Summary

- The technology described in this briefing is the Absorb Bioresorbable Vascular Scaffold (BVS). It is a drug-eluting bioresorbable stent used for widening narrowed coronary arteries.

- The innovative aspect is that over time it is resorbed in the artery, unlike metal stents.

- The intended place in therapy would be for use in place of a metallic drug-eluting stent in people with coronary artery disease who are having angioplasty.

- The key points from the evidence summarised in this briefing are from 4 good quality meta-analyses and 1 randomised controlled trial. The evidence suggests that the risks of death, myocardial infarction and target lesion failure are similar for Absorb BVS, bare-metal stents and metallic drug-eluting stents at up to 12 months' follow-up. Stent thrombosis (definite or probable) was more frequent and medium-term in-device and in-segment lumen loss was greater with Absorb BVS than with some second-generation metallic drug-eluting stents.

- Key uncertainties around the evidence are about longer-term outcomes associated with the Absorb BVS compared with metallic drug-eluting stents. NICE interventional procedures guidance recommends that bioresorbable stent implantation should only be used with special arrangements for clinical governance, consent and audit or research.

- In March 2017 a Field Safety Notice was issued. From May 2017 to summer 2018 the use of Absorb BVS is restricted to selected sites and only in patients entered into clinical registries. The situation will be reviewed in summer 2018.
The Absorb and Absorb GT1 Bioresorbable Vascular Scaffold (BVS) systems are bioresorbable, drug-eluting coronary stent systems with a delivery catheter. The Absorb and Absorb GT1 scaffolds are identical, but the Absorb GT1 BVS includes the GlideTrack delivery catheter. This is described by the manufacturer as being easier to use than the Absorb BVS delivery system. From 2017 only the Absorb GT1 BVS will be available to the NHS.

The Absorb BVS is inserted during percutaneous coronary intervention (involving angioplasty using a balloon catheter, followed by stenting) to open narrowed or constricted (stenosed) coronary arteries, usually caused by atherosclerosis.

A stent is a mesh tube that is left in an artery after angioplasty to keep the artery open. When made of fully resorbable material, the stent is usually referred to as a scaffold. Drug-eluting stents and scaffolds are coated with a drug that is slowly released to prevent restenosis, by limiting the overgrowth of tissue within the stent or scaffold.

The Absorb BVS is completely resorbed within 3 years of implantation, potentially allowing the artery to return to its natural state of vasoconstriction and vasodilation. It has a bioresorbable coating that slowly releases the drug everolimus (a protein kinase inhibitor), which is intended to prevent restenosis. Different size scaffolds are available depending on the size of the vessel.

The Absorb BVS is implanted by inserting a guiding catheter into the artery, usually through an incision in the groin. A balloon catheter is inserted into the guiding catheter, and positioned in the narrowing of the coronary artery. The balloon is inflated to dilate the artery (pre-dilation) and then removed. Following pre-dilation a catheter with the Absorb BVS is inserted and X-ray imaging is used to ensure that it is positioned at the site of the lesion. The Absorb BVS is expanded by inflating the balloon within the system to ensure full contact with the arterial wall. Fluoroscopic visualisation is used to ensure that the scaffold has been expanded to the optimum diameter for the artery. The balloon is then deflated and removed, leaving the Absorb BVS in place. An angiogram is then done to confirm that the scaffold is in the right place and has been deployed. Another balloon is usually inserted to expand the scaffold further (post-dilation).
The innovation

Within 3 years the Absorb BVS is resorbed into the artery. This means that in the longer-term the natural function of the artery could be restored and future complications associated with permanent stents, such as inflammation that can lead to thrombosis and restenosis, might be avoided. Further surgical or percutaneous treatments could be done in the same artery in the future, if needed, because the scaffold would no longer be present.

