MEDICAL POLICY	Skin and Tissue Substitutes
Effective Date: 7/1/2022  7/1/2022 Medical Officer Date	Medical Policy Number: 16 Technology Assessment Committee Approved Date: 3/09; 10/14; 1/16 Medical Policy Committee Approved Date: 4/02; 4/03; 9/04; 11/05; 5/07; 1/09; 11/09; 12/10; 4/2011; 3/12; 1/13; 1/14; 3/14; 9/14; 11/15; 12/15;12/16; 3/18; 10/18; 12/18; 8/19; 9/19; 12/19; 7/2020; 10/2020; 12/2020; 6/2021; 9/2021; 11/2022; 12/2022; 3/2022; 6/2022

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:

All lines of business

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

DOCUMENTATION REQUIREMENTS

Medical records documentation must clearly support the medical necessity of bioengineered skin and tissue substitutes. This would include the following:

- Characteristics of the wound/ulcer
- Wound/ulcer measurement
- Evidence of prior ineffective standard care, including the duration of this treatment
- The presence of qualifying or disqualifying conditions (i.e., HbA1C levels, ankle-brachial index [ABI])

POLICY CRITERIA

Medically Necessary Skin and Tissue Substitutes by Indication

Indication	Products	Product HCPCS Codes	Medical Necessity Criteria
Breast reconstruction	AlloDerm®	Q4116	I. These products may be considered **medically necessary and covered** when used for a medically necessary breast reconstruction surgery. (See policies Cosmetic and Reconstructive Surgery, SUR193, or Breast Reconstruction, SUR162, for more information)
	Dermacell™	Q4122	
	FlexHD® Accellular Hydrated Dermis	Q4128	

Indication	Products	Product HCPCS Codes	Medical Necessity Criteria
Burn wound	Biobrane®/ Biobrane®-L	Q4100 C9399	II. This product may be considered **medically necessary and covered** as a treatment of burn wounds when **all** of the following (A.-B.) criteria are met: A. The skin substitute is used as a temporary covering of a partial-thickness burn (See description section for definition); **and** B. Applied to freshly debrided or excised wounds, or meshed autografts containing less than 105 bacteria/g tissue.
	Epicel	Q4100 C9399	III. This product may be considered **medically necessary and covered** when used in accordance with the U.S. Food and Drug Administration Humanitarian Device Exemption for adult and pediatric patients who have deep dermal or full thickness burns comprising a total body surface area greater than or equal to 30%.
	– Integra® Dermal Regeneration Template – Integra® Omnigraft Dermal	Q4104 Q4105 C9363	IV. These products may be considered **medically necessary and covered** as a treatment of burn wounds when **all** of the following (A.-B.) criteria are met: A. To be used for the post-excisional treatment of life-threatening full

	Regeneration Matrix – Integra® Bilayer Matrix Wound Dressing – Integra® Meshed Bilayer Wound Matrix		thickness or deep partial-thickness thermal injuries (See description section for definition); **and** B. Sufficient autograft is not available at the time of excision or not desirable due to the physiological condition of the patient.
	TransCyte®	Q4182	V. This product may be considered **medically necessary and covered** when used as a temporary wound covering for surgically excised full-thickness and deep partial-thickness thermal burn wounds in patients who require such a covering prior to autograft placement.

Indication	Products	Product HCPCS Codes	Medical Necessity Criteria
Diabetic foot ulcer	Apligraf®	Q4101	VI. These products may be considered **medically necessary and covered** for the treatment of diabetic foot ulcers when **all** of the following (A.-H.) criteria are met: A. The skin substitute is used in conjunction with standard diabetic ulcer care; **and** B. The ulcer extends through the dermis but without tendon, muscle, joint, or bone exposure; **and** C. The ulcer is at least 1cm^2 but no more than 25cm^2 ; **and** D. The ulcer is free of infection; **and** E. The patients A1c (HbA1C) level is less than 12%; **and** F. Failure of at least 4 weeks of standard diabetic foot ulcer therapy (e.g., surgical debridement, dressing changes); **and** G. The foot to be treated has adequate blood supply as defined by **at least one** of the following (1.-2.) criteria:
	Allopatch	Q4128	
	AmnioBand Membrane	Q4151	
	Dermagraft®	Q4106	
	EpiFix® Amniotic Membrane	Q4186	
	Grafix® Core/Grafix® Prime/ Grafix® PL Prime	Q4132 Q4133	
	GraftJacket® Regenerative Tissue Matrix	Q4107	
	– Integra® Dermal Regeneration Template – Integra™ Omnigraft Dermal	Q4105	

	Regeneration Matrix		1. Ankle-brachial index (ABI) of ≥ 0.70; **and/or** 2. The presence of a palpable pedal pulse; **and** H. The skin substitute is limited to no more than 5 applications, at a minimum of 1 week between applications, over the course of 12 weeks. (Except GraftJacket® Regenerative Tissue Matrix [Q4107] which is limited to only 1 initial application.)
	Oasis® Wound Matrix/Oasis® Ultra Tri-Layer Matrix	Q4102 Q4124	
	TheraSkin®	Q4121	

Indication	Products	Product HCPCS Codes	Medical Necessity Criteria
Venous stasis ulcer	Apligraf®	Q4101	VII. These products may be considered **medically necessary and covered** for the treatment of venous stasis ulcers when **all** of the following (A.-G.) criteria are met: A. The skin substitute is used in conjunction with standard venous stasis ulcer care; **and** B. The ulcer extends through the dermis <u>but without</u> tendon, muscle, joint, or bone exposure; **and** C. The ulcer is at least 2cm^2 but no more than 20cm^2; **and** D. The ulcer is free of infection; **and** E. Failure of at least 4 weeks of standard venous stasis ulcer therapy (e.g., compression therapy); **and** F. The leg to be treated has adequate blood supply as defined by **at least one** of the following (1.-2.) criteria: 1. Ankle-brachial index (ABI) of ≥ 0.70; **and/or** 2. The presence of a palpable pedal pulse; **and** G. The skin substitute is limited to no more than 5 applications, at a minimum of 1 week between applications, over the course of 12 weeks.
	EpiFix® Amniotic Membrane	Q4186	
	Oasis® Wound Matrix	Q4102 Q4124	
	TheraSkin®	Q4121	

Traumatic Wounds

VIII. The use of the following skin and tissue substitute products may be considered **medically necessary and covered** for the treatment of traumatic wounds when autografting is not possible:

- Biobrane®/Biobrane®-L (Q4100, C9399)
- Epicel (Q4100, C9399)
- Integra Products (Q4104, Q4105, C9363):
  - Integra® Dermal Regeneration Template
  - Integra® Omnigraft Dermal Regeneration Matrix
  - Integra® Bilayer Matrix Wound Dressing
  - Integra® Meshed Bilayer Wound Matrix
- TransCyte® (Q4182)

Skin and Tissue Substitutes as a Component of Genital Surgery

IX. The use of a skin substitute as a component of a genital surgery may be **medically necessary and covered** for surgical wound coverage prior to skin grafting. Member must meet medical necessity criteria for gender affirming surgery (please see medical policy, Gender Affirming Surgical Interventions).

Skin Substitutes for prevention of Frey's Syndrome after Parotidectomy

X. The use of a skin substitute may be **medically necessary and covered** to prevent Frey's Syndrome after parotidectomy.

Repeat Treatment

XI. Repeat treatment (i.e. any additional applications after the initial 12-week treatment period outlined in criteria VI. And VII. above) of diabetic foot ulcers or venous stasis ulcers using skin and tissue substitutes may be considered **medically necessary and covered** when the ulcer continues to improve on the basis of wound documentation. Wound documentation must include **all** of the following (A.-C.):

A. The number and position of ulcers; **and**
B. Wound measurements for each ulcer, including all of the following (1.-3.):
   1. Length; **and**
   2. Width; **and**
   3. Depth; **and**
C. Descriptions of wound edge parameters, wound base quality, drainage, and infection.

