South Australian Policy Advisory Committee on Technology (SAPACT)

Health Technology Assessment (HTA) Decision Summary

Government of South Australia

SA Health

NovoSorb® Biodegradable Temporising Matrix (BTM) for Treating Burns and Complex Wounds

SAPACT MEETING DATES	18th SAPACT Meeting, 7 June 2019
APPLICATION #	1919
TECHNOLOGY	NovoSorb® BTM (PolyNovo Biomaterials Pty Ltd, Melbourne, Australia) *The primary function of the NovoSorb BTM is to 'temporise' wounds by affording physiological closure through reduction of trans-epidermal water loss.*
TECHNOLOGY CLASSIFICATION	TGA class III high-risk
PATIENT INDICATION (TGA)	NovoSorb BTM for use wherever the skin dermis is lost, regardless of (1) causes e.g. trauma, surgical removal, wounds or burns and (2) severity.

SAPACT DECISION

☒ Restricted recommendation for clinical use subjected to implementation under audit conditions.

SAPACT Advisory Recommendations

Burns and complex wounds represent a challenging and important area of patient care and BTM has the potential to improve patient outcomes. Based on the evaluation of safety, clinical-effectiveness, cost-effectiveness and budget impact, SAPACT recommends the conditional approval of the NovoSorb BTM for 25 patients (10 burns patients and 15 complex wounds patients) for the first 12 months at CALHN. The applicant should report clinical outcomes of the patients in a 12-month follow-up report to SAPACT. Any other updated published evidence, including the results (available end of 2019) from the BARDA Feasibility Burn Study and the Australian case-series study (ACTRN12615000405516) should be submitted to SAPACT for review.

SAPACT notes that the NovoSorb BTM is price equivalent to the Integra dermal template (a bovine collagen I base substitute) per square centimetre. For procurement efficiencies in SA Health, SAPACT recommends that SA Health Procurement considers a price negotiation process for the NovoSorb BTM in comparison with the Integra and any other alternatives.

SAPACT Evidence Review Conclusions

Emerging low level descriptive evidence for NovoSorb BTM found favourable and safe short-term device and clinical performance in majority of the limited number of patients across few clinical indications. However, the study designs did not allow for the validation of the clinical effectiveness of NovoSorb BTM. There remained uncertainty around long term benefits and risks to patients. High quality controlled clinical trials are recommended to establish the comparative safety, clinical-effectiveness and cost-effectiveness of this technology.

REGULATORY APPROVALS

☒ **ARTG**: 14/08/2018	☒ **US FDA**: 8/11/2017 Note: FDA-approved only for clinical indications (i.e. surgical wounds) outside of full thickness burns.	☐ **EU CE mark**: pending approval

ARTG ID: 308217 PolyNovo Biomaterials Pty Ltd - NovoSorb BTM - Dressing, absorbable

ARTG functional description: The device is a sterile, fully synthetic biodegradable temporary skin substitute intended to temporize dermal injuries, where the dermis has been lost, and to facilitate dermal repair and generate a neodermis. The device is implanted and stapled/ sutured into a debrided wound bed and integrates through vascular and cellular infiltration. The device biodegrades through hydrolysis and is eventually fully resorbed in the body. The physician removes the sealing membrane for appropriate intervention.

Sizes (cm): 20x40; 10x20; 10x10

QUALITY OF EVIDENCE	
Quality of Evidence	Comprehensive searches were conducted in eight published scientific databases and 25 grey literature sources. No Health Technology Assessment (HTA) Reports, Systematic Reviews of Randomized Controlled Trials (RCTs) or RCTs comparing NovoSorb BTM with Integra in human studies were identified. Eight studies (comprising of 35 humans + 20 mice) were included in the SAPACT Evidence Review; seven studies were National Health Medical Research Council (NHMRC) level IV evidence and the mice study was level V evidence. Out of the 35 humans in the studies, 6 had significant burns and the remaining 29 had complex wounds. The included studies were critically appraised to be of moderate methodological quality. Clinical evidence on the safety and clinical-effectiveness of the NovoSorb BTM were limited to four small case-series (total n=32), three case reports (n=3) and one mice study (n=20) comparing NovoSorb BTM and Integra dressing. Conflicts of interest were present for most papers.
CLINICAL NEED	
Burden of Illness	There were 5,430 cases of hospitalised burn injury in Australia in between 2013 to 2014. About 16% (850) of hospitalised burn cases were considered high threat to life. One in five patients with burns to more than 20% of their body ultimately die as a result of their wounds. While burn injuries make up a small fraction (1%) of all hospitalisations for injury, they are often the most serious and can result in prolonged periods of acute care, long lengths of hospital stay, rehabilitation, numerous re-admissions and outpatient visits. There are limited Australian data on the prevalence of chronic wounds.
Need	Artificial dermal substitutes play an important role in physiologic wound closure after injury. In addition to contributing to stable, durable and flexible wound closure, they provide a scaffold for tissue repair. The comparator technology is the Integra (Life Sciences Corp., New Jersey, US), a bovine-derived collagen and glycosaminoglycan with semipermeable silicone membrane, which seems to be inferior to auto/allo/xeno-graft with respect to infection and graft take. The NovoSorb BTM, on the other hand, is synthetic and seems to have theoretically reduced antigenicity and putative lower infection rates compared to the Integra.

