

SURGICAL GUIDELINES



Mark
Treated with Epicel



RECOVERING WITH EPICEL[®]

cultured
epidermal
autografts

Epicel[®]
(cultured epidermal autografts)

HUMANITARIAN DEVICE: Epicel[®] (cultured epidermal autografts) is authorized for use in adults and pediatric patients who have deep dermal or full thickness burns comprising a total body surface area greater than or equal to 30%. It may be used in conjunction with split-thickness autografts, or alone in patients for whom split-thickness autografts may not be an option due to the severity and extent of their burns. The effectiveness of the device for this use has not been demonstrated.

IMPORTANT SAFETY INFORMATION: Epicel is contraindicated in patients with a history of anaphylaxis following exposure to vancomycin, amikacin, and amphotericin, as trace quantities of these anti-infective agents may remain in the Epicel autograft. Epicel should not be used in patients with known sensitivities to materials of bovine or murine origin. It is contraindicated for use on clinically infected wounds. Because Epicel is manufactured with and contains residual amounts of murine cells, FDA considers it a xenotransplantation product. Therefore, recipients should not donate whole blood, blood components, source plasma, source leukocytes, tissues, breast milk, ova, sperm, or other body parts for use in humans because there is a potential risk of carrying an infection that is transmitted from mouse cells to humans.

Please see additional Important Safety Information on next page and [Directions for Use](#) and [Patient Information](#).

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INDICATION

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Squamous cell carcinoma (SCC) has been reported in patients with burn injury after being grafted with Epicel. Although SCC is a known complication of burn scars, the role of Epicel in the causation of SCC cannot be excluded.

The Epicel product is intended solely for autologous use. Patients undergoing the surgical procedure associated with Epicel are not routinely tested for transmissible infectious diseases. Discontinue use if the patient shows evidence of allergic reaction.

If clinical signs of infection are present or develop, do not apply Epicel until the infection is adequately treated.

The effectiveness of Epicel has not been proven in clinical studies.

The long-term safety of Epicel is unknown. Over the past 27 years, the mortality from all causes was 13% before hospital discharge.

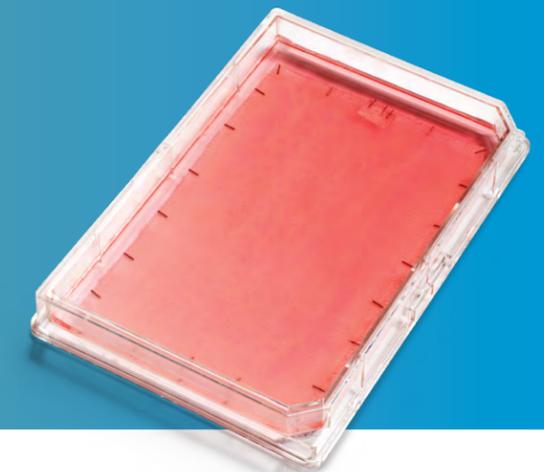
Men and women who intend to have children should be advised that the effects, if any, of Epicel on fetal development have not been assessed. In addition, the safety of Epicel has not been studied in pregnant and nursing women.

Patient information supplied by attending burn teams from 1989 to 1996 reported the adverse events of highest incidence as: death (13%), infection (13.8%), graft tear (7.8%) or graft blister (4.2%) and drainage (3.3%). Some of these events may have been due to the underlying burn injury and not the device itself.

From June 1998 through September, 2015 adverse events received by Genzyme Biosurgery (predecessor in interest to Vericel) and Vericel Corporation were similar to the previously identified adverse events. Events that were reported in $\geq 1\%$ of patients included multi-organ failure (6.6%), sepsis (5.2%) infection (4%) and skin graft failure/graft complication (2.7%). The relationship of these events to Epicel has not been established.

For more information, please see [Directions for Use](#) and [Patient Information](#).

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An adverse event is any undesirable experience associated with the use of a medical product in a patient.* To report adverse events occurring to patients after Epicel® grafting, please contact Vericel Customer Care at 800-232-7546.

*FDA website:

<http://www.fda.gov/Safety/MedWatch/HowToReport/ucm053087.htm>



Vericel Cell Therapy Specialists are thoroughly trained and experienced in all aspects of the procedures leading to grafting success with Epicel. To request additional information, please call **1-800-CEA-SKIN** (1-800-232-7546).

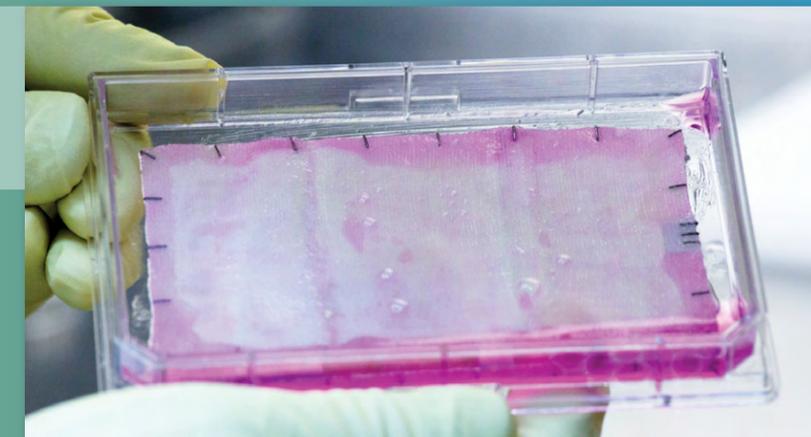
Epicel®

(cultured epidermal autografts)

Cultured Epidermal Autografts (CEAs) were first applied to the treatment of severely burned patients in the 1980s. Much has been learned since about specific techniques that can facilitate the likelihood of success.

