the use of microvascular free-tissue transfer (e.g., free TRAM flap, deep inferior epigastric perforator [DIEP] flap, superficial inferior epigastric artery perforator [SIEP] flap, inferior or superior gluteal flap, superior gluteal artery perforator flap, Reubens flap, transverse upper gracilis (TUG) flap). Breast reconstruction using these donor sites relies on harvesting the flap with its vascular pedicle, which is anastomosed using microsurgical technique to appropriate recipient vessels in the mastectomy site. The two most common types of tissue flap procedures are the TRAM flap and the LD flap. Other tissue flap surgeries are more specialized and may not be available everywhere. The choice of procedure for a given individual is affected by age, health, contralateral breast size and shape, personal preference, and the expertise of the reconstructive surgeon (Roehl, et al., 2012; Spear et al.,

2007; Mehrara et al., 2006; Alderman et al., 2006; Garvey et al., 2006; Bajaj et al., 2006; Wechselberger, et al., 2004; Behnam et al., 2003).

Deep Inferior Epigastric Perforator (DIEP) Flap: A modification of the free TRAM flap is the deep inferior epigastric perforator (DIEP) flap. This flap does not harvest any muscle or fascia from the abdomen, and reportedly has significantly less donor-site morbidity than the usual TRAM flap. Patients are thought to have reduced postoperative pain, a lower risk of abdominal bulge or hernia, and less postoperative abdominal donor-site weakness. In reducing the amount of disturbance to the abdominal wall donor site, however, use of the DIEP flap unavoidably reduces the number of perforators supplying blood to the flap. This could potentially lead to a reduced supply of blood to the flap, thereby causing an increase in partial flap loss and fat necrosis (American Society of Plastic Surgeons [ASPS], 2017; Kroll, 2000).

Latissimus Dorsi Myocutaneous (LD) Flap: The LD flap moves muscle and skin from the back to reconstruct the breast. The LD flap is ideally suited for single-stage reconstruction for individuals with small breasts and a moderate degree of ptosis and for patients with no available abdominal donor site due to scars or lack of tissue. The LD flap can be used to correct lumpectomy defects which require a smaller implant or no implant. Some individuals may have weakness in their back, shoulder, or arm after this surgery. Relative contraindications to the LD flap include: planned postoperative radiation therapy, bilateral reconstruction, and significant breast ptosis. Contraindications to the LD flap include: previous lateral thoracotomy and individuals with large breast volume who do not desire reduction (Roehl, et al., 2012).

Rubens Flap: The Rubens flap is based on the circumflex iliac vessels and is an option for individuals who have an excess of soft tissue over the hips. Because this reconstructive procedure is limited in bulk and skin envelope, and often requires a balancing procedure on the contralateral hip, it is not usually considered as a first option for breast reconstruction (Roehl, et al., 2012).

Superficial Inferior Epigastric Perforator/Artery (SIEP/SIEA) Flap: The skin and fat of the lower abdomen are supplied by perforators (vessels that perforate the rectus abdominis muscle), including the superficial inferior epigastric artery (SIEA). For this type of reconstruction, an elliptical flap of tissue is transferred from the lower abdomen to the chest while still allowing a tension-free closure of the donor site in the abdomen. The apex of the triangular flap becomes the tail of the reconstructed breast. The internal mammary artery perforators or thoracodorsal vessels are often a good size match for the SIEA; these are anastomosed to the perforators of the graft using microsurgical technique. Construction of an SIEA flap presents several technical challenges and cannot be used in all cases (Hayes, 2014, reviewed 2016).

Superior or Inferior Gluteal Free Flap: The superior or inferior gluteal free flap requires skin, fat, blood vessels, and muscle to be removed from the gluteus maximus to reconstruct the breast. This technique is an option when the abdomen is no longer an alternative for flap transfer. This flap is technically complex and has complications including: seroma, sciatica, unfavorable scar location, and asymmetrical buttock contour (Roehl, et al., 2012).

Thoracodorsal Artery Perforator (TDAP) Flap: The TDAP flap is a rarely chosen source for autogenous tissue breast reconstruction. The TDAP flap is an evolution of the LD flap. The TDAP flap allows for collection of skin and soft tissue from the upper back without sacrifice of muscle tissue. The flap is based on proximal perforating vessels that originate from the thoracodorsal artery and vein. These vessels pass through the latissimus dorsi muscle and into the overlying skin and fat (DellaCroce, 2015, updated 2023).

Transverse Rectus Abdominus Myocutaneous (TRAM) Flap: The TRAM flap is the most commonly performed autologous reconstructive procedure and is considered the gold standard in

breast reconstruction because of the lower abdominal tissue's similarities in consistency with breast tissue and its aesthetic appearance. There are three types of TRAM flaps: unipedicle, bipedicle, or free. Pedicle flaps involve leaving the flap attached to its original blood supply and tunneling it under the skin to the breast area. Free flap involves cutting the flap free of skin, fat, blood vessels, and muscle from its original location and attaching the flap to blood vessels in the chest area. These procedures are indicated for individuals with (Zenn, 2021a, 2021b, 2023; Roehl, et al., 2012):

- large tissue requirement after mastectomy
- history of radiation to the chest wall
- small or large opposite breast that is difficult to match with an implant
- previous failure of implant reconstruction
- excess lower abdominal tissue

Abdominal complications resulting from this surgery include loss of abdominal strength, abdominal bulge and hernia formations. It is recommended that reconstruction be delayed when adjuvant chemotherapy is planned, because complications of the reconstruction can be detrimental in beginning the individual's therapy.

Numerous factors place an individual at higher risk for complications and are therefore considered relative contraindications to TRAM flap surgery (e.g., cardiac and/or pulmonary disease, diabetes, history of pulmonary embolus or deep venous thrombosis) (Zenn, 2021a, 2021b, 2023; ASPS, 2017; Roehl, et al., 2012):

Transverse Upper Gracilis (TUG) Flap: The TUG flap is taken from the upper inner thigh area. Part or all of the gracilis muscle is included with the flap to ensure the most reliable blood supply. This is a breast reconstructive option for those individuals who have limited flap donor sites. Candidates for TUG flap breast reconstruction include individuals desiring autogenous breast reconstruction with sufficient upper inner thigh tissue but who have had a previous abdominoplasty, or a flap taken from their abdomen. Very thin or athletic individuals who have insufficient abdominal donor tissue may be candidates for the TUG flap. This flap may be referred to as the TUG Perforator Flap which, as a perforator flap, it is a flap made of skin and fat only (no muscle). The TUG Myocutaneous Flap includes skin, fat, a portion of the gracillis muscle and the blood vessels associated with it to keep it alive. It is not usually considered as a first option for breast reconstruction.

Omental Free Flap (LHOFF)/Omental Fat-Augmented Free Flap (O-FAFF): An omental flap can be retrieved by laparoscopic or open approach and can be free or pedicled. During the free flap procedure, the greater omentum is detached from the colon and stomach and the right gastroepiploic vein and artery are clipped and connected to the internal mammary artery via microsurgery. Reported advantages of an omental flap include: minimal blood loss, minimal donor site morbidity, mimics the feel of a natural breast, low risk of ischemic complications, can be used in obese individuals, and shows unique phenomenon of size gain. Limitations have been reported as: unpredictable volume and not suitable for reconstruction in whole breast mastectomy. Contraindications include: omental malignant nodules, omental cake, or malignant ascites, and marked abdominal adhesions (Khater, et al., 2017; Zaha, et al., 2006; Cothier-Savey, et al., 2001).

Flat Closure Chest Wall Reconstruction: Some individuals may elect to forgo breast reconstruction for a variety of personal reasons. Others may not be candidates for breast reconstruction due to health issues (e.g, obesity, blood circulation issues). In these situations, flat closure chest wall reconstruction is an option. The National Cancer Institute defines an "aesthetic flat closure" as "A type of surgery that is done to rebuild the shape of the chest wall after one or

both breasts are removed. An aesthetic flat closure may also be done after removal of a breast implant that was used to restore breast shape. During an aesthetic flat closure, extra skin, fat, and other tissue in the breast area are removed. The remaining tissue is then tightened and smoothed out so that the chest wall appears flat." (NCI, 2024; ACS, 2021)

Intraoperative Assessment of Tissue Perfusion

One of the reported causes of early complications following breast reconstructive procedures is considered to be inadequate tissue perfusion. Accurate and reliable intraoperative evaluation of tissue perfusion is needed to reduce complications and improve clinical outcomes. Besides clinical judgement, several technologies to assess tissue vascularity have been evaluated in studies and are used clinically (e.g., intraoperative laser angiography using indocyanine green (ICG); fluorescein, doppler) (Gurtner, et al., 2013). One device that is used is the SPY® Fluorescent Imaging System (Stryker, Kalamazoo, MI; formerly Novadaq Technologies Inc., Mississauga, Ontario) (510(k) Number: K083898). Intra-operative assessment of tissue perfusion is considered an integral part of a breast reconstruction procedure.

Reconstruction of the Nipple-Areolar Complex

This portion of the breast reconstruction is usually performed as a second or third stage after the breast mound has been constructed. The recreation of the nipple-areolar complex involves various proposed techniques such as skin grafts, autologous and xenograft cartilage grafts, local tissue flaps, tissue-engineered structures, and tattooing and/or transplantation of nipple-areolar tissue from the opposite breast. It has been reported that within 12 months, most reconstructed nipples undergo a 50% reduction in projection. Therefore, the nipple should be made larger than desired during the initial surgery. The rebuilding of the nipple-areolar area is conducted first, and the tattooing procedure is done when swelling has subsided, usually 3–6 weeks after nipple creation. Successful nipple-areola reconstruction is expected to maintain nipple projection and areola size; however, longevity of this reconstruction is highly variable and is influenced by factors such as tissue thickness, scar contracture, trauma and radiation. Tattooing is commonly repeated (Chun, 2017, updated 2023; Roehl, et al., 2012; Heitland, et al., 2006; Guerra, et al., 2003).

Local tissue flaps are the most frequently performed methods of nipple reconstruction. Nipple reconstruction with local flaps is achieved with various techniques, each with its own proponents and benefits. These include the skate flap, bell flap, double opposing tab flap, star flap, top-hat flap, twin flap, propeller flap, S flap, rolled dermal-fat flap, and autologous cartilage. Acellular dermal matrices used alone or in conjunction with local flaps are being proposed as well as injectable materials for nipple reconstruction. Some have also advocated creating a more stable de-epithelialized skin base for the reconstructed nipple to minimize loss of projection (Chun, 2017, updated 2021).

