Policy Number	**SUR704.011**
Policy Effective Date	**5/7/2026**

Bioengineered Skin and Soft Tissue Substitutes and Amniotic Membrane Products

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Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For Illinois only: Illinois Public Act 103-0123 (IL HB 1384) Coverage for Reconstructive Services requires the following policies amended, delivered, issued, or renewed on or after Jan. 1, 2025 (Individual and family PPO/HMO/POS; Student; Group [Small Group; Mid-Market; Large Group Fully Insured PPO/HMO/POS] or Medicaid), to provide coverage for medically necessary services that are intended to restore physical appearance on structures of the body damaged by trauma.

EXCEPTION: For members residing in the state of Arkansas, § 23-99-405 related to coverage of mastectomy and reconstruction services, should an enrollee elect

reconstruction after a mastectomy, requires coverage for surgery and reconstruction of the breast on which the mastectomy has been performed, surgery and reconstruction of the other breast to produce a symmetrical appearance, and protheses and coverage for physical complications at all stages of a mastectomy, including lymphedema. This applies to the following: Fully Insured Group, Student, Small Group, Mid-Market, Large Group, HMO, EPO, PPO, POS. Unless indicated by the group, this mandate or coverage will not apply to ASO groups.

Coverage

BIOENGINEERED SKIN AND SOFT TISSUE SUBSTITUTES

Breast Reconstructive Surgery

Breast reconstructive surgery using allogeneic acellular dermal matrix products[a] (including each of the following: AlloDerm®, Cortiva® [AlloMax™], DermACELL™, DermaMatrix™, FlexHD®, FlexHD® Pliable™) **may be considered medically necessary**:

- When there is insufficient tissue expander or implant coverage by the pectoralis major muscle and additional coverage is required;
- When there is viable but compromised or thin postmastectomy skin flaps that are at risk of dehiscence or necrosis; or
- The inframammary fold and lateral mammary folds have been undermined during mastectomy and reestablishment of these landmarks is needed.

Diabetic Lower-Extremity Ulcers

Treatment of chronic, noninfected, full-thickness diabetic lower-extremity ulcers using the following tissue-engineered skin substitutes **may be considered medically necessary**:

- AlloPatch®[a];
- Apligraf®[b];
- Dermagraft®[b];
- Integra® Omnigraft™ Dermal Regeneration Matrix (also known as Omnigraft™) and Intregra Flowable Wound Matrix;
- mVASC®;
- TheraSkin®.

Lower-Extremity Skin Ulcers due to Venous Insufficiency

Treatment of chronic, noninfected, partial- or full-thickness lower-extremity skin ulcers due to venous insufficiency, which have not adequately responded following a 1-month period of conventional ulcer therapy, using the following tissue-engineered skin substitutes **may be considered medically necessary**:

- Apligraf®[b]; or
- Oasis™ Wound Matrix[c].

Dystrophic Epidermolysis Bullosa
Treatment of dystrophic epidermolysis bullosa using the following tissue-engineered skin substitutes **may be considered medically necessary**:

- OrCel™ (for the treatment of mitten-hand deformity when standard wound therapy has failed and when provided in accordance with the humanitarian device exemption [HDE] specifications of the U.S. Food and Drug Administration)[d].

Burns
Treatment of second- and third-degree burns using the following tissue-engineered skin substitutes **may be considered medically necessary**:

- Epicel® (for the treatment of deep dermal or full-thickness burns comprising a total body surface area ≥30% when provided in accordance with the HDE specifications of the FDA)[d]; or
- Integra® Dermal Regeneration Template[b].

[a] Banked human tissue.
[b] FDA premarket approval.
[c] FDA 510(k) clearance.
[d] FDA-approved under an HDE.

All other uses of the bioengineered skin and soft tissue substitutes listed above **are considered experimental, investigational and/or unproven.**

All other skin and soft tissue substitute products not listed above **are considered experimental, investigational and/or unproven** for indications reviewed herein, including, but not limited to:

- AC5® Advanced Wound System;
- ACell® UBM Hydrated/Lyophilized Wound Dressing;
- AlloSkin™;
- AlloSkin™ RT;
- Apis®;
- Aongen™ Collagen Matrix;
- Architect® ECM, PX, FX;
- Artacent® Wound;
- ArthroFlex™ (Flex Graft);
- AxoGuard® Nerve Protector (AxoGen);
- BellaCell HD or Surederm;
- Biobrane®/Biobrane-L;
- Bio-ConneKt® Wound Matrix;
- CollaCare®;
- CollaCare® Dental;
- Collagen Wound Dressing (Oasis Research);
- CollaGUARD®;

- CollaMend™;
- CollaWound™;
- Coll-e-derm;
- Collexa®;
- Collieva®;
- Conexa™;
- Coreleader Colla-Pad;
- CorMatrix®;
- Corplex P™/Theracor P™/Allacor P™;
- Cymetra™ (Micronized AlloDerm™;
- Cytal™ (previously MatriStem®);
- DeNovoSkin™;
- Dermadapt™ Wound Dressing;
- Derma-gide;
- DermaPure™;
- DermaSpan™;
- DressSkin;
- Duragen® XS, Duragen™ Plus;
- Durepair Regeneration Matrix®;
- Endoform Dermal Template™;
- ENDURAGen™;
- Excellagen;
- ExpressGraft™;
- E-Z Derm™;
- Flexible Collagen Nerve Cuff (Collagen Matrix, Inc);
- FlowerDerm™;
- Foundation Dermal Regeneration Scaffold (DRS) Solo;
- GammaGraft;
- Geistlich Derma-Gine™;
- GraftJacket ® Xpress, injectable;
- Helicoll™;
- hMatrix®;
- Hyalomatrix®;
- Hyalomatrix® PA;
- Innovaburn™;
- InnovaMatrix®;
- Innovamatrix® XL;
- Innovamatrix® PD;
- Innovamatrix FS;
- Integra™ Bilayer Wound Matrix;
- Integra® Matrix Wound Dressing (previously Avagen);
- InteguPly®;
- Keramatrix®;

