

▶ **VIVEX'S PROPRIETARY INTEGRITY PROCESSING™ PRESERVES UPTO 600+ SIGNALING PROTEINS IN CYGNUS MATRIX, SOLO, AND MAX¹²**

VIVEX's Integrity Processing™ is a gentle process that removes blood remnants, while preserving the allograft composition without compromising structural integrity.

▶ **KNOWN GROWTH FACTORS AND EXTRACELLULAR MATRIX (ECM) PROTEINS IN AMNIOTIC ALLOGRAFTS AND THEIR CORRESPONDING ROLE^{13,14}**

GROWTH FACTORS	ROLE
MCP-1 ¹⁵ , IL1-RA ¹⁶ , TGF-β1&2 ¹⁷ , IL6 ¹⁶	Immune Modulation / Anti-Inflammatory
TNF-α ¹⁸ , GRO-α ¹⁹ , HGF ²⁰ , IGF1&2 ^{21,22} , VEGF ²³ , βFGF ²⁴ , PDGFα&β ²⁵ , Ang ²⁶	Angiogenesis
EGF ²⁷ , FGF ²⁴ , TGFβ ¹⁷ , TIMP(1-4) ²⁸ , HGF ²⁹	Cell Growth
PDGFα&β ²⁵ , EGF ²⁷ , TIMP-2&-3 ²⁸ , HGF ²⁹ , Ang ²⁶ , KGF ³⁰	Cell Migration
PDGFα&β ²⁵ , EGF ²⁷ , FGF ²⁴ , TGF-β1&2 ¹⁷ , IGF1&2 ³¹ , Ang ²⁶ , KGF ³⁰	Cell Proliferation
PDGFα&β ²⁵ , EGF ²⁷ , TIMP-2&-3 ²⁸ , TGF-β1&2 ¹⁷	Cell Differentiation

ECM PROTEINS	ROLE
Collagen, type I-VII	Main structural protein component in the body
Fibronectin	Binding protein agent, supports initial cell attachment
Hyaluronic Acid	Lubricating hydrophilic protein that coats cells and aids in hydrodynamic movements
Laminin	High molecular weight protein to which cells easily bind and migrate across
Proteoglycans	Connective proteins that fill the spaces between cells in tissue and affect the stability of the proteins and growth factors

▶ **SAFE AND TRUSTED PARTNER**

VIVEX Biologics is a regenerative solutions company focused on patient care through the innovation of tissue-based therapies in Wound Care, Ortho-Fusion, and Interventional Pain. With more than 50 years of highly safe and effective operations, VIVEX aims to provide advanced regenerative solutions.



- Amniotic tissue is recovered from healthy mothers at live births.
- Amniotic tissue is handled and processed in accordance with both FDA regulations and AATB standards.
- VIVEX maintains the trend of safely delivering over 2 million allografts with no disease transmission.

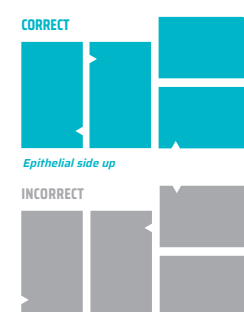
▶ **ORDERING INFORMATION**

Product HCPCS Code: Q4170 (CYGNUS) per square centimeter

CYGNUS® MATRIX

CODE	DESCRIPTION	SIZE	SQ. CM.
CAP020200S	CYGNUS® Matrix Amnion Allograft	2x2cm	4
CAP020300S	CYGNUS® Matrix Amnion Allograft	2x3cm	6
CAP030300S	CYGNUS® Matrix Amnion Allograft	3x3cm	9
CAP040400S	CYGNUS® Matrix Amnion Allograft	4x4cm	16
CAP040600S	CYGNUS® Matrix Amnion Allograft	4x6cm	24
CAP070700S	CYGNUS® Matrix Amnion Allograft	7x7cm	49
CAP015000S	CYGNUS® Matrix Amnion Allograft Disk	15mm Disk	2
CAP025000S	CYGNUS® Matrix Amnion Allograft Disk	25mm Disk	5
CAP035000S	CYGNUS® Matrix Amnion Allograft Disk	35mm Disk	10
CAP045000S	CYGNUS® Matrix Amnion Allograft Disk	45mm Disk	16
CAP055000S	CYGNUS® Matrix Amnion Allograft Disk	55mm Disk	24
CAP065000S	CYGNUS® Matrix Amnion Allograft Disk	65mm Disk	33