Loss of nipple projection commonly occurs a few years after reconstruction. This problem may be reduced with the use of bell and double opposing tab flaps. Various procedures such as re-elevating the flap; inserting autologous dermal tissue, autologous or banked cartilage; and using filler injection or AlloDerm are proposed as secondary nipple reconstruction procedures. Discoloration and uneven pigment distribution may occur over time and can usually be corrected with tattooing (Chun, 2017, updated 2021).

In a systematic review, Winocour et al. (2016) reported the efficacy, projection, and complication rates of different materials used in nipple reconstruction. A total of 31 retrospective and prospective studies with controlled and uncontrolled conditions reporting on outcomes of autologous, allogeneic, and synthetic grafts in nipple reconstruction were included. The authors reported heterogeneity in the type of material used within each category and inconsistent methodology used in outcomes assessment in nipple reconstruction. Overall, the quality of evidence is low. Synthetic materials have higher complication rates and allogeneic grafts have

nipple projection comparable to that of autologous grafts. The authors reported that further investigation with high-level evidence is necessary to determine the optimal material for nipple reconstruction.

Xenograft Cartilage Grafting: The use of cartilage is another method of nipple reconstruction, particularly in prosthetic reconstruction where there might be a soft-tissue deficiency. The procedure is applicable to both unilateral and bilateral nipple reconstruction, is reported to be an easy procedure to perform, does not involve a donor site, and maintains long-lasting projection. A reported disadvantage of donated cartilage is that the resulting nipple is unnaturally firm. If the grafts are placed too superficially and do not have a smooth contour, they can extrude through the skin, warranting revision and/or removal. Caution is recommended with thin skin flaps or irradiated tissue which can also make extrusion more likely. The use of simple nipple–areola tattooing is recommended for these patients. Autologous cartilage grafting in breast reconstruction procedures is the standard of care. There is a lack of lack of evidence in the peer reviewed published literature on the long-term outcomes, safety and efficacy of Xenograft cartilage use in breast reconstructive procedures.

Juvederm®: Juvederm (Allergan, Irvin, TX) Voluma® XC hyaluronic acid filler has been proposed to reshape nipples after reconstruction of the breast following mastectomy. On October 22, 2013, Juvederm Voluma XC received FDA premarket approval (PMA). The FDA indications for use state that the device is indicated for deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the midface in adults over the age of 21. Breast reconstruction is not specifically mentioned as an approved FDA indication (PMA Number: P110033). Evidence in the published, peer-reviewed scientific literature supporting the use of this product in breast reconstructive procedures is lacking and its role is unclear.

Radiesse®: Radiesse (BioForm Medical, Inc., San Mateo, CA) has been proposed to reshape nipples after reconstruction of the breast following mastectomy. Radiesse injections consist of very small, smooth calcium hydroxylapatite (CaHA) microspheres that are suspended in a water-based gel carrier. Radiesse has received PMA approval by the FDA as a medical device for subdermal implantation for two indications: correction of moderate to severe facial wrinkles and folds such as nasolabial folds and the correction of facial fat loss in people with human immunodeficiency virus (PMA Number: P050037). There remains a lack of evidence in the peer reviewed published literature on the long-term outcomes, safety and efficacy of Radiesse in breast reconstructive procedures.

Cook Biodesign® Nipple Reconstruction Cylinder: The Cook Biodesign Nipple Reconstruction Cylinder (Cook Biotech Incorporated, West Lafayette, IN) is a porcine non-cross-linked, non-dermis-based biologic graft material that is marketed for breast procedures including breast reconstruction, breast revision and mastopexy. It may be used in combination with Biodesign® Tissue Generation Matrix. On June 20, 2011, the Cook Biodesign Nipple Reconstruction Cylinder received FDA 510(k) approval. The FDA indications for use states it is intended for implantation to reinforce soft tissue where weakness exists in plastic and reconstructive surgery of the nipple. The cylinder is supplied sterile and is intended for one-time use. The Biodesign Nipple Reconstruction Cylinder is a rolled Small Intestinal Submucosa (SIS) mesh and available in sizes from 0.7 cm to 1.0 cm in diameter and 1.0 cm to 2.5 cm in length. The cylinder is a scaffold which becomes infiltrated by the host cells during the body's natural repair process. The device is implanted using a skin flap procedure that prevents migration of the device. The clinical performance of the Biodesign Nipple Reconstruction Cylinder was assessed in two case studies and anecdotal evidence of 186 device implants. Of the 188 implants, complications included device extrusion (number of extrusions not given). Follow-up periods ranged from 2 to 12 months. The clinical studies showed the Biodesign Nipple Reconstruction Cylinder as substantially equivalent to its predicates in its application (510(k) Number: K110402).

In the first multi-center prospective study, Collins et al. (2016) reported on the use of the Biodesign Nipple Reconstruction Cylinder (NRC) during reconstruction of the nipple after mastectomy in patients with a history of breast cancer and mastectomy. Unilateral or bilateral nipple reconstruction was performed. Skin flaps were raised, the NRC was placed beneath the flaps as a stent, and the site was protected for up to four weeks with a nipple shield. Nipple projection was measured for 12 months after surgery. Patient satisfaction was measured, and adverse events were recorded. Follow-up examinations were performed at one week, and then at one, three, six, and 12 months after surgery. A total of 82 nipple reconstructions were performed in 50 patients. Related postoperative adverse events were minor but reported in eight reconstructions (9.8%) representing seven patients (14.0%). Average projection at six and 12 months was 4.1 ± 1.6 mm and 3.8 ± 1.5 mm, respectively, compared with 10.5 ± 2.2 mm one week after surgery. Of patients completing the satisfaction questionnaire at 12 months, 70/75 (93.3%) of reconstructions were rated "pleased" or "very pleased" with the overall outcome. Overall, 45/46 (97.8%) patients would recommend nipple reconstruction to other women. This study is limited by the small homogenous sample size, lack of a control group and short-term follow-up.

There is a lack of evidence in the peer reviewed published literature regarding the long-term outcomes and efficacy of the Cook Biodesign Nipple Reconstruction Cylinder for use in breast reconstruction or for any other indication.

Contralateral Breast

Although the goal of breast reconstruction is to maintain symmetry, the process may leave the opposite or contralateral breast larger or smaller than the surgical breast. To correct this asymmetry, a mastopexy or reduction mammoplasty may be performed on the contralateral breast. If the reconstructed breast is larger, then an augmentation mammoplasty with implant may be performed on the nondiseased breast (Roehl, et al., 2012).

Oncoplastic Reconstruction

Oncoplastic procedures are performed immediately or one to two weeks after lumpectomy, once final pathology is available. They include rearrangement of the remaining breast tissue through a variety of techniques, often adhering to breast reduction principles. In addition, more tissue can be brought into the breast to correct the volume deficit, often in the form of a latissimus dorsi flap. Indications for these procedures depend on the patient's preoperative breast size, available remaining breast tissue, and overall goals for ultimate breast size and shape. All these procedures are done prior to radiation to prevent contracture of the lumpectomy defect and distortion of the nipple-areolar complex (Roehl, et al., 2012).

Radiation Tattoo Markers: Ink markers are tattooed as landmarks before radiotherapy of breast cancer with the purpose of obtaining a precise radiation field. These tattoos are permanent and are the size of a freckle. Individuals may have these tattoo markers removed via laser or punch biopsy excision as a part of the overall breast reconstruction procedure (Bregnhoj, et al., 2010).

Nonsurgical Options

Some women may choose not to have breast reconstruction or are poor candidates for reconstruction. For these women, an external breast prosthesis and/or mastectomy bras are additional options (Hu, et al., 2007).

Skin Substitutes

During breast reconstruction, acellular dermal skin substitutes (i.e., AlloDerm®, AlloMax™, DermACELL® and FlexHD®) are primarily used in the setting of tissue expander and breast implant reconstruction. Patients should be in overall good health and have no underlying condition that

would restrict blood flow or interfere with the normal healing process (e.g., uncontrolled diabetes, hypertension, previous surgery). These matrixes may be indicated when there is insufficient tissue expander or implant coverage by the pectoralis major muscle and additional coverage is required, as may be the case in a very thin patient; if there is viable but compromised or thin post-mastectomy skin flaps that are at risk of dehiscence or necrosis; or if there is a need to re-establish the inframammary fold and lateral mammary fold landmarks. When used in appropriate candidates, these skin substitutes are proposed to improve control over placement of the inframammary fold and final breast contour, enhance use of available mastectomy skin, reduce the number of expander fills necessary, reduce time to complete expansion and eventual implant exchange, potential improved management of a threatened implant, reduce the need for explantation and the potential for reduction in the incidence of capsular contracture. However, there are ongoing concerns regarding the increased risk of seroma and infection, a higher risk of an implant having to be removed, and tissue flap death (Nguyen, et al., 2011; Sbitany and Serletti, 2011).

There is a paucity of data comparing the skin substitute products directly. The products vary in many aspects, including the source of tissue, processing, storage, surgical preparation and available sizes. The most familiar product to most plastic surgeons, AlloDerm, was the first human dermis product available in 1994 (Cheng, et al., 2012).

U.S. Food and Drug Administration (FDA)
Depending on the purpose of the product and how it functions, skin substitutes are regulated by the FDA premarket approval (PMA) process, 510(k) premarket notification process, or the FDA regulations for banked human tissue.

Products that are classified by the FDA under the PMA process as a class III, high-risk device require clinical data to support their claims for use. These devices may be used as a long-term skin substitute or a temporary synthetic skin substitute. They actively promote healing by interacting directly or indirectly with the body tissues.

Other wound care devices are approved by the 510(k) process, and their primary purpose is to protect the wound and provide a scaffold for healing. They may or may not be integrated into the body tissue. Some devices are rejected by the body after approximately ten days to several weeks and removed prior to definitive wound therapy or skin grafting.

In 2021, the FDA issued a safety communication regarding acellular dermal matrix (ADM) products indicating that higher complication rates may be present in certain ADMs used in implant-based breast reconstruction. ADMs are developed from either human (e.g., FlexHD, AlloMax, AlloDerm) or animal skin (e.g., SurgiMend) and have had the cells removed leaving behind the support structure for use. The FDA has not approved any ADMs for the indication of implant-based breast reconstruction. The FDA's safety communication cited a prospective corhort study evaluating safety outcomes (i.e., reoperation, explantation, infection) from implant-based breast reconstruction surgeries after mastectomy in multiple centers in the United States and Canada that showed significantly higher complication rates in patients with FlexHD and AlloMax ADMs two years after surgery compared to a control group that did not receive an ADM. The FDA pointed to a need for additional, high-quality studies evaluating the safety and efficacy of ADMs. As a result of their analysis, the FDA has given the following recommendations for health care providers:

- "Discuss the potential benefits and risks of all relevant treatment options with your patients as part of a shared decision-making process.

