



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1429.1 – Targeted Intraoperative Radiotherapy for Early Stage Breast Cancer

Applicant: Regional Health Care Group Pty Limited

Date of MSAC consideration: MSAC 78th Meeting, 3 April 2020

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

1. Purpose of application

A resubmission requesting Medicare Benefits Schedule (MBS) listing for targeted Intraoperative Radiotherapy (IORT) for early stage breast cancer to include services delivered using the Xofig[®] Axxent[®] (California, USA) device was received from the Regional Health Care Group by the Department of Health.

2. MSAC’s advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported public funding for IORT services delivered using the Xofig[®] Axxent[®] device for early stage breast cancer. MSAC accepted the evidence of clinical equivalence for Axxent[®] and MBS-listed comparators (whole-breast external beam radiation therapy [WB-EBRT] and Intrabeam[®]), but recommended that the services for Intrabeam[®] and Axxent[®] be rigorously reviewed when the follow-up data from the upcoming clinical trials are available, to determine the place of IORT on the MBS.

MSAC considered that it was important to have IORT as a treatment option for rural and regional women, who may not be able to access three weeks of hypofractionated WB-EBRT.

The MSAC supported item descriptors are:

MBS Item	Descriptor
15900	BREAST, MALIGNANT TUMOUR, targeted intraoperative radiotherapy, using an Intrabeam [®] or Xofig [®] Axxent [®] device, delivered at the time of breast-conserving surgery (partial mastectomy or lumpectomy) for a patient who: a) is 45 years of age or more; and b) has a T1 or small T2 (less than or equal to 3cm in diameter) primary tumour; and c) has a histologic Grade 1 or 2 tumour; and d) has an oestrogen-receptor positive tumour; and e) has a node negative malignancy; and f) is suitable for wide local excision of a primary invasive ductal carcinoma that was diagnosed as unifocal on conventional examination and imaging; and g) has no contra-indications to breast irradiation Fee: \$250.00 Benefit: 75% = \$187.50

MBS Item	Descriptor
31516	BREAST, MALIGNANT TUMOUR, complete local excision of, with or without frozen section histology when targeted intraoperative radiotherapy (using an Intrabeam® or Xofigo®/Axxent® device) is performed concurrently, if the requirements of item 15900 are met for the patient (Anaes.) (Assist.) Fee: \$867.00 Benefit: 75% = \$650.25

Consumer summary

The Regional Health Care Group Pty Ltd submitted an application to list Xofigo® Axxent® on the Medicare Benefits Schedule (MBS) to treat early stage breast cancer.

Axxent® and Intrabeam® deliver intraoperative radiotherapy during breast conserving surgery. This means that a device used to deliver radiotherapy is placed inside the body temporarily during surgery, a large single dose of radiation is delivered to the tumour or tumour bed, and the device is removed before the end of the operation. Thus, patients can receive radiotherapy in one day, rather than having daily external beam radiotherapy for ~3 weeks.

The Medical Services Advisory Committee (MSAC) considered intraoperative radiotherapy to be a great advantage for patients who live in rural or regional areas, and others who may not be able to access ~3 weeks of daily radiotherapy. Also, Intrabeam® is already listed on the MBS. MSAC considered that Axxent® works in a similar way as Intrabeam®.

MSAC had some concern about the long-term effectiveness of both Axxent® and Intrabeam®; specifically, the rate at which people who have been treated develop cancer again later (recurrence rate). Therefore, MSAC recommended that the outcomes of the use of both devices be reviewed in 2–3 years after a study called the TARGIT-A trial is complete. This trial is comparing intraoperative radiotherapy using Intrabeam® with external beam radiotherapy, and will have 10 years of follow-up data, so breast cancer recurrence rates after the two technologies can be compared.

MSAC's advice to the Commonwealth Minister for Health

MSAC recommended listing Xofigo® Axxent® alongside Intrabeam®, which is already listed. MSAC felt that the two technologies are similar in terms of safety, effectiveness and cost-effectiveness. However, MSAC recommended reviewing the listing in 2–3 years as soon as the results of the TARGIT-A trial are published, to determine if intraoperative radiotherapy is as good as external beam radiotherapy.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that this application was to amend MBS items 15900 and 31516 to list delivery of target IORT for early stage breast cancer using the Axxent® device in addition to Intrabeam®.

MSAC noted the application was a resubmission, which was not supported in 2017 due to the poor data for safety, effectiveness and cost-effectiveness. In its April 2017 meeting, MSAC acknowledged the technical equivalence between Intrabeam® and Axxent®. MSAC also considered that WB-EBRT was the appropriate comparator for Axxent® and evidence of long term safety and clinical effectiveness be provided as part of a resubmission to ESC. MSAC requested the department follow-up with the Royal Australian and New Zealand College of Radiologists (RANZCR), the Royal Australasian College of Surgeons (breast surgeons) and hospitals that have purchased these devices in Western Australia and the Peter MacCallum

Cancer Centre to identify what data is being collected, explain the clinical place of these devices with respect to each other and external beam radiotherapy, and explain the very low number of MBS claims to date.

MSAC noted the updated evidence in the department contracted assessment report (DCAR) is primarily from two case series, which now provides median follow-up of 3 years for Axxent[®]. MSAC noted the applicant highlighted in their pre-MSAC response that Intrabeam[®] was approved on median follow-up of 3.2 years, but also noted that the Intrabeam[®] application was based on a large non-inferiority randomised controlled trial (RCT) (TARGIT-A; $n = 3,451$).

MSAC noted that the Prosthesis List Advisory Committee has accepted technical equivalence between Intrabeam[®] and Axxent[®]. MSAC recalled it accepted technical equivalence between the two devices with respect to the x-ray spectra, relative biological effectiveness and tissue dose distribution.

Overall, MSAC accepted the evidence of clinical equivalence for Axxent[®] and MBS-listed comparators (WB-EBRT and Intrabeam[®]), but considered that on the current evidence base, IORT is not proven to be non-inferior to WB-EBRT in terms of clinical effectiveness. However, WB-EBRT requires daily treatment over several weeks, and that the main advantage for IORT is for women based in rural or regional areas who cannot easily access WB-EBRT. In its pre-MSAC response, the applicant accepted that hypofractionated WB-EBRT is generally recommended for patients with early stage breast cancer (25 fractions down to 15 fractions), reducing the number of weeks required for treatment (from ~5 weeks to ~3 weeks). MSAC agreed that even a 15-fraction treatment regimen is inaccessible for a number of patients. MSAC considered that it was important to have IORT as a treatment option for rural and regional women, who may not be able to access three weeks of hypofractionated WB-EBRT.