- Kerecis™ Omega3;
- Keroxx™;
- MatriDerm®;
- MatriStem;
- Matrix HD™;
- Mediskin®;
- MemoDerm™;
- Microderm® biologic wound matrix;
- Microlyte® Matrix;
- MicroMatrix®;
- Miroderm®;
- Miro3D® Fibers Wound Matrix;
- Miro3d® Wound Matrix;
- MiroDry™ Wound Matrix;
- MiroTract® Wound Matrix;
- Mirragen® Advanced Wound Matrix;
- Mochida Nerve Cuff (Mochida Pharmaceutical Co.);
- MyOwn Skin;
- Myriad Matrix™;
- Myriad Morcells™;
- NervAlign Nerve Cuff (Renerve, Ltd);
- Nerve tape (BioCircuit Technologies, Inc);
- Neurowrap (Integra LifeSciences, Corp);
- NeuroMend (Stryker Orthopedics);
- NeuroShield (Monarch bioimplants, GmBH);
- NeoMatriX® Wound Matrix;
- NovoSorb SynPath;
- Novosorb™ Biodegradable Temporizing Matrix (BMT);
- Oasis® Burn Matrix;
- Oasis® Ultra;
- Ologen™ Collagen Matrix;
- Omega3 Wound (originally Merigen wound dressing);
- Omeza Collagen Matrix®;
- OviTex;
- Permacol™;
- PermeaDermB, PermeaDerm Glove, PermeaDerm C;
- Phoenix Wound Matrix;
- PriMatrix™;
- PriMatrix™ Dermal Repair Scaffold;
- Progenamatrix;
- Puracol® and Puracol® Plus Collagen Wound Dressings;
- PuraPly™ Wound Matrix (previously FortaDerm™);
- PuraPly™ AM (Antimicrobial Wound Matrix);

- Puros® Dermis;
- RegenePro™;
- Reinforce flexible Collagen Nerve Cuff (Collagen Matrix, Inc);
- Repliform®;
- ReCell®;
- Repriza™;
- Restrata;
- Restrata MiniMatrix;
- Resolve Matrix™;
- SimpiDerm;
- Skin TE™;
- StrataGraft®;
- Strattice™ (xenograft);
- SUPRA SDRM®;
- Suprathel®;
- SurgiMend®;
- Symphony™;
- Talymed®;
- TenoGlide™;
- TenSIX™ Acellular Dermal Matrix;
- TissueMend;
- TheraForm™ Standard/Sheet;
- TheraGenesis;
- TransCyte™;
- TruSkin™;
- Tutomesh™ Fenestrated Bovine Pericardium;
- Veritas® Collagen Matrix;
- Versawrap nerve protector (Alafair Biosciences, Inc);
- Xcellistem;
- XCM Biologic® Tissue Matrix; and
- XenMatrix™ AB

AMNIOTIC MEMBRANE AND AMNIOTIC FLUID PRODUCTS

Diabetic Lower-Extremity Ulcers

Treatment of nonhealing (see **Policy Guidelines**) diabetic lower-extremity ulcers using the following human amniotic membrane products (i.e., Affinity®, AmnioBand® Membrane, Biovance®, EpiCord®, Epifix®, Grafix®, NuShield®) **may be considered medically necessary**.

Ophthalmic Indications

Human amniotic membrane grafts with or without suture (e.g., Prokera®, AmbioDisk™) **may be considered medically necessary** for the treatment of the following ophthalmic indications:

- Neurotrophic keratitis with ocular surface damage and inflammation that does not

respond to conservative therapy;
- Corneal ulcers and melts that do not respond to initial conservative therapy;
- Corneal perforation when there is active inflammation after corneal transplant requiring adjunctive treatment;
- Bullous keratopathy as a palliative measure in patients who are not candidates for curative treatment (e.g., endothelial or penetrating keratoplasty);
- Partial limbal stem cell deficiency with extensive diseased tissue where selective removal alone is not sufficient;
- Moderate or severe Stevens-Johnson syndrome;
- Persistent epithelial defects that do not respond within 2 days of conservative therapy;
- Severe dry eye (Dry Eye Workshop Score [DEWS] 3 or 4) with ocular surface damage and inflammation that remains symptomatic after Steps 1, 2, and 3 of the dry eye disease management algorithm (See Policy Guidelines); or
- Moderate or severe acute ocular chemical burn.

Human amniotic membrane grafts with suture or glue **may be considered medically necessary** for the treatment of the following ophthalmic indications:
- Corneal perforation when corneal tissue is not immediately available; or
- Pterygium repair when there is insufficient healthy tissue to create a conjunctival autograft.

Human amniotic membrane grafts with or without suture **are considered experimental, investigational and/or unproven** for all other ophthalmic conditions not outlined above.

Other Indications
Injection of micronized or particulated human amniotic membrane **is considered experimental, investigational and/or unproven** for all indications, including but not limited to treatment of osteoarthritis and plantar fasciitis.

Injection of human amniotic fluid **is considered experimental, investigational and/or unproven** for all indications.

All other human amniotic membrane products (e.g., derived from amnion, chorion, amniotic fluid, umbilical cord, or Wharton's jelly) including but not limited to those in Table PG2 (see **Policy Guidelines**) for indications not listed above **are considered experimental, investigational and/or unproven** for indications reviewed herein, including but not limited to treatment of lower-extremity ulcers due to venous insufficiency and repair following Mohs micrographic surgery.

Policy Guidelines

AMNIOTIC MEMBRANE PRODUCTS

Non-healing of diabetic wounds is defined as less than a 20% decrease in wound area with standard wound care for at least 2 weeks, based on the entry criteria for clinical trials (e.g., Zelen et al. [2015] [18]).

This policy covers products that do not require U.S. Food and Drug Administration (FDA) approval or clearance. The list of products named in this review is not a complete list of all commercially available products. Table PG1 lists products included in the Policy statements, and Table PG2 lists other amniotic products that have a Healthcare Common Procedure Coding System (HCPCS) code.

Table PG1. Amniotic Products Listed in the Policy Statements

Trade Name	HCPCS Code
Affinity®	Q4159
AmnioBand® Membrane	Q4151
Biovance®	Q4154, Q4283
Epicord®	Q4187
Epifix®	Q4186
Grafix®	Q4132, Q4133, Q4304, Q4392
NuShield®	Q4160

HCPCS: Healthcare Common Procedure Code System.

Table PG2. Other Amniotic Products with HCPCS Codes

Trade Name	HCPCS Code
Abiomend Membrane and Abiomend Hydromembrane	Q4356
Abiomend XPlus Membrane and Abiomend XPlus Hydromembrane	Q4355
Acapatch™	Q4325
Acelagraft™	Q4395
Acesso	Q4311
Acesso AC	Q4312
Acesso DL	Q4293
Acesso TL	Q4300
Acesso TrifACA	Q4386
Activate™ Membrane	Q4301
Advograft Dual	Q4382
Advograft One™	Q4380
AéroGuard™	Q4370
AlloGen™	Q4212
alloPLY™	Q4323
AlloWrap™	Q4150
American Amnion™	Q4307
American Amnion AC™	Q4306