- Be aware that the FDA has not approved or cleared any ADM products for use in implant-based breast reconstruction. Data analyzed by the FDA and published literature suggest that some ADMs may have higher risk profiles than others.
- Be aware that the FDA does not recommend reoperation or removal of implanted ADM as a preventive measure.
- Report any patient adverse events to the FDA MedWatch program, using the information in the Reporting Problems with Your Device page" (FDA, 2021d).

Donated skin that requires minimal processing and is not significantly changed in structure from its natural form is classified by the FDA as banked human tissue, is not considered a medical device, and does not require PMA or 510(k) approval. Donated skin (human cells or tissue) intended for implantation, transplantation, infusion, or transfer into a human recipient is regulated as a human cell, tissue, and cellular and tissue-based product (HCT/P) by the Center for Biologics Evaluation and Research (CBER) (FDA, 2021). The American Association of Tissue Banks (AATB) sets standards for the safety and use of donated human tissue (AATB, 2019). AATB oversees a voluntary accreditation program and the FDA focuses on preventing the transmission of communicable diseases by requiring donor screening and testing. Tissue establishments must register with the FDA and list each cell or tissue produced. An example of a banked human tissue product is AlloDerm, an acellular dermal matrix (FDA, 2004).

The following skin substitutes are derived from human tissue and therefore subject to the rules and regulations for banked human tissue developed by the American Association of Tissue Banks (AATB) (this list may not be all-inclusive):

- Alloderm
- Allomax
- Cortiva
- DermACell
- DermaMatrix
- FlexHD
- hMatrix
- Repriza

The safety and efficacy of the skin substitutes listed below are supported by the evidence in the published peer-reviewed scientific literature and/or are established treatment options for post-mastectomy breast reconstruction.

AlloDerm™: AlloDerm (Allergan™, Parsippany, NJ [formerly LifeCell™ Corporation, Branchburg, NJ]) is an acellular dermal matrix allograft classified as banked human tissue by the FDA because it is minimally processed and not significantly changed in structure from the natural material. AlloDerm is an established treatment option and is supported by the evidence in the published peer-reviewed scientific literature for tissue repair during postmastectomy breast reconstruction (Lee, et al., 2018; McCarthy, et al., 2012; Cheng, et al., 2012; Vardanian, et al., 2012; Jansen and Macadam, 2011; Salzberg, et al., 2011; Joanna, et al., 2011; Antony, et al., 2010; Haddock, et al., 2010; Spear, et al., 2008; Bindingnavele, et al., 2007; Breuing and Colwell, 2007; Zienowicz, et al., 2007; Gamboa-Bobadilla, 2006; Glasberg, et al., 2006; Salzberg, 2006; Breuing, et al., 2005; Nahabedian, 2005). Various forms of AlloDerm are available including AlloDerm™ Regenerative Tissue Matrix, AlloDerm Select™ Tissue Matrix and AlloDerm Select Duo™ Tissue Matrix Bilateral Pair (Allergan Aesthetics, 2023; Hayes, 2019, reviewed 2020).

AlloMax™: AlloMax Surgical Graft (Bard Davol, Inc. Warwick, RI) is an acellular non-cross-linked human dermis allograft. Because AlloMax is a natural human product it is classified as banked human tissue and does not require FDA approval. It is regulated by the American Association of

Tissue Banks and the FDA guidelines for banked human tissue. AlloMax Surgical Graft is available in multiple sizes. The AlloMax Surgical Graft for Breast Reconstruction (previously marketed as NeoForm™) is proposed for post-mastectomy breast reconstruction and is an established skin substitute for this indication (Venturi, et al., 2013; Bard, 2017).

Cortiva®
Cortiva (RTI Surgical, Alachua, FL) is a non-crosslinked, cadaveric human acellular dermal matrix processed by Tutoplast technology using low-dose gamma irradiation. The matrix is FDA regulated as human cell, tissue, and cellular and tissue-based product (361 HCT/P) and proposed for the repair, replacement, reconstruction or augmentation of soft tissue, including supplemental support and reinforcement of soft tissue in breast reconstruction and hernia repair. There are three products: Cortiva, Cortiva 1.0 mm and Cortiva 1 mm tailored allograft dermis. The matrixes are offered in regular and 1 mm thicknesses and supplied in a range of sizes from 2x4 cm to 16x20 cm (RTI, Inc., 2021; Centers for Medicare and Medicaid Services [CMS], 2015). Cortiva has evolved into an acceptable tissue substitute for breast reconstruction and a randomized controlled trial with short-term follow-up reported that outcomes with Cortiva were not inferior to outcomes using AlloDerm.

Parikh, et al. (2018) reported the outcomes of a phase 2 randomized controlled trial that compared outcomes following breast reconstruction surgery using Cortiva 1 mm allograft or AlloDerm Ready to Use (RTU) regenerative tissue matrix. The 16x8 cm graft was used as a sling to support tissue expanders placed in the submuscular location in one study arm, and prepectoral reconstructions with tissue expanders (TEs) or direct-to-implants (DTI) in a second study arm. The interim analysis of the submuscular reconstruction group is reported herein. Breasts reconstructed with AlloDerm RTU (n=17 patients; 28 breasts) or Cortiva 1 mm (n=17 patients; 31 breasts) submuscular TE, completed the interim analysis. During the study a significant shift to prepectoral reconstructions was noted and the prepectoral arm of the study was added to optimize enrollment rates. Patients who underwent prepectoral breast reconstruction with either DTI or TE supported by a 20x16 cm ADM sheet were compared in a separate study arm. The decision to proceed with prepectoral or submuscular reconstruction with either a TE or DTI was determined preoperatively. Female patients, aged 22–70 years old, undergoing immediate prosthetic reconstruction following therapeutic or prophylactic skin- or nipple-sparing mastectomy with a body mass index (BMI) less than 36 kg/m^2 were included. Excluded patients were those who were pregnant or breastfeeding immediately before mastectomy. The primary outcome measure was premature explantation of the TE before exchange, or unintended explantation of a DTI reconstruction during the first three months postoperatively. Secondary outcome measures included other complications (e.g., seroma, cellulitis, wound or ADM dehiscence, skin flap necrosis). Patients undergoing TE placement in either study arm were followed until there was TE exchange with an implant, flap, or both, or there was premature removal of the device. Patients undergoing DTI reconstruction were followed for at least three months following surgery. Patients undergoing reoperation of the surgical site without device exchange or removal were kept in the study. Patients underwent planned exchange of TEs for implants or flaps within 145.6 ± 51.6 days in the AlloDerm group and 167.0 ± 61.5 days in the Cortiva 1 mm group (p=0.27), not statistically significant. Most patient were exchanged with breast implant alone, but 14.3% in the AlloDerm group and 26.6% in the Cortiva group (p=0.25) received an autologous flap, not statistically significant. There was no significant difference between the group in integration of the ADM to the mastectomy flap (p=0.69), in drain removal between the groups or in physical well-being, or satisfaction with information or plastic surgeon. A significant difference was seen in detectable seroma in the AlloDerm (n=3) vs. the Cortiva group (n=0). Premature explantation was performed in no Alloderm breast vs. one breast with Coriva. The initial size of the TE selected was significantly larger in patients reconstructed with Cortiva 1 mm (p=0.02). The AlloDerm RTU group was comprised of a significantly higher proportion of patients who had never smoked (p=0.009). This interim analysis of submuscular reconstructions patients revealed no evidence of

inferiority of outcomes of AlloDerm vs. Cortiva. Limitations of the study include the small patient population and short-term follow-up.

DermACELL™: DermACELL (LifeNet Health®, Virginia Beach, VA) is an acellular human dermis allograft collagen scaffold proposed for the treatment of breast reconstruction. LifeNet Health is registered with the FDA as an establishment producing tissue- and cellular-based products. MatrACELL® is a patented process that removes > 97% of donor DNA that renders Demacell acellular. Terminal sterilization is performed by low dose gamma irradiation. The use of DermACELL for breast reconstruction has evolved into an accepted standard of practice. Although the evidence supporting DermACELL for breast reconstruction is primarily in the form of case series and retrospective reviews, outcomes reported a significant improvement in time to drainage removal and fewer "red breast episodes" compared to AlloDerm (Pittman, et al., 2016). Zenn et al. (2016) reported that DermACELL was as good as Alloderm RTU in the occurrence of postoperative infection, implant loss, seroma and hematoma. Other studies have also reported favorable outcomes with DermACELL (Bullocks, et al., 2014; Vashi, 2014). Therefore, DermACELL has evolved into an accepted skin substitute for breast reconstruction (Swisher, et al., 2022; Ortiz, 2017; Chang and Liu, 2017; Pittman, et al., 2016; Zenn, et al., 2016; Bullocks, et al., 2014; Vashi, 2014).

FlexHD® Acellular Hydrated Dermis: FlexHD Acellular Hydrated Dermis (Musculoskeletal Transplant Foundation, Edison, NJ) is a matrix derived from donated human allograft skin. The product is regulated by the American Association of Tissue Banks and the FDA guidelines for banked human tissue. FlexHD is indicated for the replacement of damaged or inadequate integumental tissue or for the repair, reinforcement or supplemental support of soft tissue defects. Flex HD is available in multiple sizes and configurations including the FlexHD Pliable PRE™ which is a deeper cut of ADM consisting entirely of reticular dermis for ease of graft placement. Results of case series and retrospective reviews in the peer-reviewed literature support the safety and efficacy of FlexHD for use during postmastectomy breast reconstruction. FlexHD is an established skin substitute for this indication (Lee, et al., 2018; Liu, et al., 2014; Seth, et al., 2013; Seth, et al., 2012; Brooke, et al., 2012; Rawlani, et al., 2011; Cahan, et al., 2011; Topol, et al., 2008).

NeoForm™ Dermis: Neoform Dermis (Mentor Corp., Santa Barbara, CA) is a solvent-dehydrated, gamma-irradiated preserved human allograft dermis indicated for use as a soft tissue graft for horizontal and vertical soft tissue augmentation of thickness and length, such as breast reconstruction. NeoForm is classified as banked human tissue by the FDA. Although evidence in the published, peer-reviewed scientific literature supporting the use of this product in breast reconstruction is limited, Neoform Dermis is an established skin substitute used for tissue expansion in breast reconstruction following a mastectomy. Neoform is no longer available for distribution.

