

Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1657.1 - Rhenium-188 brachytherapy for non-melanoma skin cancer

Applicant: Oncobeta Therapeutics

Date of MSAC consideration: 3-4 April 2025

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

1. Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing of epidermal radioisotope therapy, using Rhenium-188 (Re-188) for basal cell carcinoma (BCC) or cutaneous squamous cell carcinoma (SCC) was received from Oncobeta Therapeutics 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, cost-effectiveness and total cost, MSAC deferred its advice on the public funding of Rhenium-188 brachytherapy for the treatment of non-melanoma skin cancer in patients where surgery is not possible due to lesion location or contraindicated for surgical excision, including where there are patient safety concerns. MSAC considered that despite low certainty evidence there was likely to be a clinical place for Rhenium-188 brachytherapy for a specific population of patients. Regarding the comparator therapies MSAC noted the lack of consensus on what constitutes standard of care and the limited availability of comparative safety and effectiveness evidence to inform a complex economic model. MSAC advised that a resubmission should resolve the outstanding issues regarding tighter definitions of the patient population and providing additional information and justification of the proposed MBS items, including the cost of the Rhenium-188 compound, waste disposal, consumables, and clinician time. Additionally, MSAC considered that additional cost analysis based on the cost per treatment success and/or cost per lesion would be useful for decision making, including but not limited to the risk and costs of managing adverse events related to Rhenium-188 brachytherapy.

Consumer summary

This is an application from Oncobeta Therapeutics Pty Ltd requesting Medicare Benefits Schedule (MBS) listing of Rhenium-188 (Re-188) brachytherapy as an alternative treatment to radiation therapy for patients with non-melanoma skin cancer that is not suitable for surgery or when the patient is not suitable for surgery.

Non-melanoma skin cancer is the most common form of cancer in Australia. Currently, non-melanoma skin cancers are generally treated with surgery. If a patient is not able to have surgery, then the skin cancer is usually treated with a type of radiation therapy called external beam radiotherapy (EBRT). This is a type of radiation treatment in which a machine aims radiation beams at a person's skin cancer cells to kill them. This type of treatment is often given in multiple small doses, meaning a patient may receive several treatments over a few days to weeks.

Consumer summary

The proposed service is a form of radiation treatment for non-melanoma skin cancer that uses a paste containing a radioactive substance called Rhenium-188 (Re-188). Re-188 emits radiation that targets and destroys cancer cells. During treatment, the affected area of the skin is covered with a sterile protective foil. The Re-188 paste is then applied on the foil using a special applicator. This sits on the skin for a pre-specified amount of time and is then removed by pulling the foil off the skin. This treatment can be provided in one visit in an outpatient setting.

This application is for Re-188 radiation treatment to treat non-melanoma skin cancer patients with lesions on hard-to-treat areas (nose, eyebrow, lip, ear, finger, genitals, shin or collarbone) or who are unable to have surgery for other reasons. Re-188 radiation therapy is not intended to be used instead of surgery but is intended to be used instead of radiation therapy (such as EBRT) when patients cannot have surgery.

MSAC noted that Re-188 radiation treatment may offer the advantage of being more acceptable to some patients (including those in rural and remote areas) than EBRT, if they are eligible, because only one treatment of Re-188 is required. MSAC also considered the evidence for comparative safety and effectiveness to be low certainty but acknowledged that more certain evidence was unlikely, and Re-188 radiation treatment did appear to be safe and effective for a certain group of patients. However, MSAC needed additional information to finalise its advice. This included identifying the right group of people and skin lesions for which Re-188 radiation would be the most appropriate treatment, and further details about the costs for both Re-188 and the different types of EBRT, including who would pay the costs for any wastage of unused Re-188 paste and the risks and costs of any side effects of Re-188 treatment. Instead, MSAC deferred its decision pending further information.

MSAC's advice to the Commonwealth Minister for Health and Aged Care

MSAC deferred its decision on MBS listing of Re-188 brachytherapy to treat patients with non-melanoma skin cancer who are unsuitable for surgery. MSAC could not give a recommendation until several uncertainties had been resolved, including the eligible population, the proposed MBS items and fees, costings for the treatments, and a revised economic model.

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

MSAC noted that this was a resubmission from Oncobeta Therapeutics requesting Medicare Benefits Schedule (MBS) listing of Rhenium-188 (Re-188) brachytherapy as an alternative to radiation therapy (RT) for treatment of patients with non-melanoma skin cancer (NMSC) who are not suitable for surgery or when the patient is not suitable for surgery.

MSAC recalled that it had previously considered Re-188 brachytherapy for NMSC in patients contraindicated to surgery at its July 2023 meeting. MSAC did not support public funding at the time due to uncertainty in the evidence base and concerns around the economic model and financial analysis. MSAC noted that its previous concerns about patient preference and radiation safety for patients and healthcare professionals (including disposal) had been addressed to the extent that is currently likely possible. However, most concerns remained outstanding with this resubmission.

MSAC noted that the resubmission had expanded the eligible population from the original application (MSAC application 1657)¹ to include clinician concerns for patient outcomes from

¹ <https://www.msac.gov.au/applications/1657>

surgery as a contraindication for surgical excision, rather than only based on lesion location MSAC considered that the expansion of the eligible population created uncertainty around the definition of the target population and increased uncertainty around the estimated utilisation of Re-188 brachytherapy. However, MSAC acknowledged that the treatment will likely benefit a specific cohort of patients, particularly older patients (due to radiation concerns for younger people).

MSAC noted that the applicant-developed assessment report (ADAR) proposed 3 MBS items: one each for planning, the radioisotope and service delivery. MSAC considered the planning item to be appropriate but had concerns regarding the radioisotope and service delivery items. MSAC noted that the fee for the second item (for the radioisotope) of \$393.90 was for Re-188 resin to cover a treatable area of 0.5 cm² and was based on the total production cost of one carpoule of Re-188 resin (approximately redacted; increased from \$14,000 in the original submission), which can treat a total area of redacted; cm². MSAC noted that the MBS item can be applied as many times as needed to treat any lesion up to 8 cm² in contiguous areas, or multiple lesions of any total area when any one lesion is ≤8 cm² in contiguous area. MSAC noted that the economic model assumes splitting one carpoule among 7 patients (base case) and assumes no wastage. However, at the hearing, representatives of the applicant acknowledged that 100% batching efficiency will never be achieved in practice, but for the 4 clinics currently providing Re-188 brachytherapy, more than 80% or 90% batching efficiency was achieved. MSAC considered that additional information regarding the wastage costs under realistic circumstances where batching efficiency was not 100% and clarification regarding who would pay for wastage would be needed to reduce uncertainty around potential out of pocket costs for patients. MSAC also noted uncertainty regarding changes in cost of the carpoule used to determine the MBS item fee.

MSAC also considered that, to improve equity in rural and remote areas, the referrer should be amended to any general practitioner (GP) in consultation with a dermatologist or plastic surgeon.

MSAC noted that the third item (for service delivery) was for staff time including the attendance of radiation therapists, medical physicists and a radiation oncologist and non-isotope-related consumables. The fee was determined through a breakdown of costs involved with delivering the treatment to a patient over the average time span of approximately 80 minutes. MSAC noted that most of this time comprises the patient waiting after the resin is applied, however the MBS can only reimburse the time a clinician spends with the patient, so a clinician would need to be in attendance during the entire treatment for the calculated costs related to apply. MSAC noted that the fee provided in the ADAR was 4-times that of a comparable MBS item for brachytherapy (15982) with a treatment time of approximately 20 minutes. The fee also includes nurse time (\$66.77) and consumables (\$50), which were considered inappropriate inclusions for an MBS item. MSAC also considered that, if multiple patients were treated simultaneously (as might occur if the patients were batched to receive treatment from the one carpoule of Re-188), clinicians would not be able to double-bill their time. Overall, MSAC considered the proposed MBS items to be inappropriate, and advised consultation with the department to develop a different approach was required.

MSAC noted the proposed clinical management algorithm in which Re-188 brachytherapy was not intended to be a substitute for surgery, and that patients suitable for surgery would still proceed with surgery. Re-188 brachytherapy was proposed to replace external beam radiotherapy (EBRT) in the eligible population who would otherwise receive standard care, although MSAC considered that what constituted standard care to be uncertain for these patients. MSAC noted at the hearing representatives of the applicant stated that there is no single direct comparator, as treatment differs depending on the type of NMSC and its severity.

MSAC noted that the clinical claim of non-inferior comparative safety was not adequately supported by the evidence. Considerable limitations to the evidence included heterogeneity between the studies' results, varying sample sizes (especially small sample sizes for EBRT), and a lack of uniformity in the follow-up across studies. MSAC noted from the limited evidence that Grade 3+ adverse events occurred more frequently in Re-188 brachytherapy studies than in EBRT studies. Varying rates of late toxicities were observed in different studies for both Re-188 brachytherapy and EBRT treatments. Ulceration, fibrosis and skin induration were more frequently seen in Re-188 brachytherapy studies than EBRT studies, while hyperpigmentation and telangiectasia were more frequently seen in EBRT studies than Re-188 brachytherapy studies. MSAC considered that Re-188 brachytherapy appears to be safe but has a different safety profile to EBRT.

MSAC noted that the evidence presented was inadequate to accurately assess comparative effectiveness. All the studies were single arm cohort studies with considerable heterogeneity, were assessed to be of low to very low uncertainty, and did not allow for statistical comparison. There was a lack of detailed information on lesion area or depth in the EBRT studies, so the similarity to the proposed population was unknown. The EBRT evidence base included studies with patients with all T stages (range of 1–4; describes the size and extent of the tumour), which may bias the comparison in favour of Re-188 brachytherapy. Overall, MSAC considered that it was difficult to draw conclusions around the comparison of Re-188 brachytherapy to EBRT due to the heterogeneity in this population, however MSAC considered it was likely that Re-188 brachytherapy was non-inferior in effectiveness for certain patients and lesions.

MSAC noted that the resubmission also presented skin cancer index (SCI) data relating to quality of life and treatment comfort, that were collected as part of the EPIC study. However, the data were only available for Re-188 brachytherapy, and no comparison with EBRT was made as there were no studies identified that measured quality of life (QoL) for EBRT.

