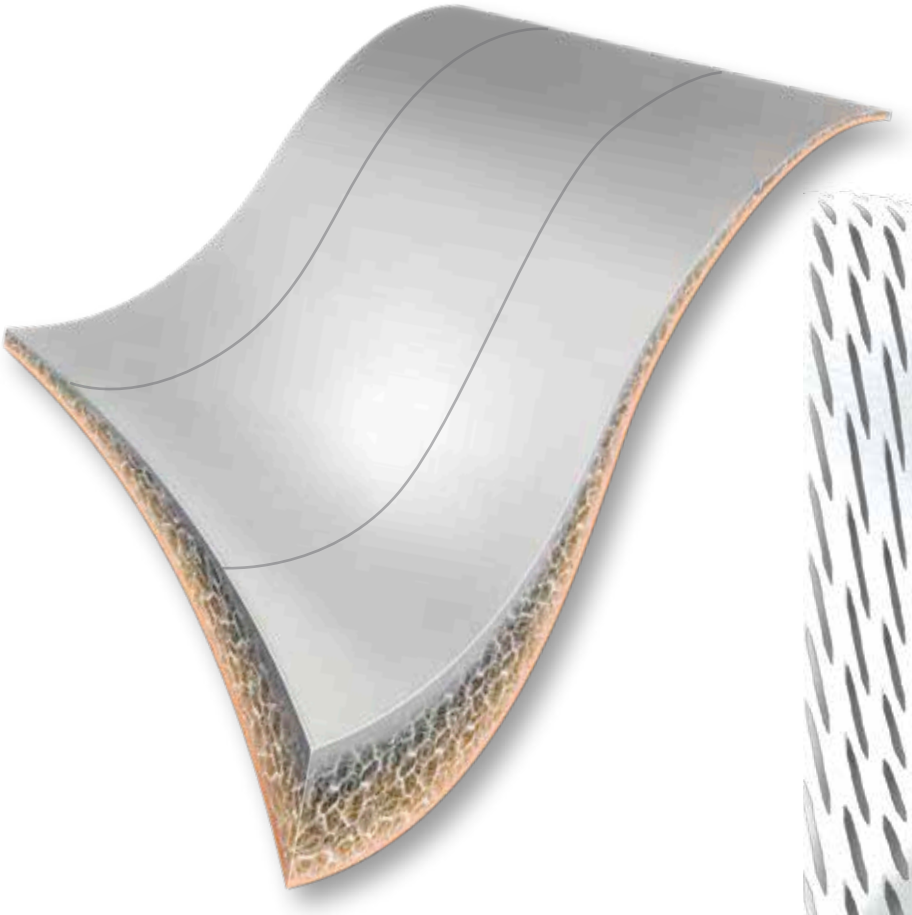
Integra®

Tissue Technologies

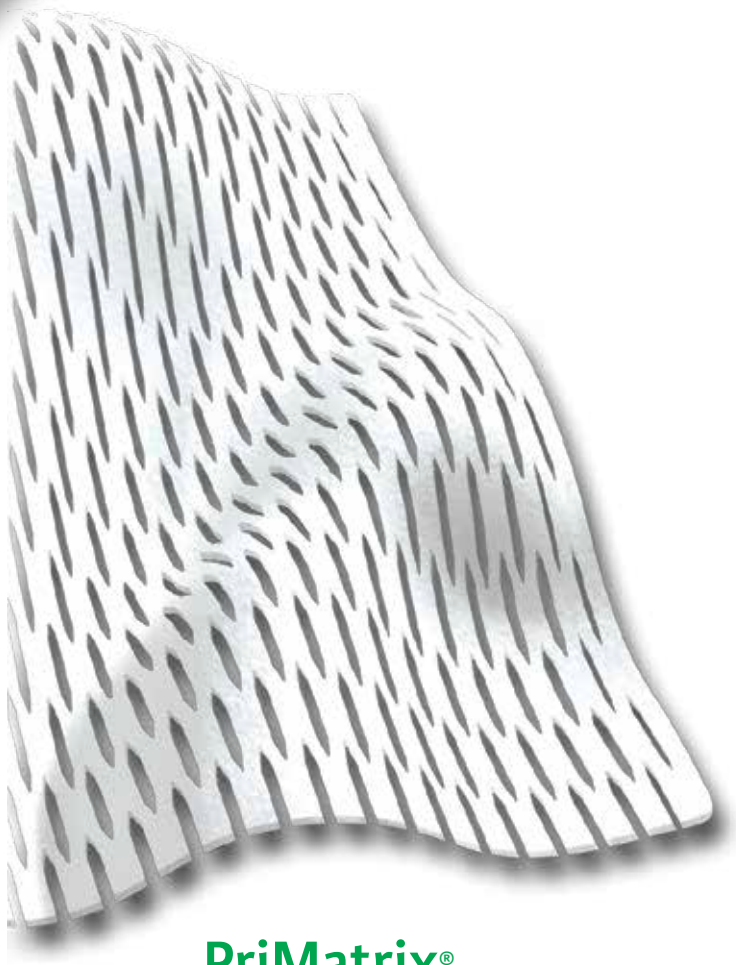
Limit uncertainty with
a leader in collagen technology

