

Skin Substitutes for Adults With Diabetic Foot Ulcers and Venous Leg Ulcers: Recommendation

Final Recommendation

- Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding skin substitutes for adults with difficult-to-heal neuropathic diabetic foot ulcers
- Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends against publicly funding skin substitutes for adults with difficult-to-heal venous leg ulcers

Rationale for the Recommendation

The Ontario Health Technology Advisory Committee has reviewed the findings of the health technology assessment¹ and determined that skin substitutes, when used as an adjunct to standard care, are more effective than standard care alone in promoting complete wound healing of difficult-to-heal neuropathic diabetic foot ulcers and are likely to be more effective in promoting complete wound healing of difficult-to-heal venous leg ulcers. The committee noted that the evidence of benefit supported two specific types of skin substitute—dermal and multi-layered—and that the benefit of epidermal skin substitutes is uncertain because no strong evidence was found. The committee also acknowledged that epidermal skin substitutes are not currently used in clinical practice in Ontario.

In making the recommendation for difficult-to-heal neuropathic diabetic foot ulcers, the committee considered the likelihood of skin substitutes being cost-effective to be moderate and the budget impact to be reasonable. They also acknowledged the lived experience of people with difficult-to-heal diabetic foot ulcers, the potential for skin substitutes to improve equity in patient care, and the importance of equity given the disproportionate risk of diabetes in some racialized communities. Committee members recognized that patient eligibility for treatment with skin substitutes should be determined by health care providers with expertise in wound care and the use of skin substitute products. Committee members also recognized that skin substitutes are an acute treatment, not meant for long-term therapy or wound prevention.

In making their recommendation for difficult-to-heal venous leg ulcers, the committee agreed that, although skin substitutes may promote complete wound healing, it was highly unlikely that the treatment would be cost-effective and that the budget impact was unfavourable at this time. Committee members acknowledged the lived experience of people with difficult-to-heal venous leg ulcers. They also acknowledged that a significant reduction in the cost of skin substitutes would be needed to improve the cost-effectiveness and budget impact profiles of this treatment before public funding could be recommended for this health condition.

Decision Determinants for Skin Substitutes for Adults with Diabetic Foot Ulcers and Venous Leg Ulcers

Decision Criteria	Subcriteria	Decision Determinants Considerations
<p>Overall clinical benefit How likely is the health technology/intervention to result in high, moderate, or low overall benefit?</p>	<p>Effectiveness How effective is the health technology/intervention likely to be (taking into account any variability)?</p>	<p>Dermal skin substitutes, when used as an adjunct to standard care, are more effective than standard care alone in promoting complete wound healing for adults with difficult-to-heal neuropathic DFUs (GRADE: High) and are likely more effective than standard care alone in promoting complete wound healing for adults with difficult-to-heal VLU (GRADE: Moderate). Multi-layered skin substitutes, when used as an adjunct to standard care, are likely to be more effective than standard care alone in promoting complete wound healing for adults with difficult-to-heal neuropathic DFUs (GRADE: Moderate) and are more effective than standard care alone in promoting complete wound healing for adults with difficult-to-heal VLU (GRADE: High). The effectiveness of epidermal skin substitutes for complete wound healing could not be determined for DFUs (no studies). Evidence was uncertain for VLU (GRADE: Very low).</p>
	<p>Safety How safe is the health technology/intervention likely to be?</p>	<p>We were unable to form conclusions about the safety of skin substitutes because of an insufficient number of adverse effects reported in the included studies. Overall, adverse effects occurred rarely.</p>
	<p>Burden of illness What is the likely size of the burden of illness pertaining to this health technology/intervention?</p>	<p>About 1.53 million people in Ontario are living with diabetes. The lifetime risk for DFUs in people with diabetes is up to 25%. The prevalence of VLU ranges from 0.8 to 1 per 1,000 population.</p>
	<p>Need How large is the need for this health technology/intervention?</p>	<p>DFUs and VLU negatively affect people's quality of life. Skin substitutes may offer an additional benefit when used as an adjunct to standard care.</p>