MSAC considered that the evidence suggests that Re-188 brachytherapy is likely effective and a suitable option for a well-defined population when EBRT is difficult (for example, based on lesion site, the number of visits). However, relative efficacy was not sufficiently quantified, which introduced issues to the economic model.

MSAC recalled that, during its previous consideration, it had requested that any resubmission should present additional research into patient preferences for the treatment. MSAC noted that the resubmission presented a brief narrative literature review of 7 studies on patient-reported outcomes regarding keratinocyte cancers (KC) and NMSC therapies. MSAC noted the commentary considered that this review was not relevant to the current submission as most studies presented patient-reported outcomes following Mohs micrographic surgery, rather than EBRT. However, the ADAR stated that the findings of the review suggest broad patient support for Re-188 brachytherapy treatment if it were indicated. MSAC noted that, in 2024, a consumer advisory board was formed by the applicant with patient advocates from the Melanoma and Skin Cancer Advocacy Network (MSCAN) to investigate patient preferences for Re-188 brachytherapy. Six participants with skin cancer experience shared their treatment journeys and discussed the importance of broad access to Re-188 brachytherapy. The participants advised that, given a choice, most of them would have preferred Re-188 brachytherapy over conventional radiotherapy. They expressed concerns about cost and availability of Re-188 brachytherapy, especially for rural and remote patients. MSAC considered that there may be equity issues for rural and remote patients due to the short half-life of Re-188 and the therapy involving an unsealed radiation source limiting the number of providers able to offer the service however, the treatment does have the benefit of only requiring a single visit, thereby reducing travel requirements for patients. The applicant stated that regional supply was not a concern as Re-188

is currently manufactured in Australia and there is sufficient logistical capacity for country-wide supply.

Overall, MSAC considered the evidence presented for comparative safety and effectiveness to be low certainty but acknowledged that higher certainty evidence was unlikely to become available.

MSAC noted that the ADAR presented a cost-minimisation approach rather than a cost-minimisation analysis as no modelling had been done. A cost-minimisation approach was chosen based on the clinical claim of Re-188 brachytherapy being non-inferior to EBRT. However, the non-inferiority claim was not substantiated by the evidence for effectiveness or safety.

Additionally, because the safety profiles of the treatments appear to differ, MSAC considered that a cost-minimisation approach was not appropriate according to the MSAC Guidelines. MSAC considered that a more complex economic model was difficult to perform due to the limited comparative data. However, MSAC considered that basic cost-effectiveness analyses covering several outcomes separately would be the most useful for decision making, including but not necessarily limited to costing studies that consider the cost per successful treatment (based on one or more appropriate patient related outcome) or the cost per lesion cured. Additionally, MSAC considered that the costs associated with the different safety profile, including costs for management of adverse events, should be included in a resubmission.

As well as the model chosen, MSAC noted that there were several other issues with the economic evaluation:

- The model was not robust and strongly favoured Re-188 brachytherapy. It only considered the time up to treatment delivery and did not include patient outcomes.
- No justification was provided for the increase in carpoule cost compared with the original submission, creating uncertainty around the costs.
- Batching and wastage were too simplistic and unrealistic, and waste management costs were not included.
- The weighted cost of EBRT types does not align with Royal Australian and New Zealand College of Radiologists (RANZCR) advice on relative use, and the cost of EBRT was too high. The assumptions, which strongly favoured Re-188 brachytherapy, have limited evidence, could not be validated and remain highly uncertain.

MSAC noted that sensitivity analyses performed by the commentary highlighted that Re-188 brachytherapy is likely to be more expensive than EBRT. MSAC considered that further clinical input regarding the fractions and type of EBRT most likely to be used for patients and lesions suitable for Re-188 brachytherapy, to ensure an accurate comparison of the total costs and relative benefits. There is also a need to compare the EBRT technologies with Re-188 brachytherapy, where the mix of EBRT in practice is directly compared with the true usage of Re-188 brachytherapy, and that also accounts for wastage and batching.

MSAC also noted that RANZCR provided advice post-ESC that the number of EBRT fractions per treatment would usually be between 1 and 7 (and not 22 as in the ADAR) and would use kilovoltage EBRT (which is less expensive than megavoltage EBRT). MSAC noted that the pre-MSAC response disagreed with the RANZCR advice and stated that kilovoltage EBRT was outdated technology. The current sensitivity analysis did not consider a lower number of fractions of EBRT; the lowest number of fractions considered was 10 per treatment, using the same mix of EBRT modalities as the ADAR base-case. This resulted in Re-188 brachytherapy being more expensive than EBRT by \$redacted/patient, whereas using 30 fractions/treatment results in a saving of \$redacted/patient. MSAC considered that it was important that the number of fractions is a shared decision between the patient and their healthcare team, particularly due to the heterogeneity of skin cancers.

MSAC noted that the financial impact used a market-share approach based on utilisation of the currently listed items related to EBRT (superficial X-ray radiation therapy [SXRT], electrons and intensity-modulated radiation therapy [IMRT]) and aligned with the updated MBS items, which MSAC considered appropriate. However, estimates of EBRT modality replacement were based on a clinician survey and an email from **redacted** with regards to their NMSC case mix. MSAC did not consider this to be appropriate because:

- there is no means of validating the results presented in the email
- the substitution of different modalities varied at different rates over time without justification, which led to a difference in the average patient cost of EBRT for different years
- the comparator varies from \$5,244.37 /patient in 2025 to \$6,592.68/patient in 2030
- the estimates assumed an average of 22 fractions per patient for EBRT, based on 7 vignettes presented to clinicians – it was unclear how representative these vignettes were of the general population, given that the range of fractions put forward ranged from 6-30.

At the hearing, representatives of the applicant stated that they had received varied advice from oncologists regarding the use of EBRT modalities, as these differ for different types of NMSC, which may explain the variation in the parameters of the above dot points. MSAC considered the variance in modality use indicated that an average may not be useful for the resubmission financial analysis, rather several scenarios could be presented the analysis, ideally using a transparent weighted approach that could be used based on prevalence of each type of lesion - if data is not available then at least some best / worst case analyses could be presented in the resubmission financial analysis.

MSAC noted that the ADAR used the full fee in the financial analysis, so did not account for the greatest permissible gap (GPG) or an 85% benefit fee when calculating the MBS costs. The ADAR's base case estimated that Re-188 brachytherapy will save the MBS an estimated **redacted** over 6 years. However, MSAC noted the commentary provided a univariate sensitivity analysis that used the 85% benefit and demonstrated the financial impact estimates ranged from a 6-year cost saving of **redacted** (if **redacted** fractions of the comparator treatment was needed) to a cost of **redacted** (if only 1 carpoule per patient was used). MSAC considered that the model was not robust. Aligning the number of fractions with RANZCR advice and adjusting for more reasonable wastage, the estimated financial impact was:

- **redacted** in year 1 to **redacted** in year 6 (assuming **redacted** fractions per treatment)
- **redacted** in year 1 to **redacted** in year 6 (assuming **redacted** patients per carpoule).

Additionally, because the costs were only considered up to treatment delivery, MSAC considered that these costs may underestimate the cost to all health budgets (in terms of post-treatment care, management of adverse effects, etc.).

MSAC considered that a resubmission should be considered first by the Evaluation Sub-committee (ESC) and the following information would be required:

- clarity around the eligible population – it should be limited to those most likely to benefit and clearly describe the patient and lesion factors that indicate likelihood of benefit from the treatment;
- an appropriate referral pathway should be defined;
- a review of the MBS items sought –including suitability of components of the MBS items, and justification of fees and variations in cost of carpoule;
- more accurate costings of both Re-188 brachytherapy (including realistic wastage) and EBRT – based on additional stakeholder engagement and feedback and preferably including independent advice, including further clinical input regarding the fractions and

type of EBRT most likely to be used for patients and lesions suitable for Re-188 brachytherapy, to ensure an accurate comparison of the total costs and relative benefits;

- Further examination of the potential costs and consequences of adverse events related to Re-188 therapy;
- a fit-for-purpose economic evaluation – preferably a basic cost-effectiveness/cost-consequence) analysis presented as the cost per treatment and/or cost per lesion treated, including the costs of retreatment and complications as well as cost of delivery, using a selection of patient outcomes in the PICO (for example, scarring/cosmesis, pain, functional impairment).

4. Background

MSAC has previously considered Re-188 brachytherapy for non-melanoma skin cancer (NMSC) in patients contraindicated to surgery at the July 2023 MSAC meeting. This resubmission will be the second time the technology has been assessed.

The key matters of concern from the previous consideration are summarised in Table 1.

