

STRATAGRAFT- allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat cellular sheet

Stratatech Corporation

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use STRATAGRAFT® safely and effectively. See full prescribing information for STRATAGRAFT.

STRATAGRAFT (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat), for topical use
Initial U.S. Approval: 2021

RECENT MAJOR CHANGES

- Warnings and Precautions (5.4)

Removed restriction regarding donation of tissues, breast milk, ova, sperm, or organs for transplantation. 01/2024

INDICATIONS AND USAGE

STRATAGRAFT (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat) is an allogeneic cellularized scaffold product indicated for the treatment of adults with thermal burns containing intact dermal elements for which surgical intervention is clinically indicated (deep partial-thickness burns). (1)

DOSAGE AND ADMINISTRATION

For topical application only.

STRATAGRAFT is applied to a surgically prepared wound bed. The number of STRATAGRAFT constructs applied will vary depending on the size of the wound bed. STRATAGRAFT constructs may be trimmed to accommodate the size and shape of the wound bed. Each STRATAGRAFT construct is for application to a single patient only. (2.1)

DOSAGE FORMS AND STRENGTHS

STRATAGRAFT is an off-white rectangular sheet of approximately 100 cm² (approximately 8 cm by 12.5 cm), consisting of a viable, bioengineered, allogeneic cellularized scaffold product derived from keratinocytes grown on gelled collagen containing dermal fibroblasts. (3)

CONTRAINDICATIONS

Do not use in patients with known allergies to murine collagen or products containing ingredients of bovine or porcine origin. (4)

WARNINGS AND PRECAUTIONS

- Potential Sensitivity (5.1)
- Hypersensitivity Reactions (5.2)
- Transmission of Infectious Diseases (5.3)
- Donation of Blood, Organs, Tissues, or Cells (5.4)

ADVERSE REACTIONS

The most common ($\geq 2\%$) adverse reactions were itching (pruritus), blisters, hypertrophic scar, and impaired healing. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Customer Care at 1-877-647-2239 or <http://www.mallinckrodt.com/stratatech> or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 1/2024

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

STRATAGRAFT is an allogeneic cellularized scaffold product indicated for the treatment of adults with thermal burns containing intact dermal elements for which surgical

intervention is clinically indicated (deep partial-thickness burns).

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

STRATAGRAFT is for topical application to a prepared wound bed (excision/debridement).

A STRATAGRAFT construct is an approximately 100 cm² (approximately 8 cm by 12.5 cm) off-white rectangle. A STRATAGRAFT construct may be trimmed to fit the shape and size of the wound area. The surface area of STRATAGRAFT to be applied should be equal to the surface area of the wound to be treated.

Multiple constructs may be applied to cover large wound areas. If multiple constructs are required to cover the wound area, abut the STRATAGRAFT constructs, and it is not necessary to overlap the edges.

Each construct is for application to a single patient only.

2.2 Preparation

STRATAGRAFT is to be prepared in an appropriate surgical environment.

STRATAGRAFT is supplied as follows:

The STRATAGRAFT carton contains a laminated foil pouch (Figure 1).

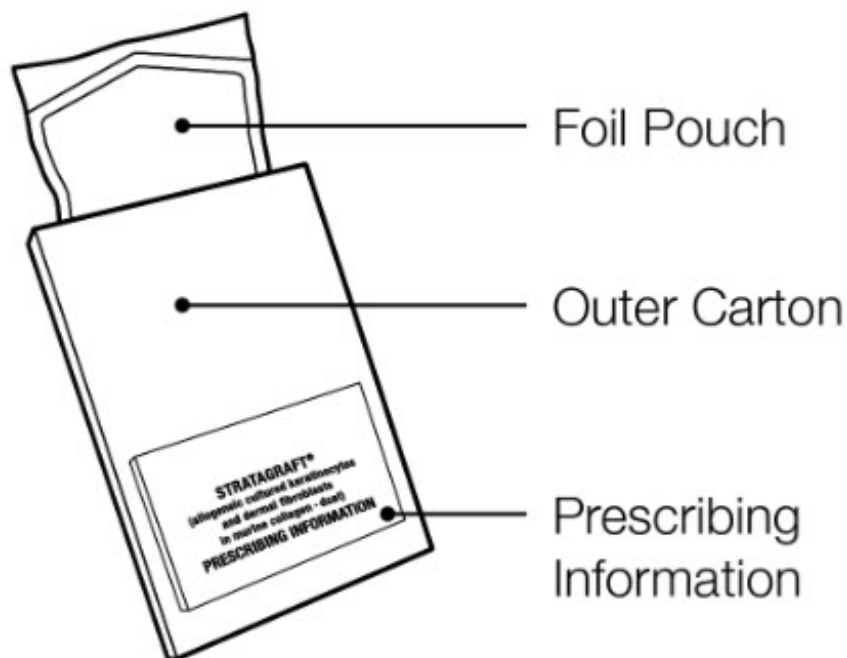


Figure 1: STRATAGRAFT carton and foil pouch

Within the pouch is the STRATAGRAFT Product Dish that contains STRATAGRAFT on a polystyrene insert tray (Figure 2).

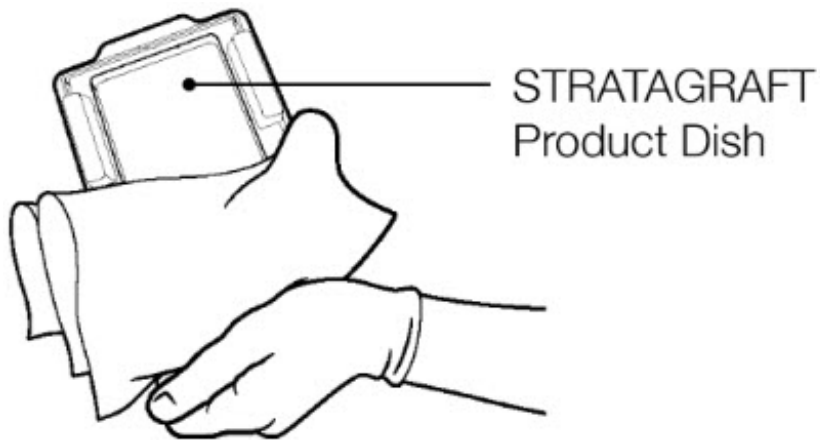


Figure 2: STRATAGRAFT Product Dish containing the STRATAGRAFT construct

Inside the STRATAGRAFT Product Dish is the polystyrene insert tray that contains the STRATAGRAFT construct (Figure 3).

STRATAGRAFT is loosely adhered to a polycarbonate membrane contained within a polystyrene insert tray frame.