INTEGRA®
LIMIT UNCERTAINTY



Integra®

Dermal Regeneration Template



PriMatrix®

Dermal Repair Scaffold

A Pioneer in Regenerative Medicine

Integra LifeSciences, a wordwide leader in medical technology, has offered innovative solutions to clinicians and patients for over 25 years.

In 1996, the FDA approved the Company's first product, Integra® Dermal Regeneration Template, a collagen matrix designed as a skin replacement system for the treatment of third-degree burns. Integra® Dermal Regeneration Template was the first product approved with a claim of regeneration of dermal tissue.

Advances in material sourcing and bioprocessing methods have led to the development of PriMatrix, a dermal repair scaffold that can be repopulated by cells and revascularized while maintaining native dermal collagen architecture. Our technology has been studied by leading physicians at top teaching institutions.

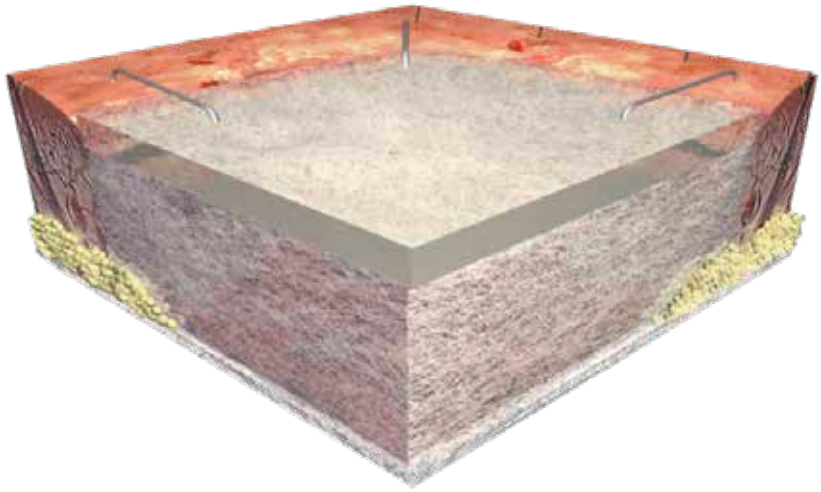
Together, these products represent over 25 years of science and innovation in the development of collagen technology. Integra now offers a broad portfolio of bioengineered and extracellular matrix products for a wide range of indications including burns, trauma, limb salvage, and chronic wounds.

What is Integra template?

Integra template is an advanced bilayer matrix for dermal regeneration.

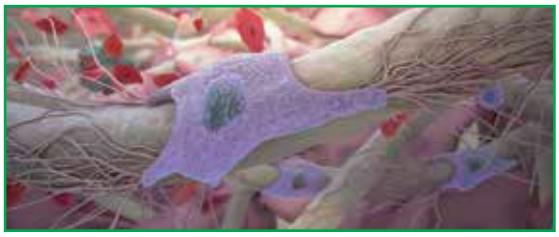
The dermal replacement layer consists of a porous, three-dimensional matrix, comprised of collagen and chondroitin-6-sulfate.

The temporary epidermal layer is made of a thin silicone layer to provide immediate wound coverage.