This document is intended to provide information about approaches recognized to enhance engraftment of Epicel. The following Surgical Guidelines ("Guidelines") are provided as general recommendations for accepted procedures to be followed before, during, and after application of Epicel. The goal is to provide specific details about techniques that have been shown over the years to achieve optimal clinical outcomes in patients treated with Epicel. The emphasis is on enhancing successful application and survival of the CEA and returning the patient to the best possible level of function.

The information provided in this document is intended for educational purposes; it is not a substitute for medical care nor should it be construed as medical advice. The Guidelines incorporate recommendations from Editorial Board members based on their extensive clinical experience with Epicel. Although time frames are suggested in these Guidelines, it is more important specific goals are attained by the end of each phase in the process before progressing to the next.



Epicel has been designated as a Humanitarian Device Exemption (HDE) by the FDA.¹

Epicel® (cultured epidermal autografts) is indicated for use in adults and pediatric patients who have deep dermal or full thickness burns comprising a total body surface area greater than or equal to 30%. It may be used in conjunction with split-thickness autografts, or alone in patients for whom split-thickness autografts may not be an option due to the severity and extent of their burns.



FIGURE 1: A patient with burns covering 60% of the total body surface area prior to debridement.

Subsequent photos of this patient are shown in Figures 21, 24, and 27.

Early burn wound excision and closure have been shown to improve survival, reduce the infection rate, and shorten hospital stays.^{2,3} The excised wounds can be covered with cadaver allograft to help reduce fluid loss and bacterial invasion during the period of immunosuppression following a burn injury.

The engrafted dermis then serves as a substrate for the Epicel (cultured epidermal autografts) grafts.⁴ Dermal substitutes can serve a similar function.^{2,6,7}

Early excision and temporary closure with allograft, which allows dermal elements to be incorporated into the wound bed over a period of weeks, appear to achieve a very good take with Epicel.^{4,8,9}



FIGURE 2: Full-thickness areas of injury are excised until clean, viable tissue is apparent.



FIGURE 3: A burn patient post-debridement, covered with allograft tissue.

- **Ideally, the patient is taken to the OR within 72 hours of admission.**
- **Excised wounds are covered with meshed, but not expanded, allograft or dermal substitute.**^{2,6,9,10}
- **The temporary covering (allograft or pigskin) or dermal substitute remains in place until full engraftment occurs.**
Temporary covering will usually take 2-3 weeks to fully engraft.
Full engraftment is critical to provide a highly vascular and clean wound surface necessary for successful placement of Epicel.
- **Patients should be taken back to the OR every 2-3 days for repeat debridement and replacement of non-adherent allograft.**

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PHASE II

PREGRAFTING: BIOPSY PROCUREMENT

The autologous keratinocytes used to prepare Epicel® (cultured epidermal autografts) are derived from a small full-thickness biopsy of skin taken from an unaffected area on the burn patient. The surface area of a single patch of biopsied skin measuring 2 cm² can be expanded in area 10,000 times.¹¹

- **At the time of initial excision, preferably within the first 24-48 hours of admission, two individual biopsies are taken from different sites on the patient's undamaged, non-diseased skin so that Epicel can be prepared.³**



FIGURE 4: A full-thickness diamond-shaped patch of skin measuring approximately 6 cm long by 2 cm wide is biopsied.

- **The biopsy site should be shaved to remove hair, thoroughly washed, and swabbed with 70% alcohol, followed by a sterile normal saline rinse.**

If contamination remains the biopsy may be lost and a repeat biopsy may be needed, causing delays in the total cell culturing process.

If it is suspected that the biopsy site is highly contaminated, the prep sequence may be repeated to remove the excessive bacterial bioburden.

- **Biopsy site suggestions include the axilla, groin, and abdomen, but any non-burned area may serve as a biopsy site.**

Ideally, the biopsy should be taken within 24-48 hours of admission to decrease the risk of a contaminated biopsy.

- **The biopsy may be taken under local or general anesthesia.**

Local anesthetic should be injected circumferentially, not directly into the biopsy site.

If the initial excision surgery is delayed, the biopsy can be taken at bedside under local anesthesia.

PHASE III

PREPARATION OF EPICEL

The patient's own skin cells are cultured ex vivo for approximately 17 days to produce Epicel.¹ If grafting surgery cannot be performed at that time, the skin cells can be cryopreserved for future use. At a later date, the cells can be thawed and grafts prepared and shipped with a 14-day advance notice.