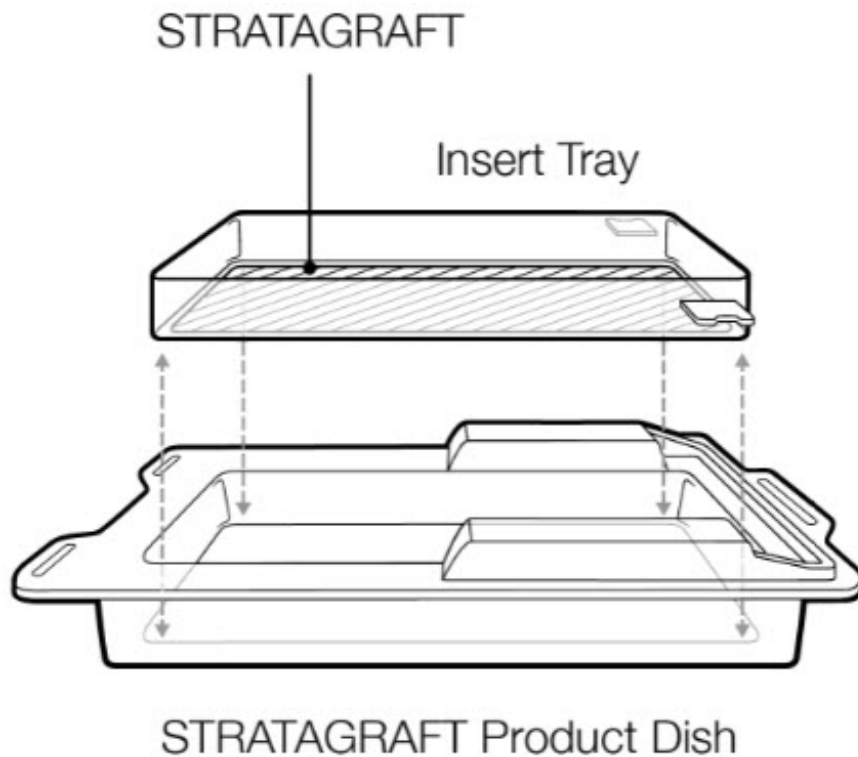


Figure 3: STRATAGRAFT Product Dish and Insert Tray containing STRATAGRAFT

Hold Solution is provided in a plastic bottle contained within a laminated, foil pouch [see *Description (11)*] (Figure 4).

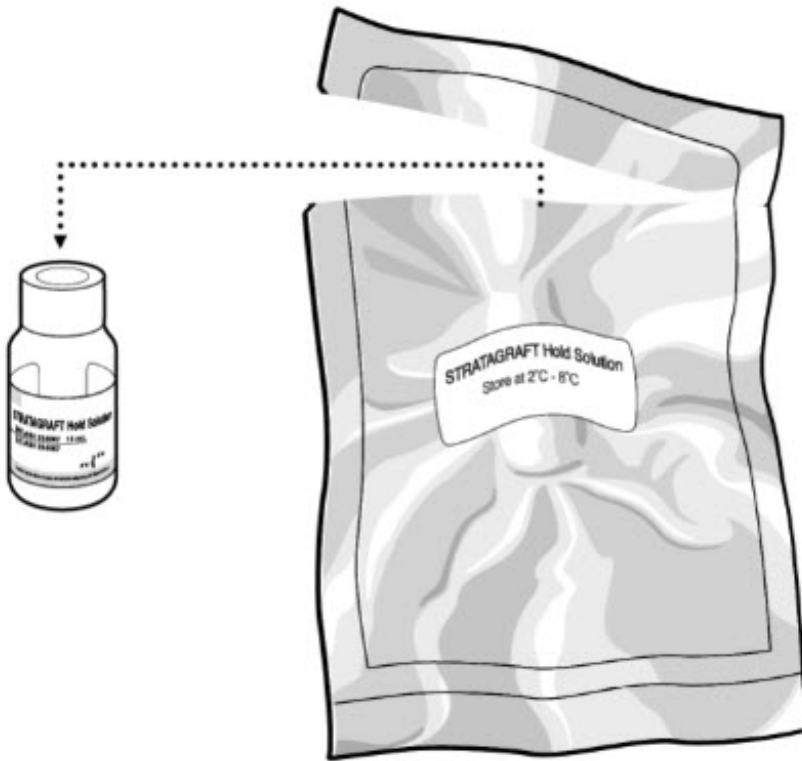
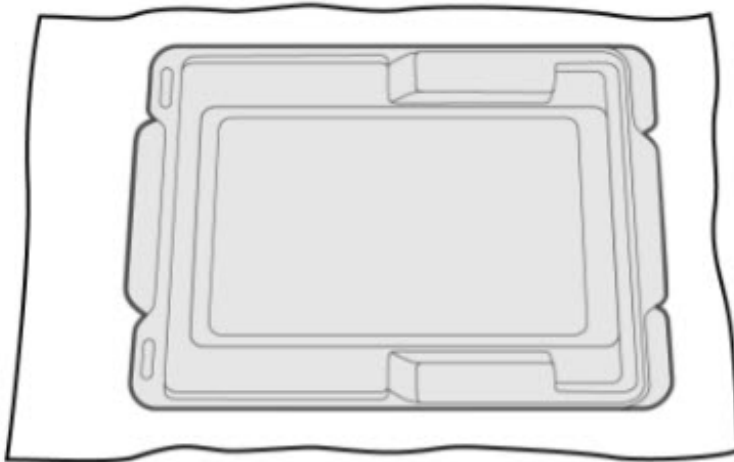


Figure 4: Hold Solution within a laminated foil pouch

The Hold Dish is contained in a clear pouch (Figure 5) and consists of identical top and bottom portions (Figure 6).



■ Sterile □ Nonsterile

Figure 5: Hold Dish contained within a clear pouch



Figure 6: Hold Dish handled in sterile field

Supplies:

The following supplies are not included but are needed for the preparation:

- Mesher: STRATAGRAFT is compatible with autograft meshing devices (crushing or noncrushing) and can be meshed at ratios up to 1:1
- Warming oven/cabinet or water bath

Preparation Instructions:

Following wound bed preparation (excision/debridement), determine the number of STRATAGRAFT constructs that need to be thawed.

The following instructions are for preparing one STRATAGRAFT construct. Two operators (one sterile operator and one non-sterile operator) are required.

If two or more STRATAGRAFT constructs are required, prepare them in one or more batches. STRATAGRAFT construct preparation should take approximately 20 minutes for a single construct or group of constructs.

1. Remove the Hold Solution bottle from the laminated, foil pouch. The Hold Solution is a clear liquid. Do not use the Hold Solution if the contents of the bottle appear cloudy or turbid. Use one bottle of Hold Solution for one construct being prepared for placement.
2. Warm the Hold Solution in a warming oven/cabinet or a water bath.
Option 1:
Place Hold Solution bottle in a warming oven/cabinet operating at 35°C to 39°C (95°F to 102°F) for AT LEAST 45 minutes prior to use.
Option 2:
Place Hold Solution bottle in a water bath at 35°C to 39°C (95°F to 102°F) for AT LEAST 15 minutes prior to use. Do not submerge the cap or threads of the bottle.
3. The nonsterile operator peels open the seal of the Hold Dish pouch and aseptically presents the Hold Dish to the sterile operator for placement in the sterile field (Figure

7). The sterile operator aseptically removes the Hold Dish presented by the nonsterile operator (Figure 7) and places it in the sterile field (Figure 8).



