South Australian Policy Advisory Committee on Technology (SAPACT)

Health Technology Assessment (HTA) Decision Summary Update

Government of South Australia

SA Health

Note: The Sponsor has removed CelluTome from the ARTG due to commercial viability, not due to safety concerns. CelluTome is no longer legally allowed for use in Australia.

CelluTome™ epidermal harvesting system for chronic wound management – Update

SAPACT MEETING DATES	20th SAPACT meeting (22 November 2019); 26th SAPACT meeting (20 August 2021)
APPLICATION #	2109 (refer to 1907 for previous decision)
TECHNOLOGY	CelluTome™ Epidermal Harvesting System (KCI Medical Australia Pty Ltd)
TECHNOLOGY CLASSIFICATION	TGA class IIa
PATIENT INDICATION (Therapeutic Goods Administration (TGA))	The CelluTome Epidermal Harvesting System is an electrically-powered dermatome intended to reproducibly cut a thin skin graft for autologous skin grafting.

SAPACT DECISION

☒ Restricted recommendation for clinical use with financial/operational restrictions and under audit conditions.

SAPACT Advisory Recommendations

Based on international and local evidence for clinical safety, effectiveness and cost effectiveness, SAPACT advises a restricted use of the CelluTome Epidermal Harvesting System with clinical audit. The use of CelluTome can provide a benefit to certain patients with failed or delayed wound healing who have not responded to standard wound care. The cost of the CelluTome harvester unit (single-use consumable) to SA Health should remain in the order of $[redacted], subject to indexation, with the company providing the CelluTome control unit and vacuum at no additional cost. Under these arrangements, CelluTome could reduce the costs of ongoing care of patients with non-healing wounds (including dressing costs, clinic time as well as costs for adverse events), although the cost benefits of local use is uncertain. The device should be used under the following conditions:

Patient selection

The following patients with wounds of significant tissue deficits (surface area >2.5cm^2) which have not responded to best standard care:

- Chronic non-healing wounds: defined as wounds which have been present for greater than 6 weeks and which have not responded to best available wound management practice. Where practicable, underlying aetiology (e.g. venous disease) shall also have been addressed
- Acute wounds that may benefit from more rapid healing: defined as wounds which have been demonstrated slow wound healing progress (e.g. less than 30% surface area reduction in a 2 week period) or where a patient is at significant risk of adverse outcome in the event of wound infection or complication (e.g. an elderly, high comorbid [e.g. due to vascular disease] or immune compromised patient)

Model of care

- The provider site should be an appropriate care setting which allows ongoing consultations with and advice from clinicians (e.g. vascular or plastic surgeons) involved in the care of patients with complex wounds.
- Nominated users at each site who are: experienced in the care of complex wounds; appropriately qualified and credentialled to provide this service within their scope of practice; have received appropriate training; have notified their local clinical governance that they are a CelluTome user.
- A maximum number of up to four nominated users per site is recommended.
- The provider site should have a documented escalation pathway if the patients suffers from a continuation of wound deterioration or in the case of an adverse event e.g. infection.
- The preferred access to this technology is that the user purchases the harvester and the sponsor (3M) provides the control module which it cleans and maintains between procedures, as per current use.

Reporting requirements

The following deidentified information should be provided to the relevant Local Health Network's new technologies committee after two years of use for patients treated with CelluTome, and patients treated with split-thickness skin grafting (SSG):

- Provider site:
- Cumulative patient number:
- Name of user:
- Patient eligibility [or characteristics]: [significant tissue deficits (surface area >2.5cm^2) AND failed standard care AND EITHER chronic non-healing wound OR acute wound which has demonstrated slow wound healing progress or where a patient is at significant risk of adverse outcome in the event of wound infection or complication]
- Wound site location and dimensions:
    - Wound aetiology:
    - Patient comorbidities: [e.g. diabetes, vascular disease, renal failure]
- Donor site location: [xxx]
- Donor site dimensions: [xxx]
- Date of CelluTome [or SSG] procedure:
- Number of harvesters used:
- Patient length of stay:

- Outcomes:
  - Graft site healing: Complete/partial/failed
  - Donor site healing: Complete/partial/failed
  - [include date(s) of observation(s)]
  - Provide pre- and post-healing photos where possible
  - Adverse events: [e.g. complications, infections]
- Additional procedures:

In order to understand activity and outcomes, SAPACT requests that patient reports are forwarded to the SAPACT executive officer for compilation.