Other Skin Substitutes

Additional skin substitutes have been proposed as treatment options in breast reconstruction as discussed below, but the evidence in the published peer-reviewed scientific literature does not support the safety and efficacy of the use of these substitutes. The number of available studies is limited and involves small, heterogeneous patient populations, short-term follow-ups, minimal comparisons to the established treatment method for the condition, and/or lack of a control group. In some cases, reported outcomes are inconsistent, and a consensus on patient selection criteria and the appropriate surgical approach and techniques that should be used have not been established.

ARTIA™ Reconstructive Tissue Matrix: ARTIA Reconstructive Tissue Matrix (Artia Tissue Matrix)/ ARTIA Tissue Matrix-Perforated (Allergan™, Parsippany, NJ [formerly LifeCell™ Corporation, Branchburg, NJ]) is a surgical mesh that is derived from porcine skin that is

processed and preserved in a patented phosphate buffered aqueous solution containing matrix stabilizers. ARTIA was originally developed by LifeCell Corporation and is currently distributed by Allergan. According to the FDA 510(k) approval, ARTIA Tissue Matrix is intended for use as a soft tissue patch to reinforce soft tissue where weakness exists and for the surgical repair of damaged or ruptured soft tissue membranes which require the use of reinforcing or bridging material to obtain the desired surgical outcome. The implant is intended for reinforcement in plastic and reconstructive surgery (510(k) Number: K162752). There is insufficient evidence to support the safety and efficacy of ARTIA Reconstructive Tissue Matrix as a skin substitute for breast reconstructive surgery.

Avance® Nerve Graft: Mastectomy can result in diminished or absent sensation which can lead to a decreased sense of femininity and sexuality and potential thermal or mechanical injury. Neurotization is a technique used to repair the loss of sensation and can be achieved through autografts, allografts, or nerve conduit tubes depending on the length of the gap (Hamilton, et al., 2021). Neurotization using allografts has been proposed as a means to bridge large nerve gaps when nerve autografts are not feasible with the potential to recover sensation earlier and with increased quality and quantity. Avance Nerve Graft (AxoGen, Inc., Alachua, FL) is an acellular, processed human peripheral nerve tissue proposed for the surgical repair of severed peripheral nerve discontinuities to support regeneration. The device maintains a 3-dimention scaffold that is proposed to support cell migration and tissue regeneration. Avance is regulated by the FDA Human Cellular and Tissue-based Products and the guidelines of the American Association of Tissue Banks (AATB). The product is available in 16 sizes (Axogen, 2024).

Literature Review
There is insufficient evidence to support the safety and efficacy of neurotization with processed nerve allografts (e.g., Avance Nerve Graft) after mastectomy either during immediate or delayed breast reconstruction. Studies are in the form of a cohort studies and case reports limited by small patient populations, short term follow-up and heterogeneity of surgical procedures. Studies were also lacking safety outcomes (Peled, et al., 2023; Momeni, et al., 2021; Djohan, et al., 2020; Peled and Peled, 2019).

Momeni et al., (2021) conducted a cohort study of individuals from a single institution to evaluate sensation outcomes of the reconstructed breast following neurotization using a processed nerve allograft. This study was an arm of the Registry study of Avance Nerve Graft utilization, Evaluations, and outcomes in peripheral nerve Repair (RANGER). Patients (n=59; breasts=96) ranged in age from 24–69 years old. A total of 33 patients were white, 14 were Asian, and 12 were Hispanic. Patients who underwent microsurgical breast reconstruction following mastectomy with free abdominal flaps by a single surgeon with follow-up of ≥12 months were included in the study. Patients who underwent autologous reconstruction using donor-sites other than the abdomen, reconstruction with stacked flaps, and implant-based reconstruction were excluded. There were two cohort groups: patients who underwent flap neurotization utilizing a 1-2mm x 50mm processed human nerve allograft (i.e., Avance, AxoGen, Alachua, FL) (n=39; breasts=59) and those who did not undergo neurotization (n=20; breasts=37). The primary outcome measured was cutaneous pressure threshold using the Semmes-Weinstein monofilaments test (SWMF) at nine pre-defined locations on the breast. Follow-up took place at three, six, twelve, and eighteen months. The majority of patients in both groups underwent bilateral immediate reconstruction following nipple-sparing mastectomy for malignancy. However, procedures also included areola-sparing, skin sparing, and simple mastectomy and reconstruction also included delayed-immediate and delayed. A total of 22 patients (group 1=22 breasts; group 2=14 breasts) had a complete data set at ≥12 months and were included in the final analysis. Compared to those who did not undergo neurotization, group one was associated with a greater likelihood for return of protective sensation in the majority of breast locations ($p<0.01$). Author noted limitations of the study included: non-randomized study design, small sample size, and a lack of

secondary outcomes (e.g., impact of medical conditions, chemotherapy, radiotherapy on sensory outcomes). Additional limitations of the study include short term follow-up, heterogeneity of mastectomy procedures, and the lack of safety outcome measures. Additional long-term, high quality studies are needed to evaluate the safety and efficacy of neurotization using processed nerve allografts on sensation outcomes in patients who underwent mastectomy and breast reconstruction.

BellaDerm® Acellular Hydrated Dermis: BellaDerm Acellular Hydrated Dermis (Musculoskeletal Transplant Foundation, Edison, NJ) is human allograft skin minimally processed to remove epidermal and dermal cells and is packaged in an ethanol solution. The process utilized preserves the extracellular matrix of the dermis. The resulting allograft serves as a framework to support cellular repopulation and vascularization at the surgical site. BellaDerm is processed to remove cells while maintaining the integrity of the matrix with the intent to address the issues of the specific and nonspecific inflammatory responses. It is used for the replacement of damaged or inadequate integumental tissue or for the repair, reinforcement or supplemental support of soft tissue defects. Grafts of BellaDerm can range between 0.8mm and 1.7mm. It is used for breast augmentation revision procedures, including correction of symmastia, capsular contracture, bottoming out and malposition. There is insufficient evidence to support the safety and efficacy of BellaDerm Acellular Hydrated Dermis as a skin substitute for breast reconstructive surgery.

DermaMatrix Acellular Dermis: DermaMatrix (formerly manufactured by Synthes Inc., West Chester, PA) is an allograft derived from human skin and is classified by the FDA as banked human tissue. DermaMatrix is proposed for use for breast reconstruction postmastectomy. Per the manufacturer, as of June 2014, DermaMatrix is no longer available for distribution.

DuraSorb® Monofilament Mesh/ Polydioxanone Surgical Scaffold™: DuraSorb® Monofilament Mesh/ Polydioxanone Surgical Scaffold™ (Surgical Innovation Associates, Inc [SIA]; Philadelphia, PA) is a resorbable, colorless, monofilament knit surgical mesh made entirely of uncolored and undyed polydioxanone (PDO) thread. Polydioxanone Surgical Scaffold is proposed for use in reinforcement of soft tissue where weakness exists. On August 1, 2018, 510(k) approval (510(k) Number: K181094) was given to Polydioxanone Surgical Scaffold™. It is manufactured in two rectangular shapes: 6x16 cm and 10x25 cm. According to the manufacturer's Instructions for Use, DuraSorb has not been studied for use in the repair of direct inguinal hernias, intraperitoneal use, contaminated and/or infected wounds or in breast reconstructive surgeries (Surgical Innovation Associates, 2021). Evidence is lacking in the published peer-reviewed literature to support the clinical effectiveness of DuraSorb Monofilament Mesh/ Polydioxanone Surgical Scaffold for any indication.

GalaFLEX® Scaffold: This surgical scaffold (Tepha, Inc., Lexington, MA) is a sterile, knitted, resorbable mesh, constructed of non-dyed monofilament fibers made from poly-4-hydroxylbutyrate (P4HB). P4HB is produced from a naturally occurring monomer and is processed into monofilament fibers and knitted into a surgical fold. It is provided in single sheets of varying widths, lengths and shapes, and may also be cut to the shape or size desired for a specific application. According to the FDA 510(k) approval GalaFLEX Scaffold is indicated for use "as a transitory scaffold for soft tissue support and to repair, elevate and reinforce deficiencies where weakness or voids exist that require the addition of material to obtain the desired surgical outcome. This includes reinforcement of soft tissue in plastic and reconstructive surgery, and general soft tissue reconstruction. Although the published literature investigating GalaFLEX in breast reconstruction is primarily in the form of retrospective reviews and case series with small patient populations (n=11-62) and short-term follow-ups (12 months) (Adams, et al., 2018; Nair et al., 2018; Adams, et al., 2016), it has evolved into a standard of care as a skin substitute for breast reconstructive surgery (Movassaghi and Stewart, 2024; Frey and Choi, 2020). (510(k) Number: K140533).

Sigalove et al. (2022) conducted a retrospective review of consecutive patients (n=263) to evaluate the safety of using GalaFLEX and AlloDerm (n=135, 250 breasts) versus AlloDerm alone (n=128, 249 breasts) in immediate, expander-implant, prepectoral breast reconstruction. Excluded were patients who underwent delayed, single-stage, revision, or hybrid autologous-prosthetic reconstruction. Primary outcomes measured was the complication rate. Follow up for the Galaflex-AlloDerm group was an average of 15 ± 7.8 months and the AlloDerm alone group follow up was an average of 41.9 ± 12 months. Rate of any complication was 6.4% (16 breasts) in the Galaflex-AlloDerm group and 7.6% (19 breasts) in the AlloDerm alone group. Complication type in the Galaflex-AlloDerm group versus (vs) the AlloDerm alone group included surgical site infection (five breasts vs four breasts), skin necrosis (three breasts vs 13 breasts), seroma (eight breasts vs seven breasts), wound dehiscence (two breasts vs five breasts), prothesis exposure (four breasts vs three breasts), return to operating room (13 breasts vs nine breasts), prothesis loss (eight breasts vs four breasts), and capsular contracture (two breasts vs two breasts). Author noted limitations include retrospective study design and short term follow up. The complication rate of Galaflex and Alloderm in in two-stage, prepectoral breast reconstruction was similar to the complication rate of Alloderm alone.

GalaFLEX™ 3DR Scaffold: GalaFLEX™ 3DR Scaffold (Tepha, Inc., Lexington, MA) is a bioresorbable surgical scaffold manufactured from P4HB. According to the FDA 510(k) approval, GalaFLEX 3DR Scaffold (formerly known as GalaFORM 3D scaffold) is indicated for use as a bioresorbable scaffold for soft tissue support and to repair, elevate and reinforce deficiencies where weakness or voids exist that require the addition of material to obtain the desired surgical outcome. This includes reinforcement of soft tissue in plastic and reconstructive surgery, and general soft tissue reconstruction. GalaFLEX™ 3DR Scaffold is also indicated for the repair of fascial defects that require the addition of a reinforcing or bridging material to obtain the desired surgical result. The predicate device is GalaFLEX™ Scaffold (510(k) Number: K162922). There is sufficient evidence to support the safety and efficacy of GalaFLEX™ 3DR Scaffold as a skin substitute for breast reconstructive surgery.

