MEDICAL POLICY

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SUBJECT: BIOENGINEERED TISSUE PRODUCTS FOR WOUND TREATMENT AND SURGICAL INTERVENTIONS	**EFFECTIVE DATE: 01/17/02**
POLICY NUMBER: 7.01.35	**REVISED DATE: 01/16/03, 03/18/04, 01/20/05, 03/16/06, 12/21/06, 01/17/08, 02/19/09, 05/27/10, 08/18/11, 08/16/12, 07/18/13, 11/20/14, 12/17/15, 2/16/17, 04/19/18**
CATEGORY: Technology Assessment	**PAGE: 1 OF: 22**

- ***If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.***
- ***If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.***
- ***If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.***

POLICY STATEMENT:

I. Based upon our criteria and review of the peer-reviewed literature, bioengineered tissue products have been proven to be medically effective and are **medically appropriate** for the treatment of *venous ulcers of the lower extremities* and for *diabetic foot ulcers* that have not responded to a comprehensive program of wound care. Only products that have received FDA approval for this purpose are considered medically appropriate.

A. For treatment of *venous ulcers*, Apligraf® or Oasis™ Wound Matrix may be used when all of the following criteria are met:
1. The patient has adequate arterial blood supply as evidenced by ankle-brachial index (ABI) of 0.65 or greater in the limb being treated;
2. The patient is competent and/or has support system required to participate in follow-up care associated with treatment with a bioengineered tissue product;
3. Ulcers are partial or full thickness and of greater than three (3) months duration;
4. Ulcers have failed to respond to conservative measures of at least one (1) month duration that have, at a minimum, included regular dressing changes, debridement of necrotic tissue, and standard therapeutic compression. ("Failure to respond" is defined as increase in size or depth or no change in size or depth with no sign or indication that improvement is likely, such as granulation, epithelialization, or progress toward closing);
5. Patient has adequate treatment of the underlying disease process(es) contributing to the ulcer; and
6. Ulcers are free of infection, redness, drainage, underlying osteomyelitis, surrounding cellulitis, tunnels and tracts, eschar or any necrotic material that would interfere with adherence of a bioengineered tissue product and wound healing.

B. For treatment of *diabetic foot ulcers*, AlloPatch® Apligraf®, Dermagraft®, Oasis™ Wound Matrix, or Integra™ Dermal Regeneration Template® (Omnigraft™) may be used when all of the following criteria are met:
1. The patient has adequate arterial blood supply as evidenced by ankle-brachial index (ABI) of 0.65 or greater in the limb being treated;
2. The patient is competent and/or has support system required to participate in follow-up care associated with treatment with a bioengineered tissue product;
3. Ulcers are full thickness and of greater than three (3) weeks duration which extend through the dermis but without tendon, muscle, capsule or bone exposure;
4. Patient has adequate treatment of underlying disease process(es) contributing to the ulcer;
5. Ulcers are located on foot or toes and are free of infection, redness, drainage, underlying osteomyelitis, surrounding cellulitis, tunnels and tracts, eschar or any necrotic material that would interfere with adherence of a bioengineered tissue product and wound healing; and
6. Patient's current HbA1C does not exceed 12%.

II. Based upon our criteria and review of the peer-reviewed literature, the use of allogeneic human acellular dermal matrix (ADM) products (e.g., AlloDerm®, AlloMax™ , Cortiva™ (formerly known as AlloMax), DermACELL AWM™, DermaMatrix™, FlexHD®, GraftJacket®) is **medically appropriate** for breast reconstruction surgery following surgical mastectomy.

III. Based upon our criteria and review of the peer-reviewed literature, the use of AlloDerm® is considered **medically appropriate** for the following indications:

A. Nasal repairs (e.g., septal repair, septal perforation repair, reconstructive septorhinoplasty), and

B. Non-primary hernia repair when chronic infection contraindicates the use of mesh or other conventional repair; and

C. Parotidectomy.

IV. Based upon our criteria and review of the peer-reviewed literature, Biobrane®, Epicel®, Integra® Dermal Regeneration Template, have been proven to be medically effective and are therefore **medically appropriate** for the treatment of *burns*.

A. For the treatment of *severe* full-thickness burns (e.g. greater than or equal to 20% total body surface area and/or excision to the fascia to remove all nonviable tissue) or deep partial-thickness thermal injury using Integra® Dermal Regeneration Template, all of the following criteria must be met:
1. The patient is competent to understand the need for immobilization and the need for a second surgical procedure for application of an ultra-thin epidermal graft, regular follow-ups, and rehabilitation;
2. Insufficient autograft is available at the time of burn excision; and
3. The burn site is free of residual eschar.

The use of Integra® Dermal Regeneration Template is contraindicated for patients with the following:
A. Known hypersensitivity to bovine collagen, silicone, or chondroitin materials;
B. Pregnancy;
C. Clinically diagnosed infected wounds.

B. For the treatment of thermal injuries, superficial scald burn or flame injury of the hand using Biobrane®, all of the following criteria must be met:
1. The patient is competent and/or has the support system required to participate in follow-up care associated with treatment with a bioengineered tissue product;
2. The burn is superficial, partial-thickness with limited involvement of the dermis (less than or equal to 25% total body surface area);
3. The burn is clean, non-infected, and free of nonviable tissue and coagulation eschar; and
4. The patient is competent to understand the need for immobilization.

V. Based upon our criteria and the lack of peer-reviewed literature, all other bioengineered tissue products have not been proven medically effective and are considered **investigational** for all other applications. These products include, but are not limited to, the following:

- ACell® UBM Hydrated/Lyophilized Wound Dressing
- Affinity™
- Alloderm for use in tympanoplasty
- AlloSkin™
- AlloSkin™ RT
- AlloSource cryopreserved human cadaver skin
- AlloWrap™
- AmbioDisk® (IOP Ophthalmics)
- AmbioDry5® (IOP Ophthalmics)
- AmnioBand™
- AmnioCare
- AmnioExCel®
- AmnioFix
- AmnioGenix
- AmnioHeal amniotic membrane
- AmnioMatrix®
- AmnioMTM
- AmnioShield
- AmnioStrip
- Amniotic fluid injection for corneal wound healing and prevention of adhesions after orthopedic surgery
- Amniox (human embryonic membrane) for tarsel tunnel repair and all other indications
- Aongen™ Collagen Matrix