MSAC considered that naming the devices in the MBS descriptor was appropriate.

MSAC noted that IORT replaces WB-EBRT planning and delivery items (MBS items 15221, 15236, 15251, 15266, 1550, 15562, 15705). MSAC noted that the costs for Intrabeam[®] and Axxent[®] are similar, and both are cheaper than WB-EBRT, even when comparing with the more appropriate hypofractionated WB-EBRT regimen (cost savings of about \$3,000 per patient; see Table 8). MSAC also noted the pre-MSAC response where the applicant provided economic findings from the Peter MacCallum Cancer Centre estimating over a \$2,000 cost reduction to healthcare system for patients with IORT. MSAC accepted that there will be no extra cost to the MBS if Axxent[®] is listed alongside Intrabeam[®]. However, depending on pathology, about 15% of patients require WB-EBRT after breast-conserving surgery.

MSAC noted the low utilisation rates for Intrabeam[®], although the technology is currently only available in Western Australia. MSAC noted the pre-MSAC response where the applicant stated that utilisation will increase due to additional machines being installed in private facilities. MSAC noted the RANZCR considered the low utilisation to be because the technology is still new.

MSAC also noted the RANZCR view does not currently support IORT as an established method for treatment of early breast cancer outside of ongoing clinical trials, and without a minimum of 10 years of follow-up data.

MSAC noted the pre-MSAC response where the applicant indicated that there is an upcoming 1,200 patient Xofigo[®] Sponsored Clinical Trial which reached median four year follow-up, and

Peter MacCallum Cancer Centre is part of the trial ([NCT01644669](#)). MSAC noted the applicant stated that prepublication ipsilateral recurrence data appear non-inferior to WB-EBRT and appear comparable to the predicate device. However, MSAC noted the supportive data was not included. MSAC also noted the non-inferiority comparison to WB-EBRT would be made at five years (primary completion date due in July 2023) and estimated study completion date is due in 2029.

MSAC considered that longer term follow-up for IORT relies heavily on 10-year patient follow-up data from the TARGIT-A trial ([NCT03501121](#)), the results of which are due in 2023 at the earliest (study completion date due in January 2023). MSAC recommended that both technologies (Intrabeam[®] and Axxent[®]) be rigorously reviewed as soon as the data available is available from TARGIT-A. The assessment process will re-assess comparative safety and effectiveness, cost-effectiveness, utilisation and patient preference data. This assessment will assist in determining the place of IORT (irrespective of technology) on the MBS in the long term; and in particular, to assess whether IORT is non-inferior to WB-EBRT in terms of recurrence rates.

MSAC also noted the department had decided to defer the predicted versus actual review because of the limited availability of MBS claims data, the yet to be available TARGIT-A follow-up data and the lack of information regarding why IORT is not being used as a treatment option.

4. Background

This is the first resubmission (department contracted assessment report; DCAR) of Application 1429.

At the April 2017 meeting, MSAC did not support public funding of IORT using the Xofig[®] Axxent[®] device for early stage breast cancer. MSAC accepted the evidence of technical equivalence between the proposed (Axxent) and listed (Intrabeam) devices, but advised that this evidence did not provide a satisfactory basis to conclude clinical equivalence. Further, MSAC considered that the clinical place for IORT has not yet been fully established and that no acceptable direct or indirect evidence of comparative safety, clinical effectiveness or cost-effectiveness was presented.

MSAC requested any resubmission would need to be considered by ESC and should provide evidence of long-term safety and clinical effectiveness. MSAC agreed that whole-breast external beam radiation therapy (WB-EBRT) is the appropriate comparator for Axxent, given that there has been virtually no utilisation of the existing MBS items for IORT.

MSAC requested the department follow-up with RANZCR, the Royal Australasian College of Surgeons (breast surgeons) and hospitals that have purchased these devices in Western Australia and the Peter MacCallum Cancer Centre to identify what data is being collected, explain the clinical place of these devices with respect to each other and external beam radiotherapy, and explain the very low number of MBS claims to date ([Public Summary Document \[PSD\] Application 1429, April 2017, p1](#)).

The DCAR provided a detailed summary of previous MSAC issues from the previous submission (1429) and how they have addressed them in the resubmission (Application 1429.1) [Table 1].

Table 1 Summary of MSAC's recommendations from MSAC 1429, and approach used in the resubmission