GalaFLEX 3D Scaffold: GalaFLEX 3D Scaffold (formerly known as GalaSHAPE 3D) (Tepha, Inc., Lexington, MA) is a 3-dimensional monofilament scaffold made from poly-4-hydroxylbutyrate (P4HB). After implantation, the scaffold is proposed to gradually bioresorb over 18-24 months providing a lattice for new tissue ingrowth and regeneration. The FDA 510(k) approval indications for use state that "GalaSHAPE™ 3D is indicated for use as a bioresorbable scaffold for soft tissue support and to repair, elevate and reinforce deficiencies where weakness or voids exist that require the addition of material to obtain the desired surgical outcome. This includes reinforcement of soft tissue in plastic and reconstructive surgery, and general soft tissue reconstruction. GalaSHAPE™ 3D is also indicated for the repair of fascial defects that require the addition of a reinforcing or bridging material to obtain the desired surgical result" (Galatea Surgical, 2024) (510(k) Number: K161092). The Galatea products are available in various sizes in oval, rectangular, triangular, circular shapes and can be custom made. There is sufficient evidence to support the safety and efficacy of Galatea products as a skin substitute for breast reconstructive surgery.

hMatrix®: hMatrix Acellular Dermis (Bacterin International Holdings Inc., Belgrade, MT) is an acellular dermal scaffold processed from donated human skin. The dermis is processed using a proprietary method and the matrix is packaged and sterilized using low-dose gamma irradiation. hMatrix is regulated by the American Association of Tissue Banks and the FDA guidelines for banked human tissue. The product is stored and supplied frozen. Bacterin hMatrix PR for breast augmentation (Bacterin, 2015). hMatrix is available in four sizes. There is insufficient evidence to support the safety and efficacy of hMatrix as a skin substitute for breast reconstruction.

OviTex®: OviTex® (TELA Bio®, Inc., Malvern, PA) is a reinforced tissue matrix composed of interwoven biologic material derived from ovine rumen and polymer reinforcement. The polymer fiber is available in resorbable or permanent variations. It is proposed for use as a surgical mesh to reinforce and/or repair soft tissue where weakness exists. Indications for use include the repair of hernias and/or abdominal wall defects that require the use of reinforcing or bridging material to obtain the desired surgical outcome. The OviTex portfolio of products includes: OviTex, a four layer device not intended for intraperitoneal placement; OviTex 1S, a six layer device with smooth external layers suitable for intraperitoneal placement; OviTex 2S, an eight layer device with two smooth external layers suitable for intraperitoneal placement; OviTex LPR, a four layer device with a smooth side suitable for laparoscopic and robotic-assisted intraperitoneal placement; and OviTex PRS, a two or three layer device available in four shapes for plastic and reconstructive surgery. In order to achieve better fluid management, tissue integration, and directional flexibility, OviTex PRS was designed with micropores, macropores, and stents to address soft tissue repair in plastic and reconstructive surgery (TelaBio® Inc., 2024). OviTex received FDA 510(k) (K141053) as Ovine Tissue Matrix (OTM) in 2014 (FDA, 2022). It is available in various sizes. Evidence in the published, peer-reviewed scientific literature supporting the use of this product in breast reconstruction is lacking and its role is unclear.

Permacol™: The Permacol Crosslinked Porcine Dermal Collagen Surgical Mesh (Tissue Sciences Laboratories PLC, Hants, United Kingdom), a xenograft, is a fibrous flat sheet comprised of acellular porcine dermal collagen and elastin. According to the FD) 510(k) approval, Permacol™ is intended for use as a soft tissue patch to reinforce soft tissue where weakness exists and for the surgical repair of damaged or ruptured soft tissue membranes (510(k) number: K992556). Breast reconstruction is not specifically mentioned as an approved FDA indication. However, muscle flap reinforcement is an FDA-approved indication for use. Permacol is available in multiple sizes. Evidence in the published, peer-reviewed scientific literature supporting the use of this product in breast reconstruction is lacking and its role is unclear (Knabben, et al., 2017; Ramsden, et al., 2009).

Phasix™ Mesh: Phasix Mesh (Bard Davol, Inc. Warwick, RI), is a fully resorbable P4HB polymer material proposed for use in breast reconstructive procedures. The P4HB is produced from a naturally occurring monomer and is processed into monofilament fiber then knitted into a surgical mesh. Phasix Mesh received FDA 510k approval on March 31, 2015 to reinforce soft tissue where weakness exists in patients undergoing plastic and reconstructive surgery, or for use in procedures involving soft tissue repair, such as the repair of hernia or other fascial defects that require the addition of a reinforcing or bridging material to obtain the desired surgical result (510(k) Number: K142818). The FDA approved indication for Phasix has no specific language related to breast reconstruction. Phasix is available in multiple sizes as round, rectangular, and square implants (Hayes, 2019, reviewed 2020). Evidence in the published, peer-reviewed scientific literature supporting the use of this product in breast reconstruction is lacking and its role is unclear.

Renuva® Allograft Adipose Matrix: Renuva® Allograft Adipose Matrix (MTF Biologics, Edison, NJ) is an injectable allograft adipose matrix processed from human adipose tissue. It has been proposed for use as part of a breast reconstruction procedure post mastectomy. According to the manufacturer's Instructions for Use, it is indicated for the replacement of damaged or inadequate integumental adipose tissue matrix in areas of the body where native fat would exist and for the reinforcement or supplemental support in underlying adipose tissue matrix as the result of damage or naturally occurring defects (MTF Biologics, 2020). Renuva Allograft Adipose Matrix is regulated by the FDA under 21 CFR Part 1271 Human Cells, Tissues and Cellular and Tissue-Based Products (HCT/Ps). It is available in 1.5cc and 3cc. Evidence in the published, peer-reviewed scientific literature supporting the use of this product in breast reconstruction is lacking and its role is unclear.

Repriza® Acellular Dermal Matrix: Repriza (Promethean Lifesciences Inc., Pittsburg, PA) is a human skin, acellular dermal matrix. The product is regulated by the American Association of Tissue Banks and the FDA guidelines for banked human tissue. Repriza is membrane free and proposed for implantation for reconstructive surgery including breast reconstruction, abdominal wall reconstruct and augmentation of soft tissue irregularities. The matrix is provided in 4X12 cm and 6X16 cm sheets. It can also be custom made. There is insufficient evidence to support the safety and efficacy of Repriza for breast reconstructive surgery.

SERI™ Surgical Scaffold: SERI Surgical Scaffold (Sofregen Medical Inc., Cambridge, MA formerly Allergan, Medford, MA) has been proposed as a skin substitute for breast reconstruction (Jewell, et al., 2015). Breast reconstruction is not specifically mentioned as an approved FDA indication. The FDA 510(k) summary states that SERI is a "knitted, multi-filament, bioengineered, long-term bioresorbable scaffold. It is derived from silk that has been BIOSILK™ purified to yield ultra-pure fibroin. The device is a mechanically strong and biocompatible bioprotein" (FDA, 2013). The FDA indications for use state, "SERI Surgical Scaffold is indicated for use as a transitory scaffold for soft tissue support and repair to reinforce deficiencies where weakness or voids exist that require the addition of material to obtain the desired surgical outcome. This includes reinforcement of soft tissue in plastic and reconstructive surgery, and general soft tissue reconstruction" (510(k) Number K123128). There is insufficient evidence in the published peer-reviewed scientific literature supporting the efficacy of SERI Surgical Scaffold for breast reconstruction.

In May 2015 the FDA issued a warning letter to Allergan stating that the FDA approval of SERI Surgical Scaffold did not include the use of SERI Surgical Scaffold for breast reconstruction. Per the FDA, this indication falls outside of the intended use "because surgical mesh has not been cleared or approved for use in breast reconstruction using a tissue expander or implant". The FDA requested Allergan "immediately cease activities that result in the misbranding or adulteration of the SERI Surgical Scaffold" for breast reconstruction" (FDA, 2015).

Sofregen Medical Inc., issued a statement indicating that as of Dec 31, 2021, Seri Surgical Scaffold is no longer commercially available. Sofregen pointed to the fact that the remaining inventory was approachign the end of the approved shelf life as the reason for discontinuation (Sofregen Medical Inc., 2021).

SimpliDerm™: SimpliDerm™ (Aziyo Biologics, Silver Spring, MD) is a pre-hydrated human acellular dermal matrix minimally processed to remove epidermal and dermal cells and then preserved in an irradiation protection solution. The process utilizes a proprietary and patented technology to preserve the remaining bioactive components and extracellular matrix of the dermis. It is proposed for the repair or replacement of damaged or insufficient integumental tissue and for the repair, reinforcement, or supplemental support of soft tissue defects or any other homologous use of human integument (Alutia, 2024). The product is classified as a human tissue and cell-based product regulated by the American Association of Tissue Banks (AATB) and in compliance with U.S. FDA regulations (21 CFR 1271). It is available in both Ellipse™ and rectangular sizes. There is insufficient evidence in the published peer-reviewed scientific literature to support the safety and efficacy of Simpliderm (Hydrated Acellular Dermal Matrix) for any indication.

Strattice™ Reconstructive Tissue Matrix or LTM Surgical Mesh: Strattice Reconstructive Tissue Matrix or LTM Surgical Mesh (Allergan™, Parsippany, NJ [formerly LifeCell™ Corporation, Branchburg, NJ]) is an acellular, xenographic tissue matrix derived from porcine dermis (FDA, 2007). It is FDA 510(k) approved as LTM-RC surgical mesh "for use as a soft tissue patch to reinforce soft tissue where weakness exists and for the surgical repair of damaged or ruptured soft tissue membranes. The implant is intended for the reinforcement of soft tissues repaired by

sutures or suture anchors, during rotator cuff surgery. Indications for use also include the repair of hernias and/or body wall defects which require the use of reinforcing or bridging material to obtain the desired surgical outcome" (FDA, 2007). Strattice is proposed for use during postmastectomy breast reconstruction to support medial repair for breast pocket size and position. Strattice is available in seven sizes with various shapes. There is insufficient evidence in the published peer-reviewed scientific literature supporting the efficacy of Strattice. Studies are primarily in the form of retrospective reviews (Dikmans, et al., 2016; Barber, et al., 2015; Lardi, et al., 2014; Kilchenmann, et al., 2014; Maxwell, et al., 2014; Glasberg and Light, 2012).