- Apligraf for nectoizing lesions
- Architect® ECM, PX, FX
- Artacent™ Wound
- ArthroFlex™ (FlexGraft)
- Atlas Wound Matrix
- Avagen Wound Dressing
- Avaulta Plus™
- AxoGuard® Nerve Protector (AxoGen)
- BioDexcel
- BioDfence/BioDfactor
- BioDmatrix
- BioDRestore Elemental Tissue Matrix
- Biostat Biologx fibrin sealant for wound healing and all other indications;
- Biotape reinforcement matrix for soft tissue
- Biovance®
- CellerateRX®
- Clarix 100
- Clarix Cord 1K
- Clarix® Flo
- CollaFix
- CollaCare®
- CollaMend™
- CollaWound™
- Collexa®
- Collieva®
- Conexa™
- CorMatrix®
- CRXa™
- Cygnus Solo™
- Cygnus Matrix™
- Cygnus Max™
- Cymetra®
- Cytal™ Burn Matrix
- Cytal™ Wound Matrix
- Dehydrated human amniotic membrane allograft (e.g. AmnioPro, BioFix, and FlowerPatch)
- DermaPure™
- DermaSpan™
- Dermavest™
- DryFlex (human amnion allograft) for shoulder repair and all other indications
- Durepair Regeneration Matrix®
- Endoform Dermal Template™
- ENDURAgen™
- EpiCord™
- EpiFix®
- EpiFix® Injectable
- *ENDURA*Gen™
- Excellagen®
- E-Z Derm™
- FlexiGraft®
- FloGraft
- Fortiva Porcine Dermis
- GammaGraft
- Glyaderm®
- Grafix® CORE
- Grafix® PRIME
- GraftJacket® Xpress, injectable
- Guardian
- hMatrix®
- HydroFix
- Hyalomatrix® PA
- Integra™ Flowable Wound Matrix
- Integra™ Bilayer Wound Matrix
- InteguPly™
- Interfyl™
- Kerecis Omega 3
- MariGen
- MatriDerm®
- Matrix HD™
- MediHoney®
- Mediskin®
- MemoDerm™
- Miroderm®
- Neox 1K
- Neox® Flo
- Neox® Wound Matrix
- NuShield™
- PalinGen® - Membrane, Hydromembrane
- PalinGen® - Flow, SportFlow
- Pelvicol™
- Permacol™
- PriMatrix™
- PriMatrix™ Dermal Repair Scaffold
- Prolifix™
- PuraPly Antimicrobial
- PuraPly Wound Matrix
- RegenePro™
- Repliform®
- Repriza™
- Revitalon™
- StrataGraft
- Strattice™

- Suprathel®
- SurgiMend®
- Talymed®
- TenoGlide™
- TenSIX™
- TheraSkin®
- TranZgraft
- TruSkin™
- Veritas® Collagen Matrix
- XCM Biologic
- XenMatrix™ AB

Refer to the Description section for further information in regard to the products listed in the Policy Statements.

Refer to Corporate Medical Policy #1.01.38 regarding Negative Pressure Wound Therapy (Vacuum Assisted Closure).

Refer to Corporate Medical Policy #2.01.24 regarding Growth Factors for Wound Healing and Other Conditions.

Refer to Corporate Medical Policy #10.01.01 regarding Breast Reconstruction Surgery.

Refer to Corporate Medical Policy #11.01.03 regarding Experimental or Investigational Services.

This policy does not address fibrin sealants (e.g., Tisseel).

POLICY GUIDELINES:

I. Utilization of specific products are medically appropriate only when used in accordance with FDA product approval and when the above policy criteria are met.

II. If a wound has not responded to standard of care by achieving a 50% closure after 4 weeks of standard of care, a single application of a bioengineered tissue product was thought to be all that was required to affect wound healing in wounds likely to be improved by this treatment. Based on clinical input from wound specialists, refractory wounds rarely heal with one graft application and may require additional graft application every week until the wound heals. Re-application of a product is appropriate only if there has been measurable response to the first application. Re-application in less than one year after successful treatment is not medically appropriate

III. Treatment of venous stasis ulcers that extend above the malleoli is beyond the scope of practice of podiatrists.

IV. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

DESCRIPTION:

Bioengineered tissue products are used for burns, chronic wounds, and rare skin diseases and are proposed for use in many other conditions. They aid in the growth of new skin or serve as a temporary cover until other grafts can be placed.

Bioengineered tissue products and their uses/ proposed uses include, but are not limited to:

Biologic tissue product	Class	Use/Proposed Use	FDA approved*	FDA exempt**
*PMA - Wound and burn dressings, class III high risk devices and require clinical data to support claims for use.				
*510(k) - Wound care devices that protect wounds and act as a scaffold for healing.				
**Human tissue - Donated, banked human skin regulated by the American Association of Tissue Banks and FDA guidelines.				
Affinity™	Human amniotic tissue membrane	Wound care		Human tissue
AlloDerm®	Acellular dermal matrix; allogeneic human derived decellularized skin	Burns, wound healing, contaminated abdominal walls, ventral hernia repair, breast reconstruction		Human tissue

Biologic tissue product	Class	Use/Proposed Use	FDA approved*	FDA exempt**
AlloMax™ (previously NeoForm™)	Acellular dermal matrix; allogeneic human derived decellularized skin	Breast reconstruction		Human tissue
AlloSkin™	Epidermal and dermal allograft	Partial and full thickness wounds		Human tissue
AlloWrap™ DS or Dry	Human amniotic tissue membrane	Wound care		Human tissue
AmnioBand™	Dehydrated human placental membrane	Wound care		Human tissue
Amnioexcel®	Human amniotic tissue membrane	Soft tissue repair, wound care		Human tissue
AmnioMatrix®	Human amniotic tissue membrane	Soft tissue repair, wound care		Human tissue
Apligraf® (previously Graftskin)	Cellular, bilayered skin substitute; human derived composite cultured skin	Venous and diabetic ulcers	x (PMA)	
ArthroFlex™ (aka FlexGraft)	Decellularized human allograft dermis	Shoulder reconstruction, Achilles tendon repair		Human tissue
Avaulta Plus™	Porcine derived polypropylene composite	Vaginal wall prolapse	X (510k)	
Biobrane®/ Biobrane l®	Synthetic, bilaminate collagen-based composite	Partial thickness burns, temporary covering	x (PMA)	
BioDFence®	Human amniotic tissue membrane	Dura repair		Human tissue
Biovance®	Human amniotic tissue membrane	Wound care		Human tissue
Clarix® Flo	Human amniotic tissue and umbilical cord membrane	Integumental tissue repair		Human tissue
Collamend	Porcine derived decellularized collagen	Soft tissue weakness, hernia and abdominal wall repair	X (510k)	
Conexa™	Porcine dermis tissue substitute	Soft tissue repair	x (510k)	
Cortiva™	Acellular dermal matrix; allogeneic human derived decellularized skin	Breast reconstruction	X (510k)	Human tissue
Cymetra®	Allogeneic cadaver derived decellularized skin; micronized particulate form of AlloDerm	Soft tissue defects (e.g., laryngoplasty)		Human tissue
Cytal™ Burn Matrix	Porcine collagen wound dressing	Burns	x (510k)	
Cytal™ Wound Matrix	Porcine collagen wound dressing	Partial and full thickness wounds, ulcers, surgical and traumatic wounds, burns	x (510k)	
DermACELL AWM™	Decellularized regenerative human tissue matrix allograft	Breast reconstruction		Human tissue