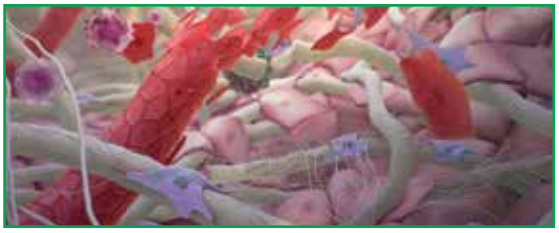


How Integra Works

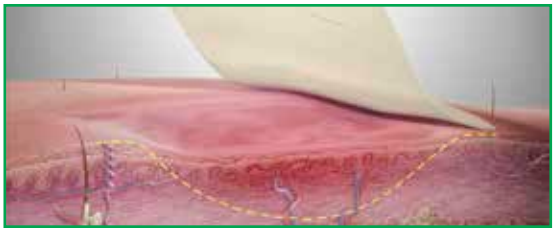
Step 1
Integra template is applied to a debrided wound bed.



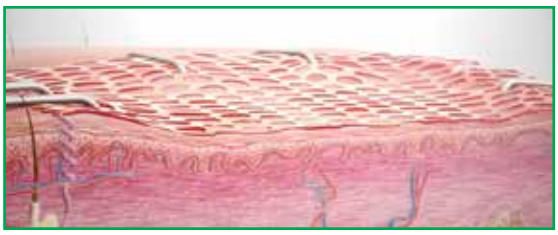
Step 2
Cells migrate from the adjacent dermis into the collagen matrix where they synthesize and deposit collagen to form a neodermis.



Step 3
Simultaneously, endothelial cells from nearby vascular supply migrate into the matrix to support neovascularization and provide essential nutrients to the neodermis.



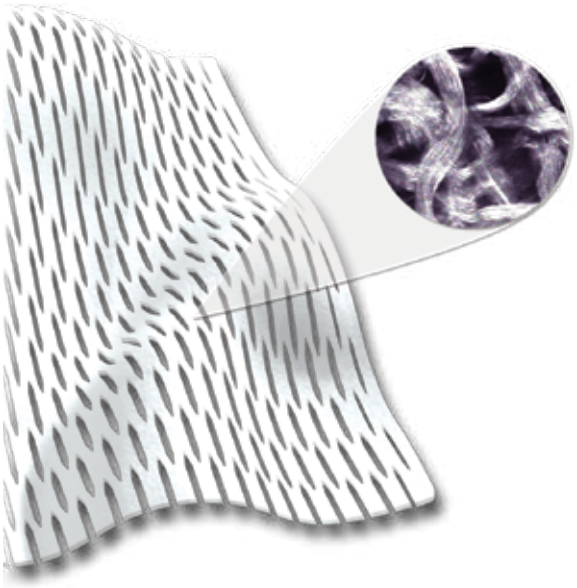
Step 4
Once the neodermis has formed the staples and silicone layer are removed, typically 14 to 21 days after application.



Step 5
A split-thickness skin graft is used for final wound closure.

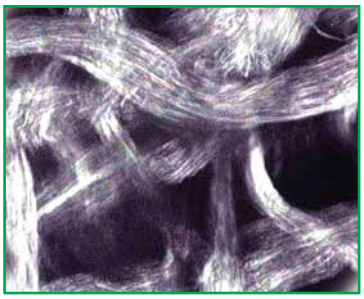
What is PriMatrix?

PriMatrix is a unique dermal repair scaffold for the management of a broad range of wound types, including diabetic and venous ulcers. Made of pure, all-natural collagen, this novel dermal matrix provides an ideal environment to support the cellular repopulation and revascularization processes critical in wound healing.



How PriMatrix Works

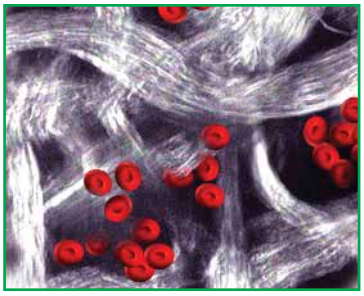
PriMatrix is cell-friendly dermal collagen and acts as a scaffold for cells and bloods vessels as the body repairs the wound.