In June 2015 the FDA issued a warning letter to LifeCell Corporation stating that the FDA approval for Strattice did not include the use of Strattice for breast reconstruction. Per the FDA, this indication falls outside of the intended use "because surgical mesh has not been cleared or approved for use in breast reconstructive surgery applications". The FDA requested that LifeCell "immediately cease activities that result in the misbranding or adulteration of the Strattice Reconstructive Tissue Matrix" for breast reconstruction.

SurgiMend® Collagen Matrix: SurgiMend or SurgiMend Collagen Matrix (Integra® LifeSciences Corp., Plainsboro, NJ formerly TEI Biosciences Inc., Boston, MA) is an acellular dermal tissue matrix derived from fetal or neonatal bovine dermis. The matrix acts as a scaffold that is progressively integrated, remodeled, and replaced by the functional host tissue. Approved as a Class II, FDA 510(k) device, SurgiMend is "intended for implantation to reinforce soft tissue where weakness exists and for the surgical repair of damage or ruptured soft tissue membranes" specifically for plastic and reconstructive surgery, muscle flap reinforcement, and hernia repair (e.g., abdominal, inguinal, femoral, diaphragmatic, scrotal, umbilical, incisional) (510(k) Number: K083898). SurgiMend is available in multiple sizes and thicknesses. SurgiMend PRS, a pure collagen product, is designed for plastic and reconstructive surgery and is available in multiple shapes, sizes and thicknesses (Integra LifeSciences Corp, 2023; Butterfield, et al., 2013, Gaster, et al., 2013, Ohkuma, et al., 2013; Endress, et al., 2012; Craft, et al., 2011; Cromwell, et al., 2009).

TEI has historically marketed SurgiMend for breast reconstruction. In May 2015, the FDA issued TEI a warning letter stating that TEI did not have FDA clearance or approval to market SurgiMend for breast reconstruction. Per the FDA, this indication falls outside of the intended use "because surgical mesh has not been cleared or approved for use in breast reconstructive surgery applications". The FDA requested that TEI "immediately cease activities that result in the misbranding or adulteration of SurgiMend" for breast reconstruction (FDA, 2015).

Veritas Collagen Matrix: Veritas Collagen Matrix (Synovis® Surgical Innovations, St. Paul, MN) is an implantable noncrosslinked biologic mesh made from bovine pericardium. Veritas is FDA approved as a surgical mesh under the 510(k) process for use as an implant for surgical repair of soft tissue deficiencies including: muscle flap reinforcement. There is also a Veritas Collagen Matrix Dry product that is FDA approved as a predicate device for the conventional Collagen Matrix (FDA, 2008; FDA, 2006). There is insufficient evidence to support the use of Veritas Collagen Matrix. The limited number of published studies investigating is primarily in the form of retrospective reviews.

Systematic Review and Meta-Analysis: Ho et al. (2012) conducted a systematic review and meta-analysis to determine an aggregate estimate of risks associated with acellular dermal matrix (ADM)-assisted breast reconstruction. AlloDerm was used in the majority of studies. ADMs other than AlloDerm were used in one study (i.e., FlexHD, Strattice). Seven complications were studied including seroma, cellulitis, infection, hematoma, skin flap necrosis, capsular contracture, and reconstructive failure. Sixteen studies met the inclusion criteria. The pooled complication rates were seroma 6.9%, cellulitis 2.0%, infection 5.7%, skin flap necrosis 10.9%, hematoma 1.3%,

capsular contracture 0.6% and reconstructive failure 5.1%. Five studies reported findings for both the ADM and non-ADM patients and were used in the meta-analysis to calculate pooled odds ratio (OR). ADM-assisted breast reconstructions had a higher likelihood of seroma, infection, and reconstructive failure than breast reconstructions without the use of ADM. The relation of ADM use to hematoma, cellulitis, and skin flap necrosis was inconclusive. In the studies evaluated, ADM-assisted breast reconstructions exhibited a higher likelihood of seroma, infection, and reconstructive failure than prosthetic-based breast reconstructions using traditional musculofascial flaps. ADM is associated with a lower rate of capsular contracture. The authors reported that given the relatively low-quality evidence that currently exists in the literature, additional randomized-controlled studies are needed to further evaluate the safety and efficacy of ADM in implant-based breast reconstruction.

Kim et al. (2012) conducted a systematic review and meta-analysis to evaluate complication outcomes from human acellular dermal matrix (ADM) used as an adjunct to traditional submuscular tissue expander/implant breast reconstruction. Forty-eight uncontrolled cohort studies met inclusion criteria. Thirteen studies had information only on human ADM matrix-based reconstruction, 29 had information only on submuscular-based reconstructions, and six reported complications on human ADM and submuscular techniques. A total of 2037 human ADM reconstructions and 12,847 submuscular reconstructions were included in the meta-analysis. A total of 877 human ADM and 3464 muscular reconstructions from six studies were used to calculate relative risks. Average follow-up time was 13.8 months in the human ADM group and 28.3 months in the submuscular cohort There was an increased rate of total complications, 15.4% vs. 14.0%; seroma, 4.8% vs. 3.5%; infection, 5.3% vs. 4.7%; and flap necrosis, 6.9% vs. 4.9% in the human ADM cohort compared to the submuscular reconstruction cohort. The rate of hematomas was greater in the submuscular cohort 1.5% vs. 1% in the human ADM. Meta-analysis revealed an increase in the risk of total complications (relative risk, 2.05; 95 percent confidence interval, 1.55 to 2.70), seroma (relative risk, 2.73; 95 percent confidence interval, 1.67 to 4.46), infection (relative risk, 2.47; 95 percent confidence interval, 1.71 to 3.57), and reconstructive failure (relative risk, 2.80; 95 percent confidence interval, 1.76 to 4.45) in the human ADM cohort. There was a trend toward increased risk of hematoma (relative risk, 2.06; 95 percent confidence interval, 0.86 to 4.95) and flap necrosis (relative risk, 1.56; 95 percent confidence interval, 0.85 to 2.85) in the human acellular dermal matrix cohort, but the results were not statistically significant. Most pooled complication analyses showed significant heterogeneity. The meta-analysis suggested that the use of human ADM increases complication rates compared to submuscular approach.

Nguyen et al (2011) conducted a systematic review of the literature to assess the quality and quantity of evidence regarding the use of acellular dermal matrices (ADM) (e.g., AlloDerm) in prosthetic breast reconstruction. Eighteen articles in the form of case reports, prospective cohort studies and retrospective reviews met inclusion criteria. The authors analyzed the evidence for the following proposed advantages of ADM: decrease or eliminate the need for expanders to create a tissue pocket for an implant; reduction in postoperative pain; decrease in operative time; increased initial fill volumes; fewer expansions; precise control of over the lateral and inframammary fold; ability to use more of the mastectomy skin flaps; faster time to completion of reconstruction; improved lower pole expansion; decreased incidence of capsular contractures; decreased rate of revisions; improved aesthetic outcome of the breast. The authors concluded that there was insufficient data to support any of the above proposed benefits of ADM for breast reconstruction due to the paucity of actual data and conflicting data. Some studies did not formally quantify or report applicable data; evidence was inconsistent due to the variations in size of the matrix, type of mastectomy, size and viability of the mastectomy flaps and surgeon judgment; and data was conflicting due to variations in surgical technique, patients' physical characteristics, and number of expansions used.

Use Outside of the US
Skin substitutes are offered outside the US by several companies. Several products have received CE Mark approval (e.g., Integra® SurgiMend PRS Meshed, Strattice, Veritas Collagen Matrix). Products approved in the US may not be approved for use outside of the US and products approved outside the US may not be approved for use in the US. Also, the approved indications for the products may not be the same within and outside of the US. Integra LifeSciences has CE Mark approval for Surgimend PRS Mesh for pre- and sub-pectoral breast reconstruction in Europe. Strattice has CE Mark approval by the Netherlands-based notified body, KEMA, for its Strattice® Reconstructive Tissue Matrix. The CE Mark allows Strattice to be marketed in 27 Europena Union member states. Strattice is proposed for use in breast reconstruction. Native® (mbp, Germany) porcine acellular dermal matrix is proposed for use in Europe for breast reconstruction.

Autologous Fat Transplant (Lipoinjection, Lipofilling, Lipomodeling)
Despite various techniques of reconstruction with autologous tissues or prostheses, autologous fat transplant (i.e., lipoinjection, lipofilling, lipomodeling) has been proposed to replace volume after breast reconstruction or to fill defects in the breast following breast conservation surgery. It has been proposed as a stand-alone procedure or as an adjunct to other breast reconstruction techniques. The use of autologous fat transplant for primary breast augmentation is controversial due to a lack of clarity regarding its safety and efficacy. It has been proposed that injection of fat into a previous tumor site may create a new environment for cancer and adjacent cells. Additionally, fat transplant to the breast has been discouraged since it has been reported that calcifications secondary to fat necrosis may mimic breast cancer or that radiological changes post fat grafting would obscure and delay the diagnosis of subsequent breast cancer. In breast reconstruction, unlike elsewhere in the body, fat is implanted in a poorly vascularized and loose space which may attribute to the poor results.

Autologous fat transplant generally involves the transfer of fat from the abdomen or thighs into the breast under local anesthesia. The harvested fat is injected into the breast, usually in small parcels and thin strips, at different levels in the subcutis. It has been reported that a certain amount of fat resorption is expected in all cases of fat grafting. Clinically, volume loss has been reported between 40%-60% and usually within the first 4-6 months. Patients usually have 2-4 sessions of lipomodelling depending on their condition. The proposed benefit of the procedure is that it can restore volume to the breast without the morbidity associated with other reconstruction techniques. Although refinement in technique has aided reproducibility of favorable results, a standardized method of fat harvest, preparation, and injection is needed. Results are dependent on technique and surgeon expertise. It is recommended that breast reconstruction using autologous fat transfer be carried out by surgeons with specialist expertise and training in the procedure.

Literature Review: The available literature consists mostly of case reports, case series and expert opinion and describes autologous fat transplant for various breast indications, both cosmetic and reconstructive. Although the published evidence supporting the role of autologous fat transplant as a breast reconstruction procedure is not robust, limited data from several small studies indicate that autologous fat transplant raises no major safety concerns and may improve outcomes in a carefully selected subset of patients. Additionally, autologous fat transplant is widely used and accepted in clinical practice as a breast reconstruction procedure (Tukiama, et al., 2022; Hayes, 2020; De Decker, et al., 2016; Claro, et al., 2012; Parikh, et al., 2012; Saint-Cyr, et al., 2012; Rosing, et al., 2011; de Blacam, et al., 2011; Losken, et al., 2011; Petit, et al., 2011a; Petit, et al., 2011b; Illouz, et al., 2009; Hyakusoku, et al., 2009; Kanchwala, et al., 2009; Chan, et al., 2008; American Society for Dermatologic Surgery (ASDS); 2008; Coleman, et al., 2007; Spear, et al., 2005). Research is ongoing to distinguish benign from malignant lesions after fat grafting (Parikh, et al, 2012).