Figure 7: Sterile operator (gray gloves) removes the sterile Hold Dish presented by the nonsterile operator (white gloves)

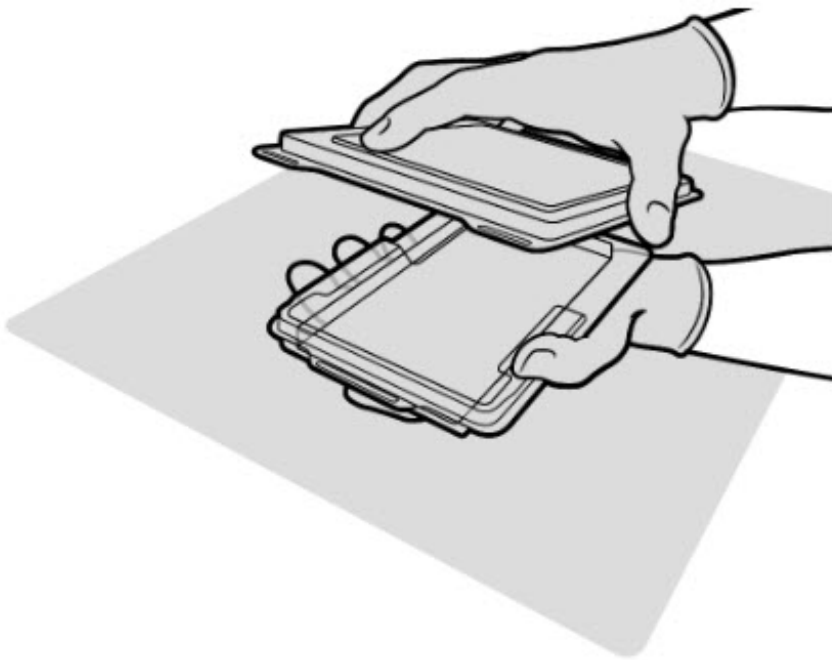


Figure 8: Sterile operator places the Hold Dish in the sterile field (gray rectangle)

4. Remove STRATAGRAFT carton from the freezer or dry ice.

Note: Steps 4-11 must be completed within 10 minutes of removal of STRATAGRAFT from the freezer or dry ice.

5. Open the STRATAGRAFT carton and remove the foil pouch (Figure 9).



Figure 9: Remove foil pouch

6. Peel the foil pouch open and carefully remove the closed STRATAGRAFT Product Dish (Figure 10).

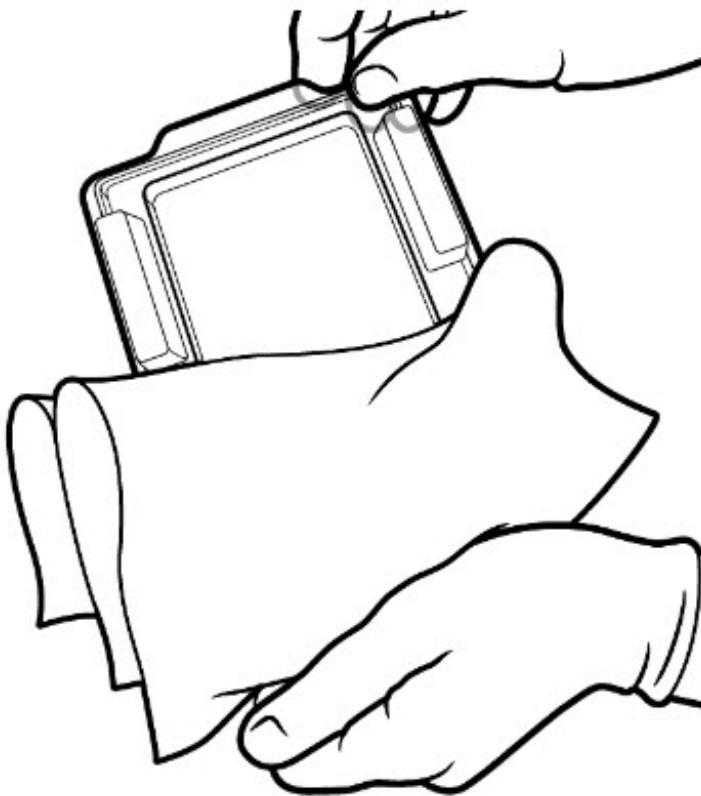


Figure 10: Remove closed STRATAGRAFT Product Dish from foil pouch

7. The unopened STRATAGRAFT Product Dish containing the construct may be placed on a flat surface outside of the sterile field (Figure 11).

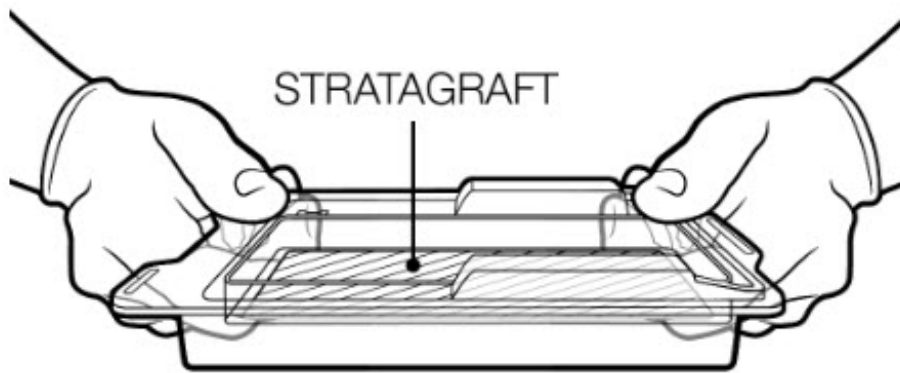


Figure 11: Placement of STRATAGRAFT Product Dish in a nonsterile area

8. The nonsterile operator pours one entire bottle of warmed Hold Solution into one sterile Hold Dish using aseptic technique per institutional procedures, immediately after removing the warmed Hold Solution from the warming device (Figure 12).