American Amnion AC™ Tri-Layer	Q4305
Amchoplast™	Q4316
AmchoplastExcel®	Q4372
Amchoplast FD™	Q4360
AmchoThick™	Q4368
AmnioAMP-MP™	Q4250
AmnioArmor™	Q4188
AmnioBand® Particulate	Q4168
AmnioBind	Q4225
Amnio Burgeon Dual-Layer Membrane	Q4365
Amnio Burgeon Membrane and Hydromembrane	Q4363
Amnio Burgeon Xplus Membrane and Xplus Hydromembrane	Q4364
AmnioCore™	Q4227
AmnioCore Pro	Q4298
AmnioCore Pro+	Q4299
AmnioCore SL	Q4367
AmnioCyte Plus	Q4242
AmnioDefend™ FT Matrix	Q4379
AmnioExcel®	Q4137
AmnioMatrix®	Q4139
Amnio-Maxx® or Amnio-Maxx Lite	Q4239
Amnion Bio™ or AxoBioMembrane	Q4211
Amnioplast 1™	Q4334
Amnioplast 2™	Q4335
Amnioplast 3™	Q4369
AmnioPlast Double	Q4391
AmniPly™	Q4249
Amnio Quad-Core	Q4294
AmnioRepair® or AltiPly™	Q4235
AmnioText™	Q4245
AmnioText™ Patch	Q4247
Amnio Tri-Core Amniotic	Q4295
AmnioTX™	Q4324
Amnio Wound™	Q4181
AmnioWrap2™	Q4221
Apollo™ FT	Q4385
ArdeoGraft®	Q4333
Artacent® AC (flowable)	Q4189
Artacent® AC (patch)	Q4190
Artacent® C	Q4336
Artacent® Cord	Q4216

Artacent® Trident	Q4337
Artacent® Velos	Q4338
Artacent® Vericlen	Q4339
Artacent® Wound	Q4169
Ascendion™	Q4390
Ascent™	Q4213
Axolotl™ Ambient or Axolotl™ Cryo	Q4215
Axolotl™ Dualgraft	Q4332
Axolotl™ Graft	Q4331
Axolotl™ Graft Ultra	Q4383
Axolotl™ DualGraft Ultra	Q4384
Barrera™ SL or Barrera™ DL	Q4281
BellaCell HD® or SureDerm®	Q4220
BioDDryFlex®	Q4138
BioDfence™	Q4140
Bionext® Patch	Q4228 (deleted)
BioWound, BioWound Plus™, BioWound XPlus™	Q4217
CaregraFT™	Q4322
carePatch™	Q4236
Celera™ Dual Layer or Celera™ Dual Membrane	Q4259
Cellesta/Cellesta Duo	Q4184
Cellesta Cord	Q4214
Cellesta Flowable Amnion	Q4185
ChoriPly	Q4359
Clarix®	Q4156
Clarix® Flo	Q4155
Cocoon™ Membrane	Q4264
Cogenex Flowable Amnion	Q4230
Cogenex Amniotic Membrane	Q4229
Complete™ AA	Q4303
Complete ACA™	Q4302
Complete™ SL	Q4270
Complete™ FT	Q4271
CoreCyte™	Q4240
Corplex™	Q4232
Corplex™ P	Q4231
Corplex™ P or Theracor P™ or Allacor P™	A2035
CoreText™ or ProText™	Q4246
Cryo-Cord™	Q4237
Cygnus®	Q4170
Cygnus® Disk	Q4362

Cygnus® Dual	Q4282
Cygnus® Matrix	Q4199
Dermabind DL™	Q4287
Dermabind CH™	Q4288
Dermabind FM™	Q4313
Dermabind SL™	Q4284
Dermacyte®	Q4248
Dermacyte® AC Matrix	Q4343
Dermavest® or Plurivest®	Q4153
Derm-Maxx®	Q4238
Dual Layer Amnio Burgeon X-Membrane	Q4366
DuoAmnion™	Q4327
duoGRAFT AC™	Q4375
duoGRAFT AA™	Q4376
E-Graft™	Q4318
Emerge™ Matrix	Q4297
Enclose™ TL Matrix	Q4351
Enverse®	Q4258
Epieffect®	Q4278
Epifix® Injectable	Q4145
Epixpress®	Q4361
Esano™ A	Q4272
Esano™ AAA	Q4273
Esano™ AC	Q4274
Esano™ ACA	Q4275
FlowerAmnioFlow™	Q4177
FlowerAmnioPatch™	Q4178
Fluid Flow™ or Fluid GF™	Q4206
Genesis	Q4198
Human Health Factor 10 Amniotic Patch (HHF10-P™)	Q4224
Impax™ Dual Layer Membrane	Q4262
InnovaMatrix AC	A2001
Interfyl®	Q4171
Lamellas	Q4291
Lamellas XT	Q4292
Mantle™ DL Matrix	Q4349
Matrion®	Q4201
Matrix DS Allograft Dermis	Q4345
Membrane Graft™ or Membrane Wrap™	Q4205
Membrane Wrap-Hydro™	Q4290
Membrane Wrap-LITE™	Q4373

MLG-Complete™	Q4256
MOST™	Q4328
Natalin™	Q4396
Néoguard™	Q4371
NeoPatch™ or Therion	Q4176
NeoStim Membrane	Q4266
NeoStim DL	Q4267
NeoStim TL™	Q4265
NeoThelium™ FT	Q4387
NeoThelium™ 4L	Q4388
NeoThelium™ 4L Plus	Q4389
Neox® Cord	Q4148
Neox® Flo	Q4155
Neox® Wound	Q4156
Novachor®	Q4194
Novafix®	Q4208
Novafix DL	Q4254
NuDYN® DL or NuDYN® DL Mesh	Q4285
NuDYN® SL or NuDYN® SLW	Q4286
Orion™	Q4276
Overlay™ SL Matrix	Q4352
PalinGen® Dual-Layer Membrane	Q4354
PalinGen® Membrane	Q4173
PalinGen® SportFlow	Q4174
Palisade™ DM Matrix	Q4350
PelloGraft®	Q4320
Plurivest™	Q4153
PolyCyte™	Q4241
Procenta®	Q4244, Q4310
Rampart™ DL Matrix	Q4347
Rebound Matrix	Q4296
Reeva FT™	Q4314
Regenelink Amniotic Membrane Allograft	Q4315
ReGUaRD™	Q4255
Relese™	Q4257
Renew™ FT matrix	Q4378
RenoGraft®	Q4321
Restorigin™	Q4191
Restorigin™ Injectable	Q4192
Revita®	Q4180
Revitalon™	Q4157

Revoshield + Amniotic Barrier	Q4289
SanoGraft®	Q4319
Sanopellis™	Q4308
Sentry™ SL Matrix	Q4348
Shelter™ DM Matrix	Q4346
Signature APatch	Q4260
SimpliGraft™	Q4340
SimpliMax™	Q4341
Singlay™	Q4329
Summit AAA	Q4397
Surgenex®, SurFactor®, and NuDYN®	Q4233
SurgiCORD®	Q4218
SurgiGRAFT™	Q4183
SurgiGraft-DUAL	Q4219
SurGraft®	Q4209
SurGraft AC	Q4393
SurGraft ACA	Q4394
SurGraft FT®	Q4268
SurGraft TL®	Q4263
SurGraft XT®	Q4269
TAG™	Q4261
Theramend™	Q4342
TOTAL™	Q4330
triGRAFT FT™	Q4377
Tri-Membrane Wrap™	Q4344
Vendaje®	Q4252
Vendaje® AC	Q4279
Via Matrix™	Q4309
VIM™	Q4251
VitoGraft®	Q4317
WoundEx®	Q4163
WoundEx® Flow	Q4162
WoundFIX™, WoundFIX™ Plus, WoundFIX™ XPlus (see BioWound above)	Q4217
WoundPlus™	Q4326
XCell Amnio Matrix™	Q4280
Xceed TL™ matrix	Q4353
Xcellerate®	Q4234
XWrap®	Q4204
XWrap Dual®	Q4358
XWrap Plus®	Q4357

Zenith™	Q4253

HCPCS: Healthcare Common Procedure Code System.