Non-Covered Indications

XII. The use of skin and tissue substitutes is considered **investigational and is not covered** when the medically necessary indication and/or product and/or criteria above are not met, including, but not limited to:

- AlloDerm for complex nasal reconstruction
- AlloDerm for tympanic membrane perforation
- Hernia repair
- Rotator cuff tear repair
- Repair of non-traumatic surgical excision of skin/soft tissue mass/lesion (e.g., Mohs surgery for squamous or basal cell carcinomas)

Investigational Skin Substitutes

XIII. Skin and tissue substitute products not listed in the tables above are considered **investigational and are not covered**, including, but not limited to, the following:

Products	Indication	Product HCPCS Codes
Affinity	Wound care	Q4159
Allogen	Wound care	Q4212
Alloskin™ AC	Wound care	Q4115 Q4141
Alloskin™ RT	Wound care	Q4123
Allowrap™	Wound care	Q4150
Altiply	Soft tissue repair	Q4235
AmnioAMP-MP	Wound care	Q4250
AmnioArmor	Wound care	Q4188
AmnioBand® Particulate	Wound care	Q4168
Amniobind	Wound care	Q4225
Amnion Bio/Axobiomembrane	Wound care	Q4211
Amniocore	Wound care	Q4227
Amniocyte Plus	Wound care	Q4242
AmnioEXCEL™/BiodExcel™	Wound care Soft tissue repair	Q4137
AmnioFix®	Tendon/nerve repair	Q4100 C9399
AmnioMatrix®/BioMatrix®	Wound care Soft tissue repair	Q4139
Amnio-maxx/Amnio-maxx Lite	Wound care	Q4239
AmnioPro-A	Wound care Soft tissue repair	Q4100
Amniorepair	Soft tissue repair	Q4235
Amniotext	Wound care	Q4245
Amniotext Patch	Wound care	Q4247

Amnio Wound	Wound care	Q4181
Amniowrap2	Wound care	Q4221
Amniply	Wound care	Q4249
Apis	Wound care	A2010
Architect™/Architect™ PX/Architect™ FX/Architect™ Extracellular Matrix	Wound care	Q4147
Artacent™ AC Powder	Surgical barrier	Q4189
Artacent™ AC Graft	Wound care Soft tissue repair	Q4190
Artracent™ Cord	Would care	Q4216
ArthroFlex™	Shoulder reconstruction Achilles tend repair	Q4125
Ascent	Wound care	Q4213
Axolotl Graft/Axolotl Dualgraft	Wound care	Q4210
Axolotl Ambient/Axolotl Cryo	Wound care	Q4215
BellaCell HD	Wound care	Q4220
Bio-conneKt™ Wound Matrix	Wound care	Q4161
BioDesign® Otologic Repair Graft	Soft tissue repair	-
BioDfactor™	Wound care Soft tissue repair	Q4100 Q9399
BioDfence™	Surgical barrier Tendon repair	Q4140
BioDfence™ Dryflex	Surgical barrier Tendon repair	Q4138
Bionext Patch	Wound care	Q4228
BioVance®	Wound care	Q4154
BioWound/Bio Wound Plus/BioWound Xplus	Wound care	Q4217
Carepatch	Wound care	Q4236
Cellesta™ Amniotic Membrane	Surgical barrier Wound care	Q4184
Cellesta™ Cord	Wound care	Q4214
Cellesta™ Flowable Amnion	Wound care	Q4185
Clarix® Flo	Integumental tissue repair	Q4155
Cogenex Amniotic Membrane	Wound care	Q4229
Cogenex Flowable Amnion	Tissue repair	Q4230
Coll-e-Derm	Tissue repair	Q4193
Conexa™	Tendon repair	Q4100
Corecyte	Wound care	Q4240
Coretext	Tissue repair	Q4246
CorMatrix	Cardiac/vascular tissue repair	Q4100 C9399
Corplex	Wound care	Q4231

		Q4232
Cryo-cord	Wound care	Q4237
Cygnus™	Wound care	Q4170 Q4199
Cymetra™ *Note: Medically necessary and covered for the treatment of vocal cord paralysis.*	Integumental tissue repair	Q4112
Cytal®	Wound care	Q4166
Dermacell™	Tissue repair	Q4122
Dermacyte Amniotic Membrane	Wound care	Q4248
Derma-gide	Wound care	Q4203
DermaMatrix Acellular Dermis	Tissue repair	Q4100
Derm-maxx	Wound care	Q4238
DermaPure™	Wound care	Q4152
DermaSpan™	Wound covering Tendon repair	Q4126
Dermavest	Wound care	Q4153
Durepair Regeneration Matrix®	Dural repair	Q4100 C9399
Endoform Dermal Template™	Wound care	Q4100 C9399
ENDURAGen	Soft Tissue Repair	C1763
Enverse	Wound Care	Q4258
Epifix® Injectable	Wound care	Q4145
EpiCord™	Wound care	Q4187
Excellagen®	Wound care	Q4149
E-Z Derm™	Wound care	Q4136
FloGraft™	Tendonitis Soft tissue trauma	Q4100 Q9399
Floweramnio™ Flo	Wound care	Q4177
Floweramnio™ Patch	Wound care	Q4178
Flowerderm™	Wound care	Q4179
Fluid Flow™	Soft Tissue Repair	Q4206
GalaFLEX Scaffold	Soft Tissue Repair	C1781
GammaGraft	Wound care	Q4111
Genesis Amniotic Membrane	Tissue repair	Q4198
Graftjacket® Xpress	Wound care	Q4113
Helicoll™	Wound care	Q4164
hMatrix®	Integumental tissue repair	Q4134
Human Health Factor 10 Patch	Wound Care	Q4224
Hyalomatrix®	Wound care	Q4117
Innovamatrix	Wound care	A2001, A2013
Integra™ Matrix	Wound care	Q4108
Integra™ Flowable Wound Matrix	Wound care	Q4114

Note: Medically necessary and covered for the treatment of vocal cord paralysis.	Tissue repair	
Interfyl™	Integuental tissue repair	Q4171
Keramatrix®	Wound care	Q4165
Kerecis Omega3	Wound care	Q4158
Keroxx	Wound care	Q4202
MariStem® Micromatrix	Wound care	Q4118
Matrion™	Wound care	Q4201
Matrix HD™	Wound care Tendon repair	Q4128
Mediskin™	Wound care	Q4135
MemoDerm™	Wound care Tendon repair	Q4126
Microlyte Matrix	Wound care	A2005
Mirragen	Wound care	A2002
Miroderm™	Wound care	Q4175
MLG-Complete	Wound care	Q4256
MyOwn Skin	Wound care	Q4226
Neopatch™	Wound care	Q4176
NEOX® 100 Quick-Peel Wound Matrix	Wound care	Q4156
NEOX® 1k Wound Matrix	Wound care	Q4148
NEOX® FLO	Wound care	Q4155
Novachor	Wound care	Q4194
Novafix	Wound care	Q4208 Q4254
NovoSorb	Wound care	A2006
NuCel™	Tendon repair	Q4100 C9399
Nudyn	Wound care	Q4233
NuShield™	Tendon repair	Q4160
Oasis® Burn Matrix	Burn wounds	Q4103
PalinGen®/Promatrx®	Soft tissue repair	Q4174
PalinGen® Xplus	Soft tissue repair	Q4173
Permacol™	Soft tissue repair	C9364
PriMatrix™	Wound care	Q4110
Procenta	Wound care	Q4244
Progenamatrix	Wound care	Q4222
Protext	Wound care	Q4246
PuraPly™/PuraPly™ AM	Wound care	Q4195 Q4196 Q4197
ReCell	Burn wound care	C1832
Reguard	Soft tissue repair	Q4255
Release	Wound care	Q4257

Repriza®	Reconstructive surgery Abdominal wall repair	Q4143
Restorigin™ Membrane	Wound care Injury healing	Q4191
Restorigin™ Fluid	Wound care Injury healing	Q4192
Restrata	Wound care	A2007
Revita®	Wound care	Q4180
Revitalon™	Wound care	Q4157
SkinTE™	Wound care Burns Surgical reconstruction	Q4200
Strattice™	Soft tissue repair	Q4130
Stravix	Wound Care	Q4133
Surederm	Surgical barrier	Q4220
Surgicord	Surgical barrier	Q4218
SURGIgraft™	Surgical barrier	Q4183
SURGIgraft™ Dual	Surgical barrier	Q4219
Surgraft	Surgical barrier	Q4209
Supra SDRM	Wound care	A2011
Suprathel	Wound care	A2012
Surfactor	Wound care	Q4233
Symphony	Wound care	A2009
Talymed™	Wound care	Q4127
TenoGlide®	Tendon repair	C9356
TenSIX™	Wound care Tendon repair	Q4146
Theragenesis	Wound care	A2008
TruSkin™	Wound care	Q4167
Vendaje	Wound care	Q4252
Veritas Collagen Matrix	Soft tissue repair	Q4100
VIM	Wound care	Q4251
WoundEx/Bioskin	Wound care	Q4163
WoundEx Flow/Bioskin Flow	Integumental tissue repair	Q4162
Woundfix/Woundfix Plus/Woundfix Xplus	Wound care	Q4217
Xcellerate	Wound care	Q4234
Xcellistem	Wound care	A2004
XCM Biologic Tissue Matrix	Soft tissue repair	Q4142
XWRAP®	Soft tissue repair	Q4204
Zenith Amniotic Membrane	Wound care	Q4253

Link to Policy Summary

BILLING GUIDELINES

Codes billed in association with the primary product code may also be denied if the product is not covered per the policy criteria above.