Biologic tissue product	Class	Use/Proposed Use	FDA approved*	FDA exempt**
Dermagraft®	Interactive wound dressing; human derived composite cultured skin; dermal replacement from neonatal foreskin fibroblasts	Diabetic foot ulcers	x (PMA)	
DermaMatrix	Human skin allograft	Facial soft tissue defects, nasal reconstruction, septal perforation, parotidectomy, cleft palate repair, breast reconstruction, abdominal wall repair		Human tissue
DermaPure™	Single layer, decellularized, dermal allograft	Wound care, diabetic foot ulcers, venous stasis ulcers, wounds refractory to conservative care		Human tissue
DermaSpan™	Acellular dermal matrix	Repair or replacement of damaged or inadequate integumental tissue		Human tissue
Dermavest™	Human placental connective tissue matrix	Replace or supplement damaged or inadequate integumental tissue		Human tissue
Endoform Dermal Template™	Ovine (sheep) derived extracellular matrix	Partial and full thickness wounds, ulcers, surgical and traumatic wounds, burns	x (510k)	
ENDURAgen™	Porcine dermal acellular collagen matrix	Soft tissue augmentation, reinforcement and repair of the head and face	x (510k)	
Epicel®	Cultured epidermal autograft; combined human and animal dermal cellular material	Full thickness burns over greater than 30% of the body	x (HDE)	
EpiCord™	Minimally manipulated lyophilized non-viable cellular umbilical cord allograft	Wound care		Human tissue
EpiFix	Human amniotic tissue membrane	Partial and full thickness diabetic foot, venous leg, arterial and pressure ulcers		Human tissue
Excellagen®	Bovine collagen gel	Partial and full thickness wounds, pressure and venous ulcers, surgical and traumatic wounds	x (510k)	
E-Z Derm™	Porcine derived 6ecellularized fetal skin	Partial thickness burns; venous, diabetic and pressure ulcers	x (510k)	
FlexHD®	Acellular dermal matrix	Breast reconstruction, hernia repair		Human tissue

Biologic tissue product	Class	Use/Proposed Use	FDA approved*	FDA exempt**
Fortaderm (see PuraPly)				
GammaGraft	Irradiated human skin composite allograft	Temporary graft for burns, chronic wounds and partial and full thickness wounds		Human tissue
Glyaderm®	Glycerol preserved acellular human dermis	Wound care		Human tissue
Grafix® CORE	Cellular matrix from human placental chorionic membrane	Acute and chronic diabetic foot ulcers, venous stasis ulcers and pressure ulcers		Human tissue
Grafix® PRIME	Cellular matrix from human placental amniotic membrane	Acute and chronic diabetic foot ulcers, venous stasis ulcers and pressure ulcers; burns; adhesion barriers; and Mohs procedures		Human tissue
GraftJacket®	Bilaminate acellular regenerative tissue; allogeneic human derived decellularized skin	Wound repair, tendon and rotator cuff repair		Human tissue
GraftJacket® Xpress	Micronized decellularized soft tissue scaffold	Deep tunneling dermal wounds		Human tissue
Graftskin (see Apligraf)				
Guardian	Dehydrated human placental membrane	Wound care		Human tissue
Hyalomatrix®	Hyaff 11 (hyaluronic acid) and silicone	Partial and full thickness wounds, ulcers, surgical and traumatic wounds, burns	x (510k)	
hMatrix®	Acellular dermal matrix	Wound covering, abdominal wall repair, breast reconstruction, craniomaxillofacial soft tissue grafting		Human tissue
Integra™	Bovine derived tendon collagen and glycosaminglycan	Partial and full thickness wounds, ulcers, surgical and traumatic wounds, burns	x (510k)	
Integra™ Bilayer Wound® Matrix	Bovine-tendon collagen, glucoseaminoglycan and silicone	Partial and full thickness wounds, ulcers, surgical and traumatic wounds, burns	x (510k)	
Integra™ Dermal Regeneration Matrix® (Omnigraft™)	Bilayered extracellular cross linked bovine collagen and chondroitin sulfate	Partial and full thickness burns; partial and full thickness diabetic foot ulcers	x (PMA)	
Integra™ Flowable Wound®	Granulated cross linked bovine tendon collagen and	Difficult to access and tunneled wounds	x (510k)	

Biologic tissue product	Class	Use/Proposed Use	FDA approved*	FDA exempt**
	glycosaminoglycan			
InteguPly™	Acellular dermal matrix	Diabetic ulcers, Charcot foot ulcers, venous ulcers, trauma wounds, pressure ulcers, partial and full thickness wounds, and surgical wounds		Human tissue
Laserskin (see Hyalomatrix)				
MariGen/ Alphaplex™ with MariGen Omega3™	Cod fish skin	Wound care	x (510k)	
Matristem® Burn Matrix (see Cytal™ Burn Matrix)				
Matristem® Wound Matrix (see Cytal™ Wound Matrix)				
Mediskin®	Porcine derived decellularized fetal skin, frozen	Partial-thickness skin ulcerations and abrasions, temporary covering for full-thickness skin loss	x (510K)	
Neoform (see Allomax)				
Neox®	Human amniotic and umbilical cord tissue membrane	Soft tissue barrier, wound care		Human tissue
Neox 1K	Human amniotic tissue membrane	Wound covering for dermal ulcers and defects		Human tissue
Neox® Flo	Human amniotic tissue and umbilical cord membrane	Wound covering for dermal ulcers and defects		Human tissue
NuShield™	Dehydrated human placental membrane	Wound repair and healing		Human tissue
OASIS® Wound Matrix	Collagen matrix from porcine small intestine submucosa, single layer	Full thickness skin injuries, ulcers, surgical wounds	x (510k)	
OASIS® Burn Matrix	Extracellular matrix from porcine small intestine submucosa, bi-layered	Burns	x (510k)	
OASIS® Ultra	Collagen matrix from porcine small intestine submucosa, tri-layered	Full thickness skin injuries, ulcers, surgical wounds	x (510k)	
Omnigraft™ (see Integra™ Dermal Regeneration Matrix®)				