Table 1 Summary of key matters of concern

Component	Matter of concern	How the current assessment report addresses it
Evidence base	MSAC noted that an improved evidence base for comparative safety and efficacy was needed.	6 month and 12 month prospective EPIC Skin Trial, European long-term safety, efficacy, quality of life (QoL), and cosmesis of Re-188 brachytherapy, local registry data of Re-188 brachytherapy and conventional radiation therapy outcomes. <i>While this adds additional data to the evidence base, it is a single arm trial and was inadequate to accurately assess the comparative safety of Re-188 brachytherapy and EBRT for BCC and SCC.</i>
Comparator estimates	MSAC noted that a more robust estimate of comparator cost will be required that considers different EBRT modalities.	Clinician advisory board, patient vignettes, questionnaires, and private radiation clinic data redacted . <i>While this added more data on the current modalities used for EBRT, the info provided from redacted was an email and there are no means to properly validate the quality of the evidence; there is still uncertainty as to how representative this is of general practice as it doesn't align with the RANZCR feedback.</i>
Eligible population	MSAC required a more “transparent” estimation of the population that would be eligible for the proposed therapy.	Volume estimates based upon current treatments and trajectory, in addition to switching rates from conventional modalities to Re-188 brachytherapy as estimated by panel of radiation oncologists. <i>While a market share approach was used, the estimates for the volume of current EBRT modalities that are used for NMSC (and eligible for Re-188 brachytherapy) were based on the redacted information and remains uncertain – see note above.</i>

Component	Matter of concern	How the current assessment report addresses it
Patient preference	MSAC noted that a formal patient preference study may inform how the population are currently treated and how this may change with a listing of the proposed therapy.	We assembled an advisory board through MSCAN of NMSC patients to gather their insights into treatments and their preferences. This included a questionnaire that was extended to additional Re-188 brachytherapy patients. We have also included analysis from a recent publication of preferences amongst a German Re-188 brachytherapy cohort. Finally, a large online survey was performed to get treatment feedback from a broad cohort of geographically diverse NMSC patients. <i>Only the online survey was relevant for patient preferences in Australia,</i>
Wastage	MSAC required specifics on how treatment could be delivered or batched between patients to minimise wastage.	Ways to mitigate wastage and the lack of commonwealth financial implication discussed in Section 1.8. <i>The ADAR provides additional information; however, the issue of wastage is still a concern with considerable uncertainty and risk given complexities of batching</i>
MBS Items	Revised items considering varying lesion sizes and batching of treatments.	New MBS items proposed on a cost per cm ² basis. <i>These have been provided with considerable changes to the ratified PICO and need further consideration.</i>
Revised economic and financial analyses.	Uncertainty regarding weighting of comparator EBRT modalities and size of the proposed population, uptake of Re-188 brachytherapy, distributions of lesion sizes, number of fractions for the comparator, and percentage split of the comparator across modalities.	Economic analysis converted to cost-minimisation with commonly used EBRT modalities. Updated analyses provided in Sections 3 and 4, with associated worksheets. <i>The ADAR has made considerable changes to the original assessment report; however, there is still uncertainty around the cost of the comparator and the size of the proposed population.</i>
Radiation Safety for patients and healthcare professionals, including disposal.	Uncertainty around radiation safety and exposure for patients and healthcare professionals, including disposal.	Detailed technical dossier with references, as well as a cross-radiation report. Inclusions of real-world Australian clinician dosimetry reports for treatment sessions. <i>The ADAR provided a comprehensive technical dossier that included radiation safety procedures.</i>

Source: Table 1.1.1 p 12 of the ADAR and *compiled during evaluation*. NMSC = Non melanoma skin cancer; MSAC = Medical Services Advisory Committee; PSD = Public Summary Document; EBRT = external beam radiation therapy; QoL = quality of life; Re-188 brachytherapy = Rhenium Skin Cancer Therapy.

5. Prerequisites to implementation of any funding advice

The proposed technology includes a therapeutic good that requires TGA approval. The entire RSCT system was registered as a class IIb medical device on the Australian Register of Therapeutic Goods (ARTG) in November 2022 (Table 2). The Rhenium-188 compound had already been listed on the ARTG as a class IIb device since December 2020. Both the compound and the system are intended to treat skin cancer using the radioisotope Rhenium-188.

Table 2 Registration summary of Re-188 brachytherapy

Product name and Sponsor	ARTG summary	Functional description	Intended purpose
Rhenium-SCT® OncoBeta Therapeutics Pty Ltd	ARTG ID: 400142 Start date: 24 November 2022 Category: Medical Devices Class IIb GMDN: 38299 Radionuclide system, therapeutic, brachytherapy, manual ARTG ID: 351390 Start date: 9 December 2020 Category: Medical Device Class IIb GMDN: 38299 Radionuclide system, therapeutic, brachytherapy, manual	High-dose brachytherapy with Rhenium-188	Treating certain keratinocyte skin cancers using the radioisotope Rhenium-188

Source: ARTG website: www.tga.gov.au/resources/artg. Abbreviations: ARTG ID= Australian Register of Therapeutic Goods identification; GMDN= Global Medical Device Nomenclature; Re-188 brachytherapy= Rhenium skin cancer therapy; TGA= Therapeutic Goods Administration.

6. Proposal for public funding

Public funding is sought via the MBS, and the proposal intends to create new MBS items.

The ADAR proposed three new items, that differed from the original PICO. These items have not previously been seen by PASC or MSAC. The applicant states that this is to address the MSAC's previous concerns:

- Single fee structure not allowing for economies of scale
 - The original submission proposed itemising lesions into size ranges, with all attendant services from specialist, nursing, and technician staff included. The MSAC was concerned that single patients with multiple lesions would attract multiple services despite being treated in a single session. ESC proposed a cost per cm² may address this concern.
- Item descriptors should align with ongoing EPIC-Skin study
- MBS item should not permit re-treatment of the same lesion

The following tables provide the group, descriptor, fee, benefits and explanatory notes for the MBS items proposed by the applicant.

During development of the commentary some changes were proposed to assist in making the item description more aligned with the PICO and MSAC feedback; however, further work may be required to ensure they meet the needs of the MBS. In all Items “Re-188 brachytherapy radioisotope therapy” was changed to the previous accepted term “Epidermal radioisotope therapy”.

Table 3 Proposed item descriptor for Re-188 brachytherapy radioisotope therapy planning

Category 3 – Therapeutic Procedures – Group T2 - Radiation Oncology; Subgroup 4 - Brachytherapy
MBS item XXXX1
Epidermal radioisotope therapy, RST radioisotope therapy planning Epidermal radioisotope therapy, using rhenium-188 Rhenium-SCT® dosimetry for treatment planning if all the following apply: (i) localisation is based on clinical mark-up, and image-based simulation is not required; (ii) delineation of structures is not possible or required necessary, with tumour borders defined using a clinician-specified margin to establish the treatment volume; (iii) surface area measurements are obtained and utilised for planning purposes to determine lesion-specific treatment times; (iv) the planning process is required to deliver a prescribed dose to a point and specified depth on the surface of the patient; (v) doses are calculated in reference to a point, either at a depth, or on the surface of the patient, using from tables, charts, or data from a treatment planning system. Applicable once per course of treatment. Fee: \$203.70 Benefit: 75% = \$152.80 85% = \$173.15

MSAC proposed modification

Item XXXX1 (Table 3) is a new item that does not align with any of the previously requested items. The ADAR based this fee on the MBS Item 15950, stating that the planning process for a single, simple-complexity SXRT treatment plan aligns closely with the proposed Re-188 brachytherapy planning service. During evaluation it was considered that the process is likely to be similar. The planning code can only be applied once per course of treatment.

Table 4 Proposed item descriptor for Re-188 brachytherapy radioisotope therapy

Category 3 – Therapeutic Procedures – Group T2 - Radiation Oncology; Subgroup 4 - Brachytherapy
MBS item XXXX2
Delivery of Epidermal radioisotope Rhenium-SCT®-radioisotope therapy Epidermal radioisotope therapy, using rhenium-188 paste per 0.5 cm² to on one or more cutaneous basal cell carcinoma (BCC) or cutaneous squamous cell carcinoma (SCC) if: a) malignancy has been confirmed and other diagnoses excluded by histological examination; and b) the maximum depth of the lesion/s is less than or equal to 3 mm; and c) the lesion contraindicated for surgical excision, or where there are clinician concerns for the patient outcomes from surgery; and d) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and e) the service is referred by a dermatologist, plastic surgeon, or a skin-specialist GP if a dermatologist or plastic surgeon is not readily available; and f) the lesion has not previously been treated g) used to implement a plan as described in item XXX1. Applicable for total surface area of lesion/s treated. Fee: \$393.90 Benefit 75% = \$295.43 85% = \$334.82

MSAC proposed modification

Item XXXX2 (Table 4) descriptor aligns with the previous submissions' three items. However, the fee structure is such that it is to be applied based on multiplications of 0.5cm² of treatable area. The ADAR based this fee on the total production cost of one carpoule (approximately **redacted**) of Rhenium-188 resin/paste which can treat **redacted** cm². Of note the cost of a Rhenium-188 carpoule has increased from \$14,000 in the previous submission to approximately **redacted**. The ADAR stated that the fee is based on the total production cost of one carpoule (approximately **redacted**). The ADAR stated the price of Re-188 carpoule production has increased due to increased material and production costs. The ADAR stated that one carpoule can treat 25cm²; however, this is likely to be variable as the quantity needed is based on both surface area and depth of the cancer and relates to previous comments around wastage and batching. If one carpoule was used to cover exactly **redacted**cm² then the cost of the carpoule would be **redacted**. The ADAR stated that the MBS item can be applied as many times as needed to treat any lesion up to 8cm² in contiguous area, or multiple lesions of any total area when any one lesion is ≤8cm² in contiguous area. These restrictions were not included in the item descriptor which was in line with the previous item descriptors; however, the previous item descriptors were limited in price as they were priced categorical and could only be charged once. The current wording poses a compliance issue that may lead to significant over expenditure, the descriptor and notes will need consideration as Services Australia may put system claiming limitations in place which will restrict the number of times an item can be claimed.

Table 5 Proposed item descriptor for Re-188 brachytherapy radioisotope therapy service

Category 3 – Therapeutic Procedures – Group T2 - Radiation Oncology; Subgroup 4 - Brachytherapy
MBS item XXXX3
Delivery of Epidermal radioisotope Rhenium-SCT®-radioisotope therapy service Service in provision of epidermal radioisotope therapy, using rhenium-188, of a cutaneous basal cell carcinoma (BCC) or cutaneous squamous cell carcinoma (SCC) Must be applied with Item XXXX2. Applicable once per course of treatment.
Fee: \$1733.77 Benefit 75% = \$1300.33 85% = \$1473.70 1,631.37

[MSAC proposed modification](#)

The ADAR did not account for the greatest permissible gap (GPG) when calculating the MBS costs. From 1 November 2024, the GPG is set at \$102.40.