The following products are considered medically necessary and covered when billed for vocal cord paralysis treatment:

Products

- Q4112 (Cymetra)
- Q4114 (Integra flowable wound matrix)

Diagnosis codes

- J38.02 Paralysis of vocal cords and larynx, bilateral
- J38.00 Paralysis of vocal cords and larynx, unspecified
- J38.01 Paralysis of vocal cords and larynx, unilateral

CPT/HCPCS CODES

All Lines of Business	
Prior Authorization Required	
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	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof (List separately in addition to code for primary procedure)
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	Application of 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 (List separately in addition to code for primary procedure)
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	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; each additional 25 sq cm wound surface area, or part thereof (List separately in addition to code for primary procedure)
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	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; 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 (List separately in addition to code for primary procedure)
15777	Implantation of biologic implant (eg, acellular dermal matrix) for soft tissue reinforcement (ie, breast, trunk) (List separately in addition to code for primary procedure)
A4100	Skin substitute, FDA cleared as a device, not otherwise specified
C1849	Skin substitute, synthetic, resorbable, per square centimeter
C9356	Tendon, porous matrix of cross-linked collagen and glycosaminoglycan matrix (tenoglide tendon protector sheet), per square centimeter
C9363	Skin substitute, integra meshed bilayer wound matrix, per square centimeter
Q4101	Apligraf, per square centimeter
Q4102	Oasis wound matrix, per square centimeter
Q4104	Integra bilayer matrix wound dressing (bmwd), per square centimeter
Q4105	Integra dermal regeneration template (drt) or integra omnigraft dermal regeneration matrix, per square centimeter
Q4106	Dermagraft, per square centimeter
Q4107	Graftjacket, per square centimeter
Q4108	Integra matrix, per square centimeter
Q4116	Alloderm, per square centimeter
Q4121	Theraskin, per square centimeter
Q4122	Dermacell, per square centimeter
Q4124	Oasis ultra tri-layer wound matrix, per square centimeter
Q4128	Flex hd, allopatch hd, or matrix hd, per square centimeter
Q4132	Grafix core, per square centimeter
Q4133	Grafix prime , grafixpl prime, stravix and stravixpl, per square centimeter
Q4182	Transcyte, per square centimeter
Q4186	Epifix, per square centimeter
Q4205	Membrane graft or membrane wrap, per square centimeter
Q4151	Amnioband or guardian, per square centimeter
Prior Authorization Required (Medicare Only)	
Q4251	Vim, per square centimeter
Q4252	Vendaje, per square centimeter
Q4253	Zenith amniotic membrane, per square centimeter
Not Covered	
A2001	Innovamatrix ac, per square centimeter
A2002	Mirragen advanced wound matrix, per square centimeter
A2004	Xcellistem, 1mg
A2005	Microlyte matrix, per square centimeter
A2006	Novosorb synpath dermal matrix, per square centimeter
A2007	Restrata, per square centimeter
A2008	Theragenesis, per square centimeter

A2009	Symphony, per square centimeter
A2010	Apis, per square centimeter
A2011	Supra sdrm, per square centimeter
A2012	Suprathel, per square centimeter
A2013	Innovamatrix fs, per square centimeter
C1832	Autograft suspension, including cell processing and application, and all system components
C9364	Porcine implant, permacol, per square centimeter
Q4103	Oasis burn matrix, per square centimeter
Q4110	Primatrix, per square centimeter
Q4111	Gammagraft, per square centimeter
Q4113	Graftjacket xpress, injectable, 1 cc
Q4115	Alloskin, per square centimeter
Q4117	Hyalomatrix, per square centimeter
Q4118	Acell Matristem micromatrix, 1 mg
Q4123	Alloskin rt, per square centimeter
Q4125	Arthroflex, per square centimeter
Q4126	Memoderm, dermaspan, tranzgraft or integuply, per square centimeter
Q4127	Talymed, per square centimeter
Q4130	Strattice tm, per square centimeter
Q4134	Hmatrix, per square centimeter
Q4135	Mediskin, per square centimeter
Q4136	Ez-derm, per square centimeter
Q4137	Amnioexcel or biodexcel, per square centimeter
Q4138	Biodfence dryflex, per square centimeter
Q4139	Amniomatrix or biodmatrix, injectable, 1 cc
Q4140	Biodfence, per square centimeter
Q4141	Alloskin ac, per square centimeter
Q4142	Xcm biologic tissue matrix, per square centimeter
Q4143	Repriza, per square centimeter
Q4145	Epifix, injectable, 1 mg
Q4146	Tensix, per square centimeter
Q4147	Architect, architect px, or architect fx, extracellular matrix, per square centimeter
Q4148	Neox 1k, per square centimeter
Q4149	Excellagen, 0.1 cc
Q4150	Allowrap ds or dry, per square centimeter
Q4152	Dermapure, per square centimeter
Q4153	Dermavest and plurivest, per square centimeter
Q4154	Biovance, per square centimeter
Q4155	Neoxflo or clarixflo, 1 mg
Q4156	Neox 100 or clarix 100, per square centimeter
Q4157	Revitalon, per square centimeter
Q4158	Kerecis omega3, per square centimeter
Q4159	Affinity, per square centimeter
Q4160	Nushield, per square centimeter

Q4161	Bio-connekt wound matrix, per square centimeter
Q4162	Woundex flow, bioskin flow, 0.5 cc
Q4163	Woundex, bioskin, per square centimeter
Q4164	Helicoll, per square centimeter
Q4165	Keramatrix, per square centimeter
Q4166	Acell Cytal, per square centimeter
Q4167	Truskin, per square centimeter
Q4168	Amnioband, 1 mg
Q4169	Artacent wound, per square centimeter
Q4170	Cygnus, per square centimeter
Q4171	Interfyl, 1 mg
Q4173	Palingen or palingen xplus, per square centimeter
Q4174	Palingen or promatrx, 0.36 mg per 0.25 cc
Q4175	Miroderm, per square centimeter
Q4176	Neopatch, per square centimeter
Q4177	Floweramnioflo, 0.1 cc
Q4178	Floweramniopatch, per square centimeter
Q4179	Flowerderm, per square centimeter
Q4180	Revita, per square centimeter
Q4181	Amnio wound, per square centimeter
Q4183	Surgigraft, per square centimeter
Q4184	Cellesta, per square centimeter
Q4185	Cellesta flowable amnion (25 mg per cc); per 0.5 cc
Q4187	Epicord, per square centimeter
Q4188	Amnioarmor, per square centimeter
Q4189	Artacent ac, 1 mg
Q4190	Artacent ac, per square centimeter
Q4191	Restorigin, per square centimeter
Q4192	Restorigin, 1 cc
Q4193	Coll-e-derm, per square centimeter
Q4194	Novachor, per square centimeter
Q4195	Puraply, per square centimeter
Q4196	Puraply am, per square centimeter
Q4197	Puraply xt, per square centimeter
Q4198	Genesis amniotic membrane, per square centimeter
Q4199	Cygnus matrix, per square centimeter
Q4200	Skin te, per square centimeter
Q4201	Matrion, per square centimeter
Q4202	Keroxx (2.5g/cc), 1cc
Q4203	Derma-gide, per square centimeter
Q4204	Xwrap, per square centimeter
Q4206	Fluid flow or fluid GF, 1 cc
Q4208	Novafix, per square cenitmeter
Q4209	Surgraft, per square centimeter
Q4210	Axolotl graft or axolotl dualgraft, per square centimeter

Q4211	Amnion bio or Axobiomembrane, per square centimeter
Q4212	Allogen, per cc
Q4213	Ascent, 0.5 mg
Q4214	Cellesta cord, per square centimeter
Q4215	Axolotl ambient or axolotl cryo, 0.1 mg
Q4216	Artacent cord, per square centimeter
Q4217	Woundfix, BioWound, Woundfix Plus, BioWound Plus, Woundfix Xplus or BioWound Xplus, per square centimeter
Q4218	Surgicord, per square centimeter
Q4219	Surgigraft-dual, per square centimeter
Q4220	BellaCell HD or Surederm, per square centimeter
Q4221	Amniowrap2, per square centimeter
Q4222	Progenamatrix, per square centimeter
Q4224	Human health factor 10 amniotic patch (hhf10-p), per square centimeter
Q4225	Amniobind, per square centimeter
Q4226	MyOwn skin, includes harvesting and preparation procedures, per square centimeter
Q4227	Amniocore, per square centimeter
~~Q4228~~	~~TERMED 10/1/2021~~ ~~Bionextpatch, per square centimeter~~
Q4229	Cogenex amniotic membrane, per square centimeter
Q4230	Cogenex flowable amnion, per 0.5 cc
Q4231	Corplex p, per cc
Q4232	Corplex, per square centimeter
Q4233	Surfactor or nudyn, per 0.5 cc
Q4234	Xcellerate, per square centimeter
Q4235	Amniorepair or altiply, per square centimeter
~~Q4236~~	~~TERMED 10/1/2021~~ ~~Carepatch, per square centimeter~~
Q4237	Cryo-cord, per square centimeter
Q4238	Derm-maxx, per square centimeter
Q4239	Amnio-maxx or amnio-maxx lite, per square centimeter
Q4240	Corecyte, for topical use only, per 0.5 cc
Q4241	Polycyte, for topical use only, per 0.5 cc
Q4242	Amniocyte plus, per 0.5 cc
Q4244	Procenta, per 200 mg
Q4245	Amniotext, per cc
Q4246	Coretext or protext, per cc
Q4247	Amniotext patch, per square centimeter
Q4248	Dermacyte amniotic membrane allograft, per square centimeter
Q4249	Amniply, for topical use only, per square centimeter
Q4250	Amnioamp-mp, per square centimeter
Q4254	Novafix dl, per square centimeter
Q4255	Reguard, for topical use only, per square centimeter
Q4256	Mlg-complete, per square centimeter
Q4257	Relese, per square centimeter
Q4258	Enverse, per square centimeter