A natural dermal collagen matrix

PriMatrix Collagen Scaffold

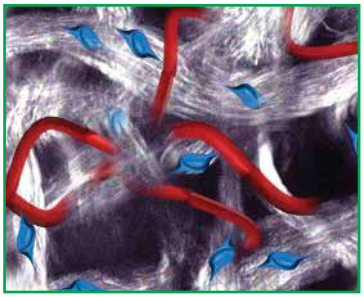
PriMatrix is a dermal repair scaffold that is consistent and non-irritating. PriMatrix is made of all-natural Type I and Type III healing collagen.



Absorbs blood, cells and growth factors

PriMatrix is Enriched

When placed in the wound, blood, cells, and growth factors infiltrate the porous dermal scaffold.



Skin cells and blood vessels begin to grow

PriMatrix Supports Cellular Repopulation and Revascularization

Cell repopulation and blood vessel growth is critical in the healing process. Cells can migrate and multiply to repopulate the dermal repair scaffold. Small and large blood vessels can then grow throughout the collagen scaffold.

Integra® Product Portfolio

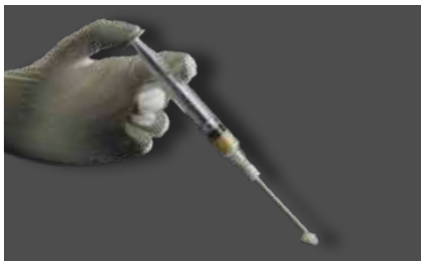
Integra® Dermal Regeneration Template
The first FDA approved bilayer matrix for dermal regeneration in 3rd degree burns and scar contractures.

Integra® Meshed Dermal Regeneration Template
The only FDA approved pre-meshed bilayer matrix for dermal regeneration in 3rd degree burn and scar contractures.

Integra® Bilayer Wound Matrix
A bilayer matrix for a variety of wounds that provides a scaffold for cellular invasion and capillary growth.

Integra® Meshed Bilayer Wound Matrix
A pre-meshed bilayer matrix for wound management that can be used in conjunction with negative pressure wound therapy.

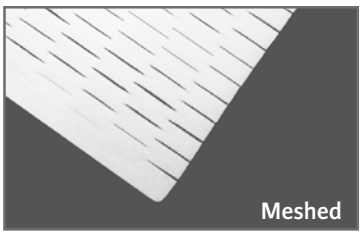
Integra® Wound Matrix
A single layer collagen matrix that supports a healing environment for wounds.

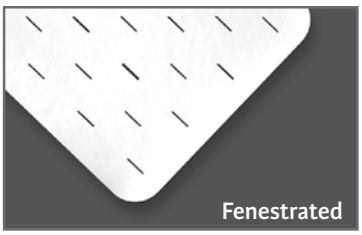


Integra® Flowable Wound Matrix
A collagen scaffold in an easy to apply syringe for use in tunneling wounds.

Integra® Wound Matrix (Thin)
A thinner collagen matrix that supports a healing environment for wound management, including partial and full-thickness wounds and donor sites.

PriMatrix® Product Portfolio





PriMatrix® Dermal Repair Scaffold
A unique dermal repair scaffold for the management of challenging wounds.

PriMatrix® Ag Dermal Repair Scaffold
A unique antimicrobial dermal scaffold containing Ionic Silver for the management of challenging wounds.

Brief Summary

Consult Package Insert for Full Prescribing Information

Integra® Dermal Regeneration Template
Integra® Meshed Dermal Regeneration Template

Description

Integra® Dermal Regeneration Template, available in Meshed and Non-Meshed configurations (Integra template) is a bilayer membrane system for skin replacement. The dermal replacement layer is made of a porous matrix of fibers of cross-linked bovine tendon collagen and glycosaminoglycan (chondroitin-6-sulfate) that is manufactured with a controlled porosity and defined degradation rate. The epidermal substitute layer is made of a thin polysiloxane (silicone) layer to control moisture loss from the wound.

Integra template is provided sterile and non-pyrogenic. The inner foil pouch and product should be handled using sterile technique. Integra template should not be re-sterilized.

Indications

Integra template is indicated for the postexcisional 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.

Integra template is also indicated for the repair of scar contractures when other therapies have failed or when donor sites for repair are not sufficient or desirable due to the physiological condition of the patient.

Integra template is also marketed as Integra® Omnigraft™ Dermal Regeneration Matrix. Omnigraft is indicated for the use in the treatment of partial and full-thickness neuropathic diabetic foot ulcers that are greater than six weeks in duration, with no capsule, tendon or bone exposed, when used in conjunction with standard diabetic care.