Tear Film and Ocular Surface Society staged management for dry eye disease (Jones et al. 2017) (17):

Step 1:

- Education regarding the condition, its management, treatment and prognosis.
- Modification of local environment.
- Education regarding potential dietary modifications (including oral essential fatty acid supplementation).
- Identification and potential modification/elimination of offending systemic and topical medications.
- Ocular lubricants of various types (if meibomian gland dysfunction is present, then consider lipid containing supplements).
- Lid hygiene and warm compresses of various types.

Step 2:

If above options are inadequate consider:

- Non-preserved ocular lubricants to minimize preservative-induced toxicity.
- Tea tree oil treatment for Demodex (if present).
- Tear conservation.
- Punctal occlusion.
- Moisture chamber spectacles/goggles.
- Overnight treatments (such as ointment or moisture chamber devices).
- In-office physical heating and expression of the meibomian glands.
- In-office intense pulsed light therapy for meibomian gland dysfunction.
- Prescription drugs to manage dry eye disease.
- Topical antibiotic or antibiotic/steroid combination applied to the lid margins for anterior blepharitis (if present).
- Topical corticosteroid (limited duration).
- Topical secretagogues.
- Topical non-glucocorticoid immunomodulatory drugs (such as cyclosporine).
- Topical lymphocyte function-associated antigen-1 (LFA-1) antagonist drugs (such as lifitegrast).
- Oral macrolide or tetracycline antibiotics.

Step 3:

If above options are inadequate consider:

- Oral secretagogues.
- Autologous/allogeneic serum eye drops.
- Therapeutic contact lens options.
- Soft bandage lenses.
- Rigid scleral lenses.

Step 4:
If above options are inadequate consider:
- Topical corticosteroid for longer duration.
- Amniotic membrane grafts.
- Surgical punctal occlusion.
- Other surgical approaches (e.g., tarsorrhaphy, salivary gland transplantation).

Dry eye severity level Dry Eye Workshop Score 3 to 4
- Discomfort, severity and frequency - severe frequent or constant
- Visual symptoms - chronic and/or constant, limiting to disabling
- Conjunctival Injection - +/- or +/+
- Conjunctive Staining - moderate to marked
- Corneal Staining - marked central or severe punctate erosions
- Corneal/tear signs - filamentary keratitis, mucus clumping, increase in tear debris
- Lid/meibomian glands - frequent
- Tear film breakup time - < 5
- Schirmer score (mm/5 min) - < 5

Description

BIOENGINEERED SKIN AND SOFT TISSUE SUBSTITUTES
Bioengineered skin and soft tissue substitutes may be either acellular or cellular. Acellular products (e.g., dermis with cellular material removed) contain a matrix or scaffold composed of materials such as collagen, hyaluronic acid, and fibronectin. Acellular dermal matrix (ADM) products can differ in a number of ways, including by species source (human, bovine, porcine), tissue source (e.g., dermis, pericardium, intestinal mucosa), additives (e.g., antibiotics, surfactants), hydration (wet, freeze-dried), and required preparation (multiple rinses, rehydration).

Cellular products contain living cells such as fibroblasts and keratinocytes within a matrix. The cells contained within the matrix may be autologous, allogeneic, or derived from other species (e.g., bovine, porcine). Skin substitutes may also be composed of dermal cells, epidermal cells, or a combination of dermal and epidermal cells, and may provide growth factors to stimulate healing. Bioengineered skin substitutes can be used as either temporary or permanent wound coverings.

Applications
There are a large number of potential applications for artificial skin and soft tissue products. One large category is nonhealing wounds, which potentially encompasses diabetic neuropathic ulcers, vascular insufficiency ulcers, and pressure ulcers. A substantial minority of such wounds do not heal adequately with standard wound care, leading to

prolonged morbidity and increased risk of mortality. For example, nonhealing lower-extremity wounds represent an ongoing risk for infection, sepsis, limb amputation, and death. Bioengineered skin and soft tissue substitutes have the potential to improve rates of healing and reduce secondary complications.

Other situations in which bioengineered skin products might substitute for living skin grafts include certain postsurgical states (e.g., breast reconstruction) in which skin coverage is inadequate for the procedure performed or for surgical wounds in patients with compromised ability to heal. Second- and third-degree burns are another indication in which artificial skin products may substitute for auto- or allografts. Certain primary dermatologic conditions that involve large areas of skin breakdown (e.g., bullous diseases) may also be conditions in which artificial skin products can be considered as substitutes for skin grafts. ADM products are also being evaluated in the repair of other soft tissues including rotator cuff repair, following oral and facial surgery, hernias, and other conditions.

Regulatory Status

The U.S. Food and Drug Administration does not refer to any single product or class of products as “skin substitutes". This policy covers products that do not require FDA approval or clearance as well as a number of products cleared through the 510(k) pathway with a variety of FDA product codes. A large number of artificial skin products are commercially available or in development. Commercial availability is not a reflection of a product's regulatory status. The following section summarizes a subset of commercially available skin and soft tissue substitutes. This is not a complete list of all commercially available products. Information on additional products is available in a 2020 Technical Brief on skin substitutes for treating chronic wounds that was commissioned by the Agency for Healthcare Research and Quality. (1)

Acellular Dermal Matrix (ADM) Products

Allograft ADM products derived from donated cadaveric human skin tissue are supplied by tissue banks compliant with standards of the American Association of Tissue Banks and FDA guidelines. The processing removes the cellular components (i.e., epidermis, all viable dermal cells) that can lead to rejection and infection. ADM products from human skin tissue are regarded as minimally processed and not significantly changed in structure from the natural material; FDA classifies ADM products as banked human tissue and, therefore, not requiring FDA approval for homologous use.