Not Covered (All Lines of Business Except Medicare)	
Q4251	Vim, per square centimeter
Q4252	Vendaje, per square centimeter
Q4253	Zenith amniotic membrane, per square centimeter
No Prior Authorization Required	
C1763	Connective tissue, non-human (includes synthetic)
C1781	Mesh (implantable)
Q4112	Cymetra, injectable, 1 cc
Q4114	Integra flowable wound matrix, injectable, 1 cc
Unlisted Codes All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then **prior-authorization is required.**	
C9399	Unclassified drugs or biologicals
Q4100	Skin substitute, not otherwise specified

DESCRIPTION

Burn Wounds

Burn injuries are classified by the depth of the wound.[1]

- First-degree burns involve only the epidermal layer (the outermost layer of skin). These burns heal completely within several days.
- Second-degree (partial-thickness) burns involve the epidermis and only part of the dermis (the thick layer of living tissue below the epidermis that forms the true skin, containing blood capillaries, nerve endings, sweat glands, hair follicles, and other structures). These burns may heal spontaneously, although healing usually requires reepithelialization from adjacent unburned skin or skin substitutes.
- Third-degree (full-thickness) burns involve all of the epidermal and dermal layers, with varying amounts of the sub-cutaneous layer. These burns cannot heal spontaneously and thus require excision and grafting.
- Fourth-degree burns involve deep structures such as tendon, muscle, and bone.

The successful treatment of burn wounds requires timely restoration of the skins protective function. “Conventionally, autologous split or full-thickness skin grafts have been recognized as the best definitive burn wound coverage, but it is constrained by the limited available sources, especially in major burns. Donor site morbidities in term of additional wounds and scarring are also of concern of the autograft application.”[2] Skin substitutes are necessary for both acute burn wounds and in patients requiring extensive reconstruction post-burn.

Diabetic Foot Ulcer

Chronic foot ulcers are common in hyperglycemia or undiagnosed poorly controlled diabetes due to damage of nerves (neuropathy), blood vessels (poor blood flow), and other body systems. "Approximately 85% of lower limb amputations among people with diabetes are preceded by a foot ulcer."[3] Diabetes-related foot ulcers are diagnosed by clinical evaluation and are classified based on the ulcer size, depth, and presence of an infection. The Wagner Ulcer Classification System is the most commonly used:

- Grade 0: No open lesions; may have deformity of cellulitis
- Grade 1: Superficial diabetic ulcer (partial- or full-thickness)
- Grade 2: Ulcer extension to ligament, tendon, joint capsule, or deep fascia without abscess or osteomyelitis
- Grade 3: Deep ulcer with abscess, osteomyelitis, or joint sepsis
- Grade 4: Gangrene localized to portion of forefoot or heel
- Grade 5: Extensive gangrenous involvement of the entire foot[3]

Treatment includes vascular and wound assessment, infection control, debridement, dressing changes, and offloading. "Offloading is the use of devices to reduce pressure on the wound, such as casts, removable cast walkers, and special shoes."[3] Amputation is required when diabetic foot ulcers do not respond to treatment or become infected.

Venous Stasis Ulcer

Venous stasis ulcers, also known as venous leg ulcers or varicose ulcers, "are partial or full-thickness defects of an area of the skin in the lower leg, usually between the knee and the ankle, due to valvular incompetence and venous reflux causing venous hypertension."[4] These ulcers are common in older patients, women, and patients with conditions causing chronic venous insufficiency (e.g., congestive heart failure) and/or venous damage (e.g., injection drug use). Longer wound duration and larger wound surface area are associated with poor ulcer healing. "Standard care for venous leg ulcers typically includes wound care and compression therapy. Wound care may include cleansing, debridement, infection control, dressing, and bandaging."[4] In patients whose venous stasis ulcers do not heal despite standard care, venous surgery to correct underlying venous pressure may be required.

Skin Substitutes

Skin substitutes, also known as bioengineered, tissue-engineered, or artificial skin, are intended to protect wounds and reconstruct defective, ulcerated tissue.[4] They function by physically covering wounds and providing structure to induce tissue regeneration and subsequent wound healing. They are generally classified into three main types:

1. Cellular—composed of living cells; or
2. Acellular—composed of synthetic materials or tissue from which living cells have been removed; or
3. A combination of cellular and acellular components.

Cellular skin substitutes are further categorized as follows:

- Autograft: A sample of the patient's own healthy skin is harvested and placed in the ulcer
- Allografts: Skin or tissue harvested from another human (e.g., cadaver)
- Xenograft: Skin or tissue is harvested from an animal with similar skin structure (e.g., pigs).

Although there are many different types of skin substitutes, they are all similarly used as an adjunct to standard wound care. Application of a skin substitute requires that no infection be present, the wound bed is properly prepared, and the wound has achieved hemostasis.

REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of skin substitutes for breast reconstruction, burn wounds, diabetic foot ulcers, or venous stasis ulcers. Below is a summary of the available evidence identified through September 2020.

Systematic Reviews

- In 2020 (updated 2021), Hayes conducted a comparative effectiveness review to evaluate cellular skin substitutes for chronic foot ulcers in adults with diabetes mellitus.[3] The evidence review identified 11 randomized controlled trials (RCT) and 2 observational retrospective database studies as eligible for inclusion. Sample sizes ranged from 23 to 180 participants in the RCTs, while the 2 observational studies assessed data from 20,482 and 13,193 patients. Outcome measures included incidence of complete ulcer closure, time to complete ulcer closure, incidence of amputation, and quality of life (QOL). Studies compared cellular skin substitutes to standard wound therapy, other cellular skin substitutes, acellular substitutes, and standard wound therapy plus acellular skin substitutes.

  Four studies reported on incidence of amputation. Two RCTs compared incidence of amputation posttreatment with 1 of 2 cellular substitutes, Hyalograft/Laserskin or Grafix, with standard wound care, and found no difference in incidence, with extremely low incidences in all groups. One retrospective study found Apligraf to significantly reduce the need for amputation compared to standard wound care (11.8% versus 16.3%, respectively). The other retrospective study compared 2 cellular skin substitutes and 2 acellular skin substitutes, and found differences in amputation incidence among the 4 treatments, ranging from 7% to 10.1%, but no pairwise analysis was performed.

  Eleven studies reported on the incidence of complete ulcer healing. In the 6 studies comparing cellular skin substitutes to standard wound care alone, incidence of complete healing ranged from 24% to 89% in the cellular substitutes group and 21% to 69% in standard care group. Five of the 6 studies reported a statistically greater incidence of complete ulcer healing in the cellular group, while one study found no difference. In 3 studies comparing different cellular skin substitutes, 1 RCT found a significantly higher incidence of complete healing the Apligraf group compared to TheraSkin. Another trial found early benefit of TheraSkin versus Dermagraft, but the significant difference diminished at follow up. The third study found no difference in healing between Grafix and Dermagraft. Four studies compare complete ulcer healing between cellular and acellular skin substitutes. One RCT found no significant difference between Dermagraft and MatriStem (acellular).

Another RCT found healing rates were higher in the Epifix (acellular) group compared to Apligraf. A third RCT found higher rates in the Amnioband group (acellular) compared with Apligraf group. The fourth study, a retrospective analysis, found higher healing rates with 2 acellular substitutes (MatriStem and Oasis) compared to Apligaf and Dermagraft.

Strengths of these studies included the randomized controlled design, large sample sizes, masked outcome assessors, and using computer programs to assess wound size and/or closure. Limitations are present in the short follow-up duration of some studies and inadequate number of patients to attain adequate power. Ultimately, Hayes concluded the following rating:

- C—"For use of cellular skin substitutes as an adjunct to standard wound care (SWC) to treat chronic, uninfected diabetes-associated foot ulcers (DFUs) that have not healed with SWC alone in adults with well-controlled blood glucose and adequate blood flow to the extremities"[3]

- In 2020, Hayes conducted a comparative effectiveness review of acellular skin substitutes for chronic foot ulcers in adults with diabetes mellitus.[5] The report included 13 RCTs and one observational retrospective study in their review. Hayes deemed 5 RCTS to be good quality, 5 of fair quality, and 3 of poor quality.

  Similar to the report on cellular substitutes, no significant differences in incidence of amputation were found comparing acellular skin substitutes and standard wound care, based on one RCT. Eleven studies compared incidence of complete ulcer healing after acellular skin substitutes versus standard wound care, with 10 finding acellular substitutes to have higher incidence (14.3% to 97% in acellular groups versus 0% to 91% in standard care groups) and one study that did not analyze results. In 4 studies that compared healing rates between acellular and cellular skin substitutes, one RCT found no difference (MatriStem [acellular] v Dermagraft), while two other RCTs and one retrospective study found acellular to have higher rates of complete healing. EpiFix (acellular) had significantly higher healing rates compared to Apligraf (cellular), Amnioband (acellular) had significantly higher rates compared to Apligraf, and MatriStem and Oasis acellular skin substitutes performed better than Apligraf and Dermagraft cellular substitutes.