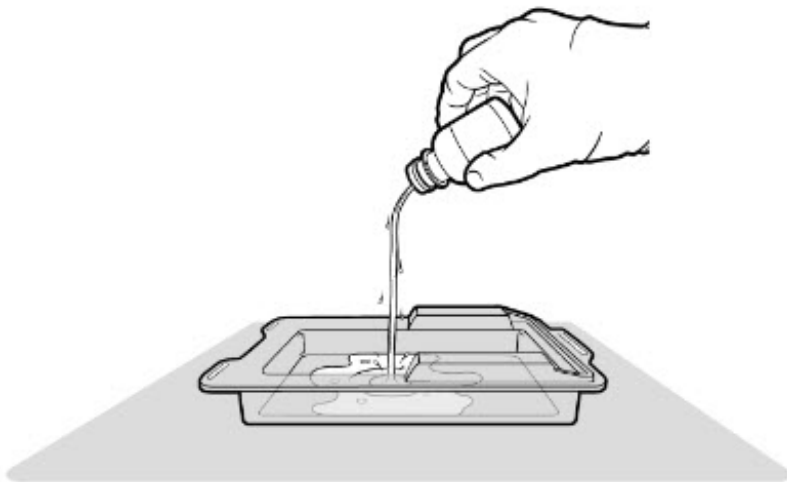


Figure 12: Nonsterile operator aseptically pours Hold Solution into the Hold Dish

9. The nonsterile operator removes the STRATAGRAFT Product Dish lid and holds the STRATAGRAFT Product Dish without contacting the insert tray (Figure 13).

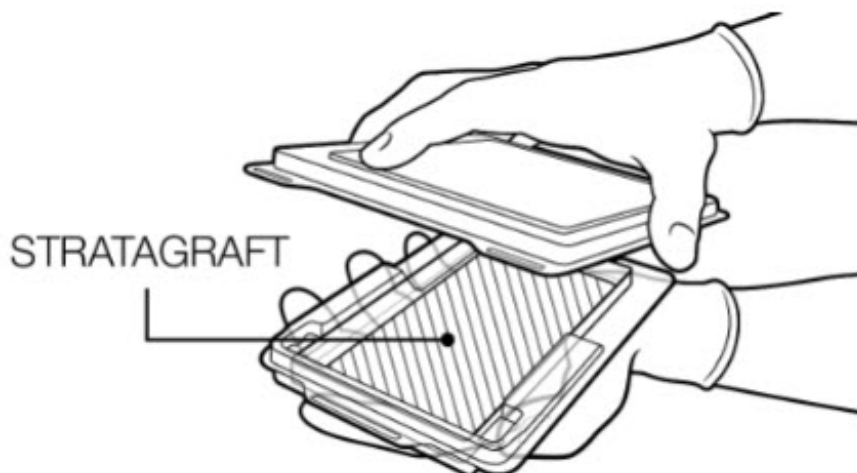
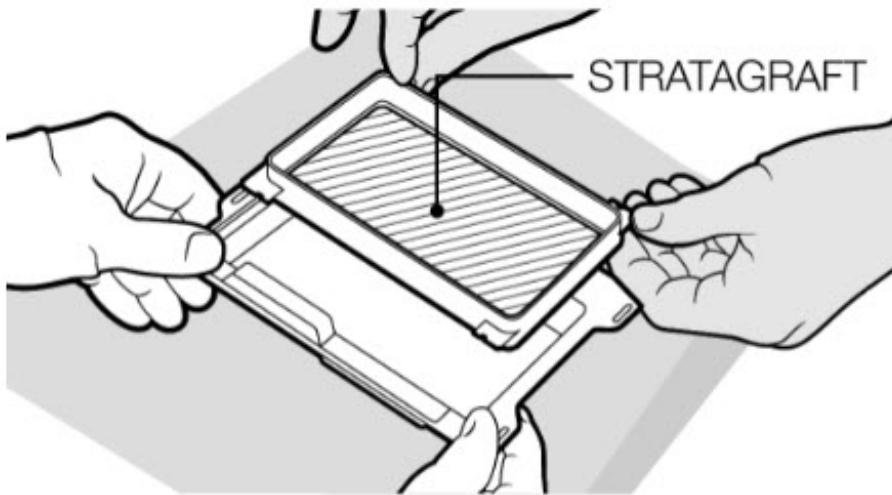


Figure 13: Nonsterile operator (white gloves) opens the STRATAGRAFT Product Dish

10. The sterile operator aseptically removes the STRATAGRAFT insert tray from the STRATAGRAFT Product Dish using either sterile forceps or sterile, gloved fingers (Figure 14).



■ Sterile □ Nonsterile

Figure 14: Sterile operator (gray gloves) removes the STRATAGRAFT insert tray

11. The sterile operator uses sterile, gloved fingers to place the insert tray into the Hold Dish beginning with one edge and lowering it to the opposite edge to minimize trapping bubbles beneath the insert tray (Figure 15).

If bubbles become trapped beneath the insert tray, gently lift the insert tray and place it slowly back down into the Hold Solution.

12. Maintain the STRATAGRAFT construct in the Hold Solution for a minimum of 15 minutes to a maximum of 4 hours.

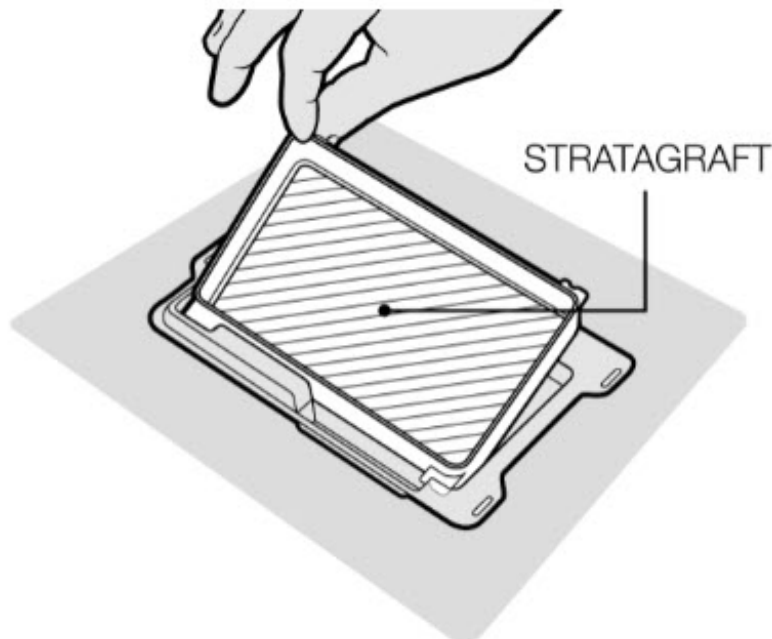


Figure 15: Sterile operator places Insert Tray into the Hold Dish

13. Remove STRATAGRAFT from the polycarbonate membrane of the insert tray with sterile, gloved fingers or a pair of atraumatic forceps and mesh the STRATAGRAFT up to a 1:1 ratio.

Do not allow STRATAGRAFT to dry. Moisten the mesher/tissue board as needed to prevent adhesion and maintain STRATAGRAFT moisture using Hold Solution, sterile 0.9% normal saline, or lactated Ringer's solution.

STRATAGRAFT is packaged with the dermal (shiny) side in contact with the polycarbonate membrane. The construct may be meshed (Figure 16) with either side up; note which side is the dermis (shiny) and which side is the epidermis (matte) prior to meshing and placement.