CLINICAL BENEFIT Many patients had diverse patient, burns and wounds demands that required individualised care, hence it was not possible to extract every outcome and descriptive nuances. The main safety and clinical outcomes from the included studies demonstrated that the NovoSorb appeared to be favourable, safe and have a good short-term device and clinical performance in majority of the patients. There remained uncertainty around long-term benefits and risks to patients.	
Safety	**Safety outcomes in burns group** > Faecal contamination BTM thigh w failure of BTM integration over shoulders (2% removed) > 4% infected BTM upper abdomen with Stenotrophomonas > 5 haematomas under BTM whilst heparinised for dialysis (8% removed) > Pseudomonas aeruginosa under BTM seal both arms (0% removed) **Failure to integrate:** > 7% total of 122% TBSA (5 burns) > Failure to integrate over lower limbs (1 burn) > Failure to integrate over devitalised muscle (1 complex wound) and seroma (1 complex wound) **SSG take** > Failure over malleolus > Failure over area where BTM has failed to integrate (2 complex wound patients) **Infection** Data from case series of 10 reconstructed free flap donor sites. Localised infection in 4/10 > One: muscle necrosis (BTM failed to adhere) > One: UTI and incontinence onto BTM – 37% BTM removed (resolved non-operatively) > Two: partial removal of seal allowed turbid fluid escape, integration continued without removal of BTM Subsequent series of 10 patients had no infection, all integrated and successfully grafted. No self-reported adverse events were reported from the Sponsor and there was no adverse event reports for the NovoSorb BTM and the Integra received by the TGA since 1 July 2012 based on the TGA Database of Adverse Event Notifications for Medical Devices.
Effectiveness	> The BTM' 'take' rate was mostly complete and uneventful without complications, however, a few patients experienced failed BTM integration in certain body areas with remedies undertaken. > The split skin graft (SSG) that followed BTM integration took and healed well in most patients, with some reports of no graft loss. In most patients, the graft take was complete and had a robust and aesthetically pleasing appearance. In cases which graft take was marred, there was adequate clinical management with successful regrafting. > The timings of delamination and definite grafting post BTM implantation were recorded in most studies and were described well; however, there are no yardsticks for comparison. > Scar outcomes evaluated using the Patient and Observer Scar Assessment Scale (POSAS) and Matching Assessment of Scars and Photographs (MAPS) found good scar characteristics and were mostly favourable to both patient and observer. > For studies that reported other patient-related outcomes, these patients recovered their functions, movements, cosmetically acceptable appearance and had regained their normal lifestyle, which are the aims of wound closure. > In two studies evaluating NovoSorb BTM for the reconstruction of free flap donor sites, localised infection was found in 40% of the patients. Subsequently, the NovoSorb BTM was improved and in the second study, no patient reported any infection. > In the laboratory mice study, the authors found that the fully synthetic NovoSorb BTM could provide wound closure, and its short-term (2 weeks) performance demonstrated its potential as an effective dermal template performing similar to the animal-derived Integra.
SUITABILITY OF PATIENT GROUP	
Suitability of Patient Group	SAPACT members noted that given the lack of comparative trials for burns and wounds indications, the FDA only approved the NovoSorb BTM for clinical indications (i.e. surgical wounds) outside of full thickness burns. The BARDA Feasibility Burn trial currently running (Nov 2016 - 2019) to assess BTM in full-thickness burns (open label single arm). TGA has approved Novosorb BTM for use wherever the skin dermis is lost, regardless of (1) cause and (2) severity. Published clinical evidence is only present for adults between 30 to 88 years old. In significant burns, patients with more than 50% TBSA burns have not been trialed (except for 1 patient in Greenwood 2016 case report) due to higher risk of morbidity and mortality. Within the approved TGA indications, there may also be a potential consideration for NovoSorb BTM in patients who are contraindicated to Integra, for example, patients who are allergic to bovine collagen or who have infected wounds.
FINANCIAL CONSIDERATION	
Device costs	In SA Health, the NovoSorb BTM seems to have price equivalence with the Integra dermal template (a bovine collagen I base substitute) per square centimetre.
Value for Money	No published costing or economic evaluation studies were found. A local SAPACT cost-effectiveness analysis was attempted but could not be performed due to the lack of evidential data from sponsor and applicant to understand the validity of underlying claims.
Australian Funding Approvals	The NovoSorb BTM has not been systematically evaluated for scientific evidence and clinical outcomes by any other international HTA and government agencies for the purposes of public funding, reimbursement, policy or consideration for uptake in routine clinical practice. The Commonwealth Medical Services Advisory Committee (MSAC) and Prostheses List Advisory Committee (PLAC)

	have not, at this time, approved NovoSorb BTM for funding. No other interstate health technology committees have reported evaluation on this technology.
FEASIBILITY OF ADOPTION	
Organizational Feasibility	The expertise at the Burns Unit, Royal Adelaide Hospital is recognized and SAPACT understands that the procedures will be carried out and followed-up appropriately.
Credentialing and Competency	The applicants have written that clinicians will ensure that patient training and support are provided. The Clinician(s) should be appropriately credentialed and approved by the SA Health Credentialing and Scope of Practice Committee to implant the NovoSorb BTM (refer to paragraph 3.4.3 New Clinical Procedures, Technologies and Treatments of the SA Health Credentialing Policy Directive).
CONSISTENCY WITH EXPECTED SOCIETAL/ ETHICAL/ LEGAL VALUES	
Values	Consistent with expected societal, ethical and legal values at this time.
QUERIES TO	Dr Deborah Chen, Senior Scientific Officer - HTA SAPACT, Medicines and Technology Programs, SA Department for Health and Ageing Level 8, Citi Centre Building, 11 Hindmarsh Square, Adelaide, SA 5000 Tel: +61 8 8226 7375; Email: Health.SAPACT@sa.gov.au
REVIEWER	Naomi Burgess, Director, Medicines and Technology Programs and Out of Hospital Pharmacy Services, SA Health
AUTHORISER	Prof Guy Maddern, SAPACT Chair