Current NHS pathway

Symptoms of coronary artery disease (mainly angina) can be managed by modifying lifestyle risk factors (smoking, exercise and diet) and drug treatment (such as antiplatelets, statins, beta-blockers, nitrates and calcium channel blockers) with the additional aim of limiting further disease and preventing cardiovascular events. If this approach is unsuccessful or unsuitable, 2 procedures can be considered: angioplasty with or without stenting, or coronary artery bypass grafting (CABG). Angioplasty has a short recovery time but the artery can narrow again so further treatment may be needed. CABG is more effective in certain people (those aged over 65 and those with diabetes, extensive disease or poor heart muscle function), but can result in pain after the operation and a long recovery time (NHS Choices 2014). Angioplasty is also used for emergency treatment of myocardial infarction, known as primary angioplasty.

NICE’s technology appraisal guidance recommends that a stent should normally be used during angioplasty for coronary artery disease, and that a drug-eluting stent should be used in certain circumstances (in particular, if the artery to be treated is less than 3 mm in diameter or the affected section of the artery is longer than 15 mm). NICE’s interventional procedure guidance on bioresorbable stent implantation recommends that the procedure should only be used with special arrangements for clinical governance, consent and audit or research. It states that although there is evidence that bioresorbable stent implantation is safe and effective in the short-term, the evidence for long-term efficacy is inadequate, and further research is recommended.

Absorb BVS would be used in place of non-bioresorbable bare-metal or drug-eluting stents, so there would be no other changes to current NHS practice, although the overall implantation process may be longer and more complex. Many patients having the Absorb BVS may have more intensive follow-up if they are part of an ongoing trial or registry, but outside this group, follow-up would be similar to patients having metallic drug-eluting stents.

NICE is not aware of other bioresorbable stents that are available to the NHS.
Population, setting and intended user

Absorb BVS systems would be used in NHS cardiac catheterisation laboratories by cardiologists who carry out angioplasty. The manufacturer provides a customer education programme to support Absorb implantation, which involves an in-service presentation and a manufacturer representative being present for the first 3 Absorb implants. Specialist commentators stated that further training is needed in addition to the support from the company.

People having the procedure would be those 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, which affects about 2 million people in the UK (NHS Choices 2014). There are over 73,000 deaths in the UK each year because of coronary artery disease. Prevalence increases with age, and it is more common in men than women and in people of South Asian family origin (British Heart Foundation). Myocardial infarction, caused by a sudden reduction in blood to the heart, occurs mostly in people over 45 years and affects around 50,000 men and 32,000 women each year in England (NHS Choices 2014).

Costs

Device costs

The list price of the Absorb and Absorb GT1 BVS systems is £2,200, excluding VAT. Consumables or calibration are not needed. Absorb BVS systems must be kept at or below 25°C, unlike metallic drug-eluting stents, so there may be additional costs associated with maintaining a temperature-controlled environment for storage if this is needed.

Costs of standard care

The NHS reference cost of a standard elective angioplasty in 2014–15 was £2,351, excluding the cost of a stent. The cost of a drug-eluting stent varies: for example, the mean cost was calculated as £529 in NICE’s technology appraisal on drug-eluting stents. The NHS reference cost of a standard elective coronary artery bypass graft, with a Complications and Co-morbidities Score of 0 to 4, was £8,952 in 2014–15.

Resource consequences

The Absorb or Absorb GT1 BVS systems are currently used in 39 hospitals in 37 NHS trusts. The manufacturer has stated that it will stop supplying the Absorb BVS at the end of 2016, and so only the Absorb GT1 BVS will be available from 2017.
If adopted, the Absorb BVS would be used instead of metallic drug-eluting stents and significant changes to current facilities or infrastructure are unlikely to be needed. Specialist commentators stated that more thorough vessel preparation is needed before Absorb implantation, with greater use of pre-dilation balloons and intravascular imaging, which will increase the cost.

**Regulatory information**

The Absorb and Absorb GT1 BVS systems were CE marked as class III devices in April 2015.