Background

This is a follow-up to an application to SAPACT in 2019 (1907) where this service was approved for use in 10 patients at SALHN, subject to more detailed clinical selection criteria, and a review of the clinical outcomes. Following the SAPACT recommendation, the applicant provided a response further clarifying their patient selection criteria to include:

- Chronic non-healing wounds: defined as wounds which have been present for greater than 6 weeks and which have not responded to best available wound management practice. Where practicable, underlying aetiology (e.g. venous disease) shall also have been addressed
- Wounds that may benefit from more rapid healing: defined as wounds which have been demonstrated slow wound healing progress (e.g. less than 30% surface area reduction in a 2 week period) or where a patient is at significant risk of adverse outcome in the event of wound infection (e.g. an elderly, high comorbid or immune compromised patient)

On 23rd February 2021 the applicant provided clinical outcomes for a 10-patient case series. In order to inform the decision on ongoing use of this technology, an updated review of international literature is provided below, together with a summary of the SALHN evidence.

Summary of international evidence

The body of evidence has improved since the previous SAPACT review in 2019. There remains a variability in study design including patient selection, wound aetiology and outcome reporting. SAPACT acknowledged the difficulty in designing RCTs and the wide variability in patient presentation for this indication.

Compared with split thickness skin grafting (SSG), graft sites treated with CelluTome epidermal grafts showed non-inferior wound healing, and superior healing of the donor sites. There was no evidence comparing CelluTome with standard care. SAPACT acknowledged that SSG is not a viable treatment option for vascular surgical patients due to the comorbid anaesthetic risk.

Summary of local evidence

Ten consecutive patients with varied indications received epidermal cell grafting with CelluTome. At up to 26 week's follow-up, there were no reported complications and complete wound healing was observed in 7 out of 10 cases, with a mean time of 10.7 weeks. All three of the patients who failed to heal their wound following epidermal grafting had a minimum of two comorbid contributors to poor wound healing. These local results and time-to-wound-healing are consistent with published outcomes.

REGULATORY APPROVALS

☒ **ARTG**: 312981 (8/1/2019)
☒ **US FDA**: 06/2013 as a class I device exempted from premarket notification 510(k). In 2015, a class II recall was issued for certain batches of harvesters due to packaging issues which may cause the blade to drift during shipping.
☒ **EU CE mark**: 04/2014, class of device is unclear

QUALITY OF EVIDENCE

Quality of Evidence	The previous SAPACT review in 2019 was restricted to five case series. Systematic searches were conducted in PubMed and Embase on 24 February 2021, supplemented by searches across a range of HTA and grey literature websites. Since the previous SAPACT review, one RCT, one non-randomised comparative study and four single arm observational series were identified. Both comparative studies compared the use of CelluTome with split thickness skin grafting (SSG): • Kanapathy 2020, RCT with 44 participants with wounds measuring more than 1cm x 1cm and less than 6cm x 6cm with a healthy granulating wound bed. The RCT was sponsored by Acelity (CelluTome manufacturer) and determined to be at some risk of bias due to a lack of multiple assessments of the data (Cochrane ROB2 tool). • Smith 2017, non-randomised comparative study of moderate quality (adjusted Downs and Black checklist) with 20 participants with chronic wounds (traumatic, acute and venous ulcer). The average wound size was 16.5 and 21cm^2 for Cellutome and SSG respectively (p value not reported). There was no reported industry support. • Bueher 2017, case series with 20 consecutive patients with chronic wounds, where epidermal cell grafts were used to assist healing of SSG donor sites of 0.33mm thickness. The wound area was not reported. The study was sponsored by Acelity (CelluTome manufacturer). • Everts 2017, case series with 78 patients with non-healing wounds of various etiologies. The most common wound