Biologic tissue product	Class	Use/Proposed Use	FDA approved*	FDA exempt**
Orcel™	Composite skin substitute; human derived composite cultured skin; bilayered cellular matrix	Donor sites in burn victims	x (PMA)	
Orthoadapt	Equine derived decellularized collagen	Soft tissue repair, reinforce tendon repairs	x (510k)	
Pelvicol	Porcine derived decellularized collagen	Soft tissue repair	x (510k)	
Pelvisoft	Porcine derived decellularized collagen	Pelvic floor reconstruction	x (510k)	
Permacol™	Acellular porcine dermal collagen and elastin xenograft	Soft tissue repair and reinforcement	x (510k)	
Primatrix	Acellular collagen dermal tissue matrix; fetal bovine derived decellularized skin product	Burns, wounds and pressure, diabetic and venous ulcers	x (510k)	
PuraPly Antimicrobial and PuraPly Wound Matrix (previously Fortaderm)	Fenestrated porcine allograft	Wound care	x (510k)	
Repriza®	Acellular dermal matrix	Wound repair		Human tissue
Restore	Porcine small intestine submucosa	Soft tissue reinforcement	x (510k)	
Revitalon™ (previously Amnioclear®)	Human amniotic tissue membrane	Wound care		Human tissue
StrataGraft	NIKS cells, tissue keratinocytes	Burns, skin defects	under develop-ment	
Strattice™	Porcine dermis xenographic tissue	Soft tissue patch	x (510k)	
SurgiMend®	Acellular dermal tissue matrix from fetal bovine dermis	Reinforce soft tissue weakness and surgical repair	x (510k)	
TenSIX™	Acellular dermal matrix	Wounds and tendons		Human tissue
TheraSkin®	Cryopreserved allogeneic human skin	Wounds and ulcers		Human tissue
Tissuemend	Bovine derived decellularized skin product	Soft tissue and tendon repair reinforcement	x (510k)	
TranZgraft	Acellular dermal matrix	Dental, orthopedic and ENT applications, hernia and ulcer repair		Human tissue
Veritas® Collagen Matrix	Non-cross linked bovine pericardium	Surgical repair of soft tissue deficiencies	x (510k)	
XCM Biologic	Porcine dermal matrix	Wound repair, soft tissue reinforcement	Not listed	

RATIONALE:

Bio-engineered skin and soft tissue substitutes are being investigated for a variety of conditions. Overall, the number of bio-engineered skin and soft-tissue substitutes is large, but the evidence is limited for any specific product. Relatively few products have been compared with the standard of care, and then only for some indications. Most trials identified were industry sponsored and were open label, with no masking indicating potential performance bias. The data on many of the industry sponsored trials had incomplete outcome data indicating attrition bias. Additional studies with larger number of subjects are needed to evaluate the effect of bio-engineered skin and soft tissue substitutes versus the current standard of care or current advanced wound therapies (i.e. Apligraf® or Dermagraft®). Overall, results of these studies do not provide convincing evidence that many of these products are more effective than SOC or current advanced wound therapies for healing diabetic foot or venous ulcers. Additional trials with a larger number of subjects are needed to determine whether these products improve health outcomes.

A systematic literature review addressing the current application and limitations of biologic dressings in dermatologic surgery was published in June 2009 (Chern, et al). The review was undertaken to review the current evidence regarding the utility, outcomes, and adverse effects of the available biologic dressings, with a particular focus on use in acute surgical wounds and applicability to dermatologic surgery. The authors concluded that although further work is necessary, biologic dressings remain a promising area of study for use in the healing of acute and chronic wounds, many case reports have described the use of various products in dermatologic disease and cutaneous surgery although further study is necessary before conclusions can be drawn, and overall, further studies, particularly randomized controlled studies, are necessary to evaluate the utility of these biologic dressings, especially in the setting of acute surgical wounds.

In December 2012, AHRQ completed a technology assessment addressing *Skin Substitutes for Treating Chronic Wounds.* The assessment addresses 57 products currently available in the U.S. that are used to manage or treat chronic wounds and are regulated by FDA. Based on FDA regulations skin substitutes can be organized into four groups: human-derived products regulated as HCT/Ps, human- and human/animal-derived products regulated through PMA or HDE, animal-derived products regulated under the 510(k) process, and synthetic products regulated under the 510(k) process. One of the report's goals was to begin to characterize the state of the evidence on skin substitutes as wound care products for chronic wounds. Eighteen RCTs examining only seven of the skin substitute products identified for the report met the inclusion criteria. The author's evaluation of the clinical literature indicates that studies comparing the efficacy of skin substitutes to alternative wound care approaches are limited in number, apply mainly to generally healthy patients, and examine only a small portion of the skin substitute products available in the United States. The results of the available studies cannot be extended to other skin substitute products because of differences in active components in the various products. The studies available were not generalizable to the broader patient populations that are not as healthy as the patients in the studies. Also missing from the evidence base were studies that compared the various types of skin substitute products. Only two of the 18 studies compared two skin substitute products. How a human dermal substitute compares with a human derived skin substitute when treating a diabetic foot ulcer or a vascular leg ulcer is unknown. Such comparisons could be useful to clinicians trying to decide which wound treatment products to use. Additional studies in the area of wound care would be helpful to provide treatment data for many of the other skin substitute products, to allow better comparisons between wound care products, and to provide better information on wound recurrence when using skin substitute products.

Product Categories:

Acellular Dermal Matrices (ADM):

There is a small amount of evidence utilizing acellular dermal matrix products in breast reconstruction that does not show any difference in outcomes among the different types of ADM products.

A retrospective review compared complication rates following breast reconstruction with AlloDerm or FlexHD in 382 consecutive women (547 breasts). 81% of the patients underwent immediate reconstructions; 165 used AlloDerm, and

97 used FlexHD. Mean follow-up was 6.4 months. Compared with breast reconstruction without use of AlloDerm or FlexHD, ADM had a higher rate of delayed healing (20.2% vs 10.3%), although this finding might be related to differences in fill volumes. In univariate analysis, there were no significant differences in complications (return to the operating room, surgical site infection, seroma, hematoma, delayed healing, or implant loss) between AlloDerm and FlexHD. In multivariate analysis, there were no significant differences between AlloDerm and FlexHD for the return to the operating room, surgical site infection, seroma, or delayed healing. Independent risk factors for implant loss included the use of FlexHD, single-stage reconstruction, and smoking. (Liu, et al, 2013).