FIGURE 6: The patient's own keratinocytes are cultured aseptically in the presence of proliferation-arrested mouse fibroblasts to produce Epicel.^{1,12}

- **Epicel consists of sheets of proliferative, autologous keratinocytes ranging from 2 to 8 cell layers thick.^{1,13}**

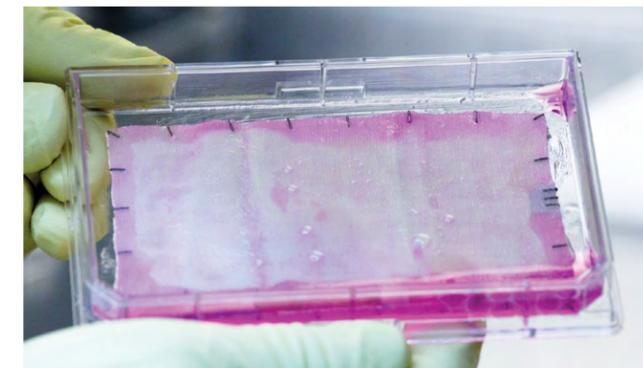


FIGURE 7: Epicel is attached to a rectangular petrolatum gauze backing with titanium surgical clips and measures approximately 50 cm² in area, about the size of a playing card.

- **In order to determine the appropriate number of grafts needed, it is important to consider the treatment plan and to measure those areas intended for Epicel (cultured epidermal autografts).**

TABLE 1: ESTIMATE # OF EPICEL GRAFTS FOR A TYPICAL ADULT PATIENT

FRONT OF PATIENT		BACK OF PATIENT	
FACE	6	BACK OF HEAD	6
FRONT OF NECK	4	BACK OF NECK	4
CHEST	50	BACK	45
FRONT OF ARM	10	BACK OF ARM	10
PALM OF HAND	N/A	BACK OF HAND	N/A
		BUTTOCKS	20
THIGH FRONT	20	THIGH BACK	20
SHIN	12	BACK OF CALF	12
TOP OF FOOT	2	SOLE OF FOOT	N/A



FIGURE 5: Once the skin biopsy has been obtained, it is packaged and delivered to Vericel in a special Skin Biopsy Transport Kit, along with the completed Epicel Transmittal Notice.

Instructions for biopsy procurement, packaging and shipping the biopsy are in Vericel's Skin Biopsy Transport Kit Directions for Use

There is no financial obligation for the biopsy kit or for taking the biopsy and starting the initial cell culture process.

4800 cm² making
up **96** Epicel grafts
cultured in **17** days*

*Individual time may vary based on unforeseen impediments to culture growth or transportation interruptions

Cuono et. al.¹⁴ demonstrated much better results could be achieved with cultured epidermal autografts by employing a technique in which Epicel® was placed on allodermis from cadaver allograft.^{4,8}

- **Condition of allograft should be monitored daily and if portions are not engrafting those segments are immediately removed, the area re-excised deeper to viable tissue, and new product placed as often as every 3-4 days.**⁵
- **Routine sensitivity testing of wound cultures (swab or preferably quantitative culture for bacteria and fungi) of the areas to be grafted with Epicel are recommended, especially at 1 week preoperative and again at 3 days preoperative.**



FIGURE 8: Allograft that has fully engrafted, prior to placement of Epicel

- **If allograft has engrafted and the alloepidermis sloughs away prior to Epicel delivery, yet there is not enough time to apply a new allograft, quickly cover areas with sterile normal saline dressings or dermal substitute.**

Dressings containing silver have been successfully used in preoperative wound bed preparation for Epicel, but their use should be discontinued 24 hours prior to grafting to reduce silver levels on the wound bed.

- **Epicel is more susceptible to wound bed conditions and bacterial colonization than split-thickness autografts.**¹⁴

Do not use cytotoxic agents (any product containing chlorhexidine gluconate) near body sites where Epicel grafts will be, or have been, placed.

The following anti-infective agents have shown significant inhibitory effects on Epicel in vitro and should be avoided: AK-Spore HC (Polymyxin B sulfate, Neomycin sulfate, Hydrocortisone), Acetic Acid, Clotrimazole and Miconazole.¹⁴

One or two days prior to the Epicel grafting date the patient is taken to the OR for final wound bed preparation.

- **Any devitalized or chronic granulation tissue is removed so that a clean, well-vascularized wound bed is produced.**

Epicel engraftment will be negatively affected unless the prepared wound bed has a low to nonexistent bacterial count, is highly vascular, and complete hemostasis has been achieved.

- **Wound cultures (swab or quantitative) are taken of prepped areas for both bacterial and fungal organisms with sensitivity testing.**
- **Wound bed is then covered and kept moist with sterile saline; or, a lightly applied dermal substitute has been successfully used to reduce drying and desiccation of the underlying tissue.**

The allograft epidermis is removed by dermabrasion prior to placement of Epicel. The allograft dermis, or "allodermis", is retained and serves as an excellent substrate, promoting rapid stratification, maturation, and integration of Epicel and the synthesis of anchoring fibrils.^{5,8}

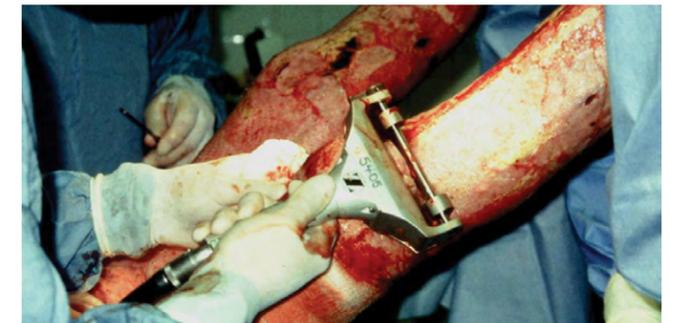


FIGURE 9: Epidermal layer of allograft is removed using a dermatome.