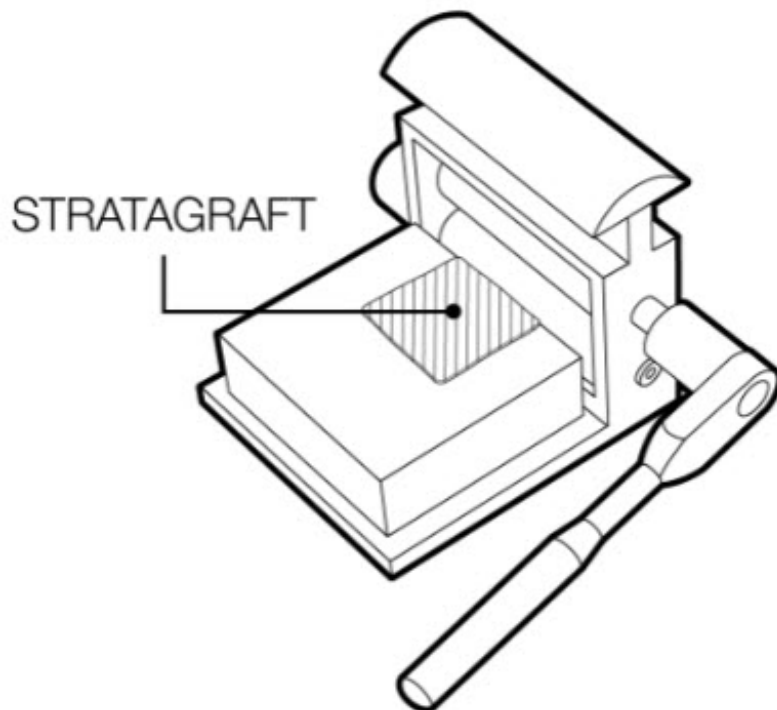


Figure 16: Meshing STRATAGRAFT

2.3 Administration

STRATAGRAFT is applied in appropriate aseptic conditions by a trained healthcare provider.

Follow the steps below for topical application of STRATAGRAFT:

1. If utilizing fibrin glue to anchor STRATAGRAFT, apply prior to placing the meshed STRATAGRAFT on the prepared wound bed. If utilizing anchoring methods other than fibrin glue, start with step 2.
2. Place the meshed STRATAGRAFT with the dermal (shiny) side down in contact with the patient's prepared wound bed. Ensure the epidermal (matte) side is facing up. Abut the constructs when placing multiple STRATAGRAFT constructs. Overlapping the STRATAGRAFT construct edges is not required.

Note: If the area to be treated is smaller than one construct, trim excess STRATAGRAFT before or after anchoring to the wound bed. Ensure that STRATAGRAFT has contact across the entire surface of the wound bed. Do not stretch or expand STRATAGRAFT, as doing so may degrade the structural integrity of

STRATAGRAFT.

- Anchor STRATAGRAFT with staples, tissue adhesive such as cyanoacrylate, or sutures to keep STRATAGRAFT from dislodging. Place a porous, nonadherent contact dressing over STRATAGRAFT and leave the dressing in place for one week before changing.
- Place a second layer of dressing that does not contain silver [see *Drug Interactions (7.2)*].
- Placement of an outer bolster or wrap that keeps STRATAGRAFT from moving as clinically appropriate is at the discretion of the physician.

3 DOSAGE FORMS AND STRENGTHS

STRATAGRAFT is an off-white, rectangular sheet of approximately 100 cm² (approximately 8 cm by 12.5 cm) consisting of a viable, bioengineered, allogeneic cellularized scaffold product derived from keratinocytes grown on gelled collagen containing dermal fibroblasts.

4 CONTRAINDICATIONS

Do not use in patients with known allergies to murine collagen or products containing ingredients of bovine or porcine origin [See *Description (11)*].

5 WARNINGS AND PRECAUTIONS

5.1 Potential Sensitivity

STRATAGRAFT contains glycerin. Avoid glycerin in patients with known sensitivity (irritant reaction) to glycerin.

5.2 Hypersensitivity Reactions

Severe hypersensitivity reactions may occur [see *Contraindications (4)*]. Monitor for both early and late symptoms and signs of hypersensitivity reaction following STRATAGRAFT application, and treat according to standard medical practice.

5.3 Transmission of Infectious Diseases

STRATAGRAFT contains cells from human donors and may transmit infectious diseases or infectious agents, e.g., viruses, bacteria, or other pathogens, including the agent that causes transmissible spongiform encephalopathy (TSE, also known as Creutzfeldt-Jakob disease (CJD) or variant CJD).

STRATAGRAFT is a xenotransplantation product because of a historic exposure of the keratinocyte cells to well-characterized mouse cells. The cell banks have been tested and found to be free of detectable adventitious agents and mouse cells are no longer used in the manufacture of STRATAGRAFT [see *Description (11)*].

STRATAGRAFT was established to be free of detectable pathogens using FDA-recommended characterization procedures and tests including molecular and analytical testing.

Transmission of infectious diseases or agents by STRATAGRAFT has not been reported.

5.4 Donation of Blood, Organs, Tissues, or Cells

Recipients of xenotransplantation products such as STRATAGRAFT are generally not eligible to donate whole blood or blood components, including source plasma and source leukocytes. However, individual blood collection establishments may request an exception.

STRATAGRAFT recipients who otherwise meet donor requirements are eligible to donate human cells, tissues, or cellular or tissue-based products (HCT/Ps), human milk, ova, sperm, or organs for transplantation.

6 ADVERSE REACTIONS

The most common adverse reactions (incidence $\geq 2\%$) were itching (pruritus), blisters, hypertrophic scar and impaired healing. (Table 1).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety data described in this section reflect exposure to STRATAGRAFT in four randomized, within-subject-controlled studies conducted in the United States, including two clinical studies in patients with deep partial-thickness thermal burns (Study 1 and Study 2) and two clinical studies in patients with full-thickness complex skin defects due to thermal burns or other causes. A total of 119 adult patients (101 patients with deep partial-thickness thermal burn, and 18 patients with full-thickness complex skin defects) received topical application of STRATAGRAFT. The patient population ranged in age from 19 to 79 years (mean age 43 years). Each patient received topical application of STRATAGRAFT at one wound site and either autografting (104 patients) or cadaver allografts (15 patients) as inpatient comparators at another wound site. The most frequent adverse reactions (incidence $\geq 2\%$) observed in the 4 studies are summarized in Table 1. No patients discontinued study participation due to adverse reactions.

Table 1: Adverse Reactions Reported at a Frequency of $\geq 2\%$ Following Treatment with STRATAGRAFT (N=119)

Adverse Reaction	Patients n (%)[*]
Pruritus (Itching)	13 (11)
Blisters	5 (4)
Hypertrophic Scar	3 (3)
Impaired Healing	3 (3)

* If a patient had more than one incidence of an adverse reaction, the patient was counted only once.