As Item XXXX2 (Table 4) only covers the cost of the Re-188, the ADAR proposed an additional item was needed to cover the cost of healthcare provider time and consumables as is seen for MBS [item 15982](#) for brachytherapy treatment. The ADAR based the fee for Item XXXX3 (Table 5) on four times the cost of item 15982 (\$404.25). This was based on the estimation that administration of Re-188 brachytherapy would take four times as long (approximately 80 minutes) compared to item 15982 (approximately 20 minutes). The commentary considered that this was likely to be overestimated; while the treatment could take up to 80 minutes, most of this time is patient waiting time while the Re-188 paste is in contact with the skin. The application process is likely to be much shorter, and therefore the commentary noted that it may be more appropriate to use the same fee as MBS Item 15982. In addition, the MBS can only pay for the actual time a clinician spends with the patient, it seems that the item request is for 80 minutes of medical practitioner time (\$1,617), nurse time (\$66.77), and consumables (\$50),

which is not appropriate. The medical provider would need to be delivering the entire service as nurses can't bill for MBS services, unless an additional 'on behalf of item' is requested similar to MBS [Item 13950](#). Currently clinicians cannot double bill their time, so there may be issues if patients are being treated at the same time.

The commentary considered that batching and wastage could still be an issue with the updated MBS items. The ADAR's approach to costing the Rhenium-188 component of the MBS fee implies that batching is required (i.e. one carpoule is used to treat multiple patients with a single lesion and/or a patient with multiple lesions), as the carpoule contains enough compound to treat **redacted** cm². Because of this, wastage may occur depending on how efficiently lesion treatments are batched. The ADAR maintains that the clinics administering the service will bear the costs of wastage. However, it is not clear how much this will be, and how much of this will be passed onto patients in out-of-pocket expenses. The potential for this to affect State Hospital budgets in a public setting and individual patients in a private setting could be significant (e.g. it could be up to \$787.8 per cm² wastage in difference between the patients' lesion size(s) and **redacted** cm²). The ADAR has not addressed the issue of batching or wastage and has not accounted for this in the economic or financial analysis.

7. Population

There was only one PICO set proposed. The ADAR defined the population as patients with histologically confirmed basal cell carcinoma (BCC) or SCC, of relatively shallow depth and moderate size (depth ≤ 3 mm and area 1.5-8.0cm²), in anatomical areas for which they are contraindicated for surgical excision, including where there are clinician concerns for patient outcomes from surgery. The commentary noted that the resubmission no longer included patients "who otherwise refuse surgery". However, the clinical assessment of comorbidities that would prevent surgical excision on a case-by-case basis still creates difficulties for defining a PICO and for tightening the proposed MBS descriptor to avoid unintended use outside of the proposed population.

The commentary noted that the resubmission removed rarer lesions, that were mentioned in the previous ADAR. Though these would still be covered under the blanket term "keratinocyte cancer", they would not be included in the proposal for public funding (i.e. keratinocyte dysplasia).

In current practice, patients with suspected keratinocyte cancer typically present initially to a general practitioner, who, in most cases, surgically excises the lesion or prescribes one of several available topical therapies, with or without concurrent histology. Higher risk lesions, those in a challenging anatomical location, or patients with relevant limiting comorbidities or other objections to surgery, would usually be referred to a dermatologist, radiation oncologist or plastic surgeon, who in many cases would collaborate with a representative of the other speciality within a multidisciplinary care model.

The proposed clinical management algorithm showing the addition of Re-188 brachytherapy as an alternative to other radiotherapy modalities is presented in [Figure 1](#). Note, this algorithm does not depict the clinical pathway for patients "who otherwise refuse surgery" but the commentary considered that this pathway may be similar to the pathway for patients contraindicated to surgery.

At an individual patient level, Re-188 brachytherapy would directly substitute other modalities of radiotherapy, with the two approaches almost never being used consecutively for the same lesion. However, at a population level, it is envisaged that Re-188 brachytherapy would sit

permanently alongside other radiation therapy techniques in the management algorithm, as an alternative treatment technique appropriate only in limited specified clinical circumstances.

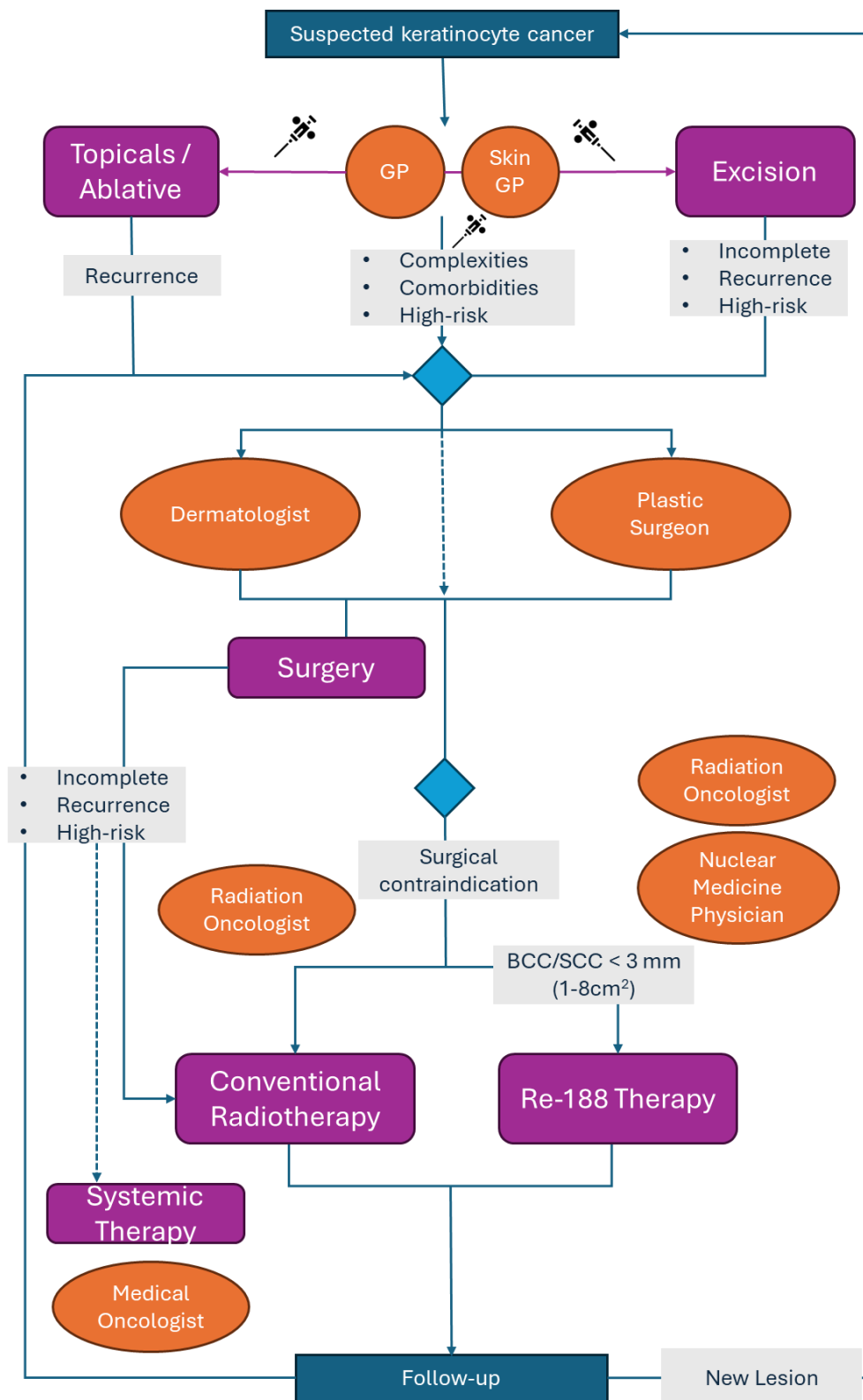


Figure 1 Proposed clinical management algorithm, following listing of Re-188 brachytherapy

Source: Figure 2 page 22 of the ADAR, BCC= basal cell carcinoma; GP = general practitioner; SCC= squamous cell carcinoma; Re-188 = Rhenium-188

8. Comparator

External beam radiation therapy (EBRT) remained the comparator in the ADAR resubmission. The original ADAR assumed that the EBRT modality would be evenly split between 3D megavoltage (50%) and Modulated Radiation Therapy/Volumetric Modulated Arc Therapy (IMRT/VMAT) (50%). The ADAR resubmission attempted to address the MSAC concerns about comparator estimates via an advisory board consultation to create a comprehensive assessment of current treatment practices of radiation oncologists across Australia. The advisory board consisted of nine Radiation Oncologists, two dermatologists and three representatives from OncoBeta. It was unclear what role the OncoBeta representatives played in the advisory board.

The clinical advisory board did not align with the MSAC feedback that orthovoltage use would be an appropriate comparator. In addition, the ADAR argued that the ESC proposed fractionation estimate of 5-10 fractions was well below what was seen in real-world data and reported by the advisory group. The commentary considered that it was unclear where the real-world data was derived from as the ADAR only reported Australian registry data for 11 patients that received EBRT modalities, and no fraction data was presented. In addition, the advisory board did not discuss fractions at length; however, the report provided case reports on eight cases where the fractions ranged from 9-30 fractions. Overall, the advisory board and case reports suggest that orthovoltage would not be used; however, it is still unclear what the mean fractions for EBRT would be from the evidence provided.

The ADAR proposed the following breakdown of EBRT modalities as the comparator for the ADAR (Table 6). This breakdown is entirely based on the clinical advisory board advice.

Table 6 Results of a survey of the clinical advisory board on the modalities used in the treatment of cutaneous basal cell carcinoma or cutaneous squamous cell carcinoma.