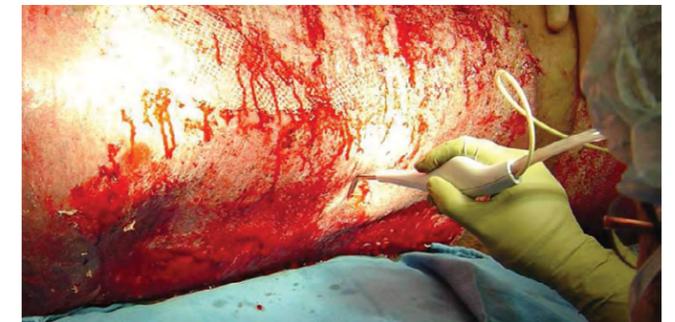


FIGURE 10: Epidermal layer of allograft is removed using Versajet™.

TABLE 2: ANTI-INFECTION AGENTS TESTED ON EPICEL IN VITRO WITH NO SIGNIFICANT INHIBITORY EFFECTS¹⁴

AGENT	MAX DOSE*
Amphotericin B	24 µg/mL
Bibiotic (Polymyxin B Sulfate and Bacitracin Zinc)	200 U/mL, 50 U/mL
Cefoperazone	100 µg/mL
Ciprofloxacin	5 µg/mL
Gentamicin Sulfate	1 mg/mL
Neomycin Sulfate	2 mg/mL
Nystatin	480 U/mL
Polymyxin B Sulfate	1000 U/mL
Polysporin® (Polymyxin B Sulfate and Bacitracin Zinc)	200 U/mL, 10 U/mL
Triple Antibiotic (Polymyxin B Sulfate, Bacitracin zinc and Neomycin Sulfate)	100 U/mL, 25 U/mL, 0.6 mg/mL
Tobramycin Sulfate	6 µg/mL
Vancomycin Hydrochloride	1 mg/mL

* Maximum dose that did not inhibit keratinocyte growth and differentiation resulting in the number of growing colonies greater than or equal to 50% of the control and the average growing colony size greater than or equal to 50% of the control.

In addition, there is a limited degree of clinical experience with topical administration of the following agents: bacitracin zinc, clavulanate potassium, fluconazole, hypochlorous solution (undiluted), imipenem, kanamycin sulfate, ketoconazole, mupirocin, ticarcillin disodium.

- **Contact your Vericel Cell Therapy Specialist for more information on appropriate use of topical antibiotic and antifungal agents.**
- **During this pregrafting period, aggressive range-of-motion exercises should be performed routinely to maximize the functional range of the patient's joints.**

After grafting with Epicel, ranging exercises of affected joints will be restricted for 7-10 days.

WOUND MANAGEMENT

Final preparation of the wound bed just prior to Epicel grafting has four advantages:

1. The time spent in surgery on the day of grafting can be significantly shortened.
2. It allows time for the prepared wound bed to gain complete hemostasis, which is essential prior to Epicel placement.
3. Cultures taken at this time can facilitate earlier detection of higher levels of bacterial or fungal colonization on the wound bed and allow more time to plan for topical treatment.
4. It provides an opportunity for physical and occupational therapy (if permitted by the physician), for range-of-motion exercises under anesthesia to achieve maximal stretching prior to the period of immobilization, and for assessment of immediate postoperative positioning and splinting needs.

TIMING OF GRAFTING PROCEDURE

- A Vericel Cell Therapy Specialist will accompany the Epicel grafts into the OR area and will stay during the procedure as a product resource.

- To ensure maximum cell viability a 24-hour expiration date is applied from the point of shipment.¹

It is important for the patient to be scheduled as early in the day as possible, preferably as first case, to allow sufficient time for the procedure.

- As required by the FDA, just prior to Epicel® application, obtain 3-5 aliquots (0.5 mL) of citrated or EDTA-anticoagulated plasma and ≥2 aliquots (1 x 10⁷ cells) of blood samples for archival purposes.

In the event a xenogeneic infectious disease is suspected, baseline patient plasma and cells may be critical to determining etiology.

Vericel will provide the kit and arrange for this blood sample to be sent to a laboratory for processing and archiving.

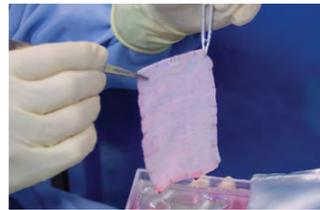


FIGURE 11: Smooth-edged pick-ups should be used rather than toothed pick-ups to prevent any tearing of the graft.

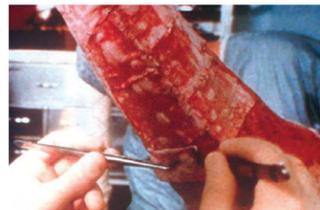


FIGURE 12: Epicel is placed with cell sheet facing down.



FIGURE 13: Epicel is stapled directly on top of the prepared wound bed.

It is important to fully release the staple before removing the stapler to minimize any graft movement or lift on the wound bed.

- It is recommended that all the grafts in an area be placed prior to stapling
- Place grafts with little to no overlap and staple grafts to adjoining grafts, 2 equidistant staples per side, locking grafts together.



FIGURE 14: Epicel over fully engrafted allograft.