Overall, the safety profile of STRATAGRAFT with regard to wound-related events,

including erythema, swelling, local warmth and wound site infections, was similar to that of autografting in these studies.

There were no reports of rejection of STRATAGRAFT in the clinical studies.

The safety of STRATAGRAFT beyond 12 months was not evaluated in the clinical studies.

7 DRUG INTERACTIONS

7.1 Mafenide Acetate

The use of mafenide acetate is not recommended following application of STRATAGRAFT. This topical antimicrobial has been shown to reduce keratinocyte viability and disrupt the integrity of tissue-engineered human skin substitutes composed of NIKS[®] keratinocytes or primary keratinocytes.¹

7.2 Silver-Containing Antimicrobials and Dressings

The use of silver-containing antimicrobials or dressings is not recommended because in vitro data suggest silver may decrease the viability of keratinocytes and human dermal fibroblasts.²

7.3 Chlorhexidine

The use of antimicrobial chlorhexidine solution on the wound following application of STRATAGRAFT is not recommended. This material has been shown to be toxic to keratinocytes and human dermal fibroblasts.³

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data regarding STRATAGRAFT use in pregnant women. No animal reproductive and developmental toxicity studies have been conducted with STRATAGRAFT to assess whether it can cause fetal harm when administered to a pregnant woman.

In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

8.2 Lactation

Risk Summary

There is no information available on the presence of STRATAGRAFT in human milk, the effect on the breastfed infant, or the effect on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for STRATAGRAFT and any potential adverse effects on the breast-fed infant from STRATAGRAFT or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of STRATAGRAFT in pediatric patients (< 18 years) have not been established.

8.5 Geriatric Use

Eight patients aged 65 years and older were enrolled in Study 1. Although no differences in safety or efficacy were observed between patients aged 65 years and older and younger patients, the number of patients aged 65 years and older was not sufficient to determine whether they responded differently from younger patients.

11 DESCRIPTION

STRATAGRAFT is a viable, bioengineered, allogeneic, cellularized scaffold product that contains a fully-stratified epithelial layer comprised of differentiated, multilayered, epidermal keratinocytes from a single human donor. The keratinocytes are grown on a purified murine Type I collagen matrix embedded with fibroblasts from a second human donor.

STRATAGRAFT is produced from well-characterized human keratinocyte and fibroblast cell banks that contain no detectable pathogens. The cells are metabolically active allogeneic NIKS keratinocytes and dermal fibroblasts.

STRATAGRAFT is a xenotransplantation product because the keratinocyte component was originally derived in the presence of a mouse cell line. However, mouse cells are no longer used to manufacture STRATAGRAFT. No mouse cells or mouse-derived infectious agents are detectable in STRATAGRAFT.

STRATAGRAFT product manufacture includes reagents derived from animal materials, including murine collagen, calf serum, porcine trypsin and purified bovine serum albumin.

STRATAGRAFT construct is loosely adherent to a supportive polycarbonate membrane insert and treated in glycerin-containing media. Each cryopreserved STRATAGRAFT construct is supplied with Hold Solution and Hold Dish, which are used for preparing STRATAGRAFT [*see How Supplied/Storage and Handling (16)*].

The Hold Solution is a cell-culture medium that is not supplemented with growth factors.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

STRATAGRAFT is an allogeneic cellularized scaffold product containing metabolically active cells that produce and secrete a variety of growth factors and cytokines. In vitro studies have shown that STRATAGRAFT secretes human growth factors and cytokines, and contains human extracellular matrix proteins. Growth factors, cytokines, and extracellular matrix proteins are known to be involved in wound repair and regeneration.

STRATAGRAFT does not remain permanently engrafted, but is replaced by the patient's own cells over time, eliminating or reducing the need for autografting to attain definitive closure of the majority of treated wounds. A total of 85 patients in Study 1 and Study 2

were evaluated at 3 months for persistence of allogeneic STRATAGRAFT DNA at the treatment site. STRATAGRAFT-associated DNA was not detected in these patients.

12.2 Pharmacodynamics

The pharmacodynamic effects of STRATAGRAFT are not known.

12.3 Pharmacokinetics

The pharmacokinetic effects of STRATAGRAFT are not known.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No animal studies were conducted to evaluate the effects of STRATAGRAFT on carcinogenesis, mutagenesis, or impairment of fertility. Evaluation of tumorigenic potential consisted of the following studies:

Karyotype Stability

The NIKS keratinocytes and human dermal fibroblasts contained in STRATAGRAFT are karyotypically stable.

In Vitro Studies

The NIKS keratinocytes and human dermal fibroblasts cultured for 43 and 6 passages, respectively, did not exhibit anchorage-independent growth (a standard assay that evaluates the potential for cellular transformation). STRATAGRAFT contains NIKS keratinocytes and human dermal fibroblasts that are at passage 40 and 7, respectively.

In Vivo Studies

A single subcutaneous injection of NIKS keratinocytes into immunodeficient mice did not result in tumor formation by 23 weeks post-injection. Topical application of STRATAGRAFT on full-thickness excisional wounds in immunodeficient mice did not result in tumor formation by 20 weeks post-dose.

Toxicity

No evidence of local or systemic toxicity was observed in immunocompromised athymic nude mice exposed to STRATAGRAFT. Administration of 14 cm² (approximately 25% Total Body Surface Area) of STRATAGRAFT was applied to full-thickness excisional wounds, followed by assessment for local or systemic toxicity from 90 to 140 days (13 to 20 weeks).

14 CLINICAL STUDIES

The efficacy of STRATAGRAFT in adult patients with thermal burns containing intact dermal elements for which surgical excision and autografting were clinically indicated was evaluated in two randomized, open-label, inpatient-controlled, multicenter clinical studies of 12 months duration (Study 1 and Study 2). In both studies, two comparable wound sites of each patient were selected and randomized to receive either topical application of STRATAGRAFT or autograft. Autografts served as the inpatient control.

Study 1 enrolled 71 adult patients with acute thermal burns containing intact dermal elements (deep partial-thickness burns) involving 3 to 37% total body surface area (TBSA). The time from burn to study treatment was 1 to 18 days. The size of the STRATAGRAFT-treated wound was 12 to 960 cm². The mean age was 44 years (19 to 79 years) with 78% male. Seventy-eight percent of patients were White, 20% were Black or African-American, and the remainder were Asian or Other. Efficacy was established on the basis of: (1) the difference in the percent area of the STRATAGRAFT treatment site and the control autograft treatment site that required autografting by 3 months following treatment, and (2) the proportion of patients achieving durable wound closure of the STRATAGRAFT treatment site at 3 months without autograft placement. Durable wound closure at 3 months was defined as wound closure at two consecutive study visits at least 2 weeks, but no more than 5 months apart, and including or encompassing the 3-month time point.