The Medicines and Healthcare Products Regulatory Agency issued 1 manufacturer Field Safety Notice (FSN) in 2015, containing advice on using the device after it was identified that procedural technique affects clinical outcomes. It recommended online quantitative coronary angiography or intravascular imaging for very small vessels, and gave revised sizing instructions for the target vessel diameter. The recommendations are reflected in the current instructions for use. In July 2016 this FSN was voluntarily updated with further revised advice on using this device.

Another FSN was issued in March 2017. It states that the device will only be available for use at selected sites in patients entered into clinical registries. This is to address safety concerns identified in the ongoing clinical trials regarding the frequency of adverse events, and to demonstrate if changes to procedural technique will mitigate them. The FSN will be in force from May 2017 until summer 2018 when the situation will be reviewed.

No Medical Device Alerts were found for this device.

**Equality considerations**

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

Coronary artery disease is more common in men and prevalence increases with age in both men and women. People of South Asian family origin are more likely to develop coronary artery disease. Sex, age and race are protected characteristics under the Equality Act 2010.
Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the published process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Six randomised controlled trials (RCTs) with a total of 3,738 patients compared the Absorb BVS with everolimus-eluting metallic stents and were summarised in 3 meta-analyses (Cassese et al. 2016; Stone et al. 2016; Bangalore et al. 2016). One of the RCTs included in the meta-analyses had a third arm using a biolimus-eluting stent (n=80; Puricel et al. 2015). Findings from this arm were excluded from the meta-analyses but are summarised in this briefing. One further network meta-analysis comparing bare-metal stents, all drug-eluting stents and the Absorb BVS included all arms of these 6 RCTs (Kang et al. 2016). The network meta-analysis did not report on lumen loss.

Risks of death, myocardial infarction and target lesion failure (which combines several clinical outcomes) were generally similar for Absorb BVS and drug-eluting stents at 6- to 12-month follow-up. Stent thrombosis (definite or probable) was more frequent and medium-term in-device late lumen loss and in-segment lumen loss were greater with Absorb BVS than some second-generation metallic drug-eluting stents. There were no differences in outcomes between Absorb BVS and bare-metal stents.

Table 1 summarises the clinical evidence as well as its strengths and limitations.