Another retrospective review published in 2013 compared complication rates following use of AlloDerm (n=136) or FlexHD (n=233) in a consecutive series of 255 patients (369 breasts). Total complication rates for the two products were similar (19.1% for AlloDerm and 19.3% for FlexHD). Analysis by type of complication showed no significant difference between the products, and regression analysis controlling for differences in baseline measures found that the type of ADM was not a risk factor for any complication (Seth, et al, 2013).

A retrospective review of complication rates when AlloDerm (n=49), DermaMatrix (n=110), or FlexHD (n=62) was used for tissue expander breast reconstruction was published in 2012. Clinically significant complications were defined as cellulitis, abscess, seroma, expander leak or puncture, skin necrosis, wound dehiscence, or hematoma. The total clinically significant complication rate was 22% with AlloDerm, 15% with DermaMatrix, and 16% with FlexHD (not significantly different). Infectious complication rates for the 3 products were the same at 10%. When compared with breast reconstruction without an ADM (n=64), there was no significant difference in the total complication rate (17% vs 11%), but there was a trend toward a higher incidence of infectious complications (10% vs 2%, p=0.09) (Brooke, et al, 2012).

Amniotic Tissue Membrane:

Human amniotic membrane is classified by the U. S. Food and Drug Administration (FDA) as banked human tissue and therefore, it does not require FDA approval. Examples of amniotic tissue membrane include, but are not limited to, EpiFix® and Amniofix®. Results from small studies are encouraging, but preliminary. Further large, randomized, controlled studies are needed before conclusions can be made regarding the efficacy of these products.

A review article, published in 2015, addresses the use of human amnion/chorion membrane (dHACM) for lower extremity repair. The article states "although there are limited data available regarding most amniotic membrane-based products, there is substantial preclinical and clinical evidence supporting the rationale and effectiveness of dHACM allograft as a treatment modality. The rapidly growing body of evidence suggests that the properties inherent in dHACM promote tissue regeneration and healing, recruiting patients' own stem cells into the wounded area. Randomized controlled trials evaluating dHACM now include more than 200 patients collectively and the results consistently show improved healing. Use of dHACM has been shown to be more clinically effective and cost-effective than other frequently used advanced wound care products. This cost-effectiveness results from dHACM showing higher healing rates and more rapid healing than other advanced wound care products. Cost-effectiveness is also enhanced through the availability of grafts of multiple sizes, which reduces wastage, and through ease of handling and storage for clinical use. Ongoing and future studies will further define and establish the value of amniotic membrane for chronic tissue repair and regeneration." (Zelen, et al, 2015).

A small, industry-sponsored, non-blinded, randomized, controlled trial comparing use of *EpiFix*® (n=13) with standard of care (SOC; moist wound therapy, n=12) for diabetic foot ulcers of at least 4 weeks' duration was published in 2013. EpiFix was applied every 2 weeks if the wound had not healed, with weekly dressing changes comprised of non-adherent dressing, moisture retentive dressing, and a compression dressing. Standard moist wound dressing was changed daily. After 4 weeks of treatment, EpiFix treated wounds had reduced in size by a mean of 97.1% compared with 32.0% for the SOC group. Healing rate (complete epithelialization of the open area of the wound) was 77% for EpiFix compared with 0% for SOC. After 6 weeks of treatment, wounds were reduced by 98.4% with EpiFix treatment compared with -1.8% for standard care. The healing rate was 92% with EpiFix compared with 8% with standard treatment alone (Zelen, et al, 2013).

Treatment with *EpiFix*®, *Apligraf*®, or standard wound care was compared in a multicenter randomized, controlled study. Sixty patients with chronic lower extremity diabetic ulcers were randomized to treatment with Epifix (dehydrated human amniotic membrane), Apligraf (human skin allograft with living fibroblasts and keratinocytes), or standard wound care. Although the patient and site investigator could not be blinded due to differences in products; wound healing was verified by 3 independent physicians who evaluated photographic images. The median wound size was 2.0 cm^2 (range, 1.0-9.0) and the median duration of the index ulcer was 11 weeks (range, 5-54). After 6 weekly treatments, the mean percent wound area healed was 97.1% for EpiFix, 80.9% for Apligraf, and 27.7% for standard care; 95% of wounds had healed in the EpiFix group compared with 45% treated with Apligraf and 35% who received standard wound care ($p<0.003$). The estimated median time to wound closure, based on Kaplan-Meier analysis, was 13 days for EpiFix compared with 49 days for both Apligraf and SOC ($p<0.001$). (Zelen, et al, 2014). Based on the updated Zelen, et. al. 2015 article, data was included on treatment of 226 diabetic foot ulcers from 99 wound care centers. Although wounds for the 2 groups were compared at baseline, the rationale for using a particular product was not reported. There were 163 wounds treated with Apligraf and 63 treated with Epifix®. By week 24, 72% of the wounds treated with Apligraf® and 47% of the wounds treated with Epifix® had closed. The median time to closure was 13.3 weeks for Apligraf® and 26.0 weeks for Epifix®.

In 2015, Kirsner et al reported an industry-sponsored observational study comparing the effectiveness of Apligraf and EpiFix in a real-world setting.13 Data were obtained from a wound care–specific database from 3000 wound care facilities. The database included 1458 diabetic ulcers treated for the first time in 2014 with Apligraf (n=994) or EpiFix (n=464). *Using the same criteria as the 2015 study by Zelen (described above),* data were included on the treatment of 226 diabetic foot ulcers from 99 wound care centers. Foot wounds were included with size between 1 cm2 and 25 cm2, duration of 1 year or less, and wound reduction of 20% or less in the 14 days prior to treatment. Although wounds for the 2 groups were comparable at baseline, the rationale for using a particular product was not reported. There were 163 wounds treated with Apligraf (mean, 2.5 applications) and 63 treated with EpiFix (mean, 3.5 applications, p=0.003). By week 24, *72% of wounds treated with Apligraf and 47% of wounds treated with EpiFix had closed* (p=0.01). Median time to closure was 13.3 weeks for Apligraf and 26.0 weeks for Amniotic Membrane and Amniotic Fluid 7.01.149.

Treatment with *Grafix*® or standard wound care was compared in a small multi-centered RCT for diabetic foot ulcers. Although the results were positive, sample size is small Grafix (50) and SOC (47). The primary end point was complete wound closure by 12 weeks. Grafix patients who achieved full closure was 62% vs. 21% in the control group receiving SOC. There is no comparison to established products e.g. Apligraf. (Lavery et.al. 2014).

AmnioBand® was compared to SOC for treatment of non-healing diabetic foot ulcers in an industry sponsored multi-center study. 40 patients were randomized to SOC or SOC with AmnioBand®.for up to 12 weeks. Complete healing by 6 weeks was observed for 70% of wounds treated with SOC and AmnioBand®vs. 15% treated with SOC alone. At 12 weeks complete healing was observed in 85% of the SOC and AmnioBand® group vs. 25% treated with SOC alone. Limitations of the study were small sample size, 9/40 drop-out rate, and the wound area in control group was larger than treatment group.

