South Australian Policy Advisory Committee on Technology (SAPACT)

Health Technology Assessment (HTA) Decision Summary Update

Government of South Australia

SA Health

TGA Update (May 2017):

TGA has removed Absorb Bioresorbable Vascular Scaffolds from the ARTG due to increased risk of heart attacks and blood clots. Product is no longer available for use in Australia.

ABSORB™ Bioresorbable Vascular Scaffolds (BVS) for Treatment of Coronary Artery Disease

SAPACT MEETING DATES	Update 16/12/16, 3/3/17, 15/05/2015 (Initial application)
APPLICATION #	1609 Review of updated evidence since February 2015 SAPACT application Absorb BVS
TECHNOLOGY	Absorb BVS System (Abbott Vascular, CA, USA) *Everolimus-eluting poly-L-lactide BVS* - an implanted medical device that opens blocked coronary arteries. It is fully absorbed by the body over time.
TECHNOLOGY CLASSIFICATION	TGA class III high-risk medical device
PATIENT INDICATION	Patients with ischemic heart disease due to de novo native coronary artery lesions inserted during percutaneous coronary intervention to open narrowed coronary arteries, usually caused by arteriosclerosis.

SAPACT DECISION

☐ Recommended for clinical use with no further need for assessment.

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

☐ Restricted recommendation for clinical use with financial or operational restrictions

☐ Not recommended for clinical adoption at this time. Re-application may be undertaken in the future.

☒ Not recommended, subjected to implementation in clinical trial with approval from SA Health Human Research and Ethics Committee.

> In December 2016, SAPACT commenced an evidence update on the clinical use of the Absorb BVS to determine the need to update the SAPACT recommendation, following approval for use of the device use in two individual cases (IPU approval via local New Technology Committees). SAPACT had previously recommended the ABSORB BVS not be adopted into routine clinical practice within SA Health due to a lack of clear evidence of clinical benefit and questions regarding costs and cost-effectiveness.

> Based on considerations of safety, efficacy and cost-effectiveness, SAPACT's previous recommendation stands, that is, that Absorb BVS is not recommended for routine clinical use in SA Health at this time. This device should only be used under ethics approved clinical trial conditions.

> Absorb BVS was expected to demonstrate enhanced long-term effectiveness and clinical outcomes compared to other stents once the device fully dissolved over 3 years, however, newly published long-term clinical data highlight significant concerns regarding long-term safety and clinical effectiveness. The pivotal studies, ABSORB II (RCT 3-year data, n=468) and ABSORB III (RCT 2-year data, n=2008) showed that at the 2-year and 3-year mark, Absorb BVS failed to demonstrate its main theoretical advantages, compared to the metallic Xience drug-eluting stent (DES).

> The evidence from these studies demonstrated:

- significant increase in major adverse cardiac events (MACE), including cardiac death, heart attack and the need for an additional procedure to re-open the treated heart vessel, particularly in small coronary vessels;
- significantly higher rate of target lesion failure (primary outcome), target-vessel myocardial infarction (secondary outcome);
- unexpected increased incidence of late scaffold thrombosis;
- significantly higher in-device and in-segment late lumen loss/binary restenosis; and
- lack of achievement of the co-primary endpoints for superiority for vasomotion and non-inferiority of late lumen loss.

> The Therapeutic Goods Administration (TGA) issued a safety alert on 3rd March 2017, advising that TGA has reviewed the 2-year data from clinical studies on Absorb BVS and highlighting the outcomes.

> The TGA issued a hazard alert[2] on 2 May 2017 and Absorb BVS was removed from the Australian Register of Therapeutic Goods (ARTG) due to increased risk of heart attacks and blood clots. The manufacturer, Abbott Vascular Australia, is recalling all unused stock of the device. Absorb BVS System will now only be available for use in Australia through clinical trials and the unapproved product pathways (Special Access Scheme and Authorised Prescriber Scheme).

> Note : Since initial application, the 2nd generation Absorb BVS (known as Absorb GT1) has received regulatory approval from US FDA and Europe, but not yet in Australia.