Contraindications

Use of Integra template is contraindicated in patients with known hypersensitivity to bovine collagen or chondroitin materials.

Integra template should not be used on clinically diagnosed infected wounds.

Warnings and Precautions

Excision of the wound must be performed thoroughly to remove all coagulation eschar and nonviable tissue. Integra template will not "take" to nonviable tissue. Leaving any remaining nonviable tissue may create an environment for bacterial growth.

Hemostasis must be achieved prior to applying Integra template. Inadequate control of bleeding will interfere with the incorporation of Integra template.

Precautions

There have been no clinical studies evaluating Integra template in pregnant women. Caution should be exercised before using Integra template in pregnant women. Such use should occur only when the anticipated benefit clearly outweighs the risk.

In clinical trials, the use of Integra template was evaluated in a small number of patients with chemical, radiation, or electrical burns. A surgeon's decision to use Integra template on these wounds should be based on their evaluation of the wound and its suitability to excisional therapy, the likelihood that a viable wound bed will be created by excision, and whether the possible benefit outweighs the risk in this patient population.

The extent of scarring associated with the use of this product has not been determined.

Adverse Events

Burn Patients

Integra template has been found to be well tolerated in 4 prospective clinical trials involving 444 burn patients. There were no reports of clinically significant immunological or histological responses to the implantation of Integra template. There were no reports of rejection of Integra template.

Adverse events reported in the Integra template clinical trials include death, sepsis, apnea, heart arrest, pneumonia, kidney failure, multisystem failure, and respiratory distress. With the exception of wound fluid accumulation, positive wound cultures, and clinical wound infection, none were directly related to the use of Integra template.

In these clinical trials, data were collected regarding wound infection. The consequences of infection at sites treated with Integra template included partial or complete loss of take (incorporation into the wound bed) of Integra template. Infection rates in sites treated with Integra template in these three clinical trials supporting the PMA ranged from 14 to 55%. The overall infection rate for the Postapproval Study was 16.3%.

Adverse events in the Postapproval study were similar to those observed in the previous clinical trials and are common in populations of critically ill burn patients regardless of type of treatment used. There were no trends noted. There were six adverse events which were rated by the investigator as being related. These events were all single occurrences except for sepsis (2). These adverse events occurring in <1% of the safety population.

Incidence of adverse events occurring in >1% of the safety population in the Post-approval Study are as follows: Sepsis (23.1%), Death (13.9%), Infection (2.8%), Thrombophlebitis (2.8%), Kidney Failure (2.8%), Necrosis (2.3%), Hemorrhage (2.3%), Heart Arrest (1.9%), Apnea (1.9%), Pneumonia (1.9%), Allergic Reaction (1.4%), Fever (1.4%), Multisystem Failure (1.4%), Atrial Fibrillation (1.4%), Gastrointestinal Hemorrhage (1.4%), Kidney Abnormal Function (1.4%).

Contracture Release Patients

The following adverse events were reported in a Reconstructive Surgery Study involving 20 patients with 30 anatomical sites and a Retrospective Reconstruction Contracture Survey involving 89 patients and 127 anatomic sites.

Incidence of adverse events in the Reconstructive Contracture Surgery Study and Retrospective Contracture Reconstruction Survey are as follows: Infection (0.0%), Fluid under Silicone Layer (0.0%), Partial graft loss (Integra) (0.0%), Failure to take (Integra) (0.0%), Shearing/Mechanical shift (3.3%), Hematoma (16.7%), Granulation tissue formation (0.0%), Delayed Healing (0.0%), Separation of the Silicone Layer (0.0%), Seroma (0.0%), Pruritis (0.0%), Epidermal autograft loss >15% (6.7%), Epidermal autograft loss <15% (23.3).

There were no infections reported in the Reconstructive Surgery Study and the reported infection rate was 20.5% in the Retrospective Contracture Reconstruction Survey. No deaths were reported.