  The overall quality of evidence among the studies was low to very low, due to limitations an individual studies, including follow up time, sample sizes, and risks of bias due to a lack of blinding. The available evidence suggests that acellular substitutes are an effective treatment for diabetic foot ulcer compared to standard wound care alone, but no definitive conclusions can be drawn on acellular skin substitutes benefit over cellular skin substitutes. More large, well-designed clinical trials are needed to evaluate comparative effectiveness and safety of acellular skin substitutes as adjuncts to standard wound care. Hayes concludes:

  - C—"For use of acellular skin substitutes as an adjunct to standard wound care (SWC) to treat chronic, uninfected diabetes-associated foot ulcers (DFUs) that have not healed with SWC alone in adults with well-controlled blood glucose and adequate blood flow to the extremities.

    This Rating reflects an overall low-quality body of evidence, which suggests that while acellular skin substitutes appear to be safe and their addition to SWC results in healing of more chronic DFUs than SWC alone in a shorter time frame, questions remain about their effect on the incidence of amputation and on ulcer recurrence due to the limited number of studies on these

outcomes. Use of acellular skin substitutes does not appear to present unique or serious safety concerns. Evidence directly comparing different acellular skin substitutes or comparing acellular with cellular skin substitutes is of very low quality, extremely limited, and insufficient to inform whether any 1 product or product type is superior."[5]

- In 2020, Hayes conducted a comparative effectiveness review to evaluate skin substitutes for chronic venous leg ulcers in adults.[4] The evidence review identified 8 studies from 10 publications on skin substitutes as adjunct to standard wound care for venous leg ulcers that met the inclusion criteria, 5 RCTs and 3 retrospective observational studies. Hayes categorized studies as follows: one good-quality RCT, 4 fair-quality RCTs, and 3 poor-quality retrospective studies. Primary outcomes measured include complete ulcer closure, time to complete ulcer closure, and time to healing.

  Eight studies (5 RCTs and 3 retrospective studies) reported on incidence of complete ulcer healing. One RCT found a significant increase in complete ulcer healing for application for Talymed once every other week relative to standard wound care (86.4% versus 45%). Two RCTs found that the Epifix group had a higher rate of complete healing compared to standard wound care alone. Another study found no significant difference between skin substitutes (Dermagraft) and standard wound care at 12 and 24 weeks. Two retrospective studies comparing cellular (Apligraf) to acellular (Oasis and Primatrix) skin substitutes found that Apligraf had significantly higher rates of complete healing compared to the acellular substitutes. Two studied compared Apligraf and Theraskin and found conflicting results. One RCT found no significant difference between the skin substitutes on incidence of complete ulcer healing, while a retrospective study found higher rates in the Apligraf group.
  Four studies reported on time to complete ulcer healing. One RCT found no difference in time comparing cellular skin substitutes to standard wound care. Two retrospective studies found quicker healing times in cellular versus acellular skin substitutes and one retrospective study found Apligraf to have quicker healing times than Theraskin. Through this analysis, Hayes concluded that skin substitutes appear to be safe and there is a low-quality body of evidence that suggests skin substitutes may improve healing of chronic venous leg ulcers when added to standard wound care. Hayes gave skin substitutes for venosus ulcer in adults a C rating.

- In 2016, Santema et al. conducted a Cochrane systematic review and meta-analysis of skin substitutes in the treatment of diabetic foot ulcers.[6] Following the Cochrane Collaboration methodology, independent reviewers systematically identified relevant literature, assessed quality and extracted data. The outcomes of interest included proportion of ulcers completely healed, time to complete ulcer healing, and incidence of lower limb amputations.

  The authors identified 17 randomized controlled trials as eligible for inclusion, encompassing 1, 655 patients with diabetic foot ulcerations. Of these trials, 13 compared a skin substitute to standard of care and 4 compared two types of skin substitutes. "When including all randomized participants, the proportion of completely healed ulcers ranged between 7.7% and 56.3% in the standard care group and 21.1% and 92.3% in the intervention group. The pooled risk ratio (RR) for complete ulcer healing was 1.55 in favor of the intervention group (95 % CI 1.30 –1.85; RD 0.25, 95 % CI 0.14–0. 37; NNT 4, 95% CI 3–8)."[6] The reporting was very heterogeneous for the outcome of time to complete ulcer healing; therefore, it was not possible to make clinical relevant comparisons. When pooling the studies that evaluated the incidence of lower limb amputations, the authors found a statistically significant lower amputation rate for the skin substitute group at 12 weeks.

This Cochrane systematic review was of good quality and had several strengths, including:

1. the systematic gathering of evidence, assessment of quality, and extraction of data by several independent reviewers following a pre-defined protocol
2. contacting authors of selected studies for additional information or data
3. assessment of heterogeneity, reporting bias, and publication bias
4. meta-analyses only being conducted when studies were determined to be homogeneous
5. sensitivity analyses to evaluate the influence of studies with a high risk of bias or high losses to follow-up

Limitations of this systematic review were the inclusion of studies with a high risk of bias and the potential for publication bias. Ultimately, the authors concluded "(t)his systematic review provides evidence that skin substitutes can, in addition to standard care, increase the likelihood of achieving complete ulcer closure compared with standard care alone in the treatment of diabetic foot ulcers."[6]

Evidence Tables

Medically Necessary Skin Substitutes

The following evidence tables are intended to succinctly list the peer-reviewed literature which supports medical necessity for the respective products. An evidence review was not performed for products which are included in the systematic reviews described above. Due to the large body of evidence, only the most recent peer-reviewed medical literature is included in the citations.

Indication	Products	Evidence
Breast reconstruction	AlloDerm®	Both AlloDerm® and FlexHD® Acellular Hydrated Dermis are established products for breast reconstruction and are supported in the peer-reviewed medical literature.[7-13]
	FlexHD® Accellular Hydrated Dermis	

Indication	Products	Evidence
Burn wound	Biobrane®/ Biobrane®-L	The peer-reviewed medical literature supports the use of Biobrane as temporary skin substitute in acute burn wounds.[14-16] In general, Biobrane performed better than the standard of care for wound healing rates, length of hospital stay, and pain.
	Epicel	Epicel received FDA approval under a Humanitarian Device Exemption (HDE); therefore, this product is exempt from the effectiveness requirements necessary for FDA approval. The evidence review did identify two nonrandomized studies which evaluated Epicel for burn wounds.[17,18] The most recent study (Carsin et al.) found that Epicel provided extensive and permanent burn coverage and improved the survival rate in severely burned patients.
	– Integra® Dermal Regeneration Template	The Integra dermal regeneration and bilayer products are well-established in the peer-reviewed medical literature as safe and effective treatments for burn wounds.[19-25]

	– Integra® Omnigraft Dermal Regeneration Matrix – Integra® Bilayer Matrix Wound Dressing – Integra® Meshed Bilayer Wound Matrix	
	TransCyte®	The peer-reviewed medical literature supports TransCyte as a safe and effective treatment for burn wounds.[26-30] Results of these clinical trials indicated that TransCyte promoted faster healing, less scaring, and shorter hospital stays.

Indication	Products	Evidence
Diabetic foot ulcer	Apligraf®	This product was included in the Hayes comparative effectiveness review and Cochrane systematic review described above.
	Allopatch	This product was included in the Hayes comparative effectiveness review
	Amnioband	This product was included in the Hayes comparative effectiveness review
	Dermagraft®	This product was included in the Hayes comparative effectiveness review and Cochrane systematic review described above.
	EpiFix® Amniotic Membrane	This product was included in the Hayes comparative effectiveness review and Cochrane systematic review described above.
	Grafix® Core/Grafix® Prime	Recent randomized controlled trials support the efficacy of Grafix products for the treatment of diabetic foot ulcers (DFU).[31,32] Both studies showed that treatment of DFU with Grafix significantly improved healing, reduced DFU- related complications, and shortened healing times. A 2019 Hayes review found consistent evidence from low-quality studies that adjunctive treatment with Grafix may improve healing of DFU.[33]
	GraftJacket® Regenerative Tissue Matrix	This product was included in the Hayes comparative effectiveness review and Cochrane systematic review described above.
	– Integra® Dermal Regeneration Template – Integra™ Omnigraft Dermal Regeneration Matrix	The use of Integra products for the treatment of diabetic foot ulcers (DFU) is supported in the peer-reviewed literature by randomized controlled trials (RCT).[34,35] A good-quality RCT by Driver et al. (2015) was conducted at 32 sites and randomized 307 patients to treatment with Integra or standard of care. Patients were treated for 16 weeks or until complete wound closure and followed-up for an additional

		12 weeks. The results showed a statistically significant increase in the rate of complete wound closure for Integra patients compared to the standard of care (51% vs. 32%; p=0.001). In addition, patients treated with Integra had increased healing times and less adverse events.
	Oasis® Wound Matrix/Oasis® Ultra Tri-Layer Matrix	This product was included in the Hayes comparative effectiveness review described above.
	TheraSkin®	This product was included in the Hayes comparative effectiveness review described above.