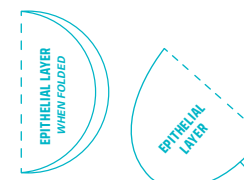
CYGNUS Matrix/Solo/Max Orientation



CYGNUS® SOLO

CODE	DESCRIPTION	SIZE	SQ. CM.
CAS020200S	CYGNUS® Solo Amnion Allograft	2x2cm	2
CAS020300S	CYGNUS® Solo Amnion Allograft	2x3cm	6
CAS030300S	CYGNUS® Solo Amnion Allograft	3x3cm	9
CAS040400S	CYGNUS® Solo Amnion Allograft	4x4cm	16
CAS040600S	CYGNUS® Solo Amnion Allograft	4x6cm	24
CAS040800S	CYGNUS® Solo Amnion Allograft	4x8cm	32
CAS070700S	CYGNUS® Solo Amnion Allograft	7x7cm	49

CYGNUS Matrix Circular-Shaped Graft Orientation



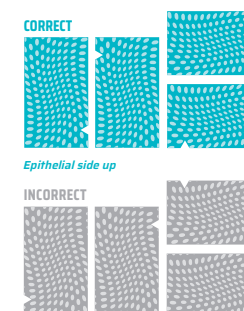
CYGNUS® MAX

CODE	DESCRIPTION	SIZE	SQ. CM.
CAM020200S	CYGNUS® Max Umbilical Cord Membrane	2x2cm	4
CAM020300S	CYGNUS® Max Umbilical Cord Membrane	2x3cm	6
CAM020400S	CYGNUS® Max Umbilical Cord Membrane	2x4cm	8

CYGNUS® MAX XL

CODE	DESCRIPTION	SIZE	SQ. CM.
CAX020300S	CYGNUS® Max XL Fenestrated Umbilical Cord Membrane	2x3cm	6
CAX030300S	CYGNUS® Max XL Fenestrated Umbilical Cord Membrane	3x3cm	9
CAX030800S	CYGNUS® Max XL Fenestrated Umbilical Cord Membrane	3x8cm	24
CAX040400S	CYGNUS® Max XL Fenestrated Umbilical Cord Membrane	4x4cm	16
CAX040600S	CYGNUS® Max XL Fenestrated Umbilical Cord Membrane	4x6cm	24
CAX040800S	CYGNUS® Max XL Fenestrated Umbilical Cord Membrane	4x8cm	32
CAX050700S	CYGNUS® Max XL Fenestrated Umbilical Cord Membrane	5x7cm	35

CYGNUS Max XL Orientation



CYGNUS® CRYOPRESERVED MAX

CODE	DESCRIPTION	SIZE	SQ. CM.
CUC020200	CYGNUS® Cryopreserved Max Umbilical Cord Membrane	2x2cm	4
CUC020400	CYGNUS® Cryopreserved Max Umbilical Cord Membrane	2x4cm	8
CUC030400	CYGNUS® Cryopreserved Max Umbilical Cord Membrane	3x4cm	12