FIGURE 15: Epicel applied to wound bed and affixed with staples and sterile nylon net.

EPICEL PRE-APPLICATION

- Reassess for any final wound bed preparation and complete preparation as appropriate.
- Obtain any follow-up or repeat quantitative wound cultures as necessary just prior to Epicel placement.
- The area to be grafted with Epicel is prepped with agents more favorable to the cultured cells and then thoroughly rinsed with sterile normal saline.
- Wide mesh autograft may be harvested and placed prior to placement of Epicel.

It is recommended that wide mesh autograft be placed over joints to minimize the occurrence of contracture.

TABLE 3: TIPS FOR PLACEMENT AND HANDLING OF EPICEL¹

- 1 If desired, autograft donor sites are harvested and wide mesh split-thickness autograft is placed just prior to placement of Epicel.
- 2 A fine mist of commercially prepared fibrin sealant may be applied immediately prior to laying the Epicel grafts, providing a full interface of cells against the wound bed.

It is important the fibrin sealant be applied in stages and to an area that will allow the Epicel grafts (approximately 6-8) to be readily applied prior to the set-up of the sealant. Please refer to the directions for use from the product's manufacturer to determine how quickly the fibrin sealant product will "set-up."
- 3 Epicel grafts should be placed with cell sheet facing down on the wound bed and the petrolatum gauze backing facing up.
- 4 The silver orientation tag on the back of the petrolatum gauze should be facing up.
- 5 During the grafting procedure, each graft carrier tray should be opened only when the graft is ready to be applied.
- 6 Grafts should be placed as close together as possible with little to no overlap.
- 7 Do not allow the grafts to dry before they are applied to the wound bed.
- 8 Handling of the grafts should be kept to a minimum as it may cause a measurable reduction in cell viability.
- 9 The graft should not be moved across the surface of the wound bed once it is applied as cell damage may result.
- 10 If a delay occurs during graft placement, the box holding the graft carrier trays should be resealed until grafting resumes.
- 11 Once grafts have been applied they are stapled directly to the wound bed.
- 12 Epicel grafts are then covered with an initial surgical dressing of sterile nylon net and secondary outer surgical dressings.

ALTERNATIVE EPICEL® GRAFTING TECHNIQUE USING WIDE MESH AUTOGRAFT^{4,16}

- Meshed autograft placed under Epicel has proven to be effective. Autograft is meshed in a ratio of 3:1, 4:1, or 6:1, and placed just prior to the placement of Epicel.¹⁶



FIGURE 16: Widely meshed autograft.¹⁶



FIGURE 17: Epicel is applied over widely meshed autograft.¹⁶

- Once the wide mesh autograft is stapled in place, a fine mist of fibrin sealant is sprayed, and the Epicel grafts are quickly applied.

Healing occurs as the spaces between the meshed autograft, or "interstices", fill in with the cultured epidermis.

The underlying mesh increases the initial durability of Epicel.

Donor sites may also be covered with Epicel to speed healing.

SURGICAL DRESSINGS FOR EPICEL

- An initial surgical dressing of hospital-sterilized bridal veil/nylon net, or commercially prepared DRYNET™ Wound Veil should be secured with staples over the petrolatum gauze backing to protect the Epicel grafts from shearing forces.

The sterile nylon net should be stretched tightly against the wound bed, with care being taken not to shear the grafts.

- A secondary outer surgical dressing consisting of four or five layers of absorbent gauze should be wrapped around the extremities or fanfolded over the anterior trunk or back.

Additionally, ace wraps may be used immediately post-graft application for light compression (in the OR). Use just for the first 24 hours to minimize concern of excessive pressure, occlusive nature, or potential shear with re-application.

- A final outer bulky dressing has also proved useful for padding the Epicel grafts to reduce shearing forces.

- The combination of dressings should not be so occlusive as to cause fluids to be trapped against the grafts, as this may lead to maceration of the delicate layers of cells.

- Depending on the condition of the wound bed and the wound culture results, topical antibiotic and/or antifungal agents may be used in the dressing application.

The secondary outer dressing can be applied dry over the sterile nylon net in the absence of drainage and infection; or dampened (wring-out procedure) with an appropriate topical antibiotic and/or antifungal agent specific to the organisms present. (Table 2).

Epicel grafts are highly sensitive to local infection.¹⁴ In the immediate postoperative period the emphasis is on monitoring the wound bed for bacterial colonization and leaving the grafted areas open to air several hours each day to allow the Epicel grafts to dry.

Bacterial contamination can cause loss of Epicel grafts, even though a similar level of colonization has little or no effect on the take of meshed split-thickness autografts.^{1,14}

Because the Epicel grafts are fragile during the postoperative period, it is also important to minimize shearing forces by immobilizing all grafted areas and using fluidized air beds.

DRESSING CHANGES

- All dressings, with the exception of the sterile nylon net, should be carefully changed once daily to prevent accumulation of fluid and bacteria and to dry the grafts; or twice daily if there are high levels of bacterial colonization or purulence.

It is important to avoid disrupting the underlying sterile nylon net and the Epicel grafts when changing the outer dressings.

- During daily dressing changes, leave all areas grafted with Epicel open to air at least 4 hours to allow Epicel to fully dry.