	types were wound dehiscence, radiation ulcer and venous ulcer, with an average wound surface area of 14·9±20·6mm^2. There was no reported industry support. • Joethy 2019, a series of 4 patients with burns. Wound size was not reported, although patients were provided with up to four sheets of epidermal grafts. There was no reported industry support. • Vinceneux 2018, a case series of 47 patients with venous or leg ulcers. The average wound area was 13cm^2 (range 3.1 to 78cm^2). There was no reported industry support. In addition, there was one case series which reported on the use of CelluTome for epidermal grafting of chronic wounds in patients with recessive dystrophic epidermolysis bullosa (Ebens 2020). There was also one systematic review from 2019 which was not able to be retrieved in full text (Qureshi 2019). These studies were not included in this summary. The etiology of the chronic wounds varied within and across the identified studies. Follow-up varied from 2 to 6 months. No evidence was identified comparing CelluTome with standard wound care.
CLINICAL NEED	
Burden of Illness	Chronic wounds are wounds that fail to progress healing or respond to treatment over the normal expected healing time frame (4 weeks) and becomes "stuck" in the inflammatory phase. These wounds have a significant impact in Australia both in terms of costs (an estimated AUD$3.5 billion per year) and on a patient's quality of life. More than 3,000 lower limb amputations are performed yearly in Australia due to non-healing leg or foot ulcers. Over 400,000 people suffer from chronic wounds. Based on the aetiology, chronic wounds are characterised as arterial ulcers, diabetic foot ulcers, venous leg ulcers, and pressure injuries.
Need	The following is taken from the 2019 SAPACT Decision Summary Document: The management of chronic wounds is through standard wound care, debridement, dressings and compression therapy. Most wounds will heal within 12 weeks if treated early. An important modality for wound coverage is autologous skin grafting, which is classified based on the thickness of the harvested skin: full-thickness skin graft (FTSG), SSG, and epidermal graft. SSG is the most common type of autologous skin grafting representing second-line strategy; however, it is an invasive procedure requiring surgery, anaesthesia (local or general), access to specialist equipment, rooms and staffing and can have high donor site morbidity. The key benefits of epidermal grafting over SSG included less pain, scarring, faster healing of donor site, simpler procedure and possible improved cost-effectiveness. Skin grafts can also be categorised based on the technique of donor site harvesting: free-hand methods, such as pinch or punch grafting—in which skin is harvested using a scalpel, other type of blade, or a punch biopsy tool—are typically employed when only a small graft is needed. When a larger amount of donor skin is harvested, powered dermatomes are used to increase efficiency. Skin grafts are not indicated for all patients due to underlying comorbidities. Epidermal grafting using the CelluTome epidermal harvesting system (powered dermatome) is an emerging option. The CelluTome is a minimally invasive skin harvesting system that is more automated and reproducible than pinch grafting. It provides minimal/pain-free epidermal skin grafts (ESG) for wound closure through autologous epithelialisation in both inpatient and outpatient settings. The CelluTome applies continuous negative pressure on normal skin to raise blisters. The procedure is purportedly low risk with minimal bleeding and infection. The CelluTome may also reduce clinical visits for patients with chronic wounds, avoid hospitalisation and theatre admissions.
CLINICAL BENEFIT The clinical evidence found non-inferior safety and non-inferior effectiveness for graft sites, non-inferior safety and superior effectiveness for donor sites compared to split thickness skin grafting.	
Safety	No adverse events were reported in the CelluTome population in both comparative studies. Two adverse events were reported in the SSG group of the non-randomised study (details not provided). Results from the case series supported the comparative evidence, with no safety issues reported in patients treated with CelluTome (Buerher 2017, Everts 2017, Joethy 2019 and Vinceneux 2018).
Effectiveness	<u>Graft sites</u> Compared to SSG, epidermal cell grafting with CelluTome showed similar wound healing at 6 weeks and 3 months (p = 0.24 and p = 0.12 respectively), and similar (Kanapathy 2020) or improved (Smith 2017) mean time for wound healing. Patient satisfaction was similar for graft site healing (p=0.096) (Smith 2017). In the non-randomised study there were two failed grafts in immunocompromised patients treated with CelluTome, and no failures in patients treated with SSC. Graft sites were fully healed in an average of 6-25 weeks (Kanapathy 2020, Smith 2017, Everts 2017, Burhrer 2017). There was also higher overall patient satisfaction in patients treated with CelluTome (p < 0.001 and p<0.05) (Kanapathy 2020 and Smith 2017 respectively), based on a validated skin grafting questionnaire. <u>Donor sites</u> Compared to SSG, epidermal cell grafting with CelluTome showed lower donor site morbidity (p = 0.001) and faster donor site healing time (EG: 4.86 days vs. SSG: 21.32 days) (p < 0.0001) (Kanapathy 2020).