In 2017, the FDA published clarification of what is considered minimal manipulation and homologous use for human cells, tissues, and cellular and tissue-based products (HCT/Ps). (2)

HCT/Ps are defined as human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. If an HCT/P does not meet the

criteria below and does not qualify for any of the stated exceptions, the HCT/P will be regulated as a drug, device, and/or biological product and applicable regulations and premarket review will be required.

An HCT/P is regulated solely under section 361 of the PHS Act and 21 CFR Part 1271 if it meets all of the following criteria:

1. "The HCT/P is minimally manipulated;
2. The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;
3. The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P; and
4. Either:
    i. The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
    ii. The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and: a) Is for autologous use; b) Is for allogeneic use in a first-degree or second-degree blood relative; or c) Is for reproductive use."

- AlloDerm® (LifeCell Corp.) is an ADM (allograft) tissue-replacement product created from native human skin and processed so that the basement membrane and cellular matrix remain intact. Originally, AlloDerm® required refrigeration and rehydration before use. It is currently available in a ready-to-use product stored at room temperature. An injectable micronized form of AlloDerm® (Cymetra) is available.
- AlloPatch® (Musculoskeletal Transplant Foundation) is an acellular human dermis allograft derived from the reticular layer of the dermis and marketed for wound care. This product is also marketed as FlexHD® for postmastectomy breast reconstruction.
- Cortiva® (previously marketed as AlloMax™ Surgical Graft and before that NeoForm™) is an acellular non-cross-linked human dermis allograft.
- FlexHD® and the newer formulation FlexHD® Pliable™ (Musculoskeletal Transplant Foundation) are acellular hydrated reticular dermis allograft derived from donated human skin.
- DermACELL™ (LifeNet Health) is an allogeneic ADM processed with proprietary technologies MATRACELL® and PRESERVON®.
- DermaMatrix™ (Synthes) is a freeze-dried ADM derived from donated human skin tissue. DermaMatrix Acellular Dermis is processed by the Musculoskeletal Transplant Foundation.
- DermaPure™ (Tissue Regenix Wound Care) is a single-layer decellularized human dermal allograft for the treatment of acute and chronic wounds.
- GraftJacket ® Regenerative Tissue Matrix (also called GraftJacket Skin Substitute; KCI) is an acellular regenerative tissue matrix that has been processed from human skin

supplied from U.S. tissue banks. The allograft is minimally processed to remove the epidermal and dermal cells while preserving dermal structure. GraftJacket Xpress® is an injectable product.
- mVASC® (MicroVascular Tissues, Inc.) is a microvascular tissue structural allograft made of small blood vessels and extracellular matrix, inherent non-viable cells, and associated biological signaling factors harvested from subcutaneous tissue of cadaveric human donors.
- TheraSkin® (LifeNet Health) is a cryopreserved split-thickness human skin allograft composed of living fibroblasts and keratinocytes and an extracellular matrix in epidermal and dermal layers. TheraSkin® is derived from human skin allograft supplied by tissue banks compliant with the American Association of Tissue Banks and FDA guidelines. It is considered a minimally processed human cell, tissue, and cellular- and tissue-based product by the FDA.

Although frequently used by surgeons for breast reconstruction, the FDA does not consider this homologous use and has not cleared or approved any surgical mesh device (synthetic, animal collagen-derived, or human collagen-derived) for use in breast surgery. The indication of surgical mesh for general use in "Plastic and reconstructive surgery" was cleared by the FDA before surgical mesh was described for breast reconstruction in 2005. The FDA states that the specific use of surgical mesh in breast procedures represents a new intended use and that a substantial equivalence evaluation via 510(k) review is not appropriate and a pre-market approval evaluation is required. (3)

In March 2019, the FDA held an Advisory Committee meeting on breast implants, at which time the panel noted that while there is data about ADM for breast reconstruction, the FDA has not yet determined the safety and effectiveness of ADM use for breast reconstruction. The panel recommended that patients are informed and also recommended studies to assess the benefit and risk of ADM use in breast reconstruction. (3)

In March 2021, FDA issued a Safety Communication to inform patients, caregivers, and health care providers that certain ADM products used in implant-based breast reconstruction may have a higher chance for complications or problems. An FDA analysis of patient-level data from real-world use of ADMs for implant-based breast reconstruction suggested that 2 ADMs—FlexHD and Allomax—may have a higher risk profile than others. (4)

In October 2021, an FDA advisory panel on general and plastic surgery voted against recommending FDA approval of the SurgiMend mesh for the specific indication of breast reconstruction. The advisory panel concluded that the benefits of using the device did not outweigh the risks. (4)

FDA product codes: FTM, OXF.

Xenogenic Products

Cytal™ (previously called MatriStem®) Wound Matrix, Multilayer Wound Matrix, Pelvic Floor Matrix, MicroMatrix, and Burn Matrix (all manufactured by ACell) are composed of porcine-derived urinary bladder matrix.

Helicoll (Encol) is an acellular collagen matrix derived from bovine dermis. In 2004, it was cleared for marketing by the FDA through the 510(k) process for topical wound management that includes partial and full-thickness wounds, pressure ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, trauma wounds (e.g., abrasions, lacerations, second-degree bums, skin tears), and surgical wounds including donor sites/grafts.

Keramatrix® (Keraplast Research) is an open-cell foam comprised of freeze-dried keratin that is derived from acellular animal protein. In 2009, it was cleared for marketing by the FDA through the 510(k) process under the name of Keratec. The wound dressings are indicated in the management of the following types of dry, light, and moderately exudating partial and full-thickness wounds: pressure (stage I-IV) and venous stasis ulcers, ulcers caused by mixed vascular etiologies, diabetic ulcers, donor sites, and grafts.

Kerecis™ Omega3 Wound (Kerecis) is an ADM derived from fish skin. It has a high content of omega 3 fatty acids and is intended for use in burn wounds, chronic wounds, and other applications.

Oasis™ Wound Matrix (Cook Biotech) is a collagen scaffold (extracellular matrix) derived from porcine small intestinal submucosa. In 2000, it was cleared for marketing by the FDA through the 510(k) process for the management of partial- and full-thickness wounds, including pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled undermined wounds, surgical wounds, trauma wounds, and draining wounds.

Permacol™ (Covidien) is xenogeneic and composed of cross-linked porcine dermal collagen. Cross-linking improves the tensile strength and long-term durability but decreases pliability.

PriMatrix™ (TEI Biosciences; a subsidiary of Integra Life Sciences) is a xenogeneic ADM processed from fetal bovine dermis. It was cleared for marketing by the FDA through the 510(k) process for partial- and full-thickness wounds; diabetic, pressure, and venous stasis ulcers; surgical wounds; and tunneling, draining, and traumatic wounds.

SurgiMend® PRS (TEI Biosciences; a subsidiary of Integra Life Sciences) is a xenogeneic ADM processed from fetal and neonatal bovine dermis.