Modality	Modality breakdown	Proportion used without Re-188 brachytherapy being available	Proportion used with Re-188 brachytherapy being available
Electrons	CT Scan - Clinical Markup	REDACTED%	REDACTED %
	CT Scan - CTV/PTV & OARs Marked w/ DVH produced	REDACTED %	REDACTED %
3D Conformal Photons	CT Scan - Clinical Markup	REDACTED %	REDACTED %
	CT Scan - CTV/PTV & OARs Marked w/ DVH produced	REDACTED %	REDACTED %
IMRT / VMAT	CT Scan - CTV/PTV & Multiple OARs Marked w/ DVH produced	REDACTED %	REDACTED 0%
SXRT	Single Fraction	REDACTED %	REDACTED %
	Single Fraction w/ Internal Eye Shield		
	Multiple Fractions	REDACTED %	REDACTED %
	Multiple Fractions w/ Internal Eye Shield	REDACTED %	REDACTED %
Re-188 brachytherapy			REDACTED %

CT = computed tomography; CTV = clinical target volume; DVH = dose volume histogram; EBRT = external beam radiation therapy; IMRT/VMAT=Modulated Radiation Therapy/Volumetric Modulated Arc Therapy; OAR = organs at risk; PTV = planned target volume; Re-188 = Rhenium-188; QoL = quality of life; Re-188 brachytherapy = Rhenium Skin Cancer Therapy; SXRT = Superficial X-Ray Radiation Therapy

9. Summary of public consultation input

Consultation input was received from five medical, health, or other (non-consumer) organisations and one individual health professional. The organisations that submitted input were:

- Private Healthcare Australia (PHA)
- The Royal Australian and New Zealand College of Radiologists (RANZCR)
- Australian Society of Plastic Surgeons (ASPS)
- Australasian College of Dermatologists (ACD)
- Australasian Association of Nuclear medicine Specialists (AANMS)

Level of support for public funding

Support for public funding of this service was mixed. Two organisations (ACD, AANMS) were supportive of public funding, however the individual health professional, PHA, RANZCR and ASPS were not supportive.

Perceived Advantages

Advantages of the service noted in the input included:

- Rhenium-188 brachytherapy is a non-invasive, non-scarring treatment that can be delivered for patients in an outpatient setting and offers reduced healing time.

- This service has a limited but definite role in the management of non-melanoma skin cancers, as an alternative to surgery or conventional radiotherapy, particularly for thin lesions; or where surgery is not appropriate because of various patient and tumour factors.

Perceived Disadvantages

Disadvantages of the service noted in the input included:

- Insufficient evidence of safety and efficacy, cost effectiveness and total funding costs of this treatment. The feedback stated that there is a lack of randomised trials and published studies to support this treatment.
- Unknown long-term effects of treatment and risk of secondary cancers or other adverse events, the follow up in the studies was poor and the duration was insufficient to establish recurrence rates and late toxicity.
- Risk of increased incidence of acute toxicity reactions, including skin inflammation and ulceration, which is painful and usually requires dressings. This would be an additional cost to patients.
- The application does not address need for radiation protection or the need to deal with radiation waste, potentially underestimating the costs of the intervention.
- Potential that this service will be more expensive than the current widely available and well-established treatments.
- Many of the lesions described in the application could be removed surgically under local anaesthetic and there is a requirement for biopsy in the protocol, therefore the theoretical benefit of avoiding a surgical procedure may not be realised.
- Lack of information on what costs would still have to be paid out-of-pocket by patients.
- Limited availability to patients, particularly in regional, rural, and remote locations, as the service will only be provided through accredited nuclear medicine facilities in specialist public and private hospitals (non-admitted patients). Additionally, the 17-hour half-life and the consequent need to quickly and safely transport the radioactive paste may limit availability to patients.
- It is unlikely to reduce linac-related capital costs as only a small proportion of any linac treatment time is devoted to skin cancer.

Support for Implementation /issues

Implementation requirements

AANMS considered that there would need to be some training of specialists and that practical experience with unsealed sources is imperative. There is the potential for contamination of patients, therapy surfaces, equipment and staff. AANMS believe the radiation specialist involved should be actively and directly involved in the application of the material.

MBS Item descriptor and fee

Suggested changes were to remove the 'per 0.5cm²' regarding the paste application and the name of the prescribing speciality should be a 'nuclear medicine specialist'.

One respondent considered the criteria as too broad, and noted 'the patient's circumstances and co-morbidities, and the cancer characteristics, must be suitable for a single fraction radiation therapy treatment'.

10. Characteristics of the evidence base

There were no randomised controlled trials nor were there any non-randomised studies directly comparing safety and effectiveness of Re-188 brachytherapy with EBRT in patients with BCC and SCC.

Characteristics of the evidence for Re-188 brachytherapy

The ADAR did not present the data from the previous ADAR. The ADAR presented three additional studies and Australian registry data (Table 7). To gather a complete picture of the available evidence, the previous ADAR studies are presented here if they included only one treatment and met the patient criteria. Risk of bias for the included studies was re-assessed using Newcastle Ottawa Scale² to be in line with the previous PSD and because the ADAR did not use an assessment tool outlined in the MSAC guidelines.

Table 7 Key features of the included evidence

References	N	Design Duration	Quality	Patient population	Surface area and thickness	Outcome(s)
EPIC-Skin ³	189	Single-arm, prospective Phase IV study 12 month follow up	Fair	Adults with BCC or SCC lesions who were unwilling or contraindicated for surgery.	Inclusion: ≤8cm ² in size, and depth of ≤3mm	Tumour response rate at 6 and 12 months Quality of life at 6 and 12 months Cosmesis at 12 months TRAEs and CTCAE grading
Vetrone 2024 (Bologna EANM24) ⁴	115	Single-arm, prospective cohort study 36 month follow up	Poor	Adults with NMSC lesions depth of ≤3mm who were unwilling or contraindicated for surgery. Sites treated: Scalp, forehead, nose, ears, cheeks, extremities (limbs), thorax, scrotum.	Mean surface area was 6.4cm ² (range, 1-60cm ²); mean thickness 1.3mm (range, 0.2-3mm)	Tumour relapses over follow-up (36 months) CTCAE graded safety Cosmesis at 24 months
Tietze 2023 ⁵	22	Single-arm, prospective pilot study 12 month follow up	Poor	Adults with BCC or SCC lesions who were contraindicated for surgery. Sites treated: Face, head without face, trunk, lower extremity.	Median size of 1.25cm ² (range, 0.04-16.8cm ²); median tumour thickness of 0.35mm (range, 0.1-2.1 mm)	Patient reported AEs Tumour response rate at 12 months Cosmesis at 12 months

² Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010 Sep;25(9):603-5. doi: 10.1007/s10654-010-9491-z. Epub 2010 Jul 22. PMID: 20652370.

³ Baxi, S., et al. (2024). "Effectiveness and Patient Experiences of Rhenium Skin Cancer Therapy for Nonmelanoma Skin Cancer: Interim Results from the EPIC-Skin Study." J Nucl Med 65(9): 1450-1455.

⁴ L. Vetrone, et al. (2024). Efficacy, Safety and Cosmetic in an Elderly Population after 188Rhenium Brachytherapy in NMSC: Long Term Follow Up Data. EANM24. Hamburg.

⁵ Tietze, J. K., et al. (2023). "Topical 188Re Ionizing Radiation Therapy Exerts High Efficacy in Curing Nonmelanoma Skin Cancer." Clin Nucl Med 48(10): 869-876.

References	N	Design Duration	Quality	Patient population	Surface area and thickness	Outcome(s)
Australian Registry	20	Retrospective registry	High	Adults with BCC or SCC lesions who were unwilling or unsuitable for surgery. All anatomic sites included.	NR	Tumour response Cosmesis Toxicity
Studies Included in previous ADAR.						
Castellucci 2021 ⁶	54	Single arm, prospective Follow-up: 33 months	Fair	BCC and/or SCC of the scalp, face, ears, fingers or another area where surgery or radiotherapy were difficult.	Surface area, mean (range) = 7.0 cm ² (1–36 cm ²), Thickness, mean (range) = 1.1 mm (0.2–2.5mm)	Response to therapy Early skin toxicity Cosmetic results
Cipriani 2020 ⁷	52	Single arm, retrospective Follow-up timelines not specified (median= 296 days)	Poor	BCC, SCC, Bowen's disease or extramammary Paget's disease. Head and neck lesions (~73%)	Treated area, mean (range) = 9.79 (0.3 – 60.5) cm ² 57% of the areas were 2-10cm ²	Response to therapy Complications

AE = adverse event; BCC = basal cell carcinoma; CTCAE = Common Terminology Criteria for Adverse Events; NR = not reported; SCC = squamous cell carcinoma; TRAE = Treatment-Related Adverse Events

The EPIC Skin Study³ is the key evidence for the ADAR submission, as it provided the largest population sample, and the lesion inclusion criteria directly matches that of the proposal for public funding. The lesions may be smaller than those seen in clinical practice, however, as the inclusion criteria was limited to patients with lesions $\leq 8\text{cm}^2$ in size.

The ADAR provided Australian registry data of patients that received either conventional radiation therapy or Re-188 brachytherapy; however, there was insufficient reporting of the patient population, or intervention modalities for the data to provide useful information on the comparative safety and efficacy of Re-188 brachytherapy.

Characteristics of the evidence for EBRT

The ADAR resubmission narrowed the inclusion/exclusion criteria to reduce the heterogeneity of the studies and to only include studies with lesions with the same target range treated by the proposed intervention. The ADAR included six studies on the safety and efficacy of EBRT in BCC and SCC (Table 8). The primary challenge in ensuring populations between Re-188 brachytherapy and EBRT studies were similar was the lack of detailed information on lesion area or depth in the EBRT studies. EBRT studies tended to use the tumour, node and metastasis (TNM) staging system, rather than thickness and depth.

The ADAR resubmission included studies that included patients with all T Stages, this may bias the comparison in favour of Re-188 brachytherapy as the T4 and some T3 tumours may be more difficult to treat than tumours that are $\leq 3\text{mm}$ deep. Caccialanza et al. 2009 and Grossi Marconi et al. 2016, should not be included in the comparative evidence as both include a much broader

⁶ Castellucci P et al. (2021) "High dose brachytherapy with non sealed (188)Re (rhenium) resin in patients with non- melanoma skin cancers (NMSCs): single center preliminary results." Eur J Nucl Med Mol Imaging 48 (5):1511-1521.

⁷ Cipriani C et al. (2020) "Personalized irradiation therapy for NMSC by rhenium-188 skin cancer therapy: a long-term retrospective study." Journal of Dermatological Treatment:1-7.

population base than the proposed population due to including severe stages of cancer. In addition, Tighe et al. 2021 should be interpreted with caution as it had a short follow up time (4 months) compared to other studies.