Table 1 Summary of evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Details of intervention and comparator/s</th>
<th>Outcomes</th>
<th>Strengths and limitations</th>
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<tr>
<td>Cassese et al. 2016</td>
<td>Everolimus-eluting BVSs (Absorb) compared with everolimus-eluting metallic stents.</td>
<td>At median follow-up of 12 months (IQR 9–12), the risks of target lesion revascularisation, target lesion failure and death were similar for Absorb and metallic stents. The risks of myocardial infarction and definite or probable stent thrombosis were higher with Absorb but these were not statistically significant. The risks of in-device late lumen loss and in-segment lumen loss were significantly higher with Absorb than with metallic stents. There was moderate heterogeneity between studies for mortality and in-device late lumen loss.</td>
<td>Good-quality systematic review including all relevant RCTs published between November 2006 and October 2015. The review was not funded by the manufacturer. Sensitivity analyses confirmed results. Heterogeneity was assessed. Limitations in trials noted by the authors were: highly selected populations, low event rates, short-term follow-up (median &lt; 1 year), differences in populations and insufficient assessment of angina recurrence. The manufacturer funded the included RCTs. One trial arm (Puricel et al. 2015) relevant to this briefing was excluded from the overall analyses.</td>
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Countries: Europe (including UK), New Zealand, Japan, China, US, Australia
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<th>Stone et al. 2016</th>
<th>Absorb compared with Xience cobalt-chromium everolimus-eluting stent.</th>
<th>1-year relative risks of the patient-oriented composite endpoint (death, myocardial infarction, or revascularisation), the device-oriented composite endpoint (target lesion failure), late target lesion failure, all-cause mortality, and all revascularisation were similar between Absorb and Xience. The risks of early target lesion failure, all myocardial infarction and definite or probable device thrombosis were higher with Absorb but not statistically significant. The risk of target vessel-related myocardial infarction was significantly higher with Absorb. Results were similar after multivariable adjustment for baseline imbalances.</th>
<th>The authors identified all relevant RCTs published between January 2010 and October 2015 (2 included in study level sensitivity analysis only). Using individual patient data allowed multivariable analysis, time to event curves and subgroup analysis. Limitations noted by the authors were: exclusion of 2 RCTs from primary analysis, meta-analysis underpowered to detect differences in low frequency events, subgroup analyses underpowered, development of procedural technique since the trials were published, trials excluded high-risk patients and complex lesions, results applied only to first-generation Absorb and that no longer-term data was available. The manufacturer funded the meta-analysis and included trials.</th>
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<tr>
<td>Meta-analysis of individual patient data from 4 RCTs with 3,389 patients</td>
<td>Countries: Europe (including UK), New Zealand, Japan, China, US, Australia</td>
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<td>Puricel et al. 2015</td>
<td>Absorb compared with Biomatrix Flex BES (Biosensors Europe SA) (n=158). This trial also included a comparison with an everolimus-eluting stent. This has not been reported here because that comparison is included in the Cassese et al. (2016) meta-analysis, whereas the BES arm was not.</td>
<td>There were no significant differences in clinical outcomes at 9 months between Absorb and BES, although more events occurred with Absorb for most outcomes. There was no significant difference between devices in the primary angiographic outcome measure (in-stent late lumen loss), although there were differences in some secondary angiographic outcomes favouring BES.</td>
<td>A good-quality RCT, but there was a risk of performance bias. The trial had a short duration (9 months) and was underpowered to detect differences in clinical event rates. No direct commercial funding was received for the study.</td>
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<td>Bangalore et al. 2016</td>
<td>Absorb BVS compared with everolimus-eluting stents.</td>
<td>The risks of target lesion revascularisation and target vessel revascularisation were similar for BVS and EES. The risks of myocardial infarction and definite or probable device thrombosis were numerically higher but not statistically significant with Absorb. Moderate heterogeneity was identified for mortality.</td>
<td>A good-quality systematic review with a wide search for evidence, including all relevant RCTs published before November 2015. Sensitivity analyses generally confirmed results. A meta-regression, heterogeneity assessment and publication bias assessment were done. Limitations noted by authors were: not an individual patient data meta-analysis, unable to adjust for other confounders, patients had uncomplicated coronary disease and the generalisability to patients with more complex disease is unknown. The manufacturer funded the meta-analysis and the trials.</td>
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<td>Kang et al. 2016</td>
<td>Absorb BVSs compared with:</td>
<td>Definite or probable stent thrombosis at 1 year:</td>
<td>A good-quality systematic review with wide search for evidence (up to December 2015).</td>
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<td>Systematic review and network meta-analysis of 147 RCTs with 126,526 patients overall (110 RCTs, 111,088 patients for the primary outcome) Countries not reported.</td>
<td>• bare-metal stents</td>
<td>Cobalt-chromium everolimus-eluting stents, platinum-chromium everolimus-eluting stents, and hybrid sirolimus-eluting stents were associated with significantly lower risk of definite or probable stent thrombosis than BVS.</td>
<td>The network meta-analysis methods were appropriate.</td>
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<td>• paclitaxel-eluting stents</td>
<td>There were no differences between stents for definite stent thrombosis and all-cause or cardiac mortality.</td>
<td>The authors reported no conflicts of interest.</td>
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<td>• sirolimus-eluting stents</td>
<td>Hybrid sirolimus-eluting stents lowered the risk of myocardial infarction compared with BVS.</td>
<td>The populations included in the studies had a wide range of subtypes and it is unclear if similarity was assessed.</td>
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<td>• Endeavor zotarolimus-eluting stents</td>
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<td>Statistical heterogeneity was not reported.</td>
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<td>• cobalt-chromium everolimus-eluting stents</td>
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<td>Closed loops were seen in the network and inconsistency was assessed; indirect evidence was stated to be consistent with direct evidence.</td>
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<td></td>
<td>• platinum-chromium everolimus-eluting stents</td>
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<td>Limitations noted by the authors were: analysis restricted to 1 year; potential bias of studies could limit the value of the results, trials with different eligibility criteria, follow-up and medication protocols were pooled, and some studies had limited sample sizes and comparisons.</td>
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<td></td>
<td>• biodegradable polymer everolimus-eluting stents</td>
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<td>The generalisability of the results is uncertain because it is unclear if all the comparators are used in the UK.</td>
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<td>• Resolute zotarolimus-eluting stents</td>
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<td></td>
<td>• biodegradable polymer biolimus A9-eluting stents</td>
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Strengths and limitations of the evidence