Background

- In early 2015, the Absorb BVS was referred via the DHA Product Standardisation Committee to SAPACT for consideration. A detailed product application was provided by a CALHN cardiologist. Following review, SAPACT and the CALHN New Procedures Committee did not support the application for adoption of the Absorb BVS into routine clinical practice at that time.
- No further devices of Absorb BVS have been implanted in CALHN. In Feb 2016 and Sept 2016, SALHN and NALHN LHN New Technology Committees approved applications to use Absorb BVS on an IPU basis. In Nov 2016, it was reported to SAPACT that the SALHN patient had no recurrent angina/cardiac event after implant and no complications were reported from the NALHN procedure.
- Data from the Coronary Angiogram Database of South Australia (CADOSA) was sought and obtained to understand safety and clinical outcomes of patients who were inserted with the Absorb BVS in SA Health.
- SAPACT notes HealthPACT decision made in January 2017 not to recommend the device for routine clinical uptake rather to monitor the technology for another 2 years on the basis of a need for device improvements (e.g. thinner struts without compromising radial strength), cost effectiveness analysis and larger accumulation of clinical outcome data.

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REGULATORY APPROVALS		
☒ **ARTG**: 03/09/2013	☒ **US FDA**: 05/07/2016 (Absorb GT1)	☒ **EU CE mark**: 12/2010 (Absorb 1st gen); 19/05/2015 (2nd gen: Absorb GT1)

ARTG ID: Removed in May 2017

Previously : 214148 Abbott Vascular Division of Abbott Australasia Pty Ltd - ABSORB BVS System - Biodegradable DES

QUALITY OF EVIDENCE Assessment of updated evidence since 2015 SAPACT evaluation	
Quality of Evidence	SAPACT note the level of evidence (II/III-1) that the updated data presented: ABSORB II RCT – 3 year outcome data (n=468) and ABSORB III RCT – 2 year outcome data (n=2008 patients at 193 centers) Comparator: Xience (Abbot Vascular) – cobalt-chromium durable polymer DES
CLINICAL NEED	
Burden of Illness	Coronary artery disease (ischaemic heart disease) is the most common form of cardiovascular disease. Coronary artery disease is the leading cause of death in Australian men and women, contributing to 20,045 deaths in 2012 (13% of all deaths). It kills 55 Australians each day, or one Australian every 25 minutes. Coronary artery disease causes significant illness, disability and poor quality of life. It contributed 7.8 per cent of the total burden of disability-adjusted life years (DALY) lost in Australia in 2010, the largest of any single condition.
Need	Conventional bare-metal stents and 1st generation DES are known to pose issues such as incomplete re-endothelialisation and polymer-induced vessel wall inflammation, resulting in late and very late thrombosis events associated with increased deaths and myocardial infarction. To address the polymer coating issues, 2 types of 2nd generation DES were pursued: metallic durable polymer DES and metallic bioresorbable polymer DES The Absorb BVS system is a new development in stent technology for the treatment of coronary artery disease, in which a temporary poly-L-lactide bioresorbable scaffold (instead of permanent metallic stent) is used together with a bioresorbable polymer drug carrier coating, hence Absorb BVS can be fully absorbed by the body over time, only leaving behind four small platinum markers denoting original placement of BVS are left embedded in artery walls. The Absorb BVS is expected to result in better outcomes and fewer complications (e.g. inflammation that can lead to thrombosis and restenosis) than conventional bare-metal stents and DES.
CLINICAL BENEFIT	
Safety	At the 2-year and 3-year mark, Absorb BVS has failed to demonstrate its main theoretical advantages, compared to the metallic Xience DES. The safety risks were notably in cases that used smaller-calibre Absorb scaffolds, hence its use should be avoided in smaller coronary vessels (reference vessel diameter <2.50mm). > Significant increase (11%, p=0.03) in major adverse cardiac events (MACE)† (Absorb III RCT 2-year) > Absorb BVS has significantly higher rate of primary outcome - target lesion failure$^{\Sigma}$ (Absorb II RCT 3-year and Absorb III RCT 2-year 11.0% vs. 7.9%, p=0.03) > Absorb BVS has significantly higher rate of secondary outcome - target-vessel myocardial infarction (Absorb II RCT 3-year 7% vs 1%; p= 0.006 and Absorb III RCT 2-year 7.3% vs. 4.9%, p=0.04) > Unexpected increased incidence of late (subacute definite or probable) scaffold thrombosis (Absorb II RCT 3-year). Six incidents of definite scaffold thrombosis occurring beyond 365 days among patients who received the Absorb stent compared with 0 reported cases of definite or probable stent thrombosis for patients who received the Xience stent. Absorb BVS are comparable to metallic Xience DES, in terms of the following measures: > Cardiac death: 1.1% vs. 0.6%, p>0.05 (Absorb III RCT 2-year) > Device thrombosis: 1.9% vs. 0.8%; p>0.05 (Absorb III RCT 2-year) > Ischemic-driven target lesion revascularization: 5.3% vs. 4.3%; p>0.05 (Absorb III RCT 2-year)