Table 8 Key features of the included evidence EBRT

References	N	Design Duration	Quality	Patient population	EBRT modality	Surface area and thickness	Outcome(s)
Caccialanza 2009 ⁸	620	Single-arm, retrospective case series mean follow-up 38 months	Poor	Adults affected by primary malignant epithelial skin neoplasms and treated with radiotherapy. Sites treated: Nose.	SXRT Fractions: 2/5 times p/w DPF: 5Gy, 2/5Gy Total dose: 30-75Gy, 60 + 20/25Gy	Included all T stages	Tumour cure rate. Cosmesis.
Ferro 2015 ⁹	31	Single-arm, prospective, Phase II study median follow-up 30 months	Fair	Adults aged ≥70 years, with NMSC <3cm, of T1 or T2 grade. Sites treated: Ear, scalp, nose, zygomatic-cheek region, temporal, frontal, chin, lumbar.	Electrons (6-9-12 MeV) or megavoltage photons (6 MV)	Inclusion: Non-melanoma skin cancer ≤ 3 cm	Acute toxicity. Tumour response.
Grossi Marconi 2016 ¹⁰	597	Single-arm, retrospective case series median follow up 44 months	Fair	Adults with NMSC. Sites treated: Face, scalp, eyelid, nose, canthus (internal/external), pinna, lips, other.	SXRT, various fractionation schedules	Included all T stages	Acute toxicity. Local control of tumour (sign to first disease progression).
Schulte 2005 ¹¹	1113	Single-arm, retrospective case series mean follow up 77 months	Poor	Adults with BCC and SCC Sites treated: Scalp, lips, ears, forehead and temple, nose, cheek and chin, periorbital region.	SXRT, various fractionation schedules	Included up to T3	Ulceration and hypopigmentation. Tumour recurrence.
Tighe 2021 ¹²	56	Single-arm, retrospective case series, Median follow-up 4 months	Poor	Adults with lower-leg NMSCs Sites treated: Lower legs	Electrons and SXRT, various fractionation schedules	Median lesion size 2 cm; 52% unknown T stage	Local recurrence of lesions. Radiation induced AEs.

⁸ Caccialanza, M., et al. (2009). "Radiotherapy of carcinomas of the skin overlying the cartilage of the nose: our experience in 671 lesions." *J Eur Acad Dermatol Venereol* 23(9): 1044-1049.

⁹ Ferro, M., et al. (2015). "Short-course radiotherapy in elderly patients with early stage non-melanoma skin cancer: a phase II study." *Cancer Invest* 33(2): 34-38.

¹⁰ Grossi Marconi, D., et al. (2016). "Head and Neck Non-Melanoma Skin Cancer Treated By Superficial X-Ray Therapy: An Analysis of 1021 Cases." *PLoS One* 11(7): e0156544.

¹¹ Schulte, K. W., et al. (2005). "Soft x-ray therapy for cutaneous basal cell and squamous cell carcinomas." *J Am Acad Dermatol* 53(6): 993-1001.

¹² Tighe, D., et al. (2021). "Lesion-based radiotherapy for non-melanoma skin cancer of the lower legs with a focus on radiation-induced ulcers." *Int J Radiat Ther* 8(2): 44-54.

References	N	Design Duration	Quality	Patient population	EBRT modality	Surface area and thickness	Outcome(s)
Patel, 2017 ¹³	369	Matched pair cohort study (EBT vs Mohs) mean follow-up of 3.4 years	Fair	Adults (80.7 years median), BCC/SCC 1-2cm on the head	Electronic brachytherapy, various fractionation schedules (30-50 Gy total in 4-5 Gy/fraction)	≤ 3 cm, up to stage T2	Tumour control Cosmesis Toxicity Patient satisfaction

* Included in previous ADAR.

AE = adverse event; BCC = basal cell carcinoma; NMSC = Non-melanoma skin cancer; NR = not reported; SCC = squamous cell carcinoma; SXRT = Superficial X-Ray Radiation Therapy

The issue persists that there is neither a direct nor an indirect comparison between Re-188 brachytherapy and EBRT.

11. Comparative safety

Safety data for Re-188 brachytherapy and EBRT in BCC and SCC are summarised in Table 9 and Table 10 respectively.

Table 9 Percentage of lesions with a Grade 1 to 3 adverse event after treatment with Re-188 brachytherapy.

Study ID	N (of lesions)	Time Point	Grade 1	Grade 2	Grade 3
EPIC-Skin ¹⁴	166	12 months	63%	31%	4%
Vetrone, et al. (2024) ¹⁵	168	90 days	48%	45%	7%
Tietze 2023 ¹⁶	40	14 days	33%	65%	0
Australian Registry	9	8 months (median)	33%	0	0
*Castellucci 2021 ¹⁷	60	Early toxicity	93%		7%
*Cipriani 2020 ¹⁸	52		NR	NR	NR

* Included in previous ADAR.

; NR= not reported Re-188 = Rhenium-188

All studies demonstrated a high level of Grade 1 and Grade 2 adverse events. Across the trials for both Re-188 brachytherapy and EBRT, it seemed that these adverse events were related to primarily mild skin reactions and Grade 3+ reactions were related to

¹³ Patel, R., et al. (2017). "Comparison of electronic brachytherapy and Mohs micrographic surgery for the treatment of early-stage non-melanoma skin cancer: a matched pair cohort study." *Journal of contemporary brachytherapy* 9(4): 338-344.

¹⁴ Baxi, S., et al. (2024). "Effectiveness and Patient Experiences of Rhenium Skin Cancer Therapy for Nonmelanoma Skin Cancer: Interim Results from the EPIC-Skin Study." *J Nucl Med* 65(9): 1450-1455.

¹⁵ L. Vetrone, et al. (2024). Efficacy, Safety and Cosmetic in an Elderly Population after 188Rhenium Brachytherapy in NMSC: Long Term Follow Up Data. EANM24. Hamburg.

¹⁶ Tietze, J. K., et al. (2023). "Topical 188Re Ionizing Radiation Therapy Exerts High Efficacy in Curing Nonmelanoma Skin Cancer." *Clin Nucl Med* 48(10): 869-876.

¹⁷ Castellucci P et al. (2021) "High dose brachytherapy with non sealed (188)Re (rhenium) resin in patients with non- melanoma skin cancers (NMSCs): single center preliminary results." *Eur J Nucl Med Mol Imaging* 48 (5):1511-1521.

¹⁸ Cipriani C et al. (2020) "Personalized irradiation therapy for NMSC by rhenium-188 skin cancer therapy: a long-term retrospective study." *Journal of Dermatological Treatment*:1-7.

more severe skin reactions such as dermatitis, ulceration, induration, and radiation skin injury.

Table 10 Percentage of lesions with a Grade 1 to 3 adverse event after treatment with EBRT

Study ID	N (of lesions)	Time Point	Grade 1	Grade 2	Grade 3
Ferro 2015 ⁹	31	Acute toxicity	61.3%	0	0
Australian Registry	11	18 months (median)	36.7%	9.1%	0

EBRT = external beam radiation therapy; Only two included studies had data on the grade of adverse events. There were no Grade 3+ adverse events in these studies, though Grade 1 adverse events were common.

Overall, Grade 3+ toxicities had a higher frequency in the Re-188 brachytherapy studies than EBRT studies. The commentary considered that there were considerable limitations to the evidence available: there was heterogeneity between the studies' results, varying sample sizes and especially small sample sizes for EBRT and there was a lack of uniformity in the follow-up across studies. Therefore, it is difficult to draw conclusions around the comparison of Re-188 brachytherapy to EBRT with regards to safety.

Late toxicities

The ADAR presented data on late toxicities across the included studies. The ADAR did not define late toxicities, but the toxicities used in the ADAR align with the Radiation Therapy Oncology Group ¹⁹ late side effects, which are those that manifest 6 months after treatment and commonly include atrophy, changes in pigmentation, hair loss, telangiectasia, fibrosis, and/or ulceration. The summary (Table 11) highlights the varying rates of late toxicities observed in different studies for both Re-188 brachytherapy and EBRT treatments. Ulceration, fibrosis and skin induration were more frequently seen in Re-188 brachytherapy studies than EBRT studies and hyper-pigmentation and telangiectasia were more frequently seen in EBRT studies than Re-188 brachytherapy studies.

¹⁹ Rubin, Philip, et al. "Overview of late effects normal tissues (LENT) scoring system." *Radiotherapy and Oncology* 35.1 (1995): 9-10.

Table 11 Summary of late toxicities (any grade) across Re-188 brachytherapy and comparator EBRT studies

Study ID, (n)	Timepoint	Ulceration	Fibrosis / Skin induration	Hypo-pigmentation	Hyper-pigmentation	Telangiectasia
Re-188 brachytherapy						
EPIC-Skin ³ , (129)	12 months	3.9%	13.9%	61.3%	4.7%	10.1%
EPIC-Skin, Australian, (33)	12 months	12.2%	18.2%	36.4%	3.0%	0
Tietze 2021 ⁵ , (40)	12 months	2.5%	NR	49%	NR	NR
Australian registry (9)	8 months (median)	0	0	33.3%	0	0
EBRT						
Ferro 2015 ⁹ , (31)	29 months	NR	3.2%	NR	12.9%	NR
Schulte 2005 ¹¹ , (1287)	77 months	0.9%	NR	72.7%	NR	23.4%
Tighe 2021 ¹² , (111)	9.6 months	NR	NR	NR	14%	NR
Patel 2017 ¹³ , (208)	38 months	1.9%	1.4%	59.36%	5.3%	31.4%
Australian registry (11)	18 months (median)	0	0	18.1%	0	0

EBRT = external beam radiation therapy; NR = not reported Re-188 = Rhenium-188

Similarly, the commentary considered that there were considerable limitations to the evidence available: there was heterogeneity between the studies' results, varying sample sizes though sample sizes for EBRT were better for long term follow up of toxicities, there was a lack of uniformity in the follow-up across studies and when the late toxicities were identified. Therefore, it is difficult to draw conclusions around the comparison of Re-188 brachytherapy to EBRT with regards to safety.

The commentary considered that the comparative safety evidence presented in the ADAR was inadequate to accurately assess the comparative safety of Re-188 brachytherapy and EBRT for BCC and SCC, noting that Grade 3+ adverse events occur more frequently with Re-188 brachytherapy than with EBRT.

