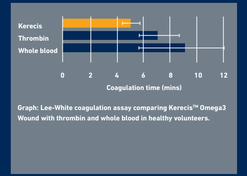
SCIENCE OF KERECIS™ OMEGA3 WOUND INTACT FISH SKIN

Haemostatic properties

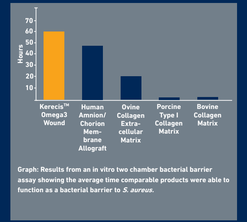
- Kerecis™ Omega3 Wound shows significantly better haemostatic properties compared to the coagulation agent thrombin or whole blood.
- In-vitro test: Lee-White coagulation assay



Graph: Lee-White coagulation assay comparing Kerecis™ Omega3 Wound with thrombin and whole blood in healthy volunteers.

Bacterial barrier[1,2]

- Kerecis™ Omega3 Wound shows superior bacterial barrier properties compared to other marketed products.
- In-vitro test: two chamber bacterial barrier assay



Graph: Results from an in vitro two chamber bacterial barrier assay showing the average time comparable products were able to function as a bacterial barrier to *S. aureus*.

Cell ingrowth[1]

- The unique structure of Kerecis™ Omega3 Wound allows deep ingrowth of cells.
- In-vitro test: Fibroblast cell ingrowth assay

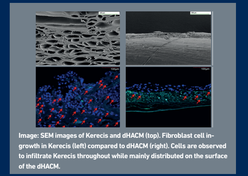


Image: SEM images of Kerecis and dHACM (top). Fibroblast cell ingrowth in Kerecis (left) compared to dHACM (right). Cells are observed to infiltrate Kerecis throughout while mainly distributed on the surface of the dHACM.

Neoangiogenesis[3]

- Kerecis™ Omega3 Wound promotes the formation of new blood vessels.
- In-vivo test: Chick embryos received hydrocortisone and VEGF 1ug/ml (positive control), hydrated filter paper (negative control) or Kerecis™ Omega3 Wound. Data is reported as percentage change in the number of branching points after 48 hours.

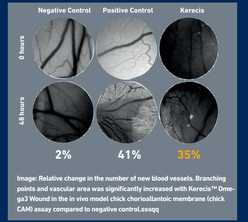


Image: Relative change in the number of new blood vessels. Branching points and vascular area was significantly increased with Kerecis™ Omega3 Wound in the in vivo model chick chorioallantoic membrane (chick CAM) assay compared to negative control.sssqq

Faster vascularization and healing[2]

- A randomized, comparative burn model in porcine provides a favourable environment for studying wound healing in deep, partial thickness burns.
- Compared with fetal bovine dermis graft, fish skin shows significantly faster vascularisation and accelerates healing of deep, partial thickness burns without the associated contracture of the wound.
- In-vivo test: Comparative porcine burn model

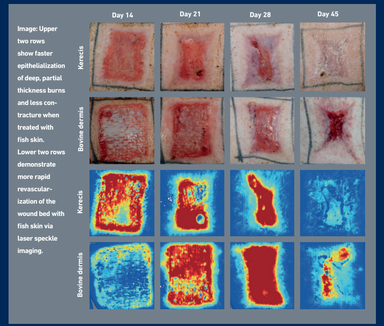


Image: Upper two rows show faster epithelialization of deep, partial thickness burns and less contracture when treated with fish skin. Lower two rows demonstrate more rapid revascularization of the wound bed with fish skin via laser speckle imaging.

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Supporting the Body's Own Ability to Regenerate

Manufacturer:	Kerecis hf, Eyrargata 2, 400 Isafjordur, Iceland www.kerecis.com
Distribution/ordering Europe:	Kerecis AG, Webereistrasse 61, 8134 Adliswil, Switzerland Tel: +41 499 15 66, Email: support@1wound.info, Fax: +41 499 15 67
Indication	■ Diabetic ulcers, chronic vascular ulcers , venous ulcers ■ Trauma wounds (including abrasions, lacerations and skin tears) ■ Acute surgical wounds (including debridement, amputation and donor sites) ■ Surgical wounds (dehiscence or failed healing after surgery) ■ Imminent failure of split thickness skin graft ■ Post-Injection necrosis
Precautions and contraindication	■ If there is necrotic tissue or biomembrane in wound, remove as much as possible with thorough debridement prior to device application. ■ Ensure that the product does not overlap the wound edges but only covers the basis of the wound. ■ Remove exudate and control bleeding prior to device application. ■ Should the wound be complicated by an infection while the device is in use, it is to be removed and the infection managed. ■ Do not reuse or re-sterilize because of cross contamination and loss of physical characteristic of the material respectively. ■ Discard unused portions of the device. ■ Sterile if package is unopened and undamaged. ■ Do not use the device if the package seal has been broken or if handling has caused damage or contamination. ■ Do not use in case of known fish allergies.
Shelf life and storage	3 years, at or below room temperture