The difference in the percent area of STRATAGRAFT and control autograft treatment sites that required autografting by 3 months was 98%±17% (p<0.0001). Three patients had part or all of their STRATAGRAFT treatment site autografted by 3 months, and two of the three patients also had part or all of their autograft control study site re-grafted. Donor site harvest was eliminated for 96% (68/71) of STRATAGRAFT-treated burn sites. As a result, pain and scarring were significantly reduced at these potential donor sites that were spared and remained intact (p<0.0001). The cosmesis was similar between STRATAGRAFT-treated sites and autograft-treated sites.

The proportion of patients achieving durable closure of the STRATAGRAFT treatment site at 3 months without autograft placement was 83% (95% CI: 74, 92). The proportion of patients achieving durable closure of the autograft control treatment site at 3 months without additional autograft placement was 86% (95% CI: 78, 94).

In subgroups of race, ethnicity, sex, age, burn size in percentage of TBSA, STRATAGRAFT treatment area, and Baux scores (a scoring system to estimate mortality due to burn), efficacy results were in general consistent with the results in the overall Study 1 population.

Study 2 enrolled 30 adult patients with acute thermal burns containing intact dermal elements (deep partial-thickness burn) and involving 3 to 49% TBSA. The time from burn to study treatment ranged from 3 to 13 days. The size of the STRATAGRAFT-treated wound was 52 to 440 cm². The mean age was 41 years (21 - 63 years). Ninety-three percent of patients were White and 7% were Black or African-American. Men accounted for 70% of the population.

Efficacy was evaluated on the basis of: (1) the percent area of STRATAGRAFT treatment site autografted by 28 days after STRATAGRAFT treatment, and (2) the proportion of treatment sites that achieved complete wound closure by 3 months. Complete wound closure was defined as ≥95% re-epithelialization in the absence of drainage.

No STRATAGRAFT treatment site required autografts by 28 days. Between 28 days and 3 months, one patient had both the STRATAGRAFT treatment site and the autograft site treated subsequently with autograft, and a second patient had 25% of the STRATAGRAFT treatment site autografted. At 3 months, 93.1% of STRATAGRAFT treatment sites and 100% of autograft treatment sites achieved complete wound closure. All STRATAGRAFT treatment sites that achieved complete wound closure at 3 months remained closed when evaluated at 6 months and 12 months after treatment.

15 REFERENCES

1. Gibson AL, Schurr MJ, Schlosser SJ, Comer AR, Allen-Hoffmann BL. Comparison of therapeutic antibiotic treatments on tissue-engineered human skin substitutes. *Tissue Eng Part A*. 2008 May; 14(5):629-38.
2. Nešporová K, Pavlík V, Šafránková B, et al. Effects of wound dressings containing silver on skin and immune cells. *Scientific Reports*. 2020 Sep;10(1):15216.
3. Boyce ST, Warden GD, Holder IA. Cytotoxicity testing of topical antimicrobial agents on human keratinocytes and fibroblasts for cultured skin grafts. *J Burn Care Rehabil*. 1995 Mar-Apr;16(2 Pt 1):97-103.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

STRATAGRAFT is an approximately 100 cm² rectangular sheet (approximately 8 cm by 12.5 cm) - (NDC 73612-200-01), loosely adherent to a polycarbonate membrane within a polystyrene frame and packaged in a sealed foil pouch contained within a carton.

STRATAGRAFT is shipped on dry ice. The Hold Solution and Hold Dish are packaged separately and shipped at ambient temperature.

16.2 Storage and Handling

Store STRATAGRAFT between -70°C and -90°C (-94°F to -130°F).

Store the Hold Solution between 2°C and 8°C (36°F and 46°F).

Store Hold Dishes at ambient temperature.

Do not use any of the above components if they have been compromised.

Dispose of unused STRATAGRAFT as surgical biohazardous waste in accordance with local requirements.

Dispose of materials that have come into contact with STRATAGRAFT as surgical biohazardous waste in accordance with local requirements.

Contact Customer Care at 1-877-647-2239 for further instructions.

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Patient Information).

Advise patients of the following risks:

- Potential Sensitivity to Glycerin
Inform patients that STRATAGRAFT contains glycerin and could cause irritation if patients are sensitive to glycerin. Advise patients to contact their healthcare provider immediately if their skin develops symptoms such as rash or itching [*see Warnings and Precautions (5.1)*].
- Hypersensitivity Reactions
Inform patients that hypersensitivity reactions are rare but may occur [*see Contraindications (4)*]. Systemic symptoms associated with immediate

hypersensitivity reactions may include dizziness or trouble breathing and are likely to occur within the first few hours after exposure. Late hypersensitivity reactions may include itching, hives, or rash. Advise patients to contact their healthcare provider if they develop symptoms of a hypersensitivity reaction [see *Warnings and Precautions (5.2)*].

- **Transmission of Infectious Diseases**

Inform patients that STRATAGRAFT may transmit infectious diseases. Advise patients to contact their healthcare provider immediately if they develop any symptoms suggestive of infection, such as redness or warmth, increased discharge / drainage or pain of skin where STRATAGRAFT is applied [see *Warnings and Precautions (5.3)*].

Xenotransplantation nature of STRATAGRAFT

Inform patients that mouse cells were used in the early development of the NIKS keratinocyte master cell bank. Therefore, STRATAGRAFT is a xenotransplantation product, even though mouse cells are no longer used in the manufacture of STRATAGRAFT. Please see the attached patient instruction sheet for additional instruction.

After application of STRATAGRAFT, provide the following post-procedure instructions:

- Expect itching, redness, swelling, bruising, and/or pain at the treatment site during the healing process. Contact the healthcare provider if experiencing fever, increased drainage, pain and/or swelling or any other adverse effect at or around the treatment site.
- Do not disturb the surgical dressing or STRATAGRAFT. Contact the healthcare provider if STRATAGRAFT is dislodged. Leave the post-procedure surgical dressing in place unless instructed otherwise by the healthcare provider [see *Dosage and Administration (2.3)*].
- Avoid touching the surgical dressing or treated areas until instructed otherwise by the healthcare provider [see *Dosage and Administration (2.3)*].
- Keep the dressing(s) dry [see *Dosage and Administration (2.3)*].

Manufactured and Distributed by:

Stratatech Corporation

510 Charmany Drive, Suite 150

Madison, WI 53719

Ph.: 1-877-647-2239

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Part number SPC-RM-0159 Rev.3

allogeneic cultured keratinocytes and dermal fibroblasts

in murine collagen-dsat

STRATAGRAFT®

Patient Information

This guide is to help you understand STRATAGRAFT and its use for the treatment of

burns. This guide does not take the place of talking with your healthcare provider about STRATAGRAFT. If you have questions about STRATAGRAFT, talk to your healthcare provider.