Professional Societies/Organizations: The 2008 American Society for Dermatologic Surgery (ASDS) guidelines of care for injectable fillers states that, "One significant concern is the safety of fat transfer into the female breast. Calcifications and nodularity may develop and require the patient to undergo numerous tests and repeated evaluations to rule out an underlying malignancy" (Alam, et al., 2008).

Australian Safety and Efficacy Register of New Interventional Procedures –Surgical (ASERNIP-S): ASERNIP-S published a systematic review on autologous fat transfer for cosmetic and reconstructive breast augmentation. The authors concluded that "the evidence base in this review is rated as poor, limited by the quality of the available evidence. Specific limitations of the evidence include absence of studies comparing autologous fat transfer to the nominated comparator procedures, as well as a lack of standardized reporting of outcomes. Autologous fat transfer for cosmetic and reconstructive breast augmentation is considered to be at least as safe as the nominated comparator procedures. It is important to note that this rating is based on indirect comparisons that have been made using overall complication rates. Important safety data examining the effect of microcalcifications following autologous fat transfer on subsequent breast cancer detection were not reported in the studies included in this review; therefore, safety in regards to this outcome cannot be determined. The efficacy of autologous fat transfer cannot be determined from the literature included in this review. Efficacy outcomes reported in the included autologous fat transfer studies varied from those reported for the nominated comparator procedures; therefore, it was not possible to compare efficacy. However, the inability of autologous fat transfer to achieve a volume increase comparable to that of prostheses or autologous tissue augmentation suggests that it is less efficacious than these comparator procedures. There is a need for controlled trials (ideally randomized), assessing the effects of microcalcifications following autologous fat transfer on immediate and long-term breast cancer detection, to be conducted. Studies to determine the maximal breast volume increase reliably achieved by autologous fat transfer would also be useful in order to define the patient population who would benefit most from the procedure, as well as which breast indications should be treated using autologous fat transfer" (Leopardi, et al., 2010).

Autologous Fat Transplant with the use of Adipose-Derived Stem Cells

Research has indicated that subcutaneous fat contains many stem and regenerative cells including cells important in tissue survival and vascularization. It is proposed that autologous adipose-derived regenerative cells (ADRCs) may increase graft survival. With the growing use of autologous fat grafting, published preclinical and clinical data describing cell enriched adipose tissue transplants in breast defect repairs and breast augmentation are increasing. After adipose harvesting using syringe liposuction, the tissue is processed with a system such as the Celution 800 System®, (Cytori Therapeutics, Inc., San Diego, CA) which washes the graft and isolates ADRCs (Kamakura, et al., 2011).

Literature Review: The available literature is limited and consists mostly of case reports and case series, both cosmetic and reconstructive (Ito, et al., 2017; Pérez-Cano, et al., 2012; Kamakura, et al., 2011). Optimal patient selection criteria have not been established through well-designed comparative clinical trials with long-term outcomes data (Kamakura, et al., 2011; Yoshimura, et al., 2008).

Pérez-Cano et al. (2012) conducted a single-arm, prospective, multicenter clinical trial of 71 women who underwent breast conserving surgery for breast cancer and autologous adipose-derived regenerative cell (ADRC)-enriched fat grafting for reconstruction of defects =150 mL (the RESTORE-2 trial). Endpoints included patient and investigator satisfaction with functional and cosmetic results and improvement in overall breast deformity at 12 months post-procedure. Females presenting with partial mastectomy defects and without breast prosthesis were eligible. The RESTORE-2 protocol allowed for up to two treatment sessions and 24 patients elected to

undergo a second procedure following the six-month follow-up visit. Of the 67 patients treated, 50 reported satisfaction with treatment results through 12 months. Sixty-one patients underwent radiation therapy as part of their treatment; two patients did not receive radiation and the status of radiation treatment was not known for the other four patients. Using the same metric, investigators reported satisfaction with 57 out of 67 patients. There were no serious adverse events associated with the ADRC-enriched fat graft injection procedure. There were no reported local cancer recurrences. The investigators reported improvement from baseline through 12 months in the degree of retraction or atrophy in 29 out of 67 patients, while 34 patients had no change and four patients reported worse symptoms. Post-radiation fibrosis at 12 months was reported as improved in 29 patients, while 35 patients had no change and three patients had worse symptoms. Management of atrophy was reported as improved in 17 patients, with 48 patients having no change and two patients reporting worse symptoms. The authors reported that future comparative studies are needed to determine the benefit of ADRC-enriched fat grafting as compared to traditional fat grafting in various clinical circumstances.

In a case series study, Kamakura et al. (2011), reported on the use of autologous adipose-derived stem cell (ADSC) enriched fat grafting for breast augmentation (n=20). After the adipose tissue was harvested by liposuction, it was processed in the Celution 800 System® to wash and isolate the adipose-derived regenerative cells and produce a fat graft enriched with the regenerative cells. The average number of cells per gram of harvested adipose tissue was 3.4×10^5, and the mean cell viability as measured with an automated cell counting system before graft delivery was 85%. Clinical outcomes measured included improvement in circumferential breast measurement from baseline state. There was improvement in circumferential breast measurement in all patients, and breast measurements were stable by three months after grafting. At nine months, the mean breast measurement had increased 3.3cm from preoperative measurements. Through nine months, overall patient satisfaction was 75%, and physician satisfaction 69%. The procedure was well-tolerated without any serious adverse events. Postoperative cyst formation was seen in two patients. This study was limited by small sample size, no control group and lack of long-term outcomes. The authors reported that to date a, a randomized, controlled study has not been performed to compare the outcomes of cell-enriched fat transfer with those of traditional fat transfer.

Suction-Assisted Lipectomy and Excision of Redundant Skin

Suction-assisted lipectomy of the trunk or extremity area is a procedure in which excess fat deposits are removed using a liposuction cannula. Excision of redundant skin is a procedure in which excess skin and/or subcutaneous tissue (e.g., dog ear, standing cone) is removed. Both procedures have the goal of recontouring the body, thereby improving appearance. These procedures may be performed alone or as one component of the flap breast reconstruction procedure. Suction-assisted lipectomy and excision of redundant skin, when performed alone and not as part of a medically necessary flap breast reconstruction procedure are considered cosmetic in nature. When these procedures are performed as part of a medically necessary flap breast reconstruction procedure, they are considered incidental to the primary procedure.

External Breast Prostheses and Mastectomy Bras Following Mastectomy or Lumpectomy

Breast reconstruction has become an integral component of the treatment of patients with breast cancer who have undergone a mastectomy or lumpectomy. External breast prostheses are available for women who have uneven- or unequal-sized breasts and who decide not to, or are waiting to, undergo surgical breast reconstruction. They may choose to wear a breast prosthesis and mastectomy bra, or elect to wear a mastectomy garment that has the prosthesis already inserted in it.

Prostheses can attach to the skin with a fabric backing and adhesive or may be worn unattached with a mastectomy bra. Prefabricated prostheses come in various shapes, sizes and skin tones.

Custom-fabricated breast prostheses are custom-designed and special ordered for the individual, based on an impression of the chest wall. In general, prefabricated prostheses can adequately meet the external prosthetic needs of most individuals. Reusable external nipple prostheses are available to cover flat or missing nipples.

U.S. Food and Drug Administration (FDA)
The FDA classifies external aesthetic restoration prostheses as Class I devices that are exempt from premarket notification (FDA, 2023).

Federal Mandate
The Women's Health and Cancer Rights Act of 1998 (WHCRA) was enacted as a federal mandate in October 1998. The federal mandate defines coverage for breast reconstruction following mastectomy as:

- reconstruction of the breast on which the mastectomy was performed
- surgery and reconstruction on the other breast to produce symmetrical appearance
- prostheses and treatment of physical complications in all stages of mastectomy, including lymphedemas

Under this mandate, benefits for breast reconstruction services following mastectomy or lumpectomy must be provided to both men and women; a diagnosis of breast cancer cannot be required; and timing of breast reconstruction services is not a factor in coverage. In addition, the mandate prohibits any limitations to the number of prostheses or the length of time from the date of the mastectomy.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Breast Reconstruction Following Mastectomy (140.2)	1/1997
LCD	CGS	External Breast Prostheses (L33317)	1/2020
LCD	Novitas	Cosmetic and Reconstructive Surgery (L35090)	7/2021
LCD	First Coast	Cosmetic and Reconstructive Surgery (L38914)	7/2021
LCD	Palmetto	Cosmetic and Reconstructive Surgery (L33428)	7/2021
LCD	Noridian	Plastic Surgery (L37020)	10/2019

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Appendix

Appendix A

Product	CPT® Code	HCPCS Code
Considered Medically Necessary		
AlloDerm®	15777	Q4116
AlloMax™	15777	C1781, Q4100
Cortiva™	15777	C9399,Q4100

Dermacell™	15777	Q4122
GalaFLEX® Scaffold	15777	C1781, C9399, Q4100
GalaFLEX 3DR Scaffold	15777	C1781, C9399 Q4100
GalaFLEX 3D Scaffold	15777	C1781, C9399,Q4100
FlexHD®	15777	Q4128
Considered Experimental, Investigational, Or Unproven		
ARTIA™ Reconstructive Tissue Matrix	15777	C1763
Avance® Nerve Graft	64912, 64913	C9399, Q4100
BellaDerm® Acellular Hydrated Dermis	15777	C1781, C9399,Q4100
Biodesign® Nipple Reconstruction Cylinder	19350	C1763
DermaMatrix Acellular Dermis	15777	C1781, C9399,Q4100
DuraSorb® Monofilament Mesh/ Polydioxanone Surgical Scaffold™	15777	C1781
Juvederm®	19350, 11950	C9399
OviTex®	15777	C1781
Permacol™	15777	C9364
Phasix™ Mesh	15777	C1781
Radiesse®	11950, 19350	Q2026
Renuva® Allograft Adipose Matrix	No specific code	J3590
SERI™ Surgical Scaffold	15777	C1781,Q4100
SimpliDerm™	15777	C9399, Q4100
Strattice™ Reconstructive Tissue Matrix	15777	Q4130
SurgiMend® Collagen Matrix	15777	C9358, C9360
Veritas Collagen Matrix	15777	C9354

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare and Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Breast Reconstruction

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
11920	Tattooing, intradermal introduction of insoluble opaque pigments to correct color defects of skin, including micropigmentation; 6.0 sq cm or less
11921	Tattooing, intradermal introduction of insoluble opaque pigments to correct color defects of skin, including micropigmentation; 6.1 to 20.0 sq cm
11970	Replacement of tissue expander with permanent implant