	All donor sites were fully healed in all studies (over a timeline of 4 to 6 weeks). Case series In observational single arm studies, all donor and all or most recipient sites were reported as being healed at a follow-up of up to 6 months (Buehrer 2017, Joethy 2019). In one study of 78 patients (Everts 2017), two wounds showed no wound surface area reduction after 3 months follow up. A further study of 47 patients reported that at 2 months follow-up, 55.3 per cent of wounds were completely healed, with the remainder partially healed (Vinceneux 2018). No repeat procedures using CelluTome were reported.
Local data	The Applicant provided clinical evidence on 10 consecutive vascular surgery patients with lower limb wounds with stalled healing secondary to chronic underlying aetiology (venous hypertension/insufficiency, peripheral arterial disease or diabetes) and delayed closure due to significant tissue deficit arising from surgery (fasciotomy, amputation or surgical debridement). The patient selection criteria were: • Wound superficial in depth (no deeper than dermis level of tissue deficit) • Wound bed contained 80 % or greater granulation tissue volume • Wound was not acutely infected, nor had signs of active tissue infection • Wound was situated in the lower extremity (lower limbs) • Wound was present on a limb with no acute ischemia • Wound healing was predicted to take longer than six weeks or more (clinical opinion of treating nurse practitioner or vascular surgeon) In selected cases, epidermal cell grafting with CelluTome was supported by two adjunctive technologies: • A novel tissue regeneration matrix – NovoSorb® Biodegradable Temporising Matrix (BTM), which provides a sealed membrane to support the proliferation of cell proliferation, was used in two patients. • VAC therapy for 1-2 weeks, to decrease air pressure on the wound bed was used in all but one patient. The mean wound size was 28cm^2. There were no reported complications. Complete wound healing was observed in 7 out of 10 cases. Failure of graft was observed in two cases: absence of new epithelial tissue was observed in a fore foot amputation and an increase in wound surface area was observed in a venous leg ulcer. In the third case, the wound failed to completely epithelialise at the maximum follow-up of 26 weeks. All 3 of the patients who failed to heal their wound following epidermal grafting had a minimum of two comorbid contributors to poor wound healing. The average time to wound healing was 10.7 weeks (range: 4-21 weeks). All donor sites completely healed within 6 weeks.
SUITABILITY OF PATIENT GROUP	
Suitability of Patient Group	No clinical guidelines were identified for the use of CelluTome. There are a range of guidelines for wound management. The identified studies reported the use of CelluTome in wounds from a range of aetologies. There appears to be no current highly targeted patient selection. There are a small number of ongoing trials, including one small RCT investigating CelluTome for burns wounds. There are also ongoing studies for the use of CelluTome for radiation wounds, for patients with vitiligo, epidermolysis bullosa, and with skin problems related to graft-versus-host disease.
FINANCIAL CONSIDERATION	
Device costs	The following is taken from the original SAPACT summary: Cost of CelluTome harvester unit (single-use consumable) to SA Health = AUD$[redacted] SALHN proposed [redacted] – [redacted] patients/year (AUD$[redacted] x [redacted] patients = AUD$[redacted] harvester unit costs only) • The cost of AUD$[redacted] does not include the cost of the nursing time to perform the procedure or any variations in the types of dressings that might be required following the graft / to support the graft during the first week or so. • The company confirmed that the use of the CelluTome control unit and vacuum (both cost a total of AUD$[redacted]) are included in the cost of the harvester. This includes the delivery and pick up of the device from the site, maintenance/cycling/QA process between patient use. The company's local technician will use the ISSO approved checklist when cycling every device between patient use. • The harvester is not currently under the SA Health Procurement wound contract. Cost of [redacted] (silicone dressing) for the harvester unit = AUD$[redacted]/piece (7.5 x 11cm) • The company manufactures and recommends using the [redacted] dressing, which is used to transfer the epidermal graft to the wound site.