Two good quality systematic reviews have synthesised 6 RCTs, providing short-term (6 to 12 months') evidence on the Absorb BVS compared with everolimus-eluting stents. A reasonable-quality meta-analysis combined individual patient data for 4 of these RCTs, giving further support for the evidence. A network meta-analysis of good-quality compared the 6 RCTs with 104 RCTs of various comparator stents by direct and indirect comparisons. Only 1 RCT compared Absorb with biolimus-eluting stents. The RCTs used composite endpoints, which have the advantage of statistical efficiency because smaller samples are needed. However, they do not explain the individual outcomes that make up the composite and results can therefore be misleading.

The manufacturer funded most of the trials, 1 of the systematic reviews and the individual patient data meta-analysis. Although there is currently no good-quality evidence on the longer-term effects of the Absorb BVS compared with any of the comparators in the trials, follow-up of patients in the RCTs is ongoing.

Recent and ongoing studies


• A multicentre prospective natural history study using multimodality imaging in patients with acute coronary syndromes – PROSPECT II (natural history study), combined with a randomized, controlled, intervention study – PROSPECT ABSORB (randomized trial).


**Specialist commentator comments**

One specialist commentator stated that the available data show equivalence of the Absorb BVS to drug-eluting stents in many pre-specified composite outcomes but also worse performance in some device- and patient-related outcomes, notably increased stent thrombosis. Some of these adverse outcomes may be associated with suboptimal use of the devices. There are practical limitations when using Absorb in small vessels because of the reduced lumen diameter of the vessel compared with metallic stents.

The commentator also remarked that at present there is no clearly defined group of people in whom Absorb would be used in preference to metallic drug-eluting stents.

One specialist commentator noted that Absorb is more expensive than metal drug-eluting stents and that the theoretical benefits have not yet been shown as improvements in clinical outcomes. They felt that there is still a need for: technology improvements (for example, thinner struts without compromise of radial strength); ongoing, larger scale accumulation of clinical-outcome data (from real-world registries and carefully designed randomised controlled trials); and cost-effectiveness analyses based on such data.
Three specialist commentators thought that training on the specific preparation of the lesion and the insertion procedure, in addition to the training currently provided by the manufacturer, is needed.

**Specialist commentators**

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE’s view.

The following clinicians contributed to this briefing:

- Ms Alison Pottle, Cardiology Nurse Consultant, Royal Brompton and Harefield NHS Foundation Trust. No conflicts of interest declared.

- Professor Keith Oldroyd, Cardiologist, Golden Jubilee National Hospital Glasgow. No conflicts of interest declared.

- Dr Divaka Perera, Cardiologist, Guy’s and St Thomas' NHS Foundation Trust. No conflicts of interest declared.

- Dr Alex Sirker, Consultant Cardiologist, St Bartholomew’s Hospital and University College London Hospital. No conflicts of interest declared.

**Development of this briefing**

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