StrataGraft®

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

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 (>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: 06/2021

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*Sections or subsections omitted from the full prescribing information are not listed.
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.

![STRATAGRAFT Product Dish and Insert Tray containing STRATAGRAFT](image)

**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).

![Hold Solution within a laminated foil pouch](image)

**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).

![Hold Dish contained within a clear pouch](image)

**Figure 5: Hold Dish contained within a clear pouch**

![Hold Dish handled in sterile field](image)

**Figure 6: Hold Dish handled in sterile field**

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**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 35ºC to 39ºC (95ºF to 102ºF) for AT LEAST 45 minutes prior to use.

   **Option 2:**
   
   Place Hold Solution bottle in a water bath at 35ºC to 39ºC (95ºF to 102ºF) 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).

![Sterile operator (gray gloves) removes the sterile Hold Dish presented by the nonsterile operator (white gloves)](image)

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

![Sterile operator places the Hold Dish in the sterile field (gray rectangle)](image)

**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](image)

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](image)

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](image)

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](image)

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](image)

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).

![Figure 14: Sterile operator (gray gloves) removes the STRATAGRAFT insert tray](image)

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](image)
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 mesh/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.
3. 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.
4. Place a second layer of dressing that does not contain silver [see Drug
Interactions (7.2)].
5. 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,
algogenic 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 an 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)]; however these measures do not
entirely eliminate the risk of transmitting infectious diseases and disease
agents.

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

5.4 Donation of Blood, Organs, Tissues, or Cells
Because STRATAGRAFT is a xenotransplantation product, STRATAGRAFT
recipients should not donate whole blood, blood components, plasma,
leukocytes, tissues, breast milk, ova, sperm, or other body parts for use
in humans.

6 ADVERSE REACTIONS
The most common adverse reactions (incidence ≥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 intrapatient comparators
at another wound site. The most frequent adverse reactions (incidence
≥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 ≥2%
Following Treatment with STRATAGRAFT (N=119)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Patients n (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus (Itching)</td>
<td>13 (11)</td>
</tr>
<tr>
<td>Blisters</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Hypertrophic Scar</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Impaired Healing</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

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

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, especially considering the xenotransplant nature of 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 keratinocytes and human dermal fibroblasts 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 of STRATAGRAFT 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.
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 by 28 days after STRATAGRAFT treatment. 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

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:
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