Strattice™ Reconstructive Tissue Matrix (LifeCell Corp.) is a xenogenic non-cross-linked porcine-derived ADM. There are pliable and firm versions, which are stored at room temperature and come fully hydrated.

FDA Product codes: KGN, FTL, FTM.

Living Cell Therapy

Apligraf® (Organogenesis) is a bilayered living cell therapy composed of an epidermal layer of living human keratinocytes and a dermal layer of living human fibroblasts. Apligraf® is supplied as needed, in 1 size, with a shelf-life of 10 days. In 1998, it was approved by the FDA for use in conjunction with compression therapy for the treatment of noninfected, partial- and full-thickness skin ulcers due to venous insufficiency and in 2001 for full-thickness neuropathic diabetic lower-extremity ulcers nonresponsive to standard wound therapy.

Dermagraft® (Organogenesis) is composed of cryopreserved human-derived fibroblasts and collagen derived from newborn human foreskin and cultured on a bioabsorbable polyglactin mesh scaffold. Dermagraft has been approved by the FDA for repair of diabetic foot ulcers.

Epicel® (Genzyme Biosurgery) is an epithelial autograft composed of a patient's own keratinocytes cultured ex vivo and is FDA-approved under a humanitarian device exemption (HDE) for the treatment of deep dermal or full-thickness burns comprising a total body surface area of 30% or more. It may be used in conjunction with split-thickness autografts or alone in patients for whom split-thickness autografts may not be an option due to the severity and extent of their burns.

OrCel™ (Forticell Bioscience; formerly Composite Cultured Skin) is an absorbable allogeneic bilayered cellular matrix, made of bovine collagen, in which human dermal cells have been cultured. It was approved by the FDA premarket approval for healing donor site wounds in burn victims and under a HDE for use in patients with recessive dystrophic epidermolysis bullosa undergoing hand reconstruction surgery to close and heal wounds created by the surgery, including those at donor sites.

FDA product codes: FTM, PFC, OCE, ODS.

Autologous Cell Harvesting Device

Recell® (Avita Medical) was initially approved by the FDA in September 2018 under the PMA process (PMA BP170122*).* It is an autologous cell harvesting device indicated for the treatment of acute partial-thickness thermal burn wound when used by an appropriately-licensed healthcare professional at the patient's point of care to prepare autologous Regenerative Epidermal Suspension (RES). The initial indication was for use in patients 18 years of age and older in combination with meshed autografting. Subsequently, indications were expanded to include direct application to acute partial-thickness thermal burn wounds in patients 18 years of age and older or application in combination with meshed autografting for acute full-thickness thermal burn wounds in pediatric as well as adult

patients and full-thickness skin defects after traumatic avulsion (e.g., degloving) or surgical excision (e.g., necrotizing tissue infection) or resection (e.g., skin cancer) in patients 15 years of age and older.

FDA product code: QCZ.

Biosynthetic Products

Biobrane®/Biobrane-L (Smith & Nephew) is a biosynthetic wound dressing constructed of a silicon film with a nylon fabric partially imbedded into the film. The fabric creates a complex 3-dimensional structure of tri-filament thread, which chemically binds collagen. Blood/sera clot in the nylon matrix, adhering the dressing to the wound until epithelialization occurs.

Integra® Dermal Regeneration Template (also marketed as Omnigraft Dermal Regeneration Matrix; Integra LifeSciences) is a bovine, collagen/glycosaminoglycan dermal replacement covered by a silicone temporary epidermal substitute. It was approved by the FDA for use in the post-excisional treatment of life-threatening full-thickness or deep partial-thickness thermal injury where sufficient autograft is not available at the time of excision or not desirable because of the physiologic condition of the patient and for certain diabetic foot ulcers. Integra® Matrix Wound Dressing and Integra® Meshed Bilayer Wound Matrix are substantially equivalent skin substitutes and were cleared for marketing by the FDA through the 510(k) process for other indications. Integra® Bilayer Matrix Wound Dressing (Integra LifeSciences) is designed to be used in conjunction with negative pressure wound therapy. The meshed bilayer provides a flexible wound covering and allows drainage of wound exudate.

TransCyte™ (Advanced Tissue Sciences) consists of human dermal fibroblasts grown on nylon mesh, combined with a synthetic epidermal layer and was approved by the FDA in 1997. TransCyte is intended as a temporary covering over burns until autografting is possible. It can also be used as a temporary covering for some burn wounds that heal without autografting.

FDA product codes: FRO, MDD, MGR.

Synthetic Products

Suprathel® (PolyMedics Innovations) is a synthetic copolymer membrane fabricated from a tripolymer of polylactide, trimethylene carbonate, and s-caprolactone. It is used to provide temporary coverage of superficial dermal burns and wounds. Suprathel® is covered with gauze and a dressing that is left in place until the wound has healed.

Nerve Wraps

Nerve wraps can be used for peripheral nerve repair. They are often made from biocompatible materials like collagen, designed to encase injured peripheral nerves. It provides a barrier between the nerve and surrounding tissue, minimizing scarring and

promoting a conducive environment for nerve healing. Their application is ideal for cases where the nerve is intact but needs protection from scarring or compression.

AxoGuard® nerve connector (Axogen, Inc) is an implant derived from small intestine submucosa designed to protect injured and compressed nerves. Other FDA 510K approved nerve wraps include: Flexibile Collagen Nerve Cuff (Collagen Matrix, Inc), Mochida Nerve Cuff (Mochida Pharmaceutical Co.), NervAlign Nerve Cuff (Renerve, Ltd), Nerve tape (BioCircuit Technologies, Inc), Neurawrap (Integra LifeSciences, Corp), NeuroMend (Stryker Orthopedics), NeuroShield (Monarch bioimplants, GmBH), Reinforce flexible Collagen Nerve Cuff (Collagen Matrix, Inc), and Versawrap nerve protector (Alafair Biosciences, Inc).

FDA product code: JXI.

AMNIOTIC MEMBRANE PRODUCTS

Several commercially available forms of human amniotic membrane and amniotic fluid can be administered by patches, topical application or injection. Amniotic membrane and amniotic fluid are being evaluated for the treatment of a variety of conditions, including chronic full-thickness diabetic lower-extremity ulcers, venous ulcers, knee osteoarthritis, plantar fasciitis and ophthalmic conditions.

Human Amniotic Membrane

Human amniotic membrane (HAM) consists of two conjoined layers, the amnion and chorion, and forms the innermost lining of the amniotic sac or placenta. When prepared for use as an allograft, the membrane is harvested immediately after birth, cleaned, sterilized, and either cryopreserved or dehydrated. Many products available using amnion, chorion, amniotic fluid, and umbilical cord are being studied for the treatment of a variety of conditions, including chronic full-thickness diabetic lower-extremity ulcers, venous ulcers, knee osteoarthritis, plantar fasciitis, and ophthalmic conditions. The products are formulated either as patches, which can be applied as wound covers, or as suspensions or particulates, or connective tissue extractions, which can be injected or applied topically.