FIGURE 18: Exposed inner surgical dressing

- If the gauze dressing immediately over the sterile nylon net sticks during removal, the area should be dampened (a bulb syringe or sterile spray bottle are effective) with sterile normal saline or commercially prepared Shur-Clens® to eliminate adhesion.

Dressing changes may need to be done in stages to best accommodate patient positioning while eliminating any cross contamination.

Patients with grafts on their back limited to the supine position should be log-rolled on each side to allow drying.

Elevate extremities slightly to allow posterior grafts to dry.

Traffic in the patient's room should be restricted and protective garb worn when patient is open to the air. Signage should be placed outside the patient's room to indicate this need.

To protect the grafts from environmental contamination, a sterile sheet may be draped over the patient, but special care should be taken to avoid shearing the delicate grafts.

APPLICATION OF TOPICAL ANTIBIOTIC OR ANTIFUNGAL AGENTS^{4,16}

- Wounds having excessive discharge may require more frequent dressing changes; if cultures show low levels of bacteria or fungi or moderate to high levels of colonization in the wound bed, topical antibiotics and/or antifungals effective against the bacteria or fungi present will also be required.^{17,18}

If necessary, gently place a gauze slightly dampened (wring-out procedure) with an appropriate antibiotic and/or antifungal solution over the sterile nylon net.

Apply to the area a maximum of twice daily; more frequent application of these agents could cause maceration of the grafts.

- The pharmacy should label individual solutions for stability and compatibility; it is often best to prepare only enough topical solution for one day of application.

Often patients receiving Epicel will require a combination of both techniques.

PROTECTING EPICEL® FROM SHEARING FORCES AND WOUND BED COLONIZATION

- Pressure and shearing forces applied to grafted areas may result in damage to Epicel, therefore all grafted areas are immobilized.

Depending on the graft placement and the patient's condition, splinting with heavy padding or chemical paralysis may be appropriate in the case of more active patients.

Hexalite splints allow air to circulate, which can aid in avoiding maceration of the Epicel graft. Hard plaster casts that cannot be removed to allow for graft drying should not be used.

Specialty beds may be needed for postoperative care; air fluidized beds for grafted posterior surfaces, or beds with Gore-tex help to reduce shear.

- Intubated patients with posterior grafted areas will need to be carefully assessed for appropriateness of prone positioning.
- No physical or occupational therapy that would flex, stretch, or in any way move the grafted areas should be permitted until after the takedown procedure.
Range-of-motion exercises applied to body sites not affecting areas grafted with Epicel are encouraged.
Therapists should monitor splints and ensure proper positioning is maintained to protect newly grafted areas.
- Wound cultures of open spaces between grafts and of any exudate should be taken twice a week or as needed to monitor wound bed colonization.
It is critical to be proactive in routine culturing of the wound bed even if active signs of infection are not evident.
Early detection of an increase in bacterial or fungal colonization can enhance the efficacy of topical antibiotic and/or antifungal therapy.
- It is important to communicate the need for gentle handling of the Epicel grafted areas to weekend staff and other shifts responsible for care of the patient, especially those nurses responsible for dressing changes.



FIGURE 19: Patient with posterior Epicel grafts is positioned "side-lying" during dressing changes



FIGURE 20: Epicel grafts with a normal appearance prior to takedown. Take note that grafts are fragile at this state.

Takedown, or removal of the petrolatum gauze backing from the Epicel (cultured epidermal autografts) grafts, usually occurs 1 week to 10 days after placement of the grafts.

- If the grafts appear dry and show no evidence of infection, the takedown procedure is best performed using strict sterile technique, either in the OR or at the bedside.
- In the case of suspicious wound exudate, or if high levels of bacterial or fungal colonization are present under the graft (i.e., purulence), it may be advisable to perform the takedown procedure earlier so topical antibiotic and/or antifungal treatment can be more effective.
Please consult your Vericel Cell Therapy Specialist concerning the need to do an early or delayed takedown procedure.
- At this phase it is best to avoid the use of products containing chlorhexidine gluconate, such as Hibiclens®.
- If needed, ungrafted areas should be prepped with an agent not harmful to cultured epidermis, such as povidone iodine, Shur-Cleans, hypochloris or other agents (Table 2), then rinsed with sterile normal saline.



FIGURE 21: Supplies needed for graft takedown

STEPS IN TAKEDOWN

1. Remove staples from the sterile nylon net and carefully remove.
2. Remove the staples used to affix the petrolatum gauze. Gently peel the gauze backing down and away from the wound bed; do not pull up on the gauze backing.
Sterile cotton-tipped applicators may help "tease" the gauze backing from the cultured epidermis if it lifts from the wound bed. If after soaking with sterile saline or Shur-Cleans (3.4 oz. bottle per 0.5L NSS) the gauze backings still adhere, the takedown procedure should be delayed. In this case, replace the outer dressing and heavily soak with Shur-Cleans overnight.
3. Wound cultures of the cultured epidermis should be obtained along with sensitivities for bacterial and fungal organisms.
4. Apply nonadherent dressings to all areas of cultured epidermis. Adaptic® is recommended, but Dermanet®, Conformant™ 2, N-terface®, Cuticerin™ and Aquaphor® Gauze may also be used.
5. Bacitracin or polysporin-type ointment may be used to lightly impregnate the non-adherent dressing before application.
6. A soft, absorbent sterile gauze wrap is applied as an outer layer over the non-adherent dressing.
If no drainage or infection is present, a dry dressing is applied; if purulence is present, a dampened dressing with appropriate antibiotic and/or antifungal solution may be used.
7. It is critical to monitor Epicel grafted areas closely for drainage, and both inner and outer dressings should be changed daily providing antibiotic and/or antifungal therapy as needed.