The limited published, peer-reviewed, medical literature does not provide sufficient information to determine that the use of *Biovance*® has a definite, positive effect on health outcomes in treating lower extremity diabetic ulcers.

Products:

AlloDerm® is classified by the FDA as human tissue and is approved for use in burns and full-thickness wounds. There is limited scientific evidence in the form of retrospective case series to support the use of AlloDerm® in rare cases of non-primary hernia repair when chronic infection contraindicates the use of mesh or other conventional repair.

Although the literature investigating the use of AlloDerm® in breast reconstruction surgery consists of small case series that lack long-term data on effectiveness and safety, they all reach favorable conclusions. The use of AlloDerm® obviates many of the current disadvantages to implant breast reconstruction including thinning of muscle layer causing visible rippling and contour irregularities. In the multi-step processing of AlloDerm®, the epidermis and all the dermal

cellular components are removed, leaving no reservoir for viral agents. As a result, no immune response is elicited after placement of the allograft.

Literature regarding the use of AlloDerm® in parotidectomy also consists of small case series; however they support that AlloDerm® is beneficial in preventing Frey's syndrome after parotidectomy.

AlloPatch Pliable human reticular acellular dermis was compared to SOC in a 2016 industry-sponsored multicenter trial by Zelen et al. The trial was powered to detect a 45% difference between groups in percent healing at 6 weeks with 20 patients per group. Evaluation of the outcome measures was not blinded. At 6 weeks, 65% (13/20) of wounds treated with AlloPatch had healed compared to 5% (1/20) in the SOC-alone group ($p<0.001$). After adjusting for wound area at baseline, the hazard ratio for healing was 168 (95% CI, 10 to 2704; $p<0.001$), indicating a lack of precision in the estimate. Per protocol, 10 patients in the SOC group and 1 in the AlloPatch group exited the study at 6 weeks because their wounds failed to reduce in area by at least 50%. According to *intent-to-treat* (ITT) analysis with last observation carried forward, the percentage of wounds healed at 12 weeks was 80% in the AlloPatch group compared to 20% in the SOC group. However, because there was a high (50%) withdrawal rate in the SOC group, this result has a high risk of bias.

Biobrane® was granted pre-market approval by the FDA as a temporary covering of full-thickness burns until autografting is clinically appropriate.

Integra® Dermal Regeneration Template was granted pre-market approval by the FDA for use in post-excisional treatment of life-threatening full-thickness or deep partial-thickness thermal injuries where sufficient autograft in not available at the time of excision or not desirable due to the physiological condition of the patients, and for the repair of scar contractures when other therapies have failed or when donor sites for repair are not sufficient or desirable due to the physiologic condition of the patient. Evidence for use of Integra for contracture release procedures consists only of a retrospective case series without controls.

In January 2016, the U. S. Food and Drug Administration approved the use *Integra® Dermal Regeneration Template,* marketed as *Omnigraft™,* for use in the treatment of partial and full-thickness neuropathic diabetic foot ulcers that are greater than six weeks in duration, with no capsule, tendon, or bone exposes, when used in conjunction with standard diabetic ulcer care. Randomized, controlled studies have been shown to improve healing of chronic, non-healing diabetic foot ulcers with the use of Omnigraft™. The Foot Ulcer New Dermal Replacement Study (FOUNDER) multicenter study on the Integra Dermal Regeneration Template for chronic, non-healing diabetic foot ulcers was conducted under an FDA-regulated investigational device exemption. 307 patients with at least 1 chronic diabetic foot ulcer were randomized to treatment with the Integra Template or a control condition (0.9% sodium chloride gel). Treatment was given for 16 weeks or until wound closure. There was a modest increase in wound closure with the Integra Template (51% vs 32%) and a shorter median time to closure (43 days vs 78 days). There was a strong correlation between investigator-assessed and computerized planimetry assessment of wound healing (r=0.97). Kaplan-Meier analysis showed the greatest difference between groups in wound closure up to 10 weeks, with diminishing differences after 10 weeks. Strengths of the study included adequate power to detect an increase in wound healing of 18%, which was considered to be clinically significant, secondary outcomes of wound closure and time to wound closure by computerized planimetry, and intention-to-treat (ITT) analysis. (Driver, et. al., 2015)

Oasis® Wound Matrix, Oasis® Burn Matrix, and Oasis® Ultra Tri-Layer Matrix have FDA 510(k) approval in the management of wounds including partial and full thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled undermined wounds, surgical wounds, trauma wounds, and draining wounds. (Cook Biotech) is a xenogeneic collagen scaffold derived from porcine small intestinal mucosa. Oasis Wound Matrix Niezgoda et al compared healing rates at 12 weeks for full-thickness diabetic foot ulcers treated with OASIS Wound Matrix (an acellular wound care product) to Regranex Gel.54 This industry-sponsored, multicenter RCT was conducted at 9 outpatient wound care clinics and involved 73 patients with at least 1 diabetic foot ulcer. Patients were randomized to receive either Oasis Wound Matrix (n=37) or Regranex

Gel (n=36) and a secondary dressing. Wounds were cleansed and débrided, if needed, at a weekly visit. The maximum treatment period for each patient was 12 weeks. After 12 weeks, 18 (49%) Oasis-treated patients had complete wound closure compared with 10 (28%) Regranex-treated patients. Oasis treatment met the noninferiority margin, but did not demonstrate that healing in the Oasis group was statistically superior (p=0.055). Post hoc subgroup analysis showed no significant difference in incidence of healing in patients with type 1 diabetes (33% vs 25%) but showed a significant improvement in patients with type 2 diabetes (63% vs 29%). There was also an increased healing of plantar ulcers in the Oasis group (52% vs 14%).

PriMatrix^{TM} received FDA 510(k) approval in 2006 for the management of wounds that include: partial and full thickness wounds; pressure, diabetic and venous ulcers; second-degree burns; surgical wounds - donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence; trauma wounds - abrasions, lacerations, and skin tears; tunneled/undermined wounds; draining wounds.