MSAC issues/recommendations based on MSAC 1429	How these recommendations have been addressed in MSAC 1429.1
MSAC agreed that whole-breast external beam radiation therapy (WB-EBRT) is the appropriate comparator for Axxent, given that there has been virtually no utilisation of the existing MBS items for IORT [PSD, p1,2].	WB-EBRT is the appropriate comparator [Application Form] and has been nominated as the main comparator in this submission.
MSAC considered that the clinical place for IORT has not yet been fully established [PSD, p1].	RANZCR agreed with the clinical algorithm proposed in the previous submission [Consolidated Consultations Feedback]. Increased utilisation of Intrabeam® suggests IORT has a place in clinical practice.
MSAC questioned the need for listing another device on the MBS, given the lack of uptake of Intrabeam (no MBS claims under Item 15900, six claims under Item 31516, between September 2015 to February 2017) – which suggests a lack of clinical need for IORT in general [PSD, p3].	There has been an increase in uptake of Intrabeam® since the previous submission. There have been 36 claims under MBS item 31516 but no claims under MBS item 15900, between September 2015 to September 2019. This suggests that IORT has a place in clinical practice with uptake likely to continue to rise.
<p>Any resubmission should provide evidence of long-term safety and clinical effectiveness [PSD, p1].</p> <p>MSAC agreed on the lack of long-term safety data for the Axxent device [PSD, p2]</p> <p>MSAC recalled its concerns regarding the Intrabeam evidence base (MSAC Public Summary Document [PSD] Application 1189, November 2014) and the limited evidence for long-term safety and efficacy of IORT using Intrabeam compared to WB-EBRT [PSD, p2].</p>	<p>An updated literature search identified a new study reporting on longer follow-up data for Axxent® with a median follow-up of three years (Silverstein <i>et al</i> 2018).</p> <p>Vaidya <i>et al</i> 2010 and 2014 reported results with Intrabeam® with a median follow-up of 5.8 years. An updated literature search identified one new RCT on Intrabeam® that reported safety outcomes from 41 patients after a median follow-up of 3.2 years (Key <i>et al</i> 2017).</p>
MSAC noted that an economic evaluation had not been presented to the Committee due to uncertainties around the reported outcomes. MSAC also noted the unknown costs for the Axxent device [PSD, p2].	<p>MSAC recommended MBS listing of Intrabeam® on a cost-minimisation basis given the claim of non-inferiority in terms of safety and effectiveness compared to WB-EBRT (PSD Application 1189 p1).</p> <p>Section B of this submission demonstrates clinical non-inferiority between Axxent® against WB-EBRT or Intrabeam® in terms of both safety and effectiveness. This is consistent with the previous submission.</p> <p>Given the evidence presented in this resubmission and MSAC recommendations for Intrabeam®, it is assumed that Axxent® can be cost-minimised against WB-EBRT. Therefore, consistent with the previous submission, no pre-modelling studies or economic evaluation were provided in the resubmission.</p>
Specific issues related to previous main comparator: IORT with Intrabeam device	
MSAC considered that no acceptable direct or indirect evidence of comparative safety, clinical effectiveness or cost-effectiveness was presented and as such no conclusion could be made regarding the relative safety or effectiveness of Axxent compared to Intrabeam. [PSD, p2].	An updated literature search identified one new study reporting on longer follow-up data for Axxent® with a median follow-up of three years (Silverstein <i>et al</i> 2018). One new RCT on Intrabeam® that reported safety outcomes from 41 patients after a median follow-up of 3.2 years (Key <i>et al</i> 2017) was also identified. A naïve indirect comparison of the safety and effectiveness of Axxent® and Intrabeam® is presented in this submission.
MSAC agreed that the level, quality and duration of follow-up of the Axxent evidence base was lower, poorer and shorter than the Intrabeam evidence base [PSD, p2].	This submission presents data from a new study reporting longer follow-up data for Axxent® with a median follow-up of three years (Silverstein <i>et al</i> 2018). Vaidya <i>et al</i> 2010 and 2014 reported data for Intrabeam® with a median follow-up of 5.8 years.

MSAC issues/recommendations based on MSAC 1429	How these recommendations have been addressed in MSAC 1429.1
MSAC queried the relevance of the Ivanov O et al 2011 study due to low quality, small sample size (n = 11) and the inclusion of a large proportion (45%) of patients with ductal carcinoma in situ (DCIS) rather than the proposed population of invasive ductal carcinoma. MSAC noted that the Epstein M et al 2016 study reported results as simple rates with no information on time to events or confidence intervals and follow-up was too short to make any conclusions about recurrence rates. MSAC observed that the included studies reported only breast cancer related mortality as opposed to all-cause mortality [PSD, p2].	An updated literature search identified one new study reporting on longer follow-up data for Axxent® with a median follow-up of three years (Silverstein et al 2018). This data is presented in this submission.

Source: Table 13, pp 28-29 of DCAR

5. Prerequisites to implementation of any funding advice

The Xoft® Axxent® Electronic Brachytherapy (eBx®) System is registered on the Australian Register of Therapeutic Goods; refer to Public Summary Document [PSD] Application 1429, April 2017, pp3-4.

6. Proposal for public funding

This was unchanged from the previous submission (Table 2).

Table 2 Proposed MBS item descriptor

<p>15900 – version 2 BREAST, MALIGNANT TUMOUR, targeted intraoperative radiotherapy, delivered at the time of breast conserving surgery (partial mastectomy or lumpectomy) for a patient who:</p> <ul style="list-style-type: none"> a) is 45 years of age or more; and b) has a T1 or small T2 (less than or equal to 3cm in diameter) primary tumour; and c) has a histologic Grade 1 or 2 tumour; and d) has an oestrogen-receptor positive tumour; and e) has a node negative malignancy; and f) is suitable for wide local excision of a primary invasive ductal carcinoma that was diagnosed as unifocal on conventional examination and imaging; and g) has no contraindications to breast irradiation <p>MBS Fee: \$250.00 Benefit: 75% = \$187.50</p>
<p>31516 – version 2 BREAST, MALIGNANT TUMOUR, complete local excision of, with or without frozen section histology when targeted intraoperative radiotherapy is performed concurrently, if the requirements of item 15900 are met for the patient (Anaes.) (Assist.)</p> <p>MBS Fee: \$867.00 Benefit: 75% = \$650.25</p>

Source: Table 1, p7 of DCAR

7. Summary of public consultation feedback/consumer Issues

This was unchanged; refer to Public Summary Document [PSD] Application 1429, April 2017, p4.

8. Proposed intervention's place in clinical management

MSAC considered that the clinical place for IORT has not yet been fully established (PSD Application No. 1429, 2017 p1).

The DCAR stated that RANZCR agreed with the clinical algorithm proposed in the previous submission [Consolidated Consultations Feedback]. Increased utilisation of Intrabeam[®] suggests IORT has a place in clinical practice (Medicare statistics, 2019).

In their pre-MSAC response, the applicant indicated that almost 20,000 patients have been treated with the Axxent[®] System as of March 2020, including 5,000 patients treated with breast IORT.

9. Comparator

The primary comparator for the resubmission is WB-EBRT, the secondary comparator is IORT with the Intrabeam[®] device.

The DCAR noted that the primary comparator for the previous assessment was IORT with the Intrabeam device, the secondary comparator was WB-EBRT. However, MSAC agreed that WB-EBRT is the appropriate comparator for Axxent[®], given that there has been virtually no utilisation of the existing MBS items for IORT (PSD Application No. 1429, 2017 p1).

10. Comparative safety

Vs. WB-EBRT

Two new studies (Lai et al. 2016; Silverstein et al. 2018) were identified for Axxent[®], giving a total of three studies on Axxent[®] involving 1,256 patients. In addition, nine randomised controlled trials (RCTs) that included WB-EBRT in the comparator arm with 5,205 patients in total were identified (Table 3).