12. Comparative effectiveness

The ADAR presented response, relapse, cosmetic and quality of life results from the included studies.

Response rates

The ADAR presented complete and partial response results for Re-188 brachytherapy at 12-months follow-up from the EPIC Skin study, and Tietze et al. 2023 (Table 12).

Table 12 Key clinical effectiveness (complete or partial response per lesion) results from the Re-188 brachytherapy studies at 12-months follow up.

Study ID	Complete Response	Partial Response
EPIC-Skin ³	174/185 (94.1%)	6/185 (3.2%)
*Castellucci 2021 ²⁰	41/41 (100%)	0
Tietze 2023 ⁵	38/40 (95%)	1/40 (2.5%)

* Included in previous ADAR.

Source: Table 21 of MSAC 1657 ADAR

PD = progressive disease; Re-188 = Rhenium-188; SD = stable disease.

The ADAR also included additional data on the Australian specific participants in the EPIC Skin study and relapse rates from the EPIC Skin study and Vetrone, et al. (2024). All the Australian cohort in the EPIC Skin study had complete response up to 12 months. Relapse occurred in 3% of lesions (over 12 months of follow up) in the EPIC Skin study and in 7% of lesions (over 36 months of follow up) in Vetrone, et al. (2024). Castellucci et al (2021) from the previous ADAR also presented complete response (23/24 (96%)) and relapse (1/24 (4%)) at 24 months of follow up.

The ADAR presented complete and partial response results for EBRT studies at varying follow up times as there was no uniformity in the follow up across studies (Table 12).

Table 13 Key clinical effectiveness (complete or partial response and relapse per lesion) results from the EBRT studies at varying follow up timepoints.

Study ID	Timepoint	Complete Response	Partial Response	PD/SD, or relapse
Ferro 2015 ⁹	3 months	30/31 (96.8%)	1/31 (3.2%)	NR
	24 months	NR	NR	6.8%
	36 months	NR	NR	11.7%
Patel 2017	3.3 years (mean)	NR	NR	1/208 (0.05%)
Schulte 2005	60 months	1174/1267 (92.6%)	47/1267 (3.7%)	65/1267 (6.2%)
Tighe 2021	4 months (median)	74/77 (96.1%)	NR	NR

* Included in previous ADAR.

Source: Table 21 of MSAC 1657 ADAR

EBRT = external beam radiation therapy; NR = Not reported; PD = progressive disease, SD = stable disease

Overall response rates were similar for both interventions and relapse tended to be low, only been demonstrated in the studies after 12 months of follow up. However, the commentary considered that the evidence presented in the ADAR was inadequate to accurately assess the comparative effective of Re-188 brachytherapy and EBRT for BCC and SCC. This was due to all the studies were single arm cohort studies, there was considerable heterogeneity between the different treatment studies, the quality of the studies were fair to poor, and evidence identified does not allow for statistical comparison.

²⁰ Castellucci P et al. (2021) "High dose brachytherapy with non sealed (188)Re (rhenium) resin in patients with non- melanoma skin cancers (NMSCs): single center preliminary results." Eur J Nucl Med Mol Imaging 48 (5):1511-1521.

Cosmesis

The ADAR presented tumour cosmesis ratings for various studies for Re-188 brachytherapy and EBRT: Ratings range from "Poor" to "Excellent," with percentages of each category provided for EPIC-Skin, Vetrone, et al. 2024, Tietze 2023, and the Australian registry. Most patients that received Re-188 brachytherapy rated as good to excellent response. This was also demonstrated for EBRT (Table 14).

Table 14 Summary of results of tumour cosmesis ratings across Re-188 brachytherapy and comparator EBRT studies

Study ID	Follow-up	Poor	Acceptable	Good	Excellent
Re-188 brachytherapy					
EPIC-Skin*	12 months	7/174 (4.0%)	18/174 (10.3%)	34/174 (19.5%)	74/174 (42.5%)
EPIC-Skin**	12 months	7/174 (4.0%)	20/174 (11.5%)	52/174 (29.9%)	56/174 (32.2%)
Bologna	24 months	3/124 (2.4%)	N/A	25/124 (20.2%)	96/124 (77.4%)
Tietze 2023	12 months	0	3/40 (7.7%)	20/40 (51.3%)	16/40 (41.0%)
Australian registry	8 months (median)	0	0	2/9 (22.2%)	7/9 (77.8%)
EBRT					
Ferro 2015	24 months	0	1/31 (3.2%)	14/31 (45.2%)	12/31 (37.8%)
Patel 2017*	3.3 years	5 (2.4%)	15 (7.2%)	48 (23.1%)	140 (67.3%)
Patel 2017**	(mean)	4 (1.9%)	1 (0.5%)	70 (33.7%)	133 (63.9%)
Australian registry	18 months (median)	0	0	3/11 (27.3%)	8/11 (72.7%)

EPIC-Skin study notes: The ITT set of 174 lesions used. * Patient rating, ** Clinician rating. 0-10 rating scale used in EPIC-Skin study converted to 0-3 Poor, 4-6 Acceptable, 7-8 Good, 9-10 Excellent.
EBRT = external beam radiation therapy; Re-188 = Rhenium-188;

MSAC considered that there was considerable heterogeneity between the studies' results, and there was no uniformity in the follow-up across studies. Therefore, it is difficult to draw conclusions around the comparison of Re-188 brachytherapy to EBRT.

Quality of Life and Treatment Comfort

The ADAR presented skin cancer index (SCI) data that was collected as part of the EPIC Skin study. The SCI is a validated disease-specific quality of life (QoL) instrument with 3 distinct subscales: Emotion, Social, and Appearance.²¹ Standardised scores range from 0 to 100, with higher scores reflecting higher QoL. The SCI is not a multi-attribute utility instrument (MAUIs) and the commentary could not identify any evidence where the Minimal Clinically Important Difference (MCID) for the SCI has been explicitly defined

²¹ Rhee JS, Matthews BA, Neuburg M, Logan BR, Burzynski M, Nattinger AB. The skin cancer index: clinical responsiveness and predictors of quality of life. *Laryngoscope*. 2007 Mar;117(3):399-405. doi: 10.1097/MLG.0b013e31802e2d88.

In the EPIC Skin study, all subscales and total scores increased from baseline to 6 months and from baseline to 12 months. The average total score improved by 8.21 points at 6 months and 9.23 points at 12 months. The emotion subscale showed an average improvement of 10.28 points at 6 months and 11.39 points at 12 months. The social subscale had an average improvement of 4.90 points at 6 months and 7.41 points at 12 months. The appearance subscale improved by an average of 9.44 points at 6 months and 8.89 points at 12 months.

This data was only available for Re-188 brachytherapy and no comparison with EBRT was made as there were no studies identified that measure QoL for EBRT.

The ADAR presents data on pain for the comparison of Re-188 brachytherapy with surgery. As this was not the PICO comparison, and no data was available for EBRT it was not applicable to the current application.

Clinical claim

The ADAR stated that the use of Re-188 brachytherapy results in noninferior safety and effectiveness compared with EBRT.

The safety results varied between studies. For the Re-188, Grade 1 adverse events results ranged from 33% to 63%, Grade 2 from 0 to 65% and Grade 3 from 0 to 7% across the different studies. For EBRT Grade 1 adverse events occurred at a range between 37% and 61% and Grade 2 events occurred from 0 to 9% across the different studies, there were no Grade 3 events reported.

The efficacy results also varied between studies. For the Re-188, complete response rates ranged from 94% to 100%, across the different studies. For EBRT complete response rates ranged from 93% to 97% across the different studies.

MSAC considered that there were considerable biases in the naive comparisons and the comparative effective evidence presented in the ADAR that does not allow for statistical comparison and cannot accurately support the clinical claim of noninferior safety and effectiveness. The heterogeneity between the study populations and how the patients were selected for inclusion means that there may be considerable selection bias, this would lead to populations being too dissimilar between the two interventions for comparison of the results (e.g. studies focusing on specific areas of the body). Using different study designs and variation in interventions by study location and health systems makes it difficult to determine whether observed effects are due to the intervention or other factors. In addition, as the studies don't include a control arm it is challenging to account for confounding variables that might influence the outcome

13. Economic evaluation

The ADAR presented a cost minimisation approach (CMA) based on a clinical claim of non-inferiority and that the MSAC guidelines recommend a cost-minimisation approach is appropriate where there is a therapeutic claim of noninferiority, the safety profile is equivalent or superior, and the proposed service is anticipated to result in equivalent or lesser costs to the health system. The commentary noted that a CMA approach might be suitable given the limited clinical evidence, differences in cost structures between the intervention and comparator, and the lack of existing economic evaluations.

The ADAR presented costings only and no model was developed for cost minimisation. The cost minimisation only compared the MBS-funded healthcare resources for EBRT against Re-188

brachytherapy. The ADAR did not include other costs, stating that all other costs are identical for both therapies. However, the commentary noted that this is unlikely to be true due to wastage, as batching would need to be 100% effective for the current cost minimisation to be accurate. This was considered as the wastage of paid product would lead to additional cost, but also treatment facilities need to have a defined waste management system or special waste containers to dispose of unused REC carpoules, protective foils with the rhenium-188 paste and any other radioactive waste, this is likely to add additional costs to the provider.

A summary of the ADAR's economic evaluation is detailed in Table 15.

Table 15 Summary of the economic evaluation

Component	Description
Perspective	Medicare Benefits Schedule Perspective
Population	Patients with confirmed Basal Cell Carcinoma or Squamous Cell Carcinoma that has a lesion size of 3.5cm ² and a maximum depth of 3.0 mm; on the nose, eyebrow, lip, ear, digit, genitalia, shin or collarbone or a contiguous area; and with comorbidities preventing surgery; or who have refused surgery
Comparator	External beam radiation therapy comprised of one simulation/dosimetry service and 22 fractions per course of treatment.
Type(s) of analysis	Cost-minimisation
Outcomes	Total treatment cost
Time horizon	Discrete time horizon
Software	Excel

Cost of Re-188 brachytherapy

The costs for Re-188 brachytherapy was solely based on the costs of the individual MBS items proposed by the ADAR. As Item XXXX2 was based on a per 0.05cm² dosing, the cost of the intervention was based on the average lesion size from the EPIC Skin Study (3.5cm²), which equates to the use of seven of Item XXXX2. The proposed cost of Re-188 brachytherapy is presented in Table 16.