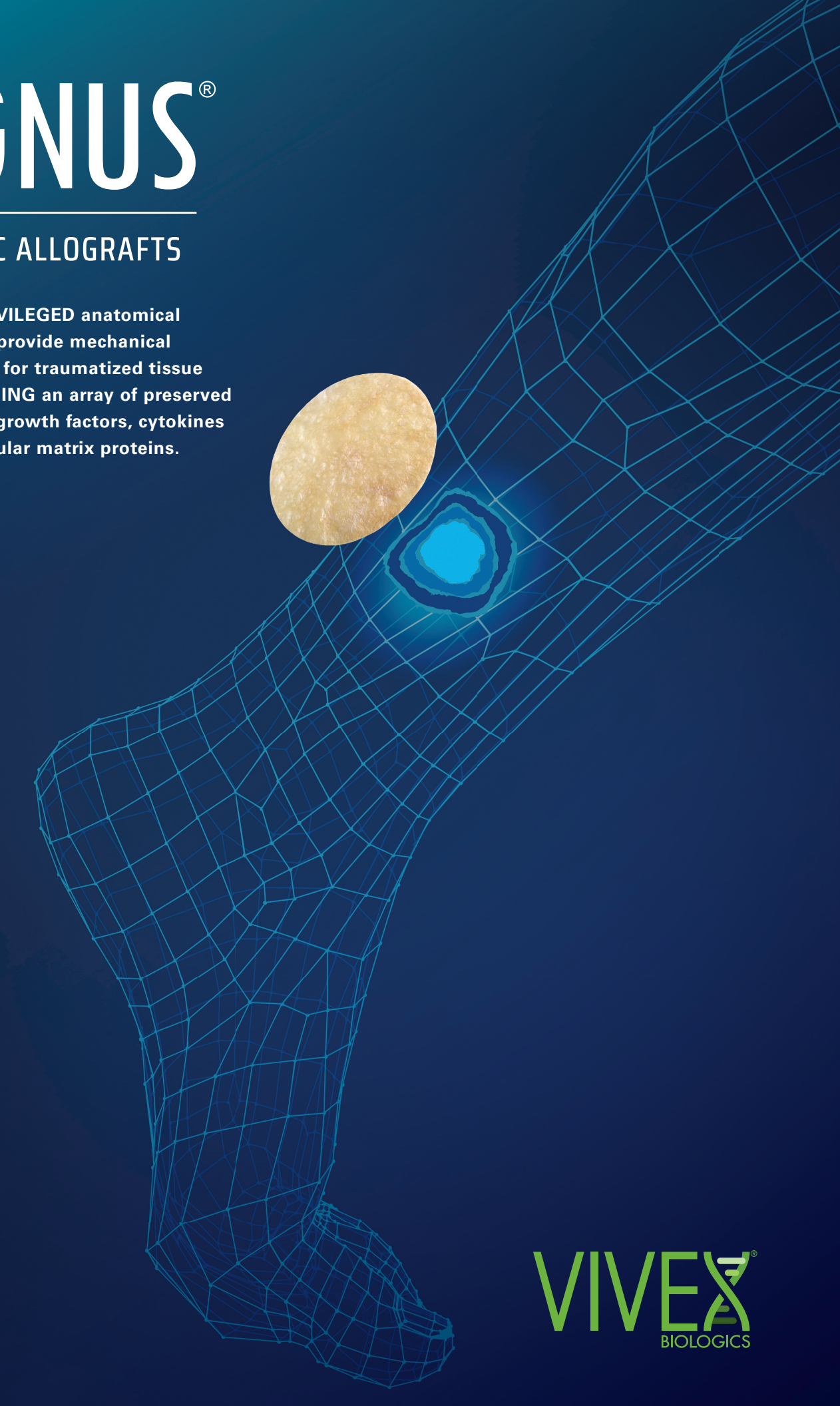
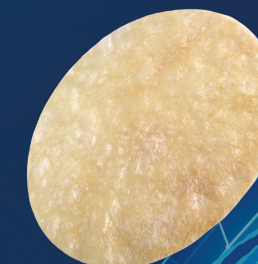
1. Rowlett, U. (1979). Intrauterine wound healing in a 20-week human fetus. *Virchows Arch A Pathol Anat Histol*, 381(3), 353-361
2. Coolen, N.A. et al. (2010). Comparison between human fetal and adult skin. *Archives of Dermatological Research*, 302(1), 47-55.
3. Coolen NA, Schouten KC, Boekema BK, Middelkoop E, Ulrich MM. Wound healing in a fetal, adult, and scar tissue model: a comparative study. *Wound Repair Regen*. 2010; 18(3):291-301. doi: 10.1111/j.1524-7531.2010.02685.x
4. Tseng SC, Espana EM, Kawakita T, et al. How does amniotic membrane work? *Ocul Surf*. 2004;2(3):177-187
5. Riordan NH, George BA, Chandler TB, McKenna RW. Case report of non-healing surgical wound treated with dehydrated human amniotic membrane. *J Transl Med*. 2015;13:242. doi: 10.1186/s12967-015-0668-8
6. Kim SS, Sohn SK, Lee KY, et al. Use of human amniotic membrane wrap in reducing perineural adhesions in a rabbit model of ulnar nerve neurotomy. *J Hand Surg Eur Vol*. 2010;35(3):214-219. doi: 10.1177/1175133409352410
7. Delcroix GJ, Namin S, D'Ipollito G, Temple HT, Marshall R. Preserving the natural regenerative potential of amniotic membrane. *Vivex Biomedical*.
8. Koob TJ, Lim JJ, Nasseef M, Zabeck N, Denoziar G. Properties of dehydrated human amnion/chorion composite grafts: implications for wound repair and soft tissue regeneration. *J Biomed Mater Res B Appl Biomater*. 2014;102(B):1353-1362. doi:10.1002/jbm.b.33141
9. "The last layer which is known as intermediate layer or spongy layer or zona spongiosa lies adjacent to the chorionic membrane and contains a meshwork of mostly type III collagen" Gupta A. HYPERLINK "http://et.al" et al. "Amnion and Chorion Membranes: Potential Stem Cell Reservoir with Wide Applications in Periodontics" *Int J Biomater*, 2015; 2015:274032
10. "Type III collagen (α2)1, expressed in early granulation tissue, has been proposed to play a prominent role in cutaneous wound repair" Volk SW. HYPERLINK "http://et.al" et al. "Diminished Type III Collagen Promotes Myfibroblast Differentiation and Increases Scar Deposition in Cutaneous Wound Healing" *Cells Tissues Organs*, 2011 Jun; 194(1): 25-37
11. Jerabek SA, Carroll KM, Michaels B, Mayman DJ. A pilot study to evaluate the safety and efficacy of amniotic membrane transplantation in patients with anterior cruciate ligament tears following total knee arthroplasty. *Hospital for Special Surgery*. http://www.amnionmedical.com/wp-content/uploads/Amniotic_Hip_Knee_Study.pdf. Accessed November 21, 2017