Table 3 Key features of the included evidence comparing Axxent[®] to WB-EBRT

Study	n using device	IORT device	Study design Setting	Follow-up time	Patient disease profile ^b	Key outcome(s)
Ivanov et al. (2011)	11	Axxent	Case series NR	1 year	Invasive ductal carcinoma - 55% Ductal carcinoma <i>in situ</i> - 45%	Recurrence Adverse events
Lai et al. (2016)	261	Axxent [®]	Case series Multicentre	Median 1.3 years	Invasive ductal carcinoma and ductal carcinoma <i>in situ</i> - 73% Invasive lobular carcinoma and lobular carcinoma <i>in situ</i> - 1.9% Ductal carcinoma <i>in situ</i> - 16.1% Mucinous or papillary carcinoma - 3.4% Unknown - 4.2%	Recurrence Mortality
Silverstein et al. (2018) ^c	984	Axxent [®]	Case series Single centre	Median 3 years	Invasive ductal carcinoma - 71% Ductal carcinoma <i>in situ</i> - 21% Invasive lobular carcinoma - 8%	Recurrence Mortality Adverse events
Coles et al. (2018) ^a	674	WB-EBRT	RCT Multicentre	Median 6 years	Invasive ductal carcinoma - 86% Mixed - 2% Other - 12%	Recurrence Mortality
Strnad et al. (2016) & Polgar et al. (2017) ^a	551	WB-EBRT	RCT Multicentre	5 years	Invasive ductal carcinoma - 77% Invasive lobular carcinoma - 9% Mixed - 11% Unknown - 4%	Recurrence Mortality Adverse events

Study	n using device	IORT device	Study design Setting	Follow-up time	Patient disease profile ^b	Key outcome(s)
Livi et al. (2014) ^a	260	WB-EBRT	RCT Single centre	Median 5.3 years	Invasive ductal carcinoma - 58.8% Ductal carcinoma <i>in situ</i> - 12.3% Invasive lobular carcinoma - 11.2% Invasive ductal and lobular carcinoma - 6.9% Other - 10.8%	Recurrence Mortality
Vaidya et al. (2010) & (2014) ^a	1730	WB-EBRT	RCT Multicentre	1 year recurrence Median 2.3 years Median 2.7 years Median 5 years	Invasive ductal carcinoma - 94% Invasive lobular carcinoma - 4% Mixed - 3% Unknown - 4%	Recurrence Mortality Adverse events
Polgar et al. (2007) & (2013) ^a	130	WB-EBRT	RCT Single centre	5 years Median 10.2 years	Invasive ductal carcinoma - 83.1% Other - 16.9%	Recurrence Mortality Adverse events
Rodriguez et al. (2013) ^a	51	WB-EBRT	RCT Single centre	Median 5 years	Invasive ductal carcinoma - 100%	Recurrence
Olivotto et al. (2013) ^a	1,065	WB-EBRT	RCT Multicentre	Median 3 years	Invasive ductal carcinoma - 81% Ductal carcinoma <i>in situ</i> - 17% Unknown - 2%	Adverse events
Veronesi et al. (2013) ^a	654	WB-EBRT	RCT Single centre	Median 5.9 years	Ductal - 79% Lobular - 9% Ductal and lobular - 3% Other - 9% ^e	Recurrence Mortality
Dodwell et al. (2005) ^a	90	WB-EBRT	RCT Single centre	Median 8 years	pT1/T2, pN0/N1 tumours included - NR	Recurrence

Source: Table 2, pp11-12 of DCAR

^a: Only WB-EBRT arm has been extracted,

^b: Patient disease profile exceeds 100%, this table replicates what was reported in the paper,

^c: Patient disease profile out of 1000 tumours. IORT = intraoperative radiation therapy, NR = not reported, RCT = randomised controlled trial, WB-EBRT = Whole Breast - External Beam Radiotherapy

Note, **grey text** is content from previous submission

The DCAR stated that patients' ages were comparable between WB-EBRT and Axxent[®] studies with the majority of patients aged 45–50 years and older. The proportion of patients with invasive ductal carcinoma varied across the studies (WB-EBRT: 58.8–100.0%; Axxent[®]: 55.0–72.0%). The proportion of patients who were Estrogen receptor (ER) positive was comparable between WB-EBRT (88.0–96.1%) and Axxent[®] (83.9–94.0%). Furthermore, 95.8% of patients who received Axxent[®] were node negative whereas with WB-EBRT the proportion of patients who were node negative ranged from 69.0–96.0%. There were minor differences in the proportion of patients with T1 and T2 tumours between Axxent[®] (T1: 75.5% and T2: 21.4%) and WB-EBRT (T1: 40.0–94.1% and T2: 5.9–46.0%). For both devices (Axxent[®] and WB-EBRT), the included populations do not directly match the PICO confirmation. Most studies included a broader patient population, including those with ductal carcinoma in-situ (DCIS) and/or higher-stage cancer. Six of the identified studies also included patients aged under 45 years old. The impact of a broader population might result in an underestimate of the treatment effect as they may be more fragile if they have a higher-stage cancer and are therefore less likely to have a positive response. The impact of a broader population might also result in an overestimate of the treatment effect as they are younger than 45 years old and therefore may have better response rates in comparison to

those over 45 years old. However, overall there will be a minimal impact as invasive ductal carcinoma, formed the majority of patients in each study and the median age of patients in each study exceeded 45 years old.

Key safety outcomes reported in the identified studies were as follows:

- infection (Axxent[®]: 0–1.2% at 1 month; WB-EBRT: 1.3% at 6 months)
- seroma (Axxent[®]: 2.3% at 6 months; WB-EBRT: 0.8% at 6 months)
- haematoma (Axxent[®]: 1.4% at 1 month; WB-EBRT: 0.6% at 6 months and 0.1 percent beyond six months)
- necrosis (Axxent[®]: 0.1% at 1 month and 0 percent at 12 months; WB-EBRT: 2.1–28.7%)
- erythema (Axxent[®]: 27.3% immediately post-surgery and 20.8% at 1 month; WB-EBRT: 66.5–85.0%)
- dehiscence (Axxent[®]: 1.3%; WB-EBRT: 1.9% at 6 months and 0.3% after 6 months)
- fibrosis (Axxent[®]: 10.0% at 6 months and 18.2% at 12 months; WB-EBRT: 11.2–35.2%)
- skin hyperpigmentation (Axxent[®]: 7.7% at 6 months; WB-EBRT: 10.2–20.1%)
- breast pain (Axxent[®]: 27.3% immediately post-surgery; WB-EBRT: 21.4–26.2%).