Indication	Products	Evidence
Venous stasis ulcer	Apligraf®	This product was included in the Hayes comparative effectiveness review described above.
	EpiFix® Amniotic Membrane	The use of EpiFix for the treatment of venous stasis ulcers is supported in the peer-reviewed literature by randomized controlled trials (RCT).[36,37] Most recently, Bianchi et al. (2017) conducted a multicenter RCT evaluating 109 patients with venous leg ulcers. Patients were recruited from 15 centers around the U.S. and followed-up for 16 weeks. The results indicated that patients receiving EpiFix in conjunction with compression therapy were statistically significantly more likely to experience complete wound healing than patients receiving standard wound care alone (60% vs. 35% at 12 weeks, p=0.0128; 71% vs. 44% at 16 weeks, p=0.0065). The older RCT by Serena et al. (2014) also showed a statistically significant difference in wound closure rates in favor of the Epifix group at 4 weeks follow-up (62% vs. 32%, p=0.005).
	Oasis® Wound Matrix	This product was included in the Hayes comparative effectiveness review described above.
	TheraSkin®	This product was included in the Hayes comparative effectiveness review described above.

Parotidectomy

- In 2013, Li et al. conducted a systematic review and meta-analysis of randomized controlled trials to evaluate the efficacy and safety of different types of grafts for the prevention of Frey syndrome after parotidectomy.[38] Independent reviewers systematically identified relevant literature, assessed quality, and extracted then pooled data. The outcomes of interest were the relative risk of Frey syndrome using skin substitute grafting or muscle flaps (another preventative measure) following parotidectomy.

  The authors identified 14 randomized controlled trails encompassing 1,098 participants as eligible for inclusion. All studies had an unclear risk of bias. Although, the results of the meta-analysis indicated that the use of an acellular dermal matrix can reduce the risk of Frey syndrome up to 82%, the muscle flaps can also reduce the risk of Frey syndrome up to 81%. Additionally, there was no

statistically significant difference was found between the acellular dermal matrix and muscle flap groups (RR 0.73, 95% CI 0.15 to 3.53, P = .70).

The strengths of this study include the systematic gathering of evidence, assessment of quality, and extraction of data by several independent reviewers following a pre-defined protocol, and the assessment of heterogeneity and sensitivity. Limitations are present in the heterogeneity of included studies and the poor quality of the RCTs (heterogenous patient populations, small sample sizes, and short follow-up periods). The authors concluded that "the evidence suggests grafts are effective in preventing Frey syndrome after peridectomy. More randomized clinical trials are needed to confirm our conclusions and prove the safety of the grafts."[38]

- In 2012, Zeng and colleagues conducted a systematic review and meta-analysis to evaluate the AlloDerm skin substitute for the prevention of Frey syndrome after parotidectomy.[39] Independent reviewers identified relevant studies, extracted and pooled data, and assessed quality. The primary outcome of interest was the relative risk reduction in objective and subjective incidence.

  Following systematic review, the authors had identified 5 studies including 409 patients as eligible for inclusion. Results of the meta-analysis showed a relative risk reduction of 85% in the objective incidence and 68% in the subjective incidence of Frey syndrome with AlloDerm implants. There was also a 91% relative risk reduction in salivary fistula. However, there was no statistically significant reduction in the incidence of facial nerve paralysis or seroma/sialocele.
  Strengths of this systematic review include the evaluation of evidence and extraction of data by independent authors following a pre-defined protocol and the inclusion of only randomized controlled trials. Limitations are present in the significant inter-study heterogeneity, the poor quality of the included studies (small sample sizes, short follow-up periods, lack of blinding, lack of intention to treat analysis), and the small number of included studies (possible publication bias). Ultimately, the authors concluded "(t)here is evidence that AlloDerm reduces the incidence of Frey syndrome effectively and safely, and also has the potential to improve facial contour and decrease salivary fistula. However, it is unclear whether AlloDerm implants improve facial contour and decrease other complications. Thus, further controlled evaluative studies incorporating more precise measures are required."[39]

Investigational Skin Substitutes

The following skin substitutes are considered investigational due to at least one of the following:

- There is no peer-reviewed literature to support the safety and/or clinical utility of the product.
- The available peer-reviewed literature is inadequate to establish the products safety and/or clinical utility due to poor quality studies with a high risk of bias. These studies had small and heterogenous patient populations, lack of randomized controlled design, lack of a control group, and/or short-term follow-up periods.
- The product requires, but has not yet received U.S. Food and Drug Administration (FDA) approval under the 510(k) premarket notification or premarket approval (PMA) process.

Products	
Affinity	Graftjacket® Xpress
Allogen	Helicoll™

Alloskin™ AC	Hyalomatrix®
Alloskin™ RT	Integra™ Matrix
Allowrap™	Integra™ Flowable Wound Matrix
AmnioArmor	Interfyl™
AmnioBand® Particulate	Kerecis Omega3
Amnion bio/Axobiomembrane	Keroxx
AmnioEXCEL™/BiodExcel™	MariStem® Micromatrix
AmnioFix®	Matrion™
AmnioMatrix®/BioMatrix®	Matrix HD™
AmnioPro-A	Mediskin™
Amnio Wound	MemoDerm™
Amniowrap 2	Microderm™
Architect™/Architect™ PX/Architect™ FX/Architect™ Extracellular Matrix	MyOwn skin
Artacent™/ Artacent™ Cord	Neopatch™
ArthroFlex™	NEOX® 100 Quick-Peel Wound Matrix
Ascent	NEOX® 1k Wound Matrix
Axolotl Graft/Axolotl Dualgraft/Axolotl Ambient/Axolotl Cryo	NEOX® FLO
BellaCell HD	Novachor
Bio-conneKt™ Wound Matrix	Novafix
BioDfactor™	NuCel™
BioDfence™	NuShield™
BioDfence™ Dryflex	Oasis® Burn Matrix
BioVance®	PalinGen®/Promatrx®
BioWound/BioWound Plus/BioWound Xplus	PalinGen® Xplus
Cellesta™ Amniotic Membrane	Permacol™
Cellesta™ Cord	PriMatrix™
Cellesta™ Flowable Amnion	Progenamatrix
Clarix® Flo	PuraPly™/PuraPly™ AM
Coll-e-Derm	Repriza®
Conexa™	Restorigin™ Membrane
CorMatrix	Restorigin™ Fluid
Cygnus™	Revita®
Cymetra™	Revitalon™
Cytal®	SkinTE™
Dermacell™	Strattice™
Derma-guide	Stravix
DermaMatrix Acellular Dermis	Surederm
DermaPure™	Surgicord
DermaSpan™	SURGIgraft™/ SURGIgraft™ Dual
Dermavest	Surgraft
Durepair Regeneration Matrix®	Talymed™
Endoform Dermal Template™	TenoGlide®
ENDURAGen	TenSIX™

Epifix® Injectable	TruSkin™
EpiCord™	Vendaje
Excellagen®	Veritas Collagen Matrix
E-Z Derm™	VIM
FloGraft™	WoundEx/Bioskin
Floweramnio™ Flo	WoundEx Flow/Bioskin Flow
Floweramnio™ Patch	XCM Biologic Tissue Matrix
Flowerderm™	XWRAP®
GalaFLEX	Woundfix/Woundfix Plus/Woundfix Xplus
GammaGraft	Zenith
Genesis Amniotic Membrane	

Investigational Indications for Skin Substitutes

Hernia Repair

Systematic Reviews

- In 2015, Antoniou et al. conducted a systematic review and meta-analysis to estimate the comparative risk of hernia recurrence following primary suture or biologic mesh repair.[40] Independent authors systematically identified relevant literature, extracted data, and evaluated quality. The primary outcomes of interest were short-term and long-term recurrence rates.

  The authors identified 5 studies (2 randomized controlled trials and 3 case-control studies) encompassing 295 patients as eligible for inclusion. "Short-term recurrence rates were 16.6% and 3.5% for suture repair and biologic mesh repair, respectively (OR 3.74, 95 % CI 1.55–8.98, p = 0.003). Long-term recurrence based on data provided by one trial only was 51.3% and 42.4 %, respectively (OR 1.43, 95 % CI 0.56–3.63, p = 0.45). Sensitivity analysis of the two randomized trials at short-term follow up demonstrated no significant difference (OR 2.54, 95 % CI 0.92–7.02, p = 0.07)."[40]

  The strengths of this study include the systematic gathering of evidence, assessment of quality, and extraction of data by several independent reviewers following a pre-defined protocol, and the assessment of heterogeneity and sensitivity. Limitations are present in the small number of included studies, leading to possible publication bias, and the poor quality of included studies. The authors concluded, "(b)iologic mesh repair of large hiatal hernias may confer short-term benefits in terms of hernia recurrence; however, the limited available information does not allow us to make conclusions about the long-term efficacy of biologic mesh in this setting. Individual biologic mesh grafts require further clinical assessment."[40]

- In 2013, Slater and colleagues conducted a systematic review to evaluate the effectiveness and safety of biologic grafts for ventral hernia repair.[41] Independent authors systematically identified relevant literature, extracted data, and evaluated quality. The primary outcomes of interest were recurrence, abdominal wall laxity, surgical morbidity, and adverse events.