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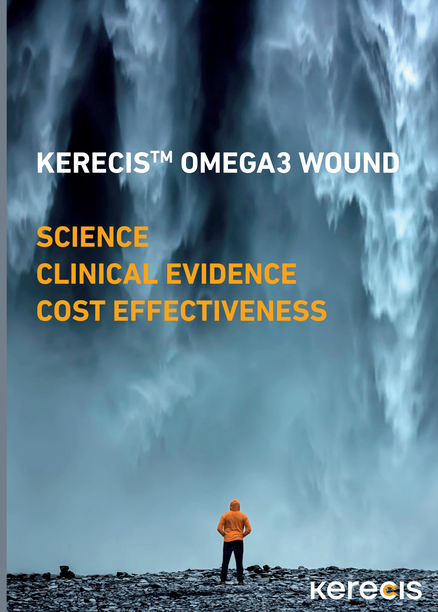


KERECIS™ OMEGA3 WOUND

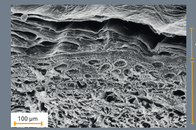
SCIENCE
CLINICAL EVIDENCE
COST EFFECTIVENESS

kerecis

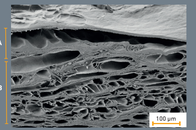
THE FISH

- Kerecis™ Omega3 Wound is an intact fish skin graft from the North Atlantic cod (Gadus morhua).
- Kerecis fish skin graft is the only skin substitute product on the market that does not originate from mammalian tissues.
- Kerecis™ Omega3 Wound is naturally rich in omega-3 polyunsaturated fatty acids (PUFAs) due to its cold-sea origin. The fish skin has both higher total amount of lipids and over 30x higher ratio of omega-3 fatty acids compared to its mammalian skin substitute counterparts.
- Fish skin shares evolutionary homology with human skin and contains all the components of normal human skin like glycosaminoglycans, proteoglycans and elastin. Due to the mild processing Kerecis® Omega3 Wound maintains its natural structure.

Human Skin



Fish Skin



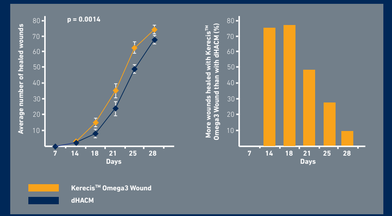
A Epidermis
B Dermis

Image: Scanned electron microscopy images of human skin (left) and Kerecis™ Omega3 Wound (right) show the structural similarities between the skin types.

CLINICAL EVIDENCE AND COST EFFECTIVENESS

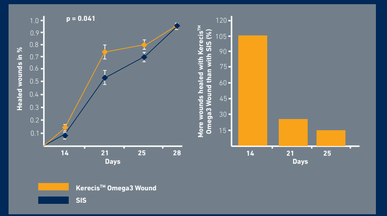
Double blind RCT - Acute biopsy wounds heal significantly faster with Kerecis™ Omega3 Wound than with dHACM[4]

- Two identical punch biopsy wounds on volunteers were randomized for treatment with either Kerecis® Omega3 Wound or dehydrated human amnion/chorion membrane allograft (dHACM).
- A total of 170 wounds were treated with 85 wounds per group.
- Primary endpoint was an FDA recognised endpoint as time-to-heal (full epithelialization).
- Wounds treated with Kerecis™ Omega3 Wound (orange) healed significantly faster than the dHACM treated wounds (blue).
- The hazard ratio was 2.37 with a highly significant p-value of 0.0014. Projected healing was 22 days for the fish skin treated group and 24 days for the dHACM group.