The DCAR stated that no material differences in type and severity of the adverse events was observed for the two devices. Thus, the resubmission concluded, it is likely that Axxent[®] is non-inferior to WB-EBRT in terms of safety. However, due to the large disparity in the evidence base of Axxent[®] relative to WB-EBRT, it is difficult to make a clear conclusion. Specifically, Axxent[®] has only been studied in case series studies, compared to WB-EBRT which is subject to several good quality RCTs. In addition, Axxent[®] has shorter follow-up data of up to three years, compared to WB-EBRT that has follow-up data for up to 10.2 years.

Vs. Intrabeam[®]

One new RCT (Key et al. 2017) on Intrabeam[®] was identified that included 41 patients. Overall, the three studies on Axxent[®] included 1,256 patients and the four studies on Intrabeam[®] included 1,784 patients. The DCAR stated that the updated review of the evidence base did not provide any new evidence to suggest that Axxent[®] is superior or inferior, relative to Intrabeam[®] in terms of safety.

The safety outcomes that were reported included the following:

- infection (Axxent[®]: 1.1% at one month and 1.2% at 36 months; Intrabeam[®]: 1.8% by six months and 10.9% by 12 months)
- seroma (Axxent[®]: 0.3% at 1 month and 2.3% at 6 months; Intrabeam[®]: 2.0–13.4%)
- haematoma (Axxent[®]: 1.4% at 1 month; Intrabeam[®]: 0.1–24.0%)
- erythema (Axxent[®]: 27.3% immediately post-surgery and 20.8% at 1 month; Intrabeam[®]: 12.9% at 1 week)
- necrosis (Axxent[®]: 0.1% at 1 month; Intrabeam[®]: 0.5%)
- dehiscence (Axxent[®]: 1.3% at 36 months; Intrabeam[®]: 2.8% at 6 months, 0.1% after 6 months, 8.1% at 12 months)
- fibrosis (Axxent[®]: 9.9% at 6 months; Intrabeam[®]: 46.3% Grade 1 and 2.4% Grade 2)
- breast pain (Axxent[®]: 27.3% immediately post-surgery and 0% at 12 months; Intrabeam[®]: 14.6% Grade 1 at three years).

The DCAR therefore concluded that Axxent[®] remains non-inferior in terms of safety.

11. Comparative effectiveness

Vs. WB-EBRT

Recurrence

Measurement of recurrence was conducted with mammogram and physical examination.

The DCAR stated that at a median follow-up of three years, the rate of any local recurrence with Axxent® was 3.1% and the rate of local recurrence for only invasive carcinoma was 2.0%. Rate of any local recurrence for WB-EBRT ranged from 0-4 to 6% depending on follow-up period. Distant recurrence was not reported for Axxent®, however, four studies reported distant recurrence with WB-EBRT (Table 4).

Table 4 Local and distant cancer recurrence results across the included studies

Study ID	Device	Follow-up time	Local recurrence rate n with event/N (%)	Distant recurrence rate n with event/N (%)
Ivanov et al. (2011)	Axxent®	1 year	0/11 (0)	Not reported
Lai et al. (2006)	Axxent®	Median 1.3 years	2/261 (0.8)	Not reported
Silverstein et al. (2018)	Axxent®	Median 3 years	Any recurrence: 26/836 (3.1) ^a For invasive carcinoma only: 17/836 (2.0)	Not reported
Coles et al. (2017)	WB-EBRT	Median 6 years	9/674 (1)	13/674 (2)
Strnad (2016) & Polgar et al. (2017)	WB-EBRT	5 years	5/551 (0.9)	5/551 (0.9)
Livi et al. (2014)	WB-EBRT	Median 5.3 years	3/260 (1.2)	4/260 (1.8)
Vaidya et al. (2010) & (2014)	WB-EBRT	1 year recurrence Median 2.3 years Median 3.7 years Median 5 years	0/1107 (0) 6/1127 (0.5) 5/710 (0.7) 3/405 (0.7)	Not reported
Polgar et al. (2007) & (2013)	WB-EBRT	5 years Median 10.2 years	4/130 (3.1) 6/130 (4.6)	11/130 (8.5)
Rodriguez et al. (2014)	WB-EBRT	Median 5 years ^e	0/51 (0)	Not reported
Veronesi et al. (2013)	WB-EBRT	Median 5.9 years	4/654 (0.6)	Not reported
Dodwell et al. (2005)	WB-EBRT	Median 8 years ^e	4/90 (4.4)	24/90 (27)
GRADE analysis	Summary ^b		Rate of local recurrence of invasive disease in Axxent® studies was 2% at 3.0 years. Rate of local recurrence for WB- EBRT ranged from 0-4 to 6% depending on follow-up period.	Rate of distant recurrence was not reported in Axxent® studies. Rate of distant recurrence for WB-EBRT ranged from 0.9 to 27% depending on follow-up period.
	Quality ^c		⊕⊕⊕⊕ VERY LOW ^{cd}	⊕⊕⊕⊕ VERY LOW ^{cd}

Source: Table 4, pp15-16 of DCAR

^a: Denominator is number of tumours ^b: All summaries are limited by a lack of comparative evidence for the Axxent® device, ^c: GRADE Working Group grades of evidence (Guyatt et al., 2013), ^d: Conclusions not based on direct comparisons, ^e: median follow-up for treatment and control arm.

⊕⊕⊕⊕ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Mortality

Mortality was measured as death due to breast cancer in the included population.

The DCAR stated that no deaths due to breast cancer was observed with the Axxent[®] device at a maximum of 3.0 years follow-up. WB-EBRT ranged from 0-2% depending on follow-up period. Axxent[®] does not appear to have substantially higher rates of breast cancer mortality compared to WB-EBRT (Table 5).