Decision Criteria	Subcriteria	Decision Determinants Considerations
<p>Patient preferences and values How likely is adoption of the health technology/ intervention to be congruent with patient preferences and values and with ethical or legal standards?</p>	<p>Patient preferences and values Do patients have specific preferences, values, or needs related to the health condition, health technology/intervention, or life impact that are relevant to this assessment? (Note: The preferences and values of family members and informal caregivers are to be considered as appropriate.)</p>	<p>Participants reported desiring an effective treatment for DFUs and VLUs to prevent potential adverse health outcomes, such as amputation.</p>
	<p>Autonomy, privacy, confidentiality, and/or other relevant ethical principles as applicable Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles that are relevant to this assessment? (Note: The preferences and values of the public are to be considered as appropriate.)</p>	<p>Awareness of this treatment option among patients is limited. To support patient autonomy and independence in decision-making, patients should have access to all relevant information about possible treatment options for DFUs and VLUs.</p>
<p>Equity and patient care How could the health technology/ intervention affect equity of access and coordination of patient care?</p>	<p>Equity of access or outcomes Are there disadvantaged populations or populations in need whose access to care or health outcomes might be improved or worsened that are relevant to this assessment?</p>	<p>Currently, skin substitutes are available only in a limited number of clinics in Ontario; this may pose a geographical barrier to access for some patients. Cost may also be a barrier to access for some patients. DFUs and VLUs have a negative effect on people’s quality of life, particularly owing to impaired mobility. These ulcers can cause personal, psychological, social, and financial burdens.</p>
	<p>Patient care Are there challenges in the coordination of care for patients or other system-level aspects of patient care (e.g., timeliness of care, care setting) that might be improved or worsened that are relevant to this assessment?</p>	<p>Skin substitutes may improve health outcomes and may result in the avoidance of amputation and its associated risks. Patients must be referred to one of the limited number of clinics in Ontario that provide skin substitutes to have access to this treatment.</p>

Decision Criteria	Subcriteria	Decision Determinants Considerations
Cost-effectiveness	Economic evaluation	DFUs
How efficient is the health technology/intervention likely to be?	How efficient is the health technology/intervention likely to be?	<p>At a willingness-to pay of \$50,000/QALY gained, the cost-effectiveness of skin substitutes plus standard care compared with standard care alone is uncertain^a (47% probability of being cost-effective). At a willingness-to pay of \$100,000/QALY gained, skin substitutes plus standard care are moderately likely to be cost-effective compared with standard care alone^a (71% probability of being cost-effective). Our model suggested that the most likely estimate of the ICER is \$48,242/QALY gained.</p>
		VLUs
		<p>At willingness-to pay of \$50,000 and \$100,000/QALY gained, skin substitutes plus standard care are highly unlikely^a to be cost-effective compared with standard care alone (0% probability of being cost-effective). Our model suggested that the most likely estimate of the ICER is \$1,868,850/QALY gained.</p>

Decision Criteria	Subcriteria	Decision Determinants Considerations
Feasibility of adoption into health system How feasible is it to adopt the health technology/intervention into the Ontario health care system?	Economic feasibility How economically feasible is the health technology/intervention?	DFUs In people with DFUs, the cost of skin substitutes is about \$3,755.12 per person (at \$629 per application for 5.97 weekly applications). We estimated that the annual budget impact of publicly funding skin substitutes over the next 5 years would range from an additional \$0.17 million in year 1 to an additional \$1.2 million in year 5. VLUs In people with VLUs, the cost of skin substitutes is about \$13,687.48 per person (at \$1,901.04 per application for 7.2 weekly applications). We estimated that the annual budget impact of publicly funding skin substitutes over the next 5 years would range from an additional \$1 million in year 1 to an additional \$7.7 million in year 5.
	Organizational feasibility How organizationally feasible is it to implement the health technology/intervention?	Given the availability of a number of skin substitute products licensed by Health Canada that can also be stored at room temperature, there are no concerns about the organizational feasibility of implementing treatment with skin substitutes for adults with difficult-to-heal neuropathic DFUs and VLUs.

Abbreviations: DFU, diabetic foot ulcer; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; VLU, venous leg ulcer.

^aUncertainty was classified into one of five categories based on the Ontario Decision Framework²: highly likely to be cost-effective (80–100% probability of being cost-effective), moderately likely to be cost-effective (60–79% probability), uncertain if cost-effective (40–59% probability), moderately likely to not be cost-effective (20–39% probability), or highly likely to not be cost-effective (0–19% probability).

References

- (1) Ontario Health. Skin substitutes for adults with diabetic foot ulcers and venous leg ulcers: a health technology assessment. Ont Health Technol Assess Ser [Internet]. 2021 June 21(7):1–165. Available from: <https://www.hqontario.ca/evidence-to-improve-care/health-technology-assessment/reviews-and-recommendations/skin-substitutes-for-adults-with-diabetic-foot-ulcers-and-venous-leg-ulcers>
- (2) Krahn M, Miller F, Bayoumi A, Brooker AS, Wagner F, Winsor S, et al. Development of the Ontario decision framework: a values based framework for health technology assessment. Int J Technol Assess Health Care. 2018;34(3):290-9.

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