Diabetic Foot Ulcer Patients

All adverse events that were reported in the study evaluating Omnigraft for the treatment of diabetic foot ulcers at a frequency of ≥ 1% in either cohort are presented in Table 1 in the Instructions for Use. This table includes adverse events that were both attributed to and not attributed to treatment. The most common adverse events experienced by patients treated with Omnigraft were: wound infection (15%); new, worsening, or recurring wounds (14%); pain around the wound (9%); infection beyond the wound (either cellulitis or osteomyelitis, 14%); swelling (5%); nausea (5%); worsening health condition (4%). These adverse events occurred in a similar or lower percentage of patients treated with Omnigraft compared to patients treated with standard wound care alone.
The sale of Integra template is restricted to clinicians who have completed a company sponsored training program. Product training is available at ilstraining.com

Integra® Bilayer Wound Matrix

Indications

Integra® Bilayer Matrix Wound Dressing is 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.

Contraindicatons

- This device should not be used in patients with known sensitivity to bovine collagen or chondroitin materials.
- The device is not indicated for use in third-degree burns.

Precautions

- Do not resterilize. Discard all opened and unused portions of Integra® Bilayer Matrix Wound Dressing.
- Device is sterile if the package is unopened and undamaged. Do not use if the package seal is broken.
- Discard device if mishandling has caused possible damage or contamination.
- Integra® Bilayer Matrix Wound Dressing should not be applied until excessive exudate, bleeding, acute swelling and infection are controlled.
- Debridement or excision must be done thoroughly to remove any remaining necrotic tissue that may cause infection.
- The following complications are possible with the use of wound dressings. If any of the conditions occur, the device should be removed: infection, chronic inflammation (initial application of wound dressings may be associated with transient, mild, localized inflammation), allergic reaction, excessive redness, pain or swelling.

Integra® Meshed Bilayer Wound Matrix

Indications

Integra® Meshed Bilayer Wound Matrix is 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. Integra® Meshed Bilayer Wound Matrix may be used in conjunction with negative pressure wound therapy. The device is intended for one-time use.

Contraindications

- This device should not be used in patients with known sensitivity to bovine collagen or chondroitin materials.
- This device is not indicated for use in third-degree burns.
- When used with Negative Pressure Wound Therapy, follow Contraindications for the specific Negative Pressure Wound Therapy device utilized, such as in the presence of:
- Exposed arteries, veins, organs, anastomotic sites or nerves
- Malignancy in the wound
- Untreated osteomyelitis
- Untreated malnutrition
- Necrotic tissue (with or without eschar present)
- Non-enteric and unexplored fistulas
- Sensitivity to silver (if silver dressings are used)

Warnings And Precautions

- Do not resterilize. Discard all opened and unused portions of Integra® Meshed Bilayer Wound Matrix.
- Device is sterile if the package is unopened and undamaged. Do not use if the package seal is broken.
- Discard device if mishandling has caused possible damage or contamination.
- Integra® Meshed Bilayer Wound Matrix should not be applied until excessive exudate, bleeding, acute swelling and infection are controlled.
- Debridement or excision must be done thoroughly to remove any remaining necrotic tissue that may cause infection.
- Do not stretch, expand, spread or remesh the device.
- The following complications are possible with the use of wound dressings. If any of the conditions occur, the device should be removed: infection, chronic inflammation (initial application of wound dressings may be associated with transient, mild, localized inflammation), allergic reaction, excessive redness, pain or swelling.
- When used with Negative Pressure Wound Therapy, follow Warnings and Precautions for the specific Negative Pressure Wound Therapy device utilized, such as:
- Precautions for patients who are or may be receiving anticoagulant therapy or suffering from difficult hemostasis;
- Excessive bleeding is a serious risk associated with the application of suction to wounds and may result in death or serious injury. Careful patient selection, in view of the above-stated contraindications, warnings and precautions, is essential. Carefully monitor the wound and collection circuit for any evidence of a change in the blood loss status of the patient. Notify the Physician of any sudden or abrupt changes in the volume or the color of exudate.

Brief Summary

Consult Package Insert for Full Prescribing Information

Integra® Wound Matrix

Indications

Integra® Matrix Wound Dressing is indicated for the management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, 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, skin tears) and draining wounds. The device is intended for one-time use.

Contraindicatons

- This device should not be used in patients with known sensitivity to bovine collagen or chondroitin materials.
- The device is not indicated for use in third degree burns.