Fresh amniotic membrane contains collagen, fibronectin, and hyaluronic acid, along with a combination of growth factors, cytokines, and anti-inflammatory proteins such as interleukin-1 receptor antagonist. (5) There is evidence that the tissue has anti-inflammatory, antifibroblastic, and antimicrobial properties. HAM is considered nonimmunogenic and has not been observed to cause a substantial immune response. It is believed that these properties are retained in cryopreserved HAM and HAM products, resulting in a readily available tissue with regenerative potential. In support, one HAM product has been shown to elute growth factors into saline and stimulate the migration of mesenchymal stem cells, both in vitro and in vivo. (6)

Use of a HAM graft, which is fixated by sutures, is an established treatment for disorders of the corneal surface, including neurotrophic keratitis, corneal ulcers and melts, following

pterygium repair, Stevens-Johnson syndrome, and persistent epithelial defects. Amniotic membrane products that are inserted like a contact lens have more recently been investigated for the treatment of corneal and ocular surface disorders. Amniotic membrane patches are also being evaluated for the treatment of various other conditions, including skin wounds, burns, leg ulcers, and prevention of tissue adhesion in surgical procedures. (5) Additional indications studied in preclinical models include tendonitis, tendon repair, and nerve repair. The availability of HAM opens the possibility of regenerative medicine for an array of conditions.

Amniotic Fluid

Amniotic fluid surrounds the fetus during pregnancy and provides protection and nourishment. In the second half of gestation, most of the fluid is a result of micturition and secretion from the respiratory tract and gastrointestinal tract of the fetus, along with urea. (5) The fluid contains proteins, carbohydrates, peptides, fats, amino acids, enzymes, hormones, pigments, and fetal cells. Use of human and bovine amniotic fluid for orthopedic conditions was first reported in 1927. (7) Amniotic fluid has been compared with synovial fluid, containing hyaluronan, lubricant, cholesterol, and cytokines. Injection of amniotic fluid or amniotic fluid-derived cells is currently being evaluated for the treatment of osteoarthritis and plantar fasciitis.

Amniotic membrane and amniotic fluid are also being investigated as sources of pluripotent stem cells. (5) Pluripotent stem cells can be cultured and are capable of differentiation toward any cell type.

This policy does not address the use of stem cells in orthopedic applications.

Regulatory Status

In 2024, the U.S. Food and Drug Administration issued a public safety notification on amniotic fluid eyedrops. (8) The notice was to inform the public and health care practitioners "that manufacturers are marketing and distributing amniotic fluid eyedrops to treat, mitigate, or cure diseases or conditions such as dry eye disease without the required premarket review and approval, raising potential significant safety concerns." A list of related warning letters issued by the FDA can be found on the FDA website's Warning Letters page using the search term “amniotic fluid.” (9)

On December 19, 2024, the FDA issued a warning letter to Integra LifeSciences Corporation stating: "FDA investigators and a microbiologist determined that the above firms manufacture a variety of neurological and neurosurgical devices, including but not limited to, cranial perforators, disposable cottonoid patties and strips as well as collagen based medical devices, that are used for wound care, soft tissue repair and reconstruction surgery. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices because they are intended for use in the

diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body." (10)

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation, Title 21, parts 1270 and 1271. In 2017, the FDA published clarification of what is considered minimal manipulation and homologous use for human cells, tissues, and cellular and tissue-based products (HCT/Ps). (2)

HCT/Ps are defined as human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. If an HCT/P does not meet the criteria below and does not qualify for any of the stated exceptions, the HCT/P will be regulated as a drug, device, and/or biological product and applicable regulations and premarket review will be required.

An HCT/P is regulated solely under section 361 of the PHS Act and 21 CFR Part 1271 if it meets all of the following criteria:

1. "The HCT/P is minimally manipulated;
2. The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;
3. The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P; and
4. Either:
    i. The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
    ii. The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and:
        a. Is for autologous use;
        b. Is for allogeneic use in a first-degree or second-degree blood relative; or
        c. Is for reproductive use."

The guidance provides the following specific examples of homologous and non-homologous use for amniotic membrane:

a. "Amniotic membrane is used for bone tissue replacement to support bone regeneration following surgery to repair or replace bone defects. This is not a homologous use because bone regeneration is not a basic function of amniotic membrane.
b. An amniotic membrane product is used for wound healing and/or to reduce scarring and inflammation. This is not homologous use because wound healing and reduction of scarring and inflammation are not basic functions of amniotic membrane.

c. An amniotic membrane product is applied to the surface of the eye to cover or offer protection from the surrounding environment in ocular repair and reconstruction procedures. This is homologous use because serving as a covering and offering protection from the surrounding environment are basic functions of amniotic membrane."

The FDA noted the intention to exercise enforcement discretion for the next 36 months after publication of the guidance.

In 2003, Prokera was cleared for marketing by the FDA through the 510(k) process for the ophthalmic conformer that incorporates amniotic membrane (K032104; product code: NQB). The FDA determined that this device was substantially equivalent to the Symblepharon Ring. The Prokera device is intended "for use in eyes in which the ocular surface cells have been damaged, or underlying stroma is inflamed and scarred." (11) The development of Prokera, a commercially available product, was supported in part by the National Institute of Health and the National Eye Institute.

Rationale

This policy is based on a review of information found on the U.S. Food and Drug Administration website regarding the use of skin substitutes and amniotic products, and applicable specialty society guidelines.

National Institute for Health and Care Excellence
In 2023, NICE updated its guidance on the prevention and management of diabetic foot problems. (12) The Institute recommended that clinicians "consider dermal or skin substitutes as an adjunct to standard care when treating diabetic foot ulcers, only when healing has not progressed and on the advice of the multidisciplinary foot care service."

In 2019, NICE published guidance on the ReCell system for treating skin loss, scarring, and depigmentation after burn injury. (13) The guidance recommended that additional research was needed to address the uncertainties regarding the potential benefits of ReCell.

Society for Vascular Surgery et al.
In 2016, the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine made the following recommendation: "For DFUs [diabetic foot ulcers] that fail to demonstrate improvement (>50% wound area reduction) after a minimum of 4 weeks of standard wound therapy, we recommend adjunctive wound therapy options. These include negative pressure therapy, biologics (platelet-derived growth factor [PDGF], living cellular therapy, extracellular matrix products, amnionic membrane products), and hyperbaric oxygen therapy. Choice of

adjuvant therapy is based on clinical findings, availability of therapy, and cost-effectiveness; there is no recommendation on ordering of therapy choice." (14)

Wound Healing Society

In 2016, the Wound Healing Society updated their guidelines on diabetic foot ulcer treatment. (15) The Society concluded that there was level 1 evidence that cellular and acellular skin equivalents improve diabetic foot ulcer healing, noting that, "healthy living skin cells assist in healing DFUs [diabetic foot ulcers] by releasing therapeutic amounts of growth factors, cytokines, and other proteins that stimulate the wound bed." References from 2 randomized controlled trials on amniotic membrane were included with references on living and acellular bioengineered skin substitutes.