Figure 22: Takedown and exposed new skin

After takedown, dressings are changed and Epicel-grafted areas are exposed to air and monitored daily. Great care is required in removing the initial dressing as it is extremely important not to disturb the cultured epidermis. Wound cultures are taken from any suspicious areas of delayed healing.

It is important to avoid exposing the Epicel-grafted areas to any shearing forces. Gentle range-of-motion exercises can, however, be initiated during this period.

DRESSING CHANGES

- **Grafted areas are exposed to air at least 4 hours daily and dressings changed.**
Gentle irrigation with sterile saline or Shur-Clens® eases nonadherent dressing removal (which can become adherent).
- **If the dressing adheres even just slightly to the fragile cultured epidermis it may dislodge when the dressing is removed.**
- **It is important to carefully remove the initial dressing so as not to pull or disturb the underlying cultured epidermis.**



FIGURE 23: Epicel grafts are in a fragile state in the initial stages after takedown

PHYSICAL REHABILITATION AND MONITORING

- **Active to gentle passive range-of-motion exercises are recommended to prevent the cultured epidermis from lifting or splitting.¹⁹**
- **Careful attention is paid during range-of-motion exercises to avoid shear.**



FIGURE 24: Therapist with patient



FIGURE 25: Evidence of damage caused by shearing

- **If medical status permits, a patient may be lifted to a recliner after the takedown procedure is completed.**
Ambulation should be delayed and re-evaluated approximately 3 days after the takedown procedure is completed.
ACE® wraps should be utilized for lower extremity venous support once stand pivot transfers and progression to ambulation occur.
Conditioning/strengthening activities can be re-evaluated approximately 7 days after takedown procedure is completed.
- **Avoid washing, scrubbing, or rubbing Epicel grafted areas until fully confluent and the grafted areas have closed.**
- **Using a team approach to keep the same "sets of eyes", continue to monitor Epicel grafted areas for change in appearance and if negative, take immediate corrective action.**

Once the Epicel grafts are fully confluent and more mature-appearing (Figure 27), the patient may shower or use the shower trolley. Pressure garments can help reduce scar formation and decrease graft contraction.¹⁹ The use of such garments can be initiated about 6 weeks after graft placement when the new epidermis has stabilized. Physical rehabilitation is an important component of burn care, and the decision when to resume physical activity is determined by the patient's physician.

- **After skin integrity has been re-established, bathing with mild soaps and moisturizing with mild lotions is encouraged; lotions containing alcohol should be avoided as they may tend to over-dry the new epidermis.**

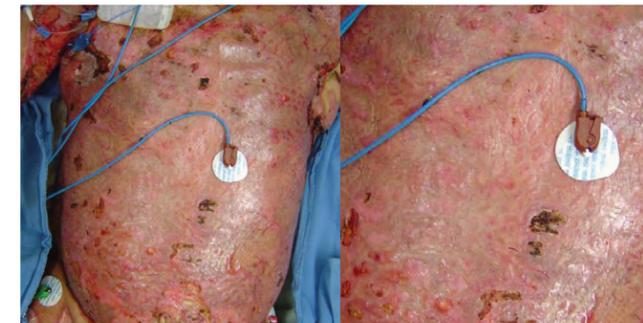


FIGURE 26: Confluent and mature appearing Epicel

- **Gently apply lotion, being careful not to over moisturize the skin to avoid graft maceration.**
- **Avoid brisk massage as this may create blisters.**
- **Showering or use of shower trolley is permitted once autografts are fully confluent and tough.**
This development process is patient specific but may extend for 4-6 weeks after the grafting procedure.
- **As the new epidermis matures and attaches to the wound bed blistering may occur; these areas should be treated with routine medical care as ordered by the physician.**

If a frictional rub is noted, please modify activity or splint to minimize or eliminate the source of friction.

- **Pressure garments are generally used after wounds are completely healed and the new epidermis is well attached and stable, approximately 6 weeks or more post grafting.¹⁶**

Initial set of garments should include zippers to avoid blistering; also, consider using soft liner inserts over fragile areas and joints to prevent disruption of the epidermis.

- **If open wounds occur, light nonadherent dressing should be applied per burn unit protocol.**
- **Physical activity can be resumed as tolerated by the patient per physician orders.²⁰**
In patients with lower extremity grafts, physical activity proceeds from dangling of the lower extremities first, followed by standing, and then walking.²⁰
- **Patients with extensive full-thickness burns may exhibit intolerance to heat or strenuous activity.**
- **Precautions concerning sun exposure and the use of sun protectants should be discussed.**