12. Data on file at VIVEX Biologics, Inc.
13. Gerhard Meisenberg, William H. Simmons, "Principals of Medical Biochemistry"; Elsevier Health Sciences. pp. 243-; ISBN 978-0-323-02942-1; February 2011.
14. Yanagishita M et al. "Function of proteoglycans in the extracellular matrix." *Acta Pathol Jen*. 1993. Jun;43(6):263-80
15. Dashkhrane, Satish L, et al. "Review of Monocyte Chemoattractant Protein-1 (MCP-1)." *Journal of Interferon & Cytokine Research*, Vol 29, #6, 2009
16. Lakshmi Srinivasan, Laurie E. Kilpatrick et al. "Cytokines and Inflammatory Response in the Fetus and Neonate"; *Fetal and Neonatal Physiology*, 5th edition, 2017
17. Hans Link, Bao-Guo Xiao, "Transforming Growth Factor Beta" *Encyclopedia of Immunology* 2nd edition, 1998
18. Narayanan Parameswaran & Sonika Patel, "Tumor Necrosis Factor-α Signaling in Macrophages." *Crit Rev Eukaryot Gene Expr*. 2010; 20(2): 87-103
19. Bednarek, Carlos et al. "Growth related oncogene-alpha (GRO-alpha): roles in atherosclerosis, angiogenesis, and other inflammatory conditions"; *Med Sci Monit*, 2007 Jun; 13(6):RA87-90
20. G.V. Sherbet, "Growth Factors and Their Receptors in Cell Differentiation, Cancer and Cancer Therapy", 2011
21. BENOIT-ST-JACQUES, JILL A; HELMUS, in *Pediatric Bone*, 2003
22. Alexander Brill, David Varon, in *Platelets (Second Edition)*, 2007
23. Angela M Duffy et al. "Vascular Endothelial Growth Factor (VEGF) and its Role in Non-Endothelial Cells: Autocrine Signaling by VEGF"
24. Ye-Ran Yun et al. "Fibroblast Growth Factors: Biology, Function, and Application for Tissue Regeneration" *Tissue Eng*, 2010;20(12):18142
25. Giannoula Lakka Klement, David Varon et al. "The Role of Platelets in Angiogenesis"; *Platelets*, 3rd Edition 2013
26. Gao X, Xu Z (2008). "Mechanisms of action of angiotensin". *Acta Biochimica et Biophysica Sinica*, 40 (7): 619-624
27. Bodnar, Richard J. "Epidermal Growth Factor and Epidermal Growth Factor Receptor: The Yin and Yang in the Treatment of Cutaneous Wounds and Cancer"
28. Masciantonio M.G. et al. "Matrix Metalloproteinases and Tissue Remodeling in Health and Disease: Cardiovascular Remodeling" *Prog in Mol Bio & Trans Sci*, 2017
29. Yinan Deng, et al. "Umbilical Cord-derived Mesenchymal Stem Cells Instruct Monocytes Towards an IL10-producing Phenotype by Secreting IL6 and HGF" *Scientific Reports* volume 6, Article number: 37566 (2016)
30. Jeffrey S. Rubin et al., "Keratinocyte Growth Factor," *Cell Biology International*, Vol 19, Issues 5, May 1995; p389-412
31. R.W. Li, A.K. Sperling, in *Brenner's Encyclopedia of Genetics (Second Edition)*, 2001

