



Bioengineered skin substitutes for wound management

This information is about the safety and effectiveness of bioengineered skin substitutes for wound management compared with standard dressings and biological skin replacements. It is based on research conducted by the Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S).

THE FOLLOWING INFORMATION IS NOT INTENDED TO REPLACE THE ADVICE OF YOUR DOCTOR, BUT RATHER TO HELP YOU AND YOUR DOCTOR MAKE DECISIONS ABOUT YOUR CARE THAT ARE BEST FOR YOU.

Main messages

(Please see the end glossary for a description of medical terms used.)

The available information was limited by the small numbers of patients, short follow-up times and differences in the way patient outcomes were reported.

- **Safety:** Bioengineered skin substitutes used with standard treatment are at least as safe (in terms of complications such as infection) as standard treatment alone for the management of venous leg ulcers, diabetic foot ulcers and other wounds.
- **Effectiveness:** There was not enough data to decide whether using bioengineered skin substitutes with standard treatment is as effective in the management of venous leg ulcers, diabetic foot ulcers and other wounds; however, healing time may be reduced for patients with diabetic foot ulcers under this regime compared to standard treatment. More high quality trials on bioengineered skin substitutes are needed to collect information on standard outcomes for patients over a longer period of time.

(For information on ASERNIP-S safety and effectiveness classifications, please visit the review process page on the website at <http://www.surgeons.org/asernip-s>)

Conventional treatments for wounds

Wounds heal in several steps. During inflammation, blood flow to the area increases and white blood cells move in to clean up dead cells and fight infection. New blood vessels grow to supply oxygen and nutrients to enable the wound to heal. Special tissue may then be deposited into the wound, which gradually contracts. Each of these steps must be completed for the wound to heal properly and restore the normal skin structure (figure 1).

Some wounds do not heal properly (i.e. the wound has not passed through all the healing steps). Poor healing may be due to lack of oxygen, bacterial infection and pressure on or injury to the wound. Other influencing factors include fluid in the body tissues, infection, circulation problems, tumour, smoking and peripheral nerve disorders. Unhealed wounds need treatment to properly close the skin and minimise pain, infection and scarring.

Management of a wound will depend on the cause.

- Venous leg ulcers between the ankle and knee do not heal because veins are not properly draining blood away and the wound cannot receive enough nutrients to heal. One in 1000 Australians suffers from this condition. It is usually treated by resting and elevating the leg and applying compression bandaging and support stockings; surgery may be needed to clean the wound and add a graft.
- Diabetic foot ulcers result from disorders of peripheral nerves, impaired blood supply and poor wound healing. Five to 15 in 100 Australians with diabetes suffer from foot ulcers, which have a risk of infection, gangrene and possible amputation. Treatment involves cleaning up dead tissue, dressings, antibacterial agents and pressure-reducing footwear.
- Other wounds may also arise from trauma, infectious disease, and removal of tumours and skin for grafts. Surgical wounds which do not heal are treated by closing the wound, using dressings, skin flaps or skin grafts.

Figure 1: Skin layers



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Skin graft may be either:

- a biological skin replacement which may be taken from elsewhere on the patient (autograft). This is the best replacement for lost skin although there may not be enough available to replace the skin in major wounds, or
- a bioengineered skin substitute.

What are bioengineered skin substitutes?

If a patient needs a graft but not enough autograft is available, bioengineered skin substitutes can be made quickly which is either:

- grown (cultured) from the patient's healthy skin cells (and will not be rejected)
- a biosynthetic skin substitute developed to cover the skin surface and encourage growth of blood vessels and wound healing. This can be made in large quantities and has a very low risk of cross-infection.

However, bioengineered skin substitutes are expensive and the practitioner needs experience to decide which material is appropriate. Uncertainty regarding safety and effectiveness of the range of bioengineered skin substitutes led ASERNIP-S to conduct a systematic review to compare them with standard methods of wound management.

What does the research show?

ASERNIP-S looked at the research, which was limited because the studies involved only a small number of patients over short periods of time and didn't all measure the same patient outcomes. Long-term benefits are unclear. The research suggests:

Venous leg ulcers. Compared to standard treatment, bioengineered skin substitutes used with standard treatment were about the same as standard treatment alone in terms of:

- wound closure, time to heal and reduction in the area of ulceration
- levels of pain experienced, recurrence of the wound and wound infection.

Diabetic foot ulcers. Compared to standard treatments, bioengineered skin substitutes used with standard treatment in some cases may:

- reduce wound healing time (Apligraf®, Dermagraft®, GraftJacket®, Hyalograft™, Laserskin™, Orcel™ and Promogran™)
- improve wound closure (Apligraf®, GraftJacket® and Orcel™)
- lower rates of infection
- result in similar recurrence rates.

Other wounds. Bioengineered skin substitutes were no better than standard treatment, although patients may have reported less pain. Compared to standard therapy:

- Apligraf® produced similar results for wounds from surgical cuts
- Biobrane® had poorer results when used to cover wounds caused by taking donor skin
- Promogran™ was as good for pressure sores.

Some of the above skin substitutes may not be available in Australia.

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What is ASERNIP-S?

Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S) is a program of the Royal Australasian College of Surgeons (RACS). ASERNIP-S conducts literature reviews on the safety and effectiveness of new surgical techniques before they are widely used, for example bioengineered skin substitutes for the management of wounds. Each review collects all relevant information, or evidence, on new and standard techniques used to treat a medical condition. The quality of evidence is assessed. ASERNIP-S then makes recommendations on the safety and effectiveness of the procedures, that are endorsed by RACS, sent to hospitals and surgeons in Australia and overseas, and published on the website with summaries for consumers.

For further information on bioengineered skin substitutes for the management of wounds, please see the full systematic review on the ASERNIP-S website:

<http://www.surgeons.org/asernip-s>

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Glossary

autograft (skin graft): a piece of skin taken from an uninjured area (donor site) of a patient to repair an injured area on the same patient

bioengineered skin substitutes: materials with both synthetic and biological components OR products created by manipulating biological tissues to alter them for a particular purpose

biological skin replacements: replacing injured skin of a patient with pieces of their own healthy skin

biosynthetic skin substitutes: dressings developed to mimic the function of skin that contains human, animal and/or synthetic material

inflammation: a normal response to tissue injury characterised by pain (caused by the release of chemicals from inflammatory cells), redness and heat (caused by widening of blood vessels allowing more blood and blood cells to an injured area for repair) and swelling (caused by leakage of fluid from the widened blood vessels). Abnormal inflammation, such as that which occurs when infection is present, results in further tissue damage, delay in healing and poor scarring.

skin flap: patient's flap of skin which is still connected to its blood supply and rolled over to cover a wound on the patient. When the flap is firmly connected to the wound base via blood vessels, the flap is disconnected from its origin.

skin graft: a piece of relatively thin tissue transplanted onto a wound

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Figure 1 is adapted from a diagram provided courtesy of Royal Adelaide Hospital - Medical Art & Design, Australia

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