Precautions

- Do not resterilize. Discard all opened and unused portions of Integra® Matrix Wound Dressing.
- Device is sterile if the package is unopened and undamaged. Do not use if the package seal is broken.
- Discard device if mishandling has caused possible damage or contamination.
- Integra® Matrix Wound Dressing should not be applied until excessive exudate, bleeding, acute swelling and infection are controlled.
- Debridement or excision must be done thoroughly to remove any remaining necrotic tissue that may cause infection.
- The following complications are possible with the use of wound dressings. If any of the conditions occur, the device should be removed: infection, chronic inflammation (initial application of wound dressings may be associated with transient, mild, localized inflammation), allergic reaction, excessive redness, pain or swelling.

Integra® Wound Matrix (Thin)

Indications

Integra® Wound Matrix (Thin) is indicated for the management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, 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, skin tears) and draining wounds. The device is intended for one-time use.

Contraindications

- This device should not be used in patients with known sensitivity to bovine collagen or chondroitin materials.
- The device is not indicated for use in third degree burns.

Precautions

- Do not resterilize. Discard all opened and unused portions of Integra Wound Matrix and Integra® Wound Matrix (Thin).
- Device is sterile if the package is unopened and undamaged. Do not use if the package seal is broken.
- Discard device if mishandling has caused possible damage or contamination.
- Integra® Wound Matrix and Integra® Wound Matrix (Thin) should not be applied until excessive exudate, bleeding, acute swelling and infection are controlled.
- Debridement or excision must be done thoroughly to remove any remaining necrotic tissue that may cause infection.
- The following complications are possible with the use of wound dressings. If any of the conditions occur, the device should be removed: infection, chronic inflammation (initial application of wound dressings may be associated with transient, mild, localized inflammation), allergic reaction, excessive redness, pain or swelling

Integra® Flowable Wound Matrix

Indications

Integra® Flowable Wound Matrix is indicated for the management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, 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, skin tears) and draining wounds. The device is intended for one-time use.

Contrindications

- This device should not be used in patients with known sensitivity to bovine collagen or chondroitin materials.
- The device is not indicated for use in third degree burns.

Precautions

- Do not resterilize. Discard all opened and unused portions of Integra® Flowable Wound Matrix.
- Device is sterile if the package is unopened and undamaged. Do not use if the package seal is broken.
- Discard device if mishandling has caused possible damage or contamination.
- Integra® Flowable Wound Matrix should not be applied until excessive exudate, bleeding, acute swelling and infection are controlled.
- Debridement or excision must be done thoroughly to remove any remaining necrotic tissue that may cause infection.
- The following complications are possible with the use of wound management products: infection, chronic inflammation (initial application of wound dressings may be associated with transient, mild, localized inflammation), allergic reaction, excessive redness, pain, or swelling. If any of these conditions occur, the device should be removed.

PriMatrix® Dermal Repair Scaffold

Description

PriMatrix is an acellular dermal tissue matrix derived from fetal bovine dermis. The device is supplied sterile in a variety of sizes to be trimmed by the surgeon to meet the individual patient's needs.

Indications

PriMatrix is intended for the management of wounds that include:

- Partial and full thickness wounds
- Pressure, diabetic, and venous ulcers
- Second-degree burns
- Surgical wounds—donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence
- Trauma wounds —abrasions, lacerations, and skin tears
- Tunneled/undermined wounds
- Draining wounds

Contraindications

PriMatrix is not designed, sold, or intended for use except as indicated.

PriMatrix should not be used for patients with a known history of hypersensitivity to collagen or bovine products.

This device is not indicated for use in third-degree burns.

Potential Complications

The following complications are possible. If any of these conditions occur, the device should be removed.

- Infection
- Chronic Inflammation
- Allergic reaction
- Excessive redness, pain, swelling, or blistering

PriMatrix® Ag Antimicrobial Dermal Repair Scaffold

Description

PriMatrix® Ag Antimicrobial is an acellular dermal tissue matrix derived from fetal bovine dermis. The device is supplied sterile in a variety of sizes to be trimmed by the surgeon to meet the individual patient's needs. The Ionic Silver content is intended to prevent microbial colonization of the device.