CHANGING APPEARANCE OF EPICEL (CULTURED EPIDERMAL AUTOGRAFTS) GRAFTS OVER TIME*

*Individual results may vary

EPICEL AT 3 WEEKS



FIGURE 27A:
Epicel on an anterior surface

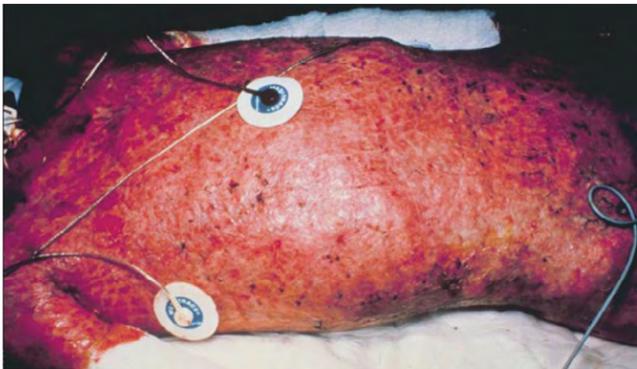


FIGURE 27B:
Epicel over 6:1 expanded meshed autograft

EPICEL AT 1 MONTH



FIGURE 28:
Epicel over 6:1 expanded meshed autograft

EPICEL AT 9 MONTHS



FIGURE 29A:
Epicel over Integra with 4:1 expanded meshed autograft



FIGURE 29B:
Epicel over allodermis

EPICEL AT 1 YEAR



FIGURE 30:
Epicel over allodermis on anterior surface of leg

EPICEL AT 3 YEARS



FIGURE 31:
Healed Epicel grafts on lower leg

RECOMMENDED SURGICAL SUPPLIES

INTRAOPERATIVE (GRAFTING) AND IMMEDIATE POSTOPERATIVE CARE

- Smooth-edged pick-ups; recommend 2 per surgeon
- Sterile normal saline
- Poloxamer 188 (Shur-Clens®) or appropriate antimicrobial solution
- Non-medicated scrub brush
- Bulb syringe or spray bottle
- Dermatome, knife or other fine mechanical dermabrasion-type methods such as a Versajet™
- Lap sponges
- Sterile specimen container for tissue sample or punch biopsy for quantitative wound culture, or wound swab culture for culture and sensitivity for bacteria and fungi
- Skin Graft Mesher (3:1, 4:1, 6:1 for autograft when used as an underlying mesh)
- Topical epinephrine or topical thrombin spray
- Staplers
- Fibrin sealant (preferably a slow setting type and mixture diluted per manufacturers' instructions)
- Inner dressings: sterilized bridal veil/nylon net or DRYNET™ Wound Veil
- Outer dressings: soft absorbent burn gauze dressings
- If needed, final outer bulky dressing for protection against shearing
- Appropriate antimicrobial solution, if required after grafting
- Stretch Net™ Tubular Elastic Dressing
- ACE® wraps
- Removable splints (preferably hexalite-type)
- For Vericel Cell Therapy Specialist: sterile gloves, basin, sturdy four-legged table without rim, towels

TAKEDOWN AND CARE OF EPICEL® (CULTURED EPIDERMAL AUTOGRAFTS)

- Smooth-edged pick-ups
- Sterile normal saline
- Poloxamer 188 (Shur-Clens®)
- Staple removers
- Sterile cotton-tipped applicators
- Bandage scissors
- Wound swab culture for culture and sensitivity for bacteria and fungi
- Bulb syringe or spray bottle
- Inner dressings: must be nonadherent such as Adaptic®, Dermanet®, Conformant™ 2, N-terface®, Cuticerin™ or Aquaphor® Gauze
- Bacitracin or polysporin-type ointment may be optional
- Outer dressings: soft absorbent burn gauze dressings
- Appropriate antimicrobial solution if required after takedown
- If needed, final outer bulky dressing for protection against shearing
- Removable splints (preferably hexalite-type)
- ACE®-wraps required for any dependent activity

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ADDITIONAL BACKGROUND REFERENCES

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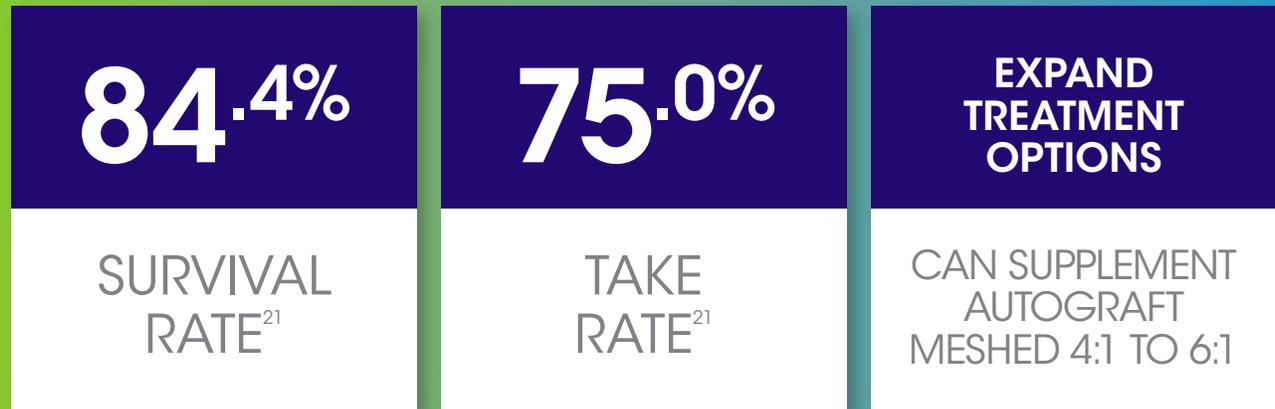
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