VIVEX Biologics will use reasonable efforts to provide accurate and complete information herein, but this information should not be construed as providing clinical advice, dictating reimbursement policy or as a substitute for the judgment of a health care provider. It is the health care provider's responsibility to determine the appropriate treatment, codes, charges for services and use of modifiers for services rendered and to submit coverage or reimbursement-related documentation.

CYGNUS®

▶ **AMNIOTIC ALLOGRAFTS**

IMMUNE PRIVILEGED anatomical barriers that provide mechanical PROTECTION for traumatized tissue while RETAINING an array of preserved endogenous growth factors, cytokines and extracellular matrix proteins.



CYGNUS®

CYGNUS® is a family of amniotic tissue allografts processed to retain the inherent mechanical properties of amniotic tissue and rich supply of extracellular matrix, growth factors, and cytokines.^{1,2}

► CYGNUS AMNIOTIC ALLOGRAFT FEATURES AND BENEFITS

Amniotic-derived tissues may be used as a soft tissue barrier and wound covering that retains endogenous extracellular matrix (ECM), growth factors, and cytokines²⁻⁵ essential for signaling. The properties of amniotic tissue help provide mechanical protection⁶ to damaged tissue while maintaining nutrient-rich growth factors.^{7,8}

WHY CYGNUS AMNIOTIC ALLOGRAFTS

- Amniotic tissue acts as a mechanical barrier between mother and fetus as well as an immune-privileged protective barrier during fetal development.¹
- CYGNUS applied as a soft tissue and wound covering helps provide the same mechanical protection to support the damaged tissue.⁵
- VIVEX's Integrity Processing™ retains the intermediate (spongy) layer and preserves the inherent properties of amniotic tissues, maintaining key extracellular matrix molecules, proteins, carbohydrates, collagen, growth factors, and cytokines.⁷
- No upfront preparation — hydrates in site
- 5-year shelf life for room temperature storage

CYGNUS Matrix: Multi-layer membrane allograft maintaining the amnion layer, its intermediate/spongy layer, and the chorion layer of the amniotic sac, and up to 4X thicker than the single amnion layer

CYGNUS Solo: Single layer membrane allograft, featuring the amnion layer of the amniotic sac