Ionic silver is a broad spectrum antimicrobial. PriMatrix® Ag Antimicrobial has been shown in CLSI Disc Susceptibility testing to be effective against a range of bacteria, including: Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Methicillin-Resistant Staphylococcus aureus (MRSA), Enterococcus faecium, Klebsiella pneumoniae, Listeria monocytogenes, Vancomycin-Resistant Enterococcus faecalis (VRE), Acinetobacter baumanni, and Streptococcus pyrogenes (Group A).

Indications

PriMatri® Ag Antimicrobial is intended for the management of wounds that include:

- Partial and full thickness wounds
- Pressure, diabetic, and venous ulcers
- Second-degree burns
- Surgical wounds—donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence
- Trauma wounds —abrasions, lacerations, and skin tears
- Tunneled/undermined wounds
- Draining wounds

Contraindications

PriMatrix® Ag Antimicrobial is not designed, sold, or intended for use except as indicated.

PriMatrix® Ag Antimicrobial should not be used for patients with a known history of hypersensitivity to silver, collagen, or bovine products.

This device is not indicated for use in third-degree burns.

Warnings and Precautions

Silver-containing compounds are known to cause a condition known as argyria, a silver-induced darkening of the skin. Frequent or prolonged use of PriMatrix® Ag Antimicrobial may result in skin discoloration.

Potential Complications

The following complications are possible. If any of these conditions occur, the device should be removed.

- Infection
- Chronic Inflammation
- Allergic reaction
- Excessive redness, pain, swelling, or blistering

Integra®
Tissue Technologies

Integra Dermal Matrices

Integra Dermal Regeneration Template (DRT)

	Integra DRT	Integra Meshed DRT
Size	Product Code	Product Code
5cm x 5cm	32021	MDRT2021
10cm x 12.5cm	34051	MDRT4051
10cm x 25cm	34101	MDRT4101
20cm x 25cm	38101	MDRT8101

Integra Single Layer Wound Matrix (without Silicone Layer)

	Integra Wound Matrix	Integra Wound Matrix (Thin)*
Size	Product Code	Product Code
5cm x 5cm	52021	52021T
10cm x 12.5cm	54051	54051T
10cm x 25cm	54101	54101T
20cm x 25cm	58101	-

*Integra Wound Matrix (Thin) is approximately 0.4mm thick, half the thickness of Integra Wound Matrix.

Integra Bilayer Wound Matrix (BWM)

	Integra BWM	Integra Meshed BWM
Size	Product Code	Product Code
5cm x 5cm	BMW2021	MWM2021
10cm x 12.5cm	BMW4051	MWM4051
10cm x 25cm	BMW4101	MWM4101
20cm x 25cm	BMW8101	MWM8101

Integra Flowable Wound Matrix

Size	Product Code
3cc	FWD301

Integra PriMatrix Scaffolds

PriMatrix® Dermal Repair Scaffold and PriMatrix Ag Antimicrobial Dermal Repair Scaffold

	Integra PriMatrix			Integra PriMatrix Ag		
Size	Solid	Fenestrated	Meshed	Solid	Fenestrated	Meshed
6cm x 6cm	607-001-660	607-004-660	607-005-660	607-101-660	607-104-660	607-105-660
8cm x 8cm	607-001-880	607-004-880	607-005-880	607-101-880	607-104-880	607-105-880
8cm x 12cm	607-001-812	-	607-005-812	607-101-812	607-104-812	607-105-812
10cm x 12cm	607-001-112	-	-	607-101-112	-	607-105-112
10cm x 25cm	607-001-125	-	607-005-125	607-101-125	607-104-125	607-105-125
20cm x 25cm	607-001-225	-	607-005-225	607-101-225	607-104-225	-

Availability of these products might vary from a given country or region to another, as a result of specific local regulatory approval or clearance requirements for sale in such country or region.
- Non contractual document. The manufacturer reserves the right, without prior notice, to modify the products in order to improve their quality.
- Warning: Applicable laws restrict these products to sale by or on the order of a physician.
- Consult product labels and inserts for any indication, contraindications, hazards, warnings, precautions, and instructions for use.

For more information or to place an order, please contact:

United States, Canada, Asia, Pacific, Latin America
USA 800-654-2873 ▪ 888-980-7742 fax
International +1 609-936-5400 ▪ +1 609-750-4259 fax
integralife.com

INTEGRA®
LIMIT UNCERTAINTY