Table 5 Mortality results across the studies

Study ID	Device	Follow-up time	Deaths due to breast cancer n with event/N (%)
Lai et al. (2016)	Axxent [®]	Median 1.3 years	0/261 (0)
Silverstein et al. (2018)	Axxent [®]	Median 1.6 years Median 3 years	0/702 (0) 0/984 (0)
Coles et al. (2017)	WB-EBRT	Median 6 years	9/674 (1)
Strnad et al. (2016) & Polgar et al. (2017)	WB-EBRT	5 years	3/551 (0.5)
Livi et al. (2014)	WB-EBRT	Median 5.3 years	3/260 (1.2)
Vaidya et al. (2010) & (2014)	WB-EBRT	Median 1 year Median 2.3 years Median 3.7 years Median 5 years	NR 15/1127 (1.3) NR NR
Polgar et al. (2007) & (2013)	WB-EBRT	Median 10.2 years ^e	28/258 (10.9) ^f
Veronesi et al. (2013)	WB-EBRT	Median 5.9 years	20/654 (2.0)
GRADE analysis	Summary ^a		No deaths due to breast cancer was observed with the Axxent [®] device at a maximum of 3.0 years follow-up. WB-EBRT ranged from 0-2% depending on follow-up period. Axxent [®] does not appear to have substantially higher rates of breast cancer mortality compared to WB-EBRT
	Quality ^b		⊕⊖⊖⊖ VERY LOW ^{c,d}

Source: Table 5, pp16-17 of DCAR

^a: All summaries are limited by a lack of comparative evidence for the Axxent[®] device, ^b: GRADE Working Group grades of evidence (Guyatt et al., 2013), ^c: Conclusions not based on direct comparisons, ^d: Few studies, ^e: median follow-up for both RCT arms, ^f: 28 breast cancer deaths in both arms of RCT. Unclear how many deaths in only WB-EBRT arm.

⊕⊖⊖⊖ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Following a complete naïve indirect comparison of the literature for Axxent[®] and WB-EBRT, the DCAR stated that it is likely that Axxent is non-inferior to WB-EBRT. However, there is a degree of uncertainty due to the large disparity in the body of evidence available for Axxent[®] relative to WB-EBRT. Specifically, Axxent[®] has only been studied in case series studies, compared to WB-EBRT which is subject to several good quality RCTs. In addition, Axxent[®] has shorter follow-up data of up to three years, compared to WB-EBRT that has follow-up data for up to 10.2 years. Therefore, although it is likely that Axxent[®] is non-inferior to WB-EBRT, it remains difficult to conclude the relative effectiveness of the two techniques.

In the pre-MSAC response, the applicant stated that Monash Health/Peter MacCallum Cancer Centre, Clayton, Victoria, Australia was one of the 28 worldwide clinical sites participating

in the 1,200 patient Xofigo Sponsored Clinical Trial which reached full enrollment July 2018, with a median 4 year follow-up ([NCT01644669](#)). The applicant also stated pre-publication ipsilateral recurrence data appear non-inferior to WB-EBRT and appear comparable to the predicate device. The estimated primary completion date and study completion date for the global randomised trial is July 2023 and December 2029, respectively. The primary outcome is rate of ipsilateral breast tumour recurrence (IBTR) at 5 years, and a non-inferiority comparison with WB-EBRT will be provided at 5 years. IBTR (and other secondary outcomes such as survival, quality of life) will also be assessed at 5 and 10-year follow-up.

In the pre-MSAC response, the applicant also highlighted the position paper from RANZCR on IORT for early stage breast cancer:

‘The Faculty of Radiation Oncology of the Royal Australian and New Zealand College of Radiologists does not currently support intraoperative radiotherapy (IORT) as an established method for treatment of early breast cancer outside of ongoing clinical trials... It is the Faculty’s view that currently available evidence is too limited to make definitive conclusions and that minimum patient follow-up data of 10 years would be required to establish an appropriate evidence base.’

The applicant acknowledged that the data for Axxent[®] is not as mature as the existing standard of care, and Monash Health has set up an IORT Trial Registry in order to further monitor the development of the therapy.

Vs. Intrabeam[®]

Recurrence

Axxent[®] does not appear to have substantially higher rates of local recurrence of ductal carcinoma in situ than Intrabeam[®]. (Table 6) Distant recurrence was not reported for Axxent[®] however, one study from the previous submission reported 3.9% of patients had a distant recurrence with Intrabeam[®] (Vaidya *et al* 2014) (Table 5).

Table 6 Local and distant cancer recurrence results across the included studies (abridged; new studies only)

Study ID	Device	Follow-up time	Local recurrence rate n with event/N (%)	Distant recurrence rate n with event/N (%)
Lai et al. (2006)	Axxent®	Median 1.3 years	1/261 (0.4)	Not reported
Silverstein et al. (2018)	Axxent®	Median 3.0 years	Any recurrence: 26/836 (3.1) ^a For invasive carcinoma only: 17/836 (2.0)	Not reported
Key et al. (2017)	Intrabeam®	Median 3.2 years	0/41 (0)	Not reported
GRADE analysis	Summary ^a		Axxent® does not appear to have substantially higher rates of local recurrence of ductal carcinoma in situ than Intrabeam®	Rate of distant recurrence was not reported in Axxent® studies. Rate of distant recurrence for Intrabeam was reported in one study as 3.9 percent
	Quality ^b		⊕⊙⊙⊙ VERY LOW ^{c,d}	⊕⊙⊙⊙ VERY LOW ^{c,d}

Source: Table 6, pp17-18 of DCAR

^a: All summaries are limited by a lack of comparative evidence for the Axxent device, ^b: GRADE Working Group grades of evidence (Guyatt et al., 2013), ^c: Conclusions not based on direct comparisons, ^d: Few studies. ⊕⊙⊙⊙ **Very low quality**: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Mortality

There were no deaths associated with the Axxent® device. The DCAR stated that Axxent® does not appear to have substantially higher rates of breast cancer mortality than Intrabeam® (Table 7).

Table 7 Mortality results across the studies (abridged; new studies only)

Study ID	Device	Follow-up time	Deaths due to breast cancer n with event/N (%)
Silverstein et al. (2018)	Axxent®	Median 3 years	0/984 (0)
Key et al. (2017)	Intrabeam®	Median 3.2 years	0/41 (0)
GRADE analysis	Summary ^a		There were no deaths associated with the Axxent® device. Axxent® does not appear to have substantially higher rates breast cancer mortality than Intrabeam®..
	Quality ^b		⊕⊙⊙⊙ VERY LOW ^{c,d}

^a: All summaries are limited by a lack of comparative evidence for the Axxent device, ^b: GRADE Working Group grades of evidence (Guyatt et al., 2013), ^c: Conclusions not based on direct comparisons, ^d: Few studies. ⊕⊙⊙⊙ **Very low quality**: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

The DCAR stated that an updated review of the evidence base did not provide any new evidence to change the conclusion of the previous assessment report. The same limitations remain as the original search as no new studies were identified that provided follow-up times longer than three years for the Axxent® device and five years for the Intrabeam® device. The lack of ten-year data means only preliminary effectiveness evidence has been reported. Despite this limitation, the evidence available indicates the effectiveness outcomes are similar for the two devices. The Axxent® device therefore remains non-inferior to Intrabeam® in both effectiveness and safety.