CPT®* Codes	Description
11971	Removal of tissue expander without insertion of implant
13100	Repair, complex, trunk; 1.1 cm to 2.5 cm
13101	Repair, complex, trunk; 2.6 cm to 7.5 cm
13102	Repair, complex, trunk; each additional 5 cm or less (List separately in addition to code for primary procedure)
15734	Muscle, myocutaneous, or fasciocutaneous flap; trunk
15771†	Grafting of autologous fat harvested by liposuction technique to trunk, breasts, scalp, arms, and/or legs; 50 cc or less injectate
15772†	Grafting of autologous fat harvested by liposuction technique to trunk, breasts, scalp, arms, and/or legs; each additional 50 cc injectate, or part thereof (List separately in addition to code for primary procedure)
15777	Implantation of biologic implant (eg, acellular dermal matrix) for soft tissue reinforcement (eg, breast, trunk) (List separately in addition to code for primary procedure)
19316	Mastopexy
19318	Breast reduction
19325	Breast augmentation with implant
19328	Removal of intact breast implant
19330	Removal of ruptured breast implant, including implant contents (eg, saline, silicone gel)
19340	Insertion of breast implant on same day of mastectomy (ie, immediate)
19342	Insertion or replacement of breast implant on separate day from mastectomy
19350††	Nipple/areola reconstruction
19357	Tissue expander placement in breast reconstruction, including subsequent expansion(s)
19361	Breast reconstruction; with latissimus dorsi flap
19364	Breast reconstruction; with free flap (eg, fTRAM, DIEP, SIEA, GAP flap)
19367	Breast reconstruction; with single-pedicled transverse rectus abdominis myocutaneous (TRAM) flap
19368	Breast reconstruction; with single-pedicled transverse rectus abdominis myocutaneous (TRAM) flap, requiring separate microvascular anastomosis (supercharging)
19369	Breast reconstruction; with bipedicled transverse rectus abdominis myocutaneous (TRAM) flap
19370	Revision of peri-implant capsule, breast, including capsulotomy, capsulorrhaphy, and/or partial capsulectomy
19371	Peri-implant capsulectomy, breast, complete, including removal of all intracapsular contents
19380	Revision of reconstructed breast (eg, significant removal of tissue, re-advancement and/or re-inset of flaps in autologous reconstruction or significant capsular revision combined with soft tissue excision in implant-based reconstruction)
19499†††	Unlisted procedure, breast

†Note: Considered experimental/investigational/unproven when used to report autologous fat transplantation using adipose-derived stem cells

††Note: Considered Experimental/Investigational/Unproven when used to report nipple reconstruction with Juvederm, Radiesse, or Cook Biodesign® Nipple Reconstruction Cylinder.

†††**Note: Considered medically necessary when used to report thoracodorsal artery perforator (TDAP) flap with a breast reconstruction procedure performed on the diseased/affected breast. Considered experimental/investigational/unproven when used to report adipose-derived stem cell autologous fat transplantation.**

HCPCS Codes	Description
C1789	Prosthesis, breast (implantable)
L8600	Implantable breast prosthesis, silicone or equal
S2066	Breast reconstruction with gluteal artery perforator (GAP) flap, including harvesting of the flap, microvascular transfer, closure of donor site and shaping the flap into a breast, unilateral
S2067	Breast reconstruction of a single breast with "stacked" deep inferior epigastric perforator (DIEP) flap(s) and/or gluteal artery perforator (GAP) flap(s), including harvesting of the flap(s), microvascular transfer, closure of donor site(s) and shaping the flap into a breast, unilateral
S2068	Breast reconstruction with deep inferior epigastric perforator (DIEP) flap or superficial inferior epigastric artery (SIEA) flap, including harvesting of the flap, microvascular transfer, closure of donor site and shaping the flap into a breast, unilateral

Not covered when used to report intraoperative assessment of tissue perfusion as it considered integral to the primary procedure and not separately reimbursable:

CPT®* Codes	Description
15860	Intravenous injection of agent (eg fluorescein) to test vascular flow in flap or graft

Considered Not Medically Necessary÷ /Cosmetic in nature when used to report correction of surgically-induced donor site asymmetry or excess tissue that results from flap breast reconstruction procedures. Considered incidental to the primary procedure when used to report suction-assisted lipectomy of the trunk as part of a medically necessary flap breast reconstruction procedure:

CPT®* Codes	Description
15839	Excision, excessive skin and subcutaneous tissue (includes lipectomy); other area
15877	Suction assisted lipectomy; trunk

Skin/Tissue Substitutes/Fillers (see Appendix A)

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
Q4116	Alloderm, per square centimeter
Q4122	Dermacell, per square centimeter
Q4128	Flex hd or allopatch hd, or matrix hd per square centimeter

Considered Medically Necessary when used to report AlloMax™:

HCPCS Codes	Description
C1781	Mesh (implantable)
Q4100	Skin substitute, not otherwise specified

Considered Medically Necessary when used to report Cortiva™:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
Q4100	Skin substitute, not otherwise specified

Considered Medically Necessary when used to report GalaFLEX Scaffold, GalaFLEX 3DR, GalaFLEX 3D:

HCPCS Codes	Description
C1781	Mesh (implantable)
C9399	Unclassified drugs or biologicals
Q4100	Skin substitute, not otherwise specified

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
C9354	Acellular pericardial tissue matrix of nonhuman origin (Veritas), per sq cm
C9358	Dermal substitute, native, nondenatured collagen, fetal bovine origin (SurgiMend Collagen Matrix), per 0.5 sq cm
C9360	Dermal substitute, native, nondenatured collagen, neonatal bovine origin (SurgiMend Collagen Matrix), per 0.5 sq cm
C9364	Porcine implant, Permacol, per sq cm
Q2026	Injection, Radiesse, 0.1 ml
Q4130	Strattice TM, per sq cm

Considered Experimental/Investigational/Unproven when used to report ARTIA™ Reconstructive Tissue or Matrix, Biodesign® Nipple Reconstruction Cylinder:

HCPCS Codes	Description
C1763	Connective tissue, nonhuman (includes synthetic)

Considered Experimental/Investigational/Unproven when used to report when used to report Phasix Mesh and OviTex®:

HCPCS Codes	Description
C1781	Mesh (implantable)

Considered Experimental/Investigational/Unproven when used to report BellaDerm® Acellular Hydrated Dermis, DermaMatrix Acellular Dermis:

HCPCS Codes	Description
C1781	Mesh (implantable)
C9399	Unclassified drugs or biologicals
Q4100	Skin substitute, not otherwise specified

Considered Experimental/Investigational/Unproven when used to report SERI™ Surgical Scaffold:

HCPCS Codes	Description
C1781	Mesh (implantable)
Q4100	Skin substitute, not otherwise specified

Considered Experimental/Investigational/Unproven when used to report Juvederm:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals

Considered Experimental/Investigational/Unproven when used to report Avance® Nerve Graft and SimpliDerm™:

CPT®* Codes	Description
64912†	Nerve repair; with nerve allograft, each nerve, first strand (cable)
64913†	Nerve repair; with nerve allograft, each additional strand (List separately in addition to code for primary procedure)

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
Q4100	Skin substitute, not otherwise specified

†**Note: CPT Codes only apply to Avance Nerve Graft**

Experimental/Investigational/Unproven when used to report the injection of a non-covered product listed in the policy statement above or when used to report autologous fat transplant using adipose-derived stem cells or xenograft cartilage grafting:

CPT®* Codes	Description
11950	Subcutaneous injection of filling material (eg, collagen); 1 cc or less
11951	Subcutaneous injection of filling material (eg, collagen); 1.1 to 5.0 cc
11952	Subcutaneous injection of filling material (eg, collagen); 5.1 to 10.0 cc
11954	Subcutaneous injection of filling material (eg, collagen); over 10.0 cc

Considered Experimental/Investigational/Unproven when used to report Biodesign® Nipple Reconstruction Cylinder:

HCPCS Codes	Description
C1763	Connective tissue, non-human (includes synthetic)

Considered Experimental/Investigational/Unproven when used to report ARTIA™ Reconstructive Tissue Matrix, BellaDerm® Acellular Hydrated Dermis, DermaMatrix Aceullular Dermis, Juvederm®, Phasix™ Mesh, or SERI™ Surgical Scaffold:

HCPCS Codes	Description
C1781	Mesh (implantable)
C9399	Unclassified drugs or biologicals
Q4100	Skin substitute, not otherwise specified

Considered Experimental/Investigational/Unproven when used to report Renuva® Allograft Adipose Matrix:

HCPCS Codes	Description
J3590	Unclassified biologics

Experimental/Investigational/Unproven when used to report breast reconstruction procedures using adipose-derived stem cells in autologous fat transplantation or xenograft cartilage grafting:

CPT®* Codes	Description
19366	Breast reconstruction with other technique
19499	Unlisted procedure, breast

<u>External Breast Prostheses and Mastectomy Bras Following Mastectomy or Lumpectomy</u>

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
19396	Preparation of moulage for custom breast implant

HCPCS Codes	Description
L8000	Breast prosthesis; mastectomy bra, without integrated breast prosthesis form, any size, any type
L8001	Breast prosthesis, mastectomy bra, with integrated breast prosthesis form, unilateral, any size, any type
L8002	Breast prosthesis, mastectomy bra, with integrated breast prosthesis form, bilateral, any size, any type
L8015	External breast prosthesis garment, with mastectomy form, post mastectomy
L8020	Breast prosthesis, mastectomy form
L8030	Breast prosthesis, silicone or equal, without integral adhesive

L8031	Breast prosthesis, silicone or equal, with integral adhesive
L8032	Nipple prosthesis, prefabricated, reusable, any type, each
L8033	Nipple prosthesis, custom fabricated, reusable, any material, any type, each
L8035	Custom breast prosthesis, post mastectomy, molded to patient model
L8039	Breast prosthesis, not otherwise specified

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• Added GalaFLEX® products as medically necessary for breast reconstruction	4/15/2025
Focused Review	• Revised policy statement for the list of non-covered products.	9/15/2024
Annual Review	• Revised policy statement for areolar and nipple reconstruction. • Added policy statement for "flat closure chest wall reconstruction". • Revised policy statement for oncoplastic reconstruction. • Added policy statement for "DuraSorb® Monofilament Mesh/ Polydioxanone Surgical Scaffold™" to the list of EIU products. • Removed policy statement for hMatrix and Repriza. • Revised policy statement for lipectomy or excision of redundant skin statement.	3/15/2024