American Diabetes Association

The 2025 American Diabetes Association Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes includes the ADA's current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Recommendations for foot care pertinent to this medical policy include:

"12.32. For chronic diabetic foot ulcers that have failed to heal with optimal standard care alone, adjunctive treatment with randomized controlled trial-proven advanced agents should be considered. Considerations might include negative-pressure wound therapy, placental membranes, bioengineered skin substitutes, several acellular matrices, autologous fibrin and leukocyte platelet patches, and topical oxygen therapy." (Level of Evidence, A) (16)

Tear Film and Ocular Surface Society

In 2017, the Tear Film and Ocular Surface Society published the Dry Eye Workshop II (DEWS) management and therapy report. (17) The report evaluated the evidence on treatments for dry eye and provided the following treatment algorithm for dry eye disease management:

Step 1:

- Education regarding the condition, its management, treatment, and prognosis.
- Modification of local environment.
- Education regarding potential dietary modifications (including oral essential fatty acid supplementation).
- Identification and potential modification/elimination of offending systemic and topical medications.
- Ocular lubricants of various types (if meibomian gland dysfunction is present, then consider lipid containing supplements).
- Lid hygiene and warm compresses of various types.

Step 2:
If above options are inadequate consider:
- Non-preserved ocular lubricants to minimize preservative-induced toxicity.
- Tea tree oil treatment for Demodex (if present).
- Tear conservation.
- Punctal occlusion.
- Moisture chamber spectacles/goggles.
- Overnight treatments (such as ointment or moisture chamber devices).
- In-office, physical heating and expression of the meibomian glands.
- In-office intense pulsed light therapy for meibomian gland dysfunction.
- Prescription drugs to manage dry eye disease.
- Topical antibiotic or antibiotic/steroid combination applied to the lid margins for anterior blepharitis (if present).
- Topical corticosteroid (limited-duration).
- Topical secretagogues.
- Topical non-glucocorticoid immunomodulatory drugs (such as cyclosporine).
- Topical lymphocyte function-associated antigen-1 (LFA-1) antagonist drugs (such as lifitegrast).
- Oral macrolide or tetracycline antibiotics.

Step 3:
If above options are inadequate consider:
- Oral secretagogues.
- Autologous/allogeneic serum eye drops.
- Therapeutic contact lens options.
- Soft bandage lenses.
- Rigid scleral lenses.

Step 4:
If above options are inadequate consider:
- Topical corticosteroid for longer duration.
- Amniotic membrane grafts.
- Surgical punctal occlusion.
- Other surgical approaches (e.g., tarsorrhaphy, salivary gland transplantation).

Medicare National Coverage
The Centers for Medicare & Medicaid Services issued the following national coverage determination: porcine (pig) skin dressings are covered, if reasonable and necessary for the individual patient as an occlusive dressing for burns, donor sites of a homograft, and decubiti and other ulcers. (19)

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description for defined coverage vs. non-coverage, benefit exclusions and benefit limitations such as dollar or duration caps.

CPT Codes	15011, 15012, 15013, 15014, 15015, 15016, 15017, 15018, 15271, 15272, 15273, 15274, 15275, 15276, 15277, 15278, 15777, 65778, 65779, 65780
HCPCS Codes	A2001, A2002, A2003, A2004, A2005, A2006, A2007, A2008, A2009, A2010, A2011, A2012, A2013, A2014, A2015, A2016, A2017, A2018, A2019, A2020, A2021, A2022, A2023, A2024, A2025, A2026, A2027, A2028, A2029, A2030, A2031, A2032, A2033, A2034, A2035, A4100, A6460, A6461, C1832, C5271, C5272, C5273, C5274, C5275, C5276, C5277, C5278, C8002, C9354, C9356, C9358, C9360, C9363, C9364, Q4100, Q4101, Q4102, Q4103, Q4104, Q4105, Q4106, Q4107, Q4108, Q4110, Q4111, Q4112, Q4113, Q4114, Q4115, Q4116, Q4117, Q4118, Q4121, Q4122, Q4123, Q4124, Q4125, Q4126, Q4127, Q4128, Q4130, Q4132, Q4133, Q4134, Q4135, Q4136, Q4137, Q4138, Q4139, Q4140, Q4141, Q4142, Q4143, Q4145, Q4146, Q4147, Q4148, Q4149, Q4150, Q4151, Q4152, Q4153, Q4154, Q4155, Q4156, Q4157, Q4158,Q4159, Q4160, Q4161, Q4162, Q4163, Q4161, Q4164, Q4165, Q4166, Q4167, Q4168, Q4169, Q4170, Q4171, Q4173, Q4174, Q4175, Q4176, Q4177, Q4178, Q4179, Q4180, Q4181, Q4182, Q4183, Q4184, Q4185, Q4186, Q4187, Q4188, Q4189, Q4190, Q4191, Q4192, Q4193 Q4194, Q4195, Q4196, Q4197, Q4198, Q4199, Q4200, Q4201, Q4202, Q4203, Q4204, Q4205, Q4206, Q4208, Q4209, Q4211, Q4212, Q4213, Q4214, Q4215, Q4216, Q4217, Q4218, Q4219, Q4220, Q4221, Q4222, Q4224, Q4225, Q4226, Q4227, Q4229, Q4230, Q4231, Q4232, Q4233, Q4234, Q4235, Q4236, Q4237, Q4238, Q4239, Q4240, Q4241, Q4242, Q4244, Q4245, Q4246, Q4247, Q4248, Q4249, Q4250, Q4251, Q4252, Q4253, Q4254, Q4255, Q4256, Q4257, Q4258, Q4259, Q4260, Q4261, Q4262, Q4263, Q4264, Q4265, Q4266, Q4267, Q4268, Q4269, Q4270, Q4271, Q4272, Q4273, Q4274, Q4275, Q4276, Q4278, Q4279, Q4280, Q4281, Q4282,

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Centers for Medicare and Medicaid Services

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at cms.hhs.gov.

Policy History/Revision	
Date	**Description of Change**
5/7/2026	New medical document. Bioengineered skin and soft tissue substitutes, including amniotic membrane products specifically addressed in Coverage, may be considered medically necessary when criteria in Coverage are met. Products not listed as medically necessary, or indications not addressed in Coverage as medically necessary, are considered experimental, investigational and/or unproven.