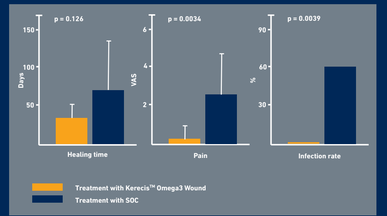
Double blind RCT - Kerecis™ Omega3 Wound heals wounds significantly faster than with porcine-derived SIS[5]

- Healthy volunteers given two 4-mm full thickness punch wounds on their arms were treated with fish skin or porcine small-intestinal submucosa (SIS).
- A total of162 wound were randomized to treatment with either Kerecis or SIS.
- Wound healing was assessed on days 14, 21, 25, and 28, by a dermatologist blinded to the treatment.
- Wound healing at day 28 was the primary end point.
- Wounds treated with fish skin grafts healed significantly faster compared to porcine-SIS, p-value = 0.041.



Prospective comparative study - Kerecis™ Omega3 Wound is superior to SOC in treating graft donor sites[6]

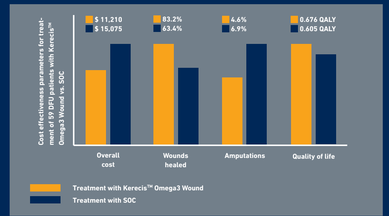
- Fish skin or standard of care (SOC) was used to treat split-thickness skin graft (STSG) donor sites in 21 patients operated on for radial forearm free flap reconstruction for head and neck wounds.
- Healing time was halved when using fish skin, from 68 to 32 days, on average, compared to SOC.
- Fish skin reduced pain levels and local infection rates:
  - Fish skin significantly reduced pain (p = 0.0034 on Day 5) as assessed by the Visual Analogue Scale (VAS).
  - Infection rate was reduced from 60% with SOC to 0% with fish skin (p=0.0039).



COST EFFECTIVENESS- Kerecis™ Omega3 Wound is more cost effective than Standard of Care (SOC)*

- Single centre retrospective study using data for 59 DFUs treated with fish skin between 2014-2017.
- Data were used to calculate transition probabilities for a Markov model comparing hypothetical cohorts fish skin-treated patients versus standard of care (SOC).
- Cost was from the payer's perspective and the time horizon set at 1 year.
- A probabilistic sensitivity analysis based on a Monte Carlo simulation indicated that fish skin treatment of DFUs would be 93.6% likely to be cost effective for a Willingness to Pay at $100,000 per QALY.

* Manuscript in preparation



CASE SERIES- Kerecis™ Omega3 Wound has an extensive record of success in case series

Indication	Investigator	Summary
Diabetic foot ulcer[7]	Michael, S Winters, C Khan, M	A rapid increase in wound healing was observed during the initial 4 weeks following graft application. Fish graft encourages wound healing by enabling the wound to transition from a chronic to an acute stage of healing.
Split thickness donor sites and partial thickness burns[8]	Alam, K Jeffery, SLA	The fish skin was found to be easy to use, resulted in no adverse reactions or immune response and produced high quality donor site healing in all cases. In addition, patients reported analgesic properties with the fish skin.
Diabetic foot ulcer[9]	Woodrow, T Chant, T Chant, H	Fish skin grafts showed promise in accelerating wound healing when used early (<3 months) in the healing process.
Chronic vascular wounds[10]	Dorweiler, B, et Al.	Fish skin was reported as being an effective treatment option in 25 complicated wounds.
Diabetic foot ulcer[11]	Winters, C	Effective healing of a chronic ulcer by fish skin, and avoidance of amputation.
Wound dehiscence[12]	Winters, C	The fish skin was effectively used to treat a chronic wound unresponsive to previous treatments.
Chronic vascular ulcers, venous ulcers[13]	Clasen, TJ	Fish skin grafts successfully kickstarted granulation in all of the wounds.
Chronic vascular ulcers, venous ulcers[14]	Cyrek, A, et Al.	Fish skin achieved a progressive wound reduction, robust granulation, and epithelialization resulting in complete long-term wound healing. A potential beneficial analgesic effect of the fish skin was noted.
Chronic wounds[15]	Fagerdahl, A	There was efficient and rapid granulation tissue formation seen in many of the wounds and improved aesthetic outcomes in the form of reduced scar formation.
Chronic wound[16]	Winters, C	The fish skin was effectively used to treat a chronic wound unresponsive to previous treatments.
Chronic vascular ulcers, venous ulcers[17]	Trinh, TT, et Al.	Fish skin represented a viable treatment option in complicated wounds in the lower limb of diabetic patients to circumvent any otherwise necessary proximalisation of amputation level.
Chronic ulcers[18]	Yang, CK Polanco, TO Lantis, JC	This fish-skin product provided an effective wound closing adjunctive ECM. This is true when used in this compassionate setting, where many other products fail.