Theraskin® was reported in a small (n=23) industry-funded randomized comparison of TheraSkin® (human skin allograft with living fibroblasts and keratinocytes) versus Dermagraft® (human-derived fibroblasts cultured on mesh) for diabetic foot ulcers. Wound size at baseline ranged from 0.5 to 18.02 cm^2; the average wound size was about 5 cm^2 and was similar for the 2 groups (p=0.51). Grafts were applied according to the manufacturer's instructions over the first 12 weeks of the study until healing, with an average of 4.4 TheraSkin grafts (every 2 weeks) compared with 8.9 Dermagraft applications (every week). At week 12, complete wound healing was observed in 63.6% of ulcers treated with TheraSkin and 33.3% of ulcers treated with Dermagraft (p<0.049). At 20 weeks, complete wound healing was observed in 90.9% of the TheraSkin-treated ulcers compared with 66.67% of the Dermagraft group (p=0.428). (Sanders, et al, 2014). Further large, randomized, controlled studies are needed before conclusions can be made regarding the efficacy of Theraskin®.

CODES: Number Description

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

CPT:	15271	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
	15272	each additional 25 sq cm wound surface area, or part thereof
	15273	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
	15274	each additional 100 sq cm wound surface area, or part thereof, or each additional 1% body area of infants and children, or part thereof
	15275	Application of skin substitute graft to face, scalp, eyelids, mouth, neck ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
	15276	each additional 25 sq cm wound surface area, or part thereof
	15277	Application of skin substitute graft to face, scalp, eyelids, mouth, neck ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of

		infants and children
	15278	each additional 100 sq cm wound surface area, or part thereof, or each additional 1% body area of infants and children, or part thereof
	15777	Implantation of biologic implant (eg, acellular dermal matrix) for soft tissue reinforcement (ie, breast, trunk)

HCPCS:	C5271	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
	C5272	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; each additional 25 sq cm or less wound surface area, or part thereof
	C5273	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
	C5274	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof
	C5275	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
	C5276	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; each additional 25 sq cm or less wound surface area, or part thereof
	C5277	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
	C5278	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof
	C9354 **(E/I)**	Acellular pericardial tissue matrix of non-human origin (Veritas), per square cm
	C9356 **(E/I)**	Tendon, porous matrix of cross-linked collagen and glycosaminoglycan matrix (TenoGlide Tendon Protector Sheet), per square cm
	C9358 **(E/I)**	Dermal substitute, native, non-denatured collagen, fetal bovine origin (SurgiMend Collagen Matrix), per 0.5 square cms
	C9360 **(E/I)**	Dermal substitute, native, non-denatured collagen, neonatal bovine origin (SurgiMend Collagen Matrix), per 0.5 square cms

C9363 **(E/I)**	Skin substitute, Integra Meshed Bilayer Wound Matrix, per square cm
C9364 **(E/I)**	Porcine implant, Permacol, per square cm
Q4100	Skin substitute, not otherwise specified
Q4101	Apligraf, per square cm
Q4102	Oasis wound matrix, per square cm
Q4103	Oasis burn matrix, per square cm
Q4104 **(E/I)**	Integra bilayer matrix wound dressing (BMWD), per square cm
Q4105	Integra dermal regeneration template (DRT) or Integra Omnigraft dermal regeneration matrix, per square cm
Q4106	Dermagraft, per square cm
Q4107	GRAFTJACKET, per square cm
Q4108	Integra matrix, per square cm
Q4110	PriMatrix, per square cm
Q4111 **(E/I)**	GammaGraft, per square cm
Q4112 **(E/I)**	Cymetra, injectable, 1 cc
Q4113 **(E/I)**	GRAFTJACKET XPRESS, injectable, 1 cc
Q4114 **(E/I)**	Integra flowable wound matrix, injectable, 1 cc
Q4115 **(E/I)**	AlloSkin, per square cm
Q4116	AlloDerm, per square cm
Q4117 **(E/I)**	HYALOMATRIX, per square cm
Q4118 **(E/I)**	MatriStem micromatrix, 1 mg
Q4121 **(E/I)**	TheraSkin, per square cm
Q4122	Dermacell, per square cm
Q4123 **(E/I)**	AlloSkin RT, per square cm
Q4124	OASIS ultra tri-layer wound matrix, per square cm
Q4125 **(E/I)**	Arthroflex, per square cm
Q4126 **(E/I)**	MemoDerm, dermaspan, tranzgraft or integuply, per square cm
Q4127 **(E/I)**	Talymed, per square cm
Q4128	FlexHD, AllopatchHD, or Matrix HD, per square cm
Q4130	Strattice TM, per square cm
Q4131 **(E/I)**	Epifix or Epicord, per square cm (revised 1/1/17)
Q4132 **(E/I)**	Grafix Core and GrafixPL Core, per square cm
Q4133 **(E/I)**	Grafix Prime and GrafixPL Prime, per square cm

Q4134 **(E/I)**	Hmatrix, per square cm
Q4135 **(E/I)**	Mediskin, per square cm
Q4136 **(E/I)**	Ez-derm, per square cm
Q4137 **(E/I)**	Amnioexcel or biodexcel, per square cm
Q4138 **(E/I)**	Biodfence dryflex, per square cm
Q4139 **(E/I)**	Amniomatrix or biodmatrix, injectable, 1 cc
Q4140 **(E/I)**	Biodfence, per square cm
Q4141 **(E/I)**	Alloskin ac, per square cm
Q4142 **(E/I)**	XCM biologic tissue matrix, per square cm
Q4143 **(E/I)**	Repriza, per square cm
Q4145 **(E/I)**	Epifix, injectable, 1 mg
Q4146 **(E/I)**	Tensix, per square cm
Q4147 **(E/I)**	Architect, architect PX, or architect FX, extracellular matrix, per square cm
Q4148 **(E/I)**	Neox Cord 1K, Neox Cord RT, or Clarix Cord 1K, per square cm
Q4149 **(E/I)**	Excellagen, 0.1 cc
Q4150 **(E/I)**	AlloWrap DS or dry, per square cm
Q4151 **(E/I)**	Amnioband or Guardian, per square cm
Q4152 **(E/I)**	DermaPure, per square cm
Q4153 **(E/I)**	Dermavest and Plurivest, per square cm
Q4154 **(E/I)**	Biovance, per square cm
Q4155 **(E/I)**	Neoxflo or Clarixflo, 1 mg
Q4156 **(E/I)**	Neox 100 or Clarix 100, per square cm
Q4157 **(E/I)**	Revitalon, per square cm
Q4158 **(E/I)**	Marigen, per square cm Kerecis Omega3, per square cm
Q4159 **(E/I)**	Affinity, per square cm
Q4160 **(E/I)**	NuShield, per square cm
Q4161 **(E/I)**	Bio-ConneKt wound matrix, per square centimeter
Q4162 **(E/I)**	WoundEx Flow, BioSkin Flow, 0.5 cc
Q4163 **(E/I)**	WoundEx, BioSkin, per square cm
Q4164 **(E/I)**	Helicoll, per square centimeter
Q4165 **(E/I)**	Keramatrix, per square centimeter
Q4166 **(E/I)**	Cytal, per square centimeter
Q4167 **(E/I)**	TruSkin, per square centimeter