Clinical claim

The primary clinical claim for the resubmission is that the relative biological effectiveness and health outcomes of the Axxent[®] device are equivalent to those of WB-EBRT. The primary health outcome is local recurrence of breast cancer. Secondary health outcomes are mortality rates, adverse events and toxicity.

12. Economic evaluation

The DCAR stated that consistent with the previous submission, no pre-modelling studies or economic evaluation were provided in the resubmission. MSAC recommended MBS listing of Intrabeam[®] on a cost-minimisation basis given the claim of non-inferiority in terms of safety and effectiveness compared to WB-EBRT (PSD Application 1189 p1). Given the evidence presented in this resubmission (summarised above) and MSAC recommendations for Intrabeam[®], the DCAR assumed that Axxent[®] can also be cost-minimised against WB-EBRT.

The DCAR stated this would result in cost savings equivalent to that calculated by the budget impact analysis as presented in Scenario 1 for Application 1189 (i.e., patients treated with Axxent concurrent with BCS plus 15% having three weeks of WB-EBRT as a tumour boost dose based on pathology taken at the time of surgery versus patients treated with BCS followed by six weeks of WB-EBRT). This is based on the assumption that the costs of treatment with Axxent and the market share and uptake of Axxent would mirror that modelled for Intrabeam[®].

13. Financial/budgetary impacts

The DCAR stated the previous application (1429) did not provide any budget impact model. However, the DCAR presented the estimated cost savings per patient that could be achieved when using the proposed IORT as opposed to WB-EBRT, with the Applicant's assumption that 15% of patients will require a tumour boost dose (Table 8).

Table 8 Estimated costs of IORT with the Axxent[®] device and cost savings per patient compared to WB-EBRT, and hypofractionated WB-EBRT calculated for MSAC

Treatment	IORT	WB-EBRT	Incremental
IORT in conjunction with BCS	\$1,117	\$0	+\$1,117
Additional OR and physicist time – 30 minutes	\$1,500	\$0	+\$1,500
Supplemental WB-EBRT following pathology for 15% of patients	\$1,280	\$0	+\$1,280
WB-EBRT (25 treatment attendances)	\$0	\$9,830	-\$9,830
Hypofractionated WB-EBRT (15 treatment attendances)		\$6,398 ^a	-\$6,830
Total	\$3,897	\$9,830	-\$5,933
Total- using hypofractionated WB-EBRT	\$3,897	\$6,398^a	-\$3,041

Source: Table 12, p23 of the DCAR, and calculated by Department for MSAC

IORT = intraoperative radiotherapy, BCS = breast conserving surgery, OR = operation room

^a Calculated by changing number of attendances from 25 to 15 in Table 11 of DCAR

The DCAR stated that the cost saving yielded through the utilisation of the IORT with the Axxent[®] device relative to WB-EBRT is marginally higher in comparison to the IORT with Intrabeam[®] relative to WB-EBRT. Application 1189 for IORT with the Intrabeam[®] device calculated that, compared to BCS followed by WB-EBRT, IORT would yield cost savings of: \$5,130 per patient for those treated with IORT concurrent with BCS followed by “boost” WB-EBRT (Scenario 1) and \$5,637 per patient for those treated with post-pathology IORT

following BCS (PSD Application 1189 2014, p9). In comparison, the total average cost for six weeks of WB-EBRT was estimated to be \$15,971 (\$6,025 for BCS plus \$9,946 for WB-EBRT).

In the pre-MSAC response, the applicant acknowledged that hypofractionated WB-EBRT is generally recommended for patients with early stage breast cancer shortening from five to three weeks (25 fractions down to 15 fractions). Despite hypofractionated WB-EBRT reducing the number of attendances from 25 to 15, the overall cost reduction for treatment still favours IORT with the Axxent[®] or Intrabeam[®] devices over hypofractionated WB-EBRT.

The DCAR stated that ESC acknowledged that due to the very low uptake of the Intrabeam[®] MBS items, that there would be no impact on the MBS should Axxent[®] replace Intrabeam[®]. However, the ESC noted that, based on the budget impact analysis reported in MSAC Application 1189, that replacement of WB-EBRT by Axxent[®] would also likely result in cost savings. Therefore, in this resubmission, based on non-inferiority compared to Intrabeam[®] and WB-EBRT, the DCAR expected that Axxent[®] will also yield in cost savings to the MBS and health budgets.

The DCAR stated MSAC also acknowledges the clinical need for an IORT device to negate the excessive travel required to undertake a WB-EBRT regimen, especially for patients in rural and remote areas (PSD Application 1189). MSAC therefore accepted, that equity of access to radiotherapy for these patients is improved (PSD Application 1189). The lack of utilisation of the current IORT device, Intrabeam[®] means that having an additional option of the Axxent[®] device is going to be beneficial to improve equity of access.

In the pre-MSAC response, the applicant stated that the low number of Medicare claims for IORT is largely attributable to the fact that the two operational systems are performing IORT on public patients in a public hospital environment and are therefore funded differently.

14. Key issues from ESC for MSAC

Table 9 Summary of key issues from ESC for MSAC

ESC key issue	ESC advice to MSAC
The device is not associated with high-level 1 evidence compared to Intrabeam [®] or WB-EBRT	MSAC may wish to check with the applicant if there is likely to be any higher level evidence available in the future. ESC considers it not unreasonable to request NHMRC level II (randomised controlled trial) evidence to support the application for public funding.
Approval of application 1189 (Intrabeam [®]) was primarily based on RCT data (TARGIT-A) with a median 2.5 years of follow-up. Axxent [®] has lower level evidence and 3-year follow-up. The short follow-up results in uncertainty regarding the comparative safety and effectiveness of Axxent versus Intrabeam or WB-EBRT.	Consideration should be given to the duration of follow-up data that would be informative for MSAC in considering the comparative safety of Axxent versus Intrabeam or WB-EBRT, noting the potential value in reviewing the extended safety data for Intrabeam when the TARGIT-A trial is completed in 2023 (NCT03501121).
MBS item descriptors – limits	ESC considered it reasonable to restrict the item to once per lifetime, as there are no data on repeated use. However, this was not raised at the time of application 1189 and subsequent MBS listing for Intrabeam [®] .