STRATAGRAFT is a biologic drug approved by the Food and Drug Administration (FDA) for use in adult patients who have a specific type of burn. STRATAGRAFT is placed onto your burn by your healthcare provider. Over time, your skin cells should grow to replace the skin cells lost to the burn.

STRATAGRAFT is available by prescription only.

U.S. License Number: 2144

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Glossary/Definitions of Terms

Autograft: a piece of your own skin tissue used to replace skin lost to burn.

Bilayer construct: product containing two different layers of skin cells in a format similar to human skin.

Biologic drug: a drug product that is produced from living organisms or contains components of living organisms.

Bovine: relating to cattle.

Dermal fibroblasts: a type of cell from the inner layer of skin that helps the skin to recover from injury.

ex-vivo: outside of the living body.

Hypersensitivity: condition in which there is an exaggerated response by the body to something foreign.

Infectious agent: organisms that might cause an infection or infectious disease; includes bacteria, fungi, viruses, and parasites.

Keratinocytes: cells that make up the outer surface of the skin that helps the skin to recover from injury.

Murine: relating to rodents.

Porcine: relating to pigs.

Skin grafts: a piece of tissue used for replacing skin lost to burn.

Xenotransplantation product: product that contains live cells, tissues, or organs from a non-human animal source or human body fluids, cells, tissues, or organs that have come into *ex-vivo* contact with live non-human animal cells, tissues, or organs.

What is STRATAGRAFT?

STRATAGRAFT construct is produced from two kinds of human skin cells (keratinocytes and dermal fibroblasts). To produce STRATAGRAFT, the cells are allowed to grow together to make a bilayered construct that is similar to skin.

STRATAGRAFT is a xenotransplantation product because in the past, one of the cell types used to make STRATAGRAFT was grown with mouse cells. The cell banks have been tested and found to be free of detectable infectious agents and mouse cells are no longer used in the manufacture of STRATAGRAFT.

There have been no identified health concerns associated with these mouse cells.

No infectious agents have been detected in STRATAGRAFT.

Who should use STRATAGRAFT?

Adults may need STRATAGRAFT if they have a deep burn(s). Your doctor will evaluate if STRATAGRAFT may be right to treat your burn(s).

Why may STRATAGRAFT help your condition?

For many deep burns, one treatment type is the removal of the damaged, burned skin, and replacement with a skin graft. These skin grafts may be taken from your own healthy skin on your body and moved to the burned area to help it heal. When skin grafts are taken from your body, it is called an autograft. This procedure leaves a new wound where the healthy skin was taken.

If your doctor recommends that your burn wound be treated with STRATAGRAFT, then your healthcare provider will place STRATAGRAFT on your burn instead of using a piece of your own healthy skin. In most cases, treatment with STRATAGRAFT avoids or greatly decreases the amount of healthy skin that is taken for grafting.

STRATAGRAFT will likely allow your own skin cells to grow and heal the burned area over time.

When should STRATAGRAFT not be used?

You should not be treated with STRATAGRAFT if you have an allergy to STRATAGRAFT or any of the components of STRATAGRAFT, including murine collagen or bovine or porcine products.

What are the risks associated with STRATAGRAFT?

- STRATAGRAFT contains glycerin. In patients who have a glycerin sensitivity, there is a risk of an allergic reaction.
- Because STRATAGRAFT contains human cells, there is the possibility of transmission of an infectious agent.

The safety of STRATAGRAFT was similar to that of autografting in clinical studies.

To report SUSPECTED ADVERSE REACTIONS, contact Customer Care at 1-877-647-2239 or <http://www.mallinckrodt.com/stratatech> or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Recipients of xenotransplantation products are generally not eligible to donate whole blood, blood components, source plasma or source leukocytes. However, individual blood banks may request an exception, so if you wish to donate blood or blood products check with your donation center.

STRATAGRAFT recipients who otherwise meet the donor requirements are eligible to donate human cells, tissues, breast milk, ova, sperm, or body parts for transplantation.

What are the potential complications of burns and skin grafting?

Severe burns may cause many complications to both the skin and other parts of the body. These complications can be very serious and life-threatening.

In the clinical studies, complications seen after treatment with STRATAGRAFT were typical of severe burns. Patients experienced itching, blisters, scarring, and impaired healing at the treatment site.

To help avoid complications after surgery, follow these instructions:

- Leave the dressing(s) in place unless instructed otherwise by your healthcare provider. Contact your healthcare provider if STRATAGRAFT gets shifted out of place.
- Avoid touching the dressing or treated areas until instructed otherwise by your healthcare provider.
- Keep the dressing(s) dry.
- Expect itching, redness, swelling, bruising, and/or pain after the surgery. **Contact your healthcare provider if you develop fever, increased drainage, pain and/or swelling, or any other adverse effect at or around the treatment site.**

SPC-LBL-0982 Rev.3

01/2024

PRINCIPAL DISPLAY PANEL - 1 Pouch Carton

NDC 73612-200-01

Rx Only

allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat

STRATAGRAFT®

For Single-Use Only

For Topical Application Only

Contains 1 Construct



PRINCIPAL DISPLAY PANEL - 1 Pouch Carton - NDC 73612-201-01

NDC 73612-201-01

Rx Only

allogeneic cultured keratinocytes and dermal
fibroblasts in murine collagen - dsat

STRATAGRAFT®

Sample - Not for Resale

For Single-Use Only
For Topical Application Only
Contains 1 Construct



STRATAGRAFT

allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat cellular sheet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:73612-200
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Viable and Metabolically Active Allogeneic Human NIKS Keratinocytes and Human Dermal Fibroblasts Cellularized Layered Scaffold (UNII: DYB2T93463) (Viable and Metabolically Active Allogeneic Human NIKS Keratinocytes and Human Dermal Fibroblasts Cellularized Layered Scaffold - UNII:DYB2T93463)	Viable and Metabolically Active Allogeneic Human NIKS Keratinocytes and Human Dermal Fibroblasts Cellularized Layered Scaffold	1 cm ² in 1 cm ²

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:73612-200-01	1 in 1 CARTON	06/15/2021	
1		100 cm2 in 1 POUCH; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125730	06/15/2021	

STRATAGRAFT

allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat cellular sheet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:73612-201
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Viable and Metabolically Active Allogeneic Human NIKS Keratinocytes and Human Dermal Fibroblasts Cellularized Layered Scaffold (UNII: DYB2T93463) (Viable and Metabolically Active Allogeneic Human NIKS Keratinocytes and Human Dermal Fibroblasts Cellularized Layered Scaffold - UNII:DYB2T93463)	Viable and Metabolically Active Allogeneic Human NIKS Keratinocytes and Human Dermal Fibroblasts Cellularized Layered Scaffold	1 cm2 in 1 cm2

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:73612-201-01	1 in 1 CARTON	10/29/2021	
1		100 cm2 in 1 POUCH; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125730	06/15/2021	

Labeler - Stratatech Corporation (160392168)