WHY CYGNUS MAX UMBILICAL CORD MEMBRANE ALLOGRAFT

- Thickest dehydrated amniotic membrane allograft, ~400µm (0.4mm)
- Retains inherent extracellular matrix molecules, growth factors and cytokines
- Robust enough to be sutured in place
- Excellent handling properties
- No upfront preparation — hydrates in site
- 5-year shelf life for room temperature storage

CYGNUS Max and CYGNUS Cryopreserved Max: Umbilical cord membrane that is up to 4X thicker than the single amnion layer (also available cryopreserved with a 9-month shelf life at storage of -65°C or colder, with minimal preparation required)

CYGNUS Max XL: Umbilical cord membrane fenestrated to allow for wound drainage and increases the size of the available allograft

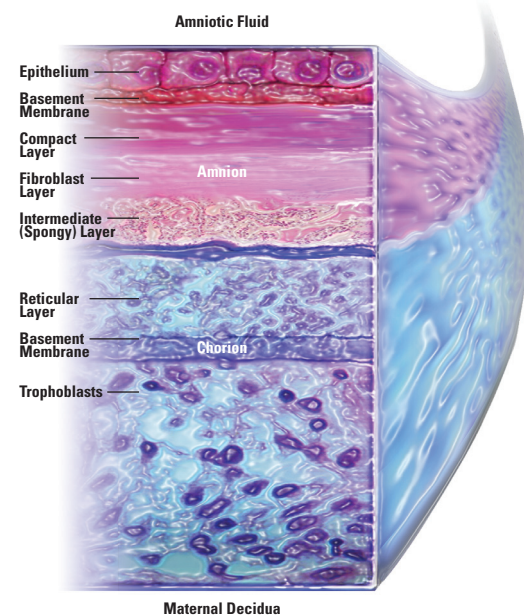


Figure 1: The Layers of Amniotic Sac

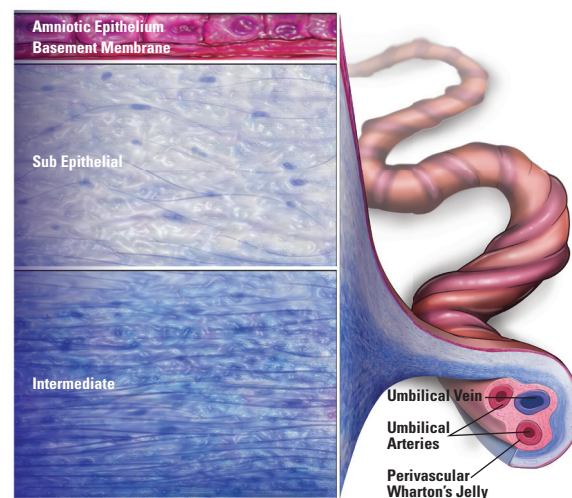


Figure 2: The Layers of the Umbilical Cord Membrane

Multi-layer membrane allograft maintaining the amnion layer, its intermediate/spongy layer, and the chorion layer of the amniotic sac, containing inherent growth factors, collagen, cytokines, and extracellular matrix.^{1,2}

Multi-layer amniotic membrane allograft, ~400µm (0.4mm) thick, up to 4X thicker than the single amnion layer

The intermediate/spongy layer contains a meshwork of mostly type III collagen which plays a prominent role in cutaneous wound repair^{9,10}

5-year shelf life at room temperature storage

No upfront preparation – hydrates rapidly in surgical site

Ideal for both internal and external application

Available in a variety of sizes and shapes to meet clinical needs and allow use throughout the course of wound repairs

Available circular shape saves time by reducing the need to trim and associated potential to waste tissue



Single layer membrane allograft, featuring the amnion layer of the amniotic sac, offering inherent growth factors, cytokines, chemokines, and extracellular matrix of the amnion layer.^{1,2}