  The authors identified 25 retrospective studies as eligible for inclusion. A total of 17 studies encompassing 531 patients were included in the recurrence rate outcome analysis. Overall, the recurrence rate was 13.8%. "Postoperative infection (r^2=.325, P =.011) and total surgical morbidity

(r^2=.189, P=.038) were revealed as significant explanatory variables for recurrent hernia."[41] Laxity was reported in 10.5% of patients, and all cases occurred with the Alloderm product. The surgical morbidity rate was 46.3% (95% CI, 33.3-59.6), and infection occurred in 15.9% (95% CI, 9.8-23.2) of patients.

Strengths of this study include the systematic review of evidence and extraction of data by independent authors; however, the methodological quality of this study is limited due to the poor quality of the included studies (all nonrandomized retrospective studies). The authors concluded that because no randomized trials were available, the efficacy of biologic grafts for ventral hernia repair could not be properly evaluated.

Randomized Controlled Trials (RCTs)

The evidence review did not identify any RCTs evaluating skin substitutes for hernia repair that were not included in the systematic reviews described above.

Nonrandomized Studies

The evidence review identified four additional recent nonrandomized studies evaluating allographic mesh for hernia repair.[42-45] Meaningful conclusions cannot be drawn from the results of these studies due to methodological limitations; including, but not limited to, lack of randomized controlled design, lack of comparison group, small sample sizes, and short-term follow-up period.

Tympanic Membrane Perforation

No systematic reviews, randomized controlled studies, or prospective cohort studies were found on AlloDerm for tympanic membrane perforations. Retrospective studies, summarized below, are considered low quality of evidence due to high risk of bias from study design, small sample sizes, and confounding variables potentially present in analyses.

A 2005 retrospective investigated the efficacy of AlloDerm versus temporalis fascia in repairing perforations in patients who require surgery for chronic otitis media with perforation. The study reviewed records of 50 patients between 1999 and 2004 and found no significant difference in closure rates between the two grafting materials, but healing time was shortened with AlloDerm. Overall perforation closure rate was 92%, with an 84% success rate for AlloDerm and a 97% success rate for native temporalis fascia.[46]

A 2006 retrospective study was conducted to compare lateral graft type 1 tympanoplasty with traditional underlay type 1 tympanoplasty using AlloDerm for tympanic membrane reconstruction in children. The study reviewed 34 records undergoing tympanoplasty between 2004 and 2005 and found that both groups significantly improved post-surgery, with a perforation closures rate of 94% for the lateral graft group and a closure rate of 88% for the underlay group. The authors conclude, "Results suggest that lateral graft type 1 tympanoplasty using AlloDerm® is effective for tympanic membrane reconstruction in children and should be used when temporalis fascia is not available or the extent of the perforation limits its use."[47]

A 2009 retrospective study on AlloDerm in type I tympanoplasty compared AlloDerm (n=25), fascia reconstruction (n=56), and fascia plus cartilage reconstruction (n=33) and found that AlloDerm significantly reduced operative time when controlled for surgeon and choice of approach, and all grafting approaches had similar success rates. Success rates were 88%, 96.7% and 89% in AlloDerm, fascia, and fascia plus cartilage reconstruction, respectively. [48]

Complex Nasal Reconstruction

The evidence review identified 4 nonrandomized trials evaluating acellular human dermal allograft (AlloDerm) for various nasal reconstruction and repair.[49-52] Studies included 2 case series and 2 observational studies that had sample sizes of 12-54 participants. Conclusions cannot be drawn from the results of these studies due to their methodological limitations; including, but not limited to, lack of randomized controlled design, lack of comparison group, small sample sizes, and short-term follow-up period.

Rotator Cuff Tear

In 2017 (archived), the ECRI Institute conducted a clinical comparison review of allografts for repairing rotator cuff tears.[53] The authors identified two studies (1 small retrospective case series and 1 small prospective comparative trial) evaluating the AlloPatch HD and Arthroflex products for this indication. Overall, the evidence was inconclusive because of insufficient data. There was no published peer-reviewed literature that examined how well these products worked compared to the standard of care. The authors concluded by stating that randomized controlled trials comparing rotator cuff tear repair with and without these products, with a minimum of 2-year follow-up, are required to determine if there is an improvement in surgical outcomes.

Repair of Non-Traumatic Surgical Wounds

The evidence related to skin substitutes for the repair of non-traumatic surgical wounds (e.g., Mohs surgery for squamous or basal cell carcinomas) is limited to small case series and nonrandomized studies.[54-63] Due to the poor methodological quality of these studies (lack of randomized design, lack of a control group, small sample sizes, short follow-up period, and lack of statistical analysis), there is insufficient evidence to establish the safety and medical necessity of skin substitutes for this indication. Further studies of good-methodological quality are required to support the effectiveness of skin substitutes for repair of non-traumatic surgical wounds, specifically Mohs surgery for squamous or basal cell carcinomas.

CLINICAL PRACTICE GUIDELINES

National Institute for Health and Care Excellence (NICE)

The 2016 (updated in 2019) evidence-based NICE guideline for the prevention and management of diabetic foot problems recommended, “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.”[64]

Society for Vascular Surgery/American Venous Forum

The 2014 evidence-based Society for Vascular Surgery/American Venous Forum guideline for the management of venous leg ulcers recommended the following:[65]

- The Committee suggests against split-thickness skin grafting as primary therapy in treatment of venous leg ulcers. [Grade - 2; Level of Evidence - B] The Committee suggests split-thickness skin grafting with continued compression for selected large venous leg ulcers that have failed to show signs of healing with standard care for 4 to 6 weeks. [Grade - 2; Level of Evidence - B]
- The Committee suggests the use of cultured allogeneic bilayer skin replacements (with both epidermal and dermal layers) to increase the chances for healing in patients with difficult to heal venous leg ulcers in addition to compression therapy in patients who have failed to show signs of healing after standard therapy for 4 to 6 weeks. [Grade - 2; Level of Evidence - A]
- We recommend serial venous leg ulcer wound measurement and documentation. [BEST PRACTICE]. "Serial VLU wound measurement and documentation is important to determine baseline markers and effect of subsequent treatment measures on healing parameters. Documentation should include number and position of ulcers on the leg. Wound measurements should be made for each VLU, including area, perimeter, and depth, with additional descriptors of wound edge parameters, wound base quality, drainage, and infection."
- We suggest reapplication of cellular therapy as long as the venous leg ulcer continues to respond on the basis of wound documentation. [GRADE - 2; LEVEL OF EVIDENCE - C]. "The optimal frequency and timing of reapplication of biologic skin substitutes to VLUs remain controversial with little consensus in published studies…With no comparative dosing studies published to determine clinical or economic outcomes, the frequency of application remains at the discretion of the clinician. Current clinical practice has included application of grafts followed by a period of 1 to 3 weeks of observation to determine effectiveness before reapplication is considered."

CENTERS FOR MEDICARE & MEDICAID SERVICES

As of November 2021, the following Centers for Medicare & Medicaid Services (CMS) guidance for the Company service area was identified which addresses skin substitutes for any indication:

- National Coverage Determination (NCD) for Porcine Skin and Gradient Pressure Dressings (270.5)

The local Medicare Administrative Contractor (MAC) – Noridian – ***used to*** have a local coverage article (LCA) for Use of Amniotic Membrane Derived Skin Substitutes (A56156); however, Noridian recently retired this LCA on September 30, 2021. Therefore, for any service not addressed by an active Medicare policy or guideline in the bulleted list above, the Company policy criteria will be applied.

Of note, an MLN Matters® (MLN# MM9923) article was identified which addresses skin substitute procedure edits.[66] This article states, "(t)he fact that a drug, device, procedure or service is assigned a HCPCS code and a payment rate under the ASC payment system does not imply coverage by the Medicare program, but indicates only how the product, procedure, or service may be paid if covered by the program. Medicare Administrative Contractors (MACs) determine whether a drug, device, procedure, or other service meets all program requirements for coverage. For example, MACs determine that it is reasonable and necessary to treat the beneficiary's condition and whether it is

excluded from payment."[66] Thus, the existence of a HCPCS code or payment rate does not imply that Medicare considers a product to be medically reasonable or necessary.