ESC key issue	ESC advice to MSAC
Economic evaluation and financial impact	<p>DCAR’s financial estimates rely on the treatment costs for WB-EBRT in MSAC application 1189, and the assumption that the costs of treatment with Axxent[®] and the market share and uptake of Axxent would mirror that modelled for Intrabeam[®]. However, several uncertainties were identified:</p> <ul style="list-style-type: none"> • Since Intrabeam[®] was considered by MSAC hypofractionated radiation therapy (HFRT) regimens for WB-EBRT is now recommended for the majority of patients with early breast cancer, and this translates to lower treatment costs due to the use of fewer fractions; the DCARs ‘cost savings’ are therefore overestimated • The costs associated with Axxent[®] were not explained and the device cost remains unknown. <p>However, ESC also noted the continued low uptake of Intrabeam[®] on the MBS and recalled previously it considered that there should be no impact on the MBS should Axxent[®] replace Intrabeam[®] in clinical practice.</p>
RANZCR support	ESC noted that RANZCR is not currently supportive of IORT technology.

ESC discussion

ESC recalled that MSAC previously did not support an application for this device in this indication on the basis of uncertain clinical effectiveness and safety. MSAC previously accepted that the Axxent[®] device was technically equivalent to Intrabeam[®] based on *ex vivo* simulations. ESC noted existing MBS items 31516 and 15900 for IORT, approved in 2015 for Intrabeam[®].

ESC noted that at the time Intrabeam[®] was supported for public funding it was scheduled for review (of utilisation and additional outcomes data) in September 2018. The department had decided to defer the predicted versus actual review because of the limited availability of the service, the TARGIT-A trial follow-up data [[NCT03501121](#)] that should be available in 2023 (which will provide longer follow-up data for recurrence rates) and the lack of information regarding why IORT is not being used as a treatment option. ESC considered a review for Intrabeam[®] to be important before Axxent[®] could be supported for MBS listing.

ESC considered it appropriate to limit the proposed service to once per lifetime, as there are no data to support re-irradiation.

ESC noted the updated evidence in the DCAR is primarily from two case series, which provide follow-up of 3.0 years. However, there is no direct comparative evidence for Axxent[®] compared with whole-breast external beam radiotherapy (WB-EBRT) or Intrabeam[®]. ESC noted the pre-ESC response stating that Intrabeam[®] was approved on follow-up of 3.2 years, but also noted that the Intrabeam[®] application was based on a large randomised controlled trial (RCT) ($n = 3,451$).

ESC considered the *naive* comparisons between Axxent[®] (case studies) and WB-EBRT (high-level RCTs), and noted the non-matched cohorts (the WB-EBRT studies included a much broader population). Although the studies might suggest non-inferior effectiveness and safety, the disparities in the evidence and shorter follow-up for Axxent[®] vs. WB-EBRT (3.0 vs. 10.2 years, respectively), make it difficult to draw conclusions regarding comparative effectiveness. Compared with Intrabeam[®], Axxent[®] might be non-inferior in terms of

effectiveness and safety, but this conclusion is again uncertain due to the short follow-up times for Axxent[®].

Overall, ESC expressed concern about the lack of RCTs for Axxent[®], and the precedent it may set if Axxent[®] is listed without such evidence.

ESC noted the claim by the sponsor in their pre-ESC response that, because MSAC accepted Axxent[®] as technically equivalent to Intrabeam[®], the clinical evidence for Intrabeam[®] should be considered as directly applicable to Axxent[®]. However, ESC considered that there are technical differences between the two devices, and was uncertain that the clinical evidence for Intrabeam[®] could be assumed to apply to Axxent[®]. ESC recalled that the technical equivalence that MSAC determined for the two devices was based on dosimetry performance, and that no determination of equivalence in terms of safety or effectiveness was made by MSAC.

ESC noted the DCAR did not include any pre-modelling studies: the DCAR relied upon the MSAC recommendation for Intrabeam[®] (in MSAC Application 1189) and assumed that Axxent[®] can also be cost-minimised against WB-EBRT. This assumption was on the basis that Axxent[®] and Intrabeam[®] are interchangeable, and the costs of treatment with Axxent[®] would mirror that modelled for Intrabeam[®]. However, ESC queried if technical differences between the two devices would lead to cost differences. ESC also noted that Axxent[®] services would require specialist training, which did not appear to be taken into account in the resubmission.

ESC also noted that the DCAR relied on the costing of WB-EBRT as presented in Scenario 1 for MSAC Application 1189, that replacement of WB-EBRT by Axxent[®] would also likely result in cost savings. This assumption was on the basis that the market share of Axxent[®] would mirror that modelled for Intrabeam[®]. However, ESC noted several uncertainties:

- Hypofractionated radiation therapy (HFRT) regimens for WB-EBRT are now recommended in Australian national guidelines. This means that the number of fractions per course of treatment has reduced from 25 attendances over 5 weeks to 15 attendances over 3 weeks. As MBS payments for WB-EBRT are paid per fraction, reliance on a conventional fractionation regimen for costing the comparator favours Axxent[®].
- The cost for IORT with Axxent[®] (\$1,117) was also not sufficiently explained; ESC recalled from the previous application that the cost for the Axxent device was also unknown.

Overall, ESC considered the DCARs claim that Axxent[®] vs. WB-EBRT would provide greater cost savings (relative to Intrabeam vs. WB-EBRT) is misleading. In addition, ESC considered that the DCAR did not discuss if there would be a change to the net budget impact to the MBS and other Government budgets with the addition of Axxent[®] to the current IORT market (with Intrabeam[®]). However, ESC noted the continued low uptake of Intrabeam[®] on the MBS and recalled previously it considered that there would be no impact on the MBS should Axxent[®] replace Intrabeam[®] (i.e. Axxent[®] becomes an alternative to Intrabeam[®]).

ESC further discussed the low uptake of Intrabeam[®], based on MBS claim data. They noted the possibility that surgeons feel that using IORT (with any device) during a breast conserving surgery (BCS) disrupts and extends theatre time, which has implications for the patient (extra anaesthesia time) and impacts on service delivery and costs. ESC also noted the lack of support from RANZCR for IORT.

ESC noted the pre-ESC response stating the recent sale of another IORT unit along with a strong likelihood of a further two IORT units entering service in 2020, which the applicant claimed will further drive the uptake of IORT.

15. Other significant factors

Nil

16. Applicant comments on MSAC's Public Summary Document

The applicant had no comment.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website:
[visit the MSAC website](#)