	Q4168 **(E/I)**	AmnioBand, 1 mg
	Q4169 **(E/I)**	Artacent™ Wound, per square centimeter
	Q4170 **(E/I)**	CYGNUS, per square centimeter
	Q4171 **(E/I)**	Interfyl, 1 mg
	Q4172 **(E/I)**	PuraPly or PuraPly AM, per square centimeter
	Q4173 **(E/I)**	PalinGen or PalinGen Xplus, per square centimeter
	Q4174 **(E/I)**	PalinGen or ProMatrX, 0.36 mg per 0.25 cc
	Q4175 **(E/I)**	Miroderm, per square centimeter
	Q4176 **(E/I)**	NeoPatch, per square cm (effective 1/1/18)
	Q4177 **(E/I)**	FlowerAmnioFlo, 0.1 cc (effective 1/1/18)
	Q4178 **(E/I)**	FlowerAmnioPatch, per square cm (effective 1/1/18)
	Q4179 **(E/I)**	FlowerDerm, per square cm (effective 1/1/18)
	Q4180 **(E/I)**	Revita, per square cm (effective 1/1/18)
	Q4181 **(E/I)**	Amnio Wound, per square cm (effective 1/1/18)
	Q4182 **(E/I)**	Transcyte, per square cm (effective 1/1/18)
ICD10:	C07	Malignant neoplasm of parotid gland
	C50.011-C50.019	Malignant neoplasm of nipple and areola, right female breast (code range)
	C50.111-C50.119	Malignant neoplasm of central portion of female breast (code range)
	C50.211-C50.219	Malignant neoplasm of upper-inner quadrant of female breast (code range)
	C50.311-C50.319	Malignant neoplasm of lower-inner quadrant of female breast (code range)
	C50.411-C50.419	Malignant neoplasm of upper-outer quadrant of female breast (code range)
	C50.511-C50.519	Malignant neoplasm of lower-outer quadrant of female breast (code range)
	C50.611-C50.619	Malignant neoplasm of axillary tail of female breast (code range)
	C50.811-C50.819	Malignant neoplasm of overlapping sites of female breast (code range)
	C50.911-C50.919	Malignant neoplasm of unspecified site of female breast (code range)
	D05.00-D05.92	Carcinoma in situ of breast (code range)
	D11.0-D11.9	Benign neoplasm of major salivary gland (code range)
	D37.030-D37.039	Neoplasm of uncertain behavior of the salivary glands (code range)
	E10.10-E10.69	Type 1 diabetes mellitus with specified complication (code range)
	E11.00-E11.8	Type 2 diabetes mellitus with specified complication (code range)
	E11.9	Type 2 diabetes mellitus without complications
	E13.00-E13.9	Other specified diabetes mellitus with specified complication (code range)
	E13.9	Other specified diabetes mellitus without complications

I70.232-I70.269	Atherosclerosis of native arteries (code range)
I70.333-I70.744	Atherosclerosis of bypass graft(s) (code range)
I83.003-I83.005	Varicose veins of unspecified lower extremity with ulcer (code range)
I83.011-I83.022	Varicose veins of lower extremity with ulcer (code range)
I83.029	Varicose veins of left lower extremity with ulcer of unspecified site
I83.10-I83.12	Varicose veins of lower extremity with inflammation (code range)
I183.201-I83.202	Varicose veins of unspecified lower extremity with both ulcer and inflammation (code range)
I83.205-I83.228	Varicose veins of lower extremity with both ulcer and inflammation (code range)
K11.1-K11.9	Disease of salivary gland (code range)
L97.301-L97.303	Non-pressure chronic ulcer of unspecified ankle (code range)
L97.311-L97.329	Non-pressure chronic ulcer of ankle (code range)
L97.401-L97.409	Non-pressure chronic ulcer of unspecified heel and midfoot (code range)
L97.413-L97.429	Non-pressure chronic ulcer of heel and midfoot (code range)
L97.501-L97.529	Non-pressure chronic ulcer of other part of foot (code range)
R68.2	Dry mouth, unspecified
T30.0	Burn of unspecified body region, unspecified degree
T30.4	Corrosion of unspecified body region, unspecified degree
T31.0-T31.99	Burns (code range)
T32.0-T32.99	Corrosions (code range)
Z85.3	Personal history of malignant neoplasm of breast
Z90.10-Z90.13	Acquired absence of breast and nipple (code range)

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KEY WORDS:

Affinity™, AlloDerm®, AlloMax™, AlloSkin™, AlloWrap™, AmnioBand™, Amnioexcel®, AmnioMatrix®, Apligraf®, Artacent™ Wound, ArthroFlex™, Artificial skin, Avaulta Plus™, Biobrane®, Biobrane l®, Bioengineered skin, Biologic tissue, Biovance®, Clarix® Flo, Collamend, Conexa™, Cygnus Solo™, Cygnus Matrix™, Cygnus Max™, Cymetra®, Cytal™ Burn Matrix, Cytal™ Wound Matrix, DermACELL AWM™, DermaMatrix, DermaPure™, DermaSpan™, Dermavest™, Endoform Dermal Template™, ENDURAgen™, Epicel®, EpiCord™, EpiFix, Excellagen®, E-Z Derm™, FlexHD®, GammaGraft, Grafix® CORE, Grafix® PRIME, GraftJacket®, GraftJacket® Xpress, Graftskin, Guardian, hMatrix®, Hyalomatrix®, Integra™, Integra™ Bilayer Wound® Matrix, Integra™ Dermal Regeneration Matrix®, Integra™ Flowable Wound® Matrix, InteguPly™, Interfyl™, Laserskin, MariGen, Mediskin®, Miroderm®, Neoform, Neox®, Neox 1K, Neox® Flo, NuShield™, OASIS® Wound Matrix, OASIS® Burn Matrix, OASIS® Ultra, Omnigraft™, Orcel™, Orthoadapt, PalinGen® - Membrane, Hydromembrane, Flow, and SportFlow, Pelvicol, Pelvisoft, Permacol™, Primatrix, PuraPly, Restore, Revitalon™, Skin substitute, StrataGraft, Strattice™, SurgiMend®, TenSIX™, TheraSkin®, Tissuemend, TranZgraft, TruSkin™, Veritas® Collagen Matrix, XCM Biological Tissue Matrix.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently no Local Coverage Determination (LCD) or National Coverage Determination addressing bioengineered tissue products.
Note: LCD and related articles were retired as of 9/1/16