POLICY SUMMARY

The evidence supports the efficacy and safety of select skin substitute products for the indications of breast reconstruction, burn wounds, diabetic foot ulcers, and venous stasis ulcers. The National Institute for Health and Care Excellence (NICE) recommends the use of skin substitutes as an adjunct to standard care when treating refractor diabetic foot ulcers. The Society for Vascular Surgery and the American Venous Forum also recommends skin substitutes in patients with refractory venous stasis ulcers.
The evidence is insufficient to establish the efficacy, safety, and medical necessity of several products due to a lack of high-quality peer-reviewed literature or a lack of appropriate regulation. In addition, there is not enough evidence to support the use of skin substitutes for other indications, including hernia repair, repair of rotator cuff tears, repair of non-traumatic surgical wounds (e.g., Mohs surgery), and for the prevention of parotidectomy complications. Further studies of good methodological quality are required to establish the safety, effectiveness, and clinical utility of these products and indications.

INSTRUCTIONS FOR USE

Providence Health Plan (PHP) and Providence Health Assurance (PHA) Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. PHP and PHA Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. PHP and PHA reserve the right to determine the application of Medical Policies and make revisions to its Medical Policies at any time. Providers will be given at least 60-days' notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and PHP and PHA Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

U.S. Food and Drug Administration (FDA)

Depending on the purpose or function of the skin substitute, FDA regulation is through the premarket approval (PMA) process or 510(k) premarket notification process. Products derived from donated human tissue are overseen by the FDA regulations for banked human tissue and the American Association of Tissue Banks (AATB) guidelines.

PMA Process

Skin substitutes that are classified by the FDA as an interactive wound and burn dressing are approved under the PMA process as a class III, high-risk device. These are considered interactive because they actively promote healing by interacting directly or indirectly with body tissues.

510(k) Premarket Notification Process

Skin substitutes approved under the 510(k) premarket notification processes are typically those whose primary purpose is to protect the wound and provide a foundation for proper healing. These skin substitutes may or may not interact with body tissues.

FDA Regulations for Tissue and Tissue Products

Donated skin or tissue "intended for implantation, transplantation, infusion, or transfer into a human recipient is regulated as a human cell, tissue, and cellular and tissue-based product or HCT/P."[67] The Center for Biologics Evaluation and Research (CBER) regulates HCT/Ps under 21 CFR Parts 1270 and 1271.

The following products are addressed in the policy criteria above as medically necessary for breast reconstruction, burn wounds, diabetic foot ulcers, or venous stasis ulcers.
Humanitarian Device Exemption (HDE)[8,68]

HDE is a special FDA approval that allows a device to be marketed on a limited basis provided that:

1. The device is used to treat or diagnose a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year
2. The device would not be available to a person with such a disease or condition unless the exemption is granted
3. No comparable device is available to treat or diagnose the disease or condition; and
4. The device will not expose patients to an unreasonable or significant risk of illness or injury, and the probable benefit to health from using the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment

HDE applications are not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury. The labeling must also indicate that the effectiveness of the device for the specific indication has not been demonstrated.

Humanitarian use devices may only be used in facilities that have obtained an institutional review board (IRB) approval to oversee the usage of the device in the facility, and after an IRB has approved the use of the device to treat or diagnose the specific rare disease. The HDE holder (defined as the person who or entity that obtains the approval of an HDE from FDA) is responsible for ensuring that a device approved under an HDE is administered only in facilities having an IRB constituted and acting in accordance with the FDA's regulation governing IRBs (21 CFR Part 56), including continuing review of use of the device.

Products	Indications for Use
AlloDerm®[69]	AlloDerm is to be used for repair or replacement of damaged or inadequate integumental tissue or for other homologous uses of human integument.

Apligraf®[70]	• Apligraf is indicated for use with standard therapeutic compression for the treatment of non-infected partial and full-thickness skin ulcers due to venous insufficiency of greater than 1 month duration and which have not adequately responded to conventional ulcer therapy. • Apligraf is also indicated for use with standard diabetic foot ulcer care for the treatment of full-thickness neuropathic diabetic foot ulcers of greater than three weeks duration which have not adequately responded to conventional ulcer therapy and which extend through the dermis but without tendon, muscle, capsule, or bone exposure.
Biobrane®/Biobrane®-L[71,72]	• Temporary wound dressing for coverage of superficial burns, donor sites and meshed autographs. • Application should be to freshly debrided or excised wounds, or meshed autografts containing less than 105 bacteria/g tissue. • The debridement or excision must be done thoroughly to remove all coagulum or eschar. BIOBRANE/BIOBRANE-L will not adhere to dead tissue and any remaining necrotic tissue may cause infection. • Establish hemostatis prior to application of BIOBRANE/BIOBRANE-L. • Apply fabric (dull) side down, wrinkle-free against the wound surface with slight tension. • If less secondary adherence is desired (e.g. deeper donor sites or meshed autografts), BIOBRANE-L is recommended. • Under slight tension immobilize BIOBRANE/BIOBRALE-L using staples, tape, sutures, or skin closure strips and wrap area with dry gauze dressing or other stenting device to hold the dressing firmly in contact with the wound surface for 24 to 36 hours.
Dermacell™[73]	Intended for use as bio-implant during breast reconstruction surgery or during the treatment of chronic wounds.
Dermagraft®[74]	Dermagraft is indicated for use in the treatment of full-thickness diabetic foot ulcers greater than six weeks duration, which extend through the dermis, but without tendon, muscle, joint capsule, or bone exposure. Dermagraft should be used in conjunction with standard wound care regimens and in patients that have adequate blood supply to the involved foot.
Epicel[75]	Epicel is indicated for use in adult and pediatric patients who have deep dermal or full thickness burns comprising a total body surface area greater than or equal to 30%. 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.
EpiFix® Amniotic Membrane[76]	EpiFix is an amnion/chorion membrane allograft for acute and chronic wound care.

FlexHD® Acellular Hydrated Dermis[77]	FlexHD is used for the replacement of damaged or inadequate integumental tissue or for the repair, reinforcement, or supplemental support of soft tissue defects.
GalaFLEX Mesh[78]	The GalaFLEX mesh is indicated for use as a transitory scaffold for soft tissue support and to repair, elevate and reinforce deficiencies where weakness or voids exist that require the addition of material to obtain the desired surgical outcome. This includes reinforcement of soft tissue in plastic and reconstructive surgery, and general soft tissue reconstruction.
Grafix®[79]	Grafix is a cryopreserved placental membrane comprised of an extracellular matrix (ECM) rich in collagen, growth factors, fibroblasts, mesenchymal stem cells (MSCs), and epithelial cells native to the tissue. Designed for application directly to acute and chronic wounds with a flexible, conforming cover that adheres to complex anatomies.
GraftJacket™ Regenerative Tissue Matrix[80]	The GRAFTJACKET™ Matrix is used to provide supplemental support, protection, and reinforcement of tendon and ligamentous tissue; to be used as a periosteal patch or covering; or for protection and support of bone and tendons in foot & ankle and hand surgery.
Integra® Dermal Regeneration Template/Omnigraft® Dermal Regeneration Matrix [81]	The original PMA (P900033), Integra Dermal Regeneration Template (Integra Template) was approved for post-excisional treatment of life-threatening full thickness or deep partial-thickness thermal injuries where sufficient autograft is not available at the time of excision or not desirable due to the physiological condition of the patient. Another indication was added (supplement S042) for 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 exposed, when used in conjunction with standard diabetic ulcer care. Integra Template is also marketed as Integra Omnigraft Dermal Regeneration Matrix (Omnigraft), specifically for the indication 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 exposed, when used in conjunction with standard diabetic ulcer care.
− Integra® Bilayer Matrix Wound Dressing[82] − Integra® Meshed Bilayer Wound Matrix[83]	The Integra Bilayer Matrix Wound Dressing and the Integra Meshed Bilayer Wound Matrix Dressing are substantially equivalent to the Integra Dermal Regeneration Template. These products are indicated for the management of wounds including: partial and full thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) and draining wounds. The device is intended for one-time use.

Oasis® Wound Matrix[84]	The OASIS® Wound Matrix device's intended use is for the management of wounds including: • partial and full-thickness wounds, • pressure ulcers, • venous ulcers, • diabetic uicers, • chronic vascular ulcers, • tunneled/undermined wounds, • surgical wounds (donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), • trauma wounds (abrasions, lacerations, second-degree burns, and skin tears), • draining wounds.
TheraSkin®[85]	TheraSkin is a biologically active, cryopreserved real human skin allograft, composed of living cells, fibroblasts and keratinocytes, and a fully developed extra cellular matrix (ECM) in its epidermis and dermis layers. TheraSkin can be used on chronic wounds with exposed muscle, bone, tendon and joint capsule including, but not limited to, DFUs, VLUs, Arterial ulcers, dehisced surgical wounds, pressure sores and wounds that might otherwise require an autograft.
TransCyte®[86]	Indicated for use as a temporary wound covering for surgically excised full-thickness and deep partial-thickness thermal burn wounds in patients who require such a covering prior to autograft placement; and for the treatment of mid-dermal to indeterminate depth burn wounds that typically require debridement and that may be expected to heal without autografting.

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

MEDICAL POLICY CROSS REFERENCES

- Cosmetic and Reconstructive Surgery
- Breast Reconstruction

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