	• The [redacted] was submitted on the SA Health wound care tender and was accepted for use and is cost-effective in comparison to the other two brands available. • [redacted] is not recommended by the applicant and company to transfer the microdomes/epidermal graft to the site. As a cover dressing the clinician can choose from a range of products available on the SA Health wound care tender.
Value for Money	<u>SA Health</u> Due to limitations of available local data, a cost-effectiveness analysis of the use of CelluTome in SA was not possible. In the original document, a single cost analysis publication set in the US suggested improved outcomes and cost-savings of approximately USD$1,000 per patient. A recent non-randomised comparative study included a simple cost evaluation (Smith 2017). Costs are taken from a UK NHS perspective (OPCS (Office of Population Censuses and Surveys) Classification of Interventions and Procedures). The overall cost per patient for ESG was GBP£431 and GBP£1,489 for SSG, resulting in a saving of approximately GBP$1,000. There is no published study comparing the costs of CelluTome with standard wound management. The following is taken from the original SAPACT summary: In SA Health, if standard wound management is taken to be the appropriate comparator, weekly dressing costs may vary considerably depending on the frequency of the dressing, and the types of dressings. The applicant has provided an estimate of the cost of weekly dressing for two of the patients prior to undergoing the CelluTome procedure. The estimate was AUD$[redacted] for one patient and AUD$[redacted] for another. Any reduction in time to healing will accompany some utility gains, and a reduction in out-of-pocket costs including travel expenses for patients. For CelluTome to be cost-effective, it would likely take only a small proportion of healed wounds that would not otherwise have healed, or that consequently became infected, or resulted in amputation. The applicant also advised that a chronic wound has ongoing health care costs whilst it is unhealed: Community nursing, wound dressings and speciality outpatient encounters (if a speciality like vascular surgery is involved). These costs vary, however best-case scenario for any chronic wound is a minimum of twice weekly wound dressings, which generally involve multi-product complex wound dressings, wound management trained nursing care and intermittent tertiary outpatient input. Other factors to consider include patient quality of life improvement in the event of wound healing; avoidance of hospital admission secondary to infection; improved life expectancy and reduced risk of lower limb amputation secondary to infection. Current Medical Benefits Schedule (MBS) items for skin grafting relate to traditional surgical procedures, hence the CelluTome procedure could be classified under 10.13 (minor medical procedures) or item 40.13 (wound management) under Tier 2 Non-Admitted Services. Should the CelluTome™ technology continue to diffuse into the health sector, appropriate treatment classification and subsidies may require further consideration (HealthPACT Brief 2016).
Funding Approvals	<u>Australian recommendations</u> • This service has not been assessed by the Medical Services Advisory Committee (MSAC) • As reported in the previous SAPACT summary, CelluTome was reviewed by HealthPACT in 2016. At the time, the recommendation was for the technology to be restricted for use in clinical trials. <u>International recommendations</u> • No international recommendations were identified.
FEASIBILITY OF ADOPTION	
Organizational Feasibility	In SA Health, sites will use existing staff and infrastructure. This procedure may be used provided that standard arrangements are in place for clinical governance, consent and audit by the LHN(s). Patients should be clearly informed of the benefits and limitations of this technology, including that CelluTome is a novel technology to SA Health.
Credentialing and Competency	No credentialing issues were identified. The procedure should only be provided by clinicians with specific training and accreditation.
CONSISTENCY WITH EXPECTED SOCIETAL/ ETHICAL/ LEGAL VALUES	
Values	The service is consistent with expected societal, ethical and legal values at this time. CelluTome provides an option for certain patients where standard therapies have become ineffective, and provides a less invasive alternative to SSG.
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