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	Σ Target lesion failure: Cardiac death, target vessel myocardial infarction or ischemic-driven target lesion revascularization. *† MACE: Cardiac death, myocardial infarction, or ischemic-driven target lesion revascularization.*
Effectiveness	At the 2-year and 3-year mark, Absorb BVS has failed to demonstrate its main theoretical advantages, compared to the metallic Xience DES. > Did not achieve co-primary endpoint – superiority for vasomotion: 0.047mm vs 0.056mm; p(superiority)=0.49 (Absorb II RCT 3-year) > Did not achieve co-primary endpoint - non-inferiority of late lumen loss: 0.37mm vs 0.25mm, p(non-inferiority)=0.78 (Absorb II RCT 3-year) > Significantly higher in-device late lumen loss/binary restenosis: 7% vs 0.7%, p=0.0031 (Absorb II RCT 3-year) > Significantly higher in-segment late lumen loss/binary restenosis: 8.4% vs 3.3% p=0.0418 (Absorb II RCT 3-year) Absorb BVS are comparable to metallic Xience DES, in terms of the following patient-oriented measures: > Seattle Angina Questionnaire score - 5 domains (Absorb II RCT 3-year) > Exercise testing - 17 parameters (Absorb II RCT 3-year)
SUITABILITY OF PATIENT GROUP	
Suitability of Patient Group	Absorb BVS is not listed on ARTG. Only available through clinical trials and TGA SAS approvals. At present, there is no clearly defined group of people in whom Absorb BVS would be used in preference to metallic DES (NICE Medtech 2016[5]). The suitable group of patients to have the Absorb BVS insertions is patients with coronary artery disease in whom medical management has failed or is unsuitable, or people who have had a myocardial infarction. The main symptom of coronary artery disease is angina. Patients may also be on dual antiplatelet therapy (Absorb II RCT 3-year). Exclusion criteria Patients whose treated vessels are less than 2.5mm, as they were found to have significantly worse outcomes at 2-years compared to metallic DES. Patients with known hypersensitivity or allergy to everolimus, poly-L-lactide or platinum; not candidates for angioplasty; have sensitivity to contrast; or who cannot take long-term aspirin therapy along with other blood-thinning medications (antiplatelet agents) are also excluded from the procedure.
FINANCIAL CONSIDERATION	
Device costs	Approx. $[redacted] per Absorb BVS (comparator metallic DES approx. $[redacted])
Value for Money	Two cost-effectiveness studies were identified on Absorb BVS. These conference abstracts each compared the Absorb BVS to the XIENCE everolimus-eluting stent. One analysed data from the ABSORB II clinical trial, reported potential cost savings with the use of Absorb owing to a reduced number of repeat percutaneous coronary interventions. The other analysed data from the ABSORB III clinical trial, reported no significant difference in the total one-year costs between BVS and everolimus-eluting stents. Absorb BVS systems must be kept at or below 25°C, unlike metallic DES, so there may be additional costs associated with maintaining a temperature-controlled environment for storage if this is needed. A more thorough vessel preparation is needed before Absorb BVS implantation, with greater use of pre-dilation balloons and intravascular imaging, which will increase the cost.
Australian Funding Approvals	HealthPACT advice (January 2017): HealthPACT does not support public investment in Absorb BVS in clinical practice at this time, and not until after consideration of published results of studies demonstrating clinical equivalence or superiority with long-term patient outcome data. Therefore, HealthPACT recommends that the evidence for the BVS technology be reviewed in 24 months. The currently available evidence raises some doubts as to whether patient outcomes with the BVS technology are equivalent in effectiveness and safety compared to those achieved in patients treated with conventional DES. MSAC: No reimbursement review has been conducted for Absorb BVS within percutaneous coronary insertion.
FEASIBILITY OF ADOPTION – Not applicable	
CONSISTENCY WITH EXPECTED SOCIETAL/ ETHICAL/ LEGAL VALUES – Not applicable	
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