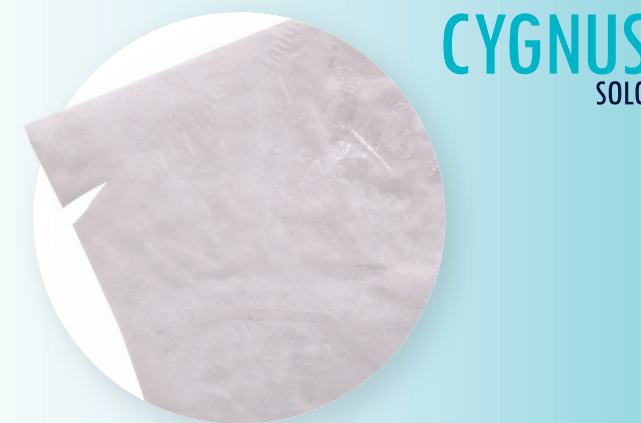
Thin amniotic membrane allograft, ~100µm (0.1mm) thick

5-year shelf life at room temperature storage

No upfront preparation – hydrates rapidly in surgical site

Ideal for superficial wounds and topical application

Burn treatment, acute wounds, non-healing/chronic wounds, diabetic ulcers



Comprised of the umbilical cord membrane, this tissue is the thickest of the VIVEX dehydrated amniotic allograft products and is robust enough to be sutured in place.

Thick umbilical cord membrane, ~400µm (0.4mm) thick, up to 4X thicker than the single amnion layer

5-year shelf life at room temperature storage

No upfront preparation – hydrates rapidly in surgical site

Tissue can be sutured into place

Excellent handling properties



Comprised of fenestrated umbilical cord membrane, increasing the available allograft size to cover a larger wound while also allowing the wound to drain.

Thick umbilical cord membrane, 400µm (0.4mm) thick, up to 4X thicker than the single amnion layer

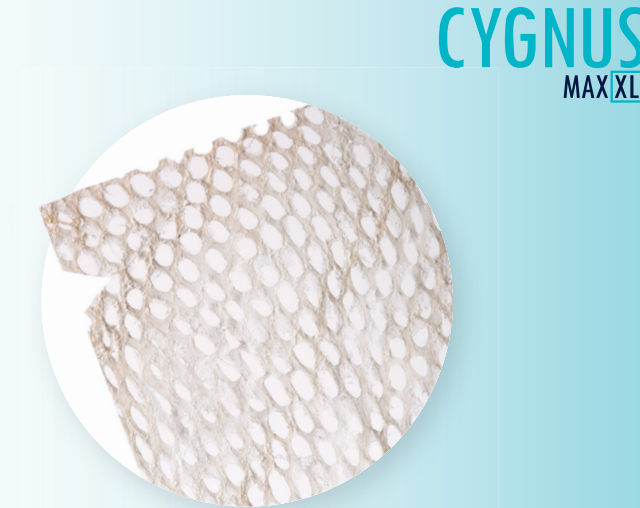
5-year shelf life at room temperature storage

No upfront preparation – hydrates rapidly in surgical site

Tissue can be sutured into place

Excellent handling properties

Fenestrated to allow for wound drainage and increases the size of the umbilical cord membrane



Comprised of the cryopreserved umbilical cord membrane, this tissue is the thickest amniotic allograft of the VIVEX products and is robust enough to be sutured in place.

Thick umbilical cord membrane, ~800–2,000µm (0.8-2.0mm) thick, up to 8X thicker than the single amnion layer

9-month shelf life at temperature of -65°C or colder

Thaws quickly in 3-5 minutes

Tissue can be sutured into place



► POTENTIAL CLINICAL APPLICATIONS

In general wound care, such as diabetic foot ulcers, venous leg ulcers, pressure wounds, hard-to-heal wounds, and surgical wound dehiscence, CYGNUS has been used as a protective barrier to provide essential mechanical protection for wounds. Other potential clinical applications include general orthopedics, arthroplasty, hand and wrist, and foot and ankle procedures.

- Wounds
- Burns
- Diabetic Foot Ulcers
- Venous Leg Ulcers
- Pressure Wounds
- Hard-to-Heal Wounds
- Surgical Wound Dehiscence