Table 16 Proposed MBS items and fees for Re-188 brachytherapy

Proposed MBS Item	Proposed MBS Fee	Cost used in the calculations
XXXX3 Service Item	\$1,733.77	\$1,733.77
XXXX1 Planning Item	\$203.70	\$203.70
XXXX2 Treatment Item	\$393.90	\$2,757.30
Total Treatment		\$4,694.77

The proposed fee structure for Re-188 brachytherapy resulted in a total cost of \$4,694.77 for the average treated patient. This would leave enough of the carpoule to treat an additional **redacted**cm², or an approximate cost of **\$redacted** to the clinic or out-of-pocket to the patient, if the clinic passes on the costs. Alternatively, the clinic would have to see seven patients in a certain period to ensure batching can be carried out. The ADAR did not present adequate information to inform how batching can be achieved, i.e. the length of time a carpoule can be open before it is no longer useful, or if there are additional steps required for the equipment when batching is done, compared to when a new carpoule is used. Further details on how

batching has been achieved in the South African example would be beneficial and clinical feedback on whether this could be achieved in an Australian setting should be sought.

If batching cannot be achieved, the cost of treating an average patient with a 3.5cm² lesion would increase to approximately \$redacted (assuming a carpoule would cost redacted, though exact pricing has not been provided by the ADAR).

Cost of EBRT

The calculation of the costs of EBRT were based on the proportion of the different MBS items (15904, 15906, 15930, 15910, 15938, 15950 and 15952) used for simulation, dosimetry, and treatment of the different treatment modalities (electrons, IMRT and SXRT) and weighted for non-melanoma skin cancers (based on an email from redacted). redacted provided the proportion of the different modalities that are used for NMSC, i.e., of all the VMAT/IMRT treated patients, redacted% were NMSC; for electron – redacted% were NMSC, and for SXRT – redacted% were NMSC. These rates were applied to the current use of MBS items to get a weighted average of the treatment modalities for EBRT.

Table 17 Proportion of patients receiving the different treatment modalities in the costing analysis

Modality	Proportion of NMSC Patients (2023)	Proportion of NMSC Patients (2030)	Proportion of NMSC Patients (used in the cost minimisation)
Electrons	55%	46%	52%
IMRT	32%	48%	42%
SXRT	13%	6%	6%

Calculated during evaluation.

IMRT = Intensity-modulated radiation therapy; NMSC = non-melanoma skin cancer; SXRT = Superficial X-ray.

The ADAR calculated the weighted usage of the different MBS items, based on 2023 Medicare statistics and applied the above table to calculate the weighted numbers of MBS items for simulation/dosimetry across all modalities for NMSC. The ADAR used these numbers and the average number of EBRT fractions of 22 (as advised by the advisory board convened by the applicant) to calculate the usage of MBS treatment items for the different modalities and projects usage and costs out to 2030. From that, the ADAR calculated the average cost per treatment for each year and then the overall average weighted cost per patient for EBRT. The weighted average cost for EBRT was \$5,952.53.

This method to estimate the average cost of treatment likely overestimated the cost of EBRT. It was reliant on a two key factors, replacement rates and projected growth/market share of the different modalities for EBRT. There was no justification for these varying rates, just that the ADAR generated rates of replacement based on their own commercial experience.

The most expensive modality (IMRT/VMAT) was estimated to take up an increasing proportion of the market share from year one to year six, whereas the two cheaper modalities either had no change (SXRT) or were assumed to have a reducing market share (Electrons)(Table 17). This meant that the average cost per patient went from \$5,244.37 in 2025 to \$6,592.68 in 2030, leading to a weighted average cost for the comparator (used in the cost minimisation) of \$5,952.53 per patient. The commentary calculated the weighted cost for the comparison to be redacted based on the assumed breakdown of modalities used for NMSC and 2023 MBS usage data (tested in the sensitivity analysis). EBRT

Table 18 Costings of the comparator used in the sensitivity analysis of the economic model.

Modality	Cost
Electron	
Simulation	\$1,505
Cost of Fractions	\$2,008
Sub Total	\$3,513
IMRT	
Simulation	\$4,143
Cost of Fractions	\$6,125
Sub Total	\$10,268
SXRT	
Dosimetry	\$203
Fractions	\$1,207
Sub Total	\$1,410
Combined (weighted average based on 2023 MBS usage)	
55% Electron, 32% IMRT, 13%, SXRT	\$5,373

Calculated during evaluation.

IMRT = Intensity modulated radiation therapy; NMSC = non-melanoma skin cancer; SXRT = Superficial X-ray.

In Addition, consultation feedback received previously from the Faculty of Radiation Oncology at the Royal Australian & New Zealand College of Radiologists (RANZCR) is that the main comparator should be superficial radiation therapy (RT) using a kilovoltage machine. The costs to government of a 22 -fraction course of kilovoltage treatment is approximately \$1,410. And a minority of cases electron radiation therapy from a linear accelerator (LINAC) would be used. The costs to the government of a 22 -fraction course of treatment is approximately \$3,513. The results of the cost minimisation are presented in Table 19.

Table 19 Total cost of treatment for Re-188 brachytherapy and EBRT

Description	Value
Re-188 brachytherapy average cost per course of treatment	\$4,694.77
EBRT average cost per course of treatment	\$5,952.53
Average cost saved per course of treatment	\$1,257.76

EBRT = external beam radiation therapy; Re-188 = Rhenium-188

The results of the cost minimisation suggests that Re-188 brachytherapy would lead to a cost saving to the health budgets of over **redacted** per patient treated. Due to the uncertainty in the data presented by the ADAR, a sensitivity analysis was conducted during evaluation (Table 20).

Table 20 Sensitivity analysis of the economic evaluation conducted during the evaluation

Changes made	Average cost of Re-188 brachytherapy	Average cost of EBRT	Difference
Assuming a consistent weighted cost of EBRT	\$REDACTED	\$REDACTED	\$REDACTED
Adjustment based on RANZCR advice (80% SXRT and 20% Electron)	\$REDACTED	\$REDACTED	\$REDACTED
Fractions redacted per treatment* (based on highest from advisory board)	\$REDACTED	\$REDACTED	\$REDACTED
Fractions redacted per treatment*	\$REDACTED	\$REDACTED	\$REDACTED
Fractions redacted per treatment*	\$REDACTED	\$REDACTED	\$REDACTED
Half carpoule wasted*	\$REDACTED	\$REDACTED	\$REDACTED
Only one average patient per carpoule*	\$REDACTED	\$REDACTED	\$REDACTED

Source: Calculated during evaluation.

EBRT = external beam radiation therapy

* The simplistic calculations for EBRT done during evaluation (line 1 in the table) were used for the rest of the sensitivity analysis.

MSAC noted that due to the high level of uncertainty regarding the relationship between lesion size, fractionation for EBRT, batching for Re-188 brachytherapy and average patients per carpoule, the robustness of the economic model's results were undermined. The sensitivity analysis highlighted that Re-188 brachytherapy is likely to be more expensive than EBRT. MSAC commentary considered that more clinical evidence comparing on the relationship between these two technologies is needed to ensure an accurate comparison of their total costs. Specifically, there is a need to compare the EBRT technologies with Re-188, where the mix of EBRT in practice is directly compared with the true usage of Re-188 patients where wastage and batching is taken into consideration.

14. Financial/budgetary impacts

A market share approach was used to estimate the uptake of the proposed technology in the ADAR. The market share was based on utilisation of the currently listed items related to EBRT (SXRT, Electrons and IMRT) and aligned with the updated items as a result of the MBS²². The commentary considered this was appropriate.

Key assumptions

The following key cost assumptions/drivers were used for the budgetary impact analysis:

- The estimates of EBRT modality replacement were based on a clinician survey and an email from **redacted** with regards to their NMSC case mix.
- The ADAR generated rates of replacement based on their own commercial experience without justification
- The ADAR estimated that there would be an overall growth in the market over the forward estimates, based on the growth in usage of IMRT in the past 5 years.
- The ADAR assumed 22 fractions per patient on average for EBRT.

²² [Updates to the Medicare Benefits Schedule for radiation therapy items](#)

The ADAR used the full fee in the financial analysis, so did not account for the greatest permissible gap (GPG) or an 85% benefit fee when calculating the MBS costs. The commentary specified a new base case where the 85% benefit is used in the financial model.

Results

The financial implications to the MBS resulting from the proposed listing of Epidermal radioisotope therapy, using rhenium-188 paste are summarised in Table 21. It was estimated that the addition of MBS items for Re-188 brachytherapy would lead to a cost saving of just over **redacted** in the first year of listing, with an estimated cost saving of **redacted** over the first six years of listing.

Table 21 Net financial implications of Re-188 brachytherapy to the MBS

Parameter	Year 2025	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030
Estimated use and cost of the proposed health technology						
Number of people eligible for Re-188 brachytherapy	16,801	16,381	16,073	15,867	15,759	15,742
Number of people who receive Re-188 brachytherapy	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Number of services of Re-188 brachytherapy	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Cost to the MBS [85% benefit] (with appropriate copayments excluded)	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Change in use and cost of other health technologies						
Change in use of number of services of EBRT	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Net change in costs to the MBS (with appropriate copayments excluded)	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Net financial impact to the MBS	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED

Source: *Calculated during evaluation using the 85% benefit.*

EBRT = external beam radiation therapy; Re-188 = Rhenium-188

The average cost of the Re-188 brachytherapy per patient per course is: **redacted** (excluding co-pay), The out-of-pocket cost or cost to the hospital budgets has the potential to be substantial, but difficult to estimate. If no batching is achieved and the only patient has a small lesion this cost will likely be absorbed by State Health governments – if the treatment is carried out in a public hospital – or by patients – if it is carried out in a private setting. As mentioned above, the ADAR has not covered the batching of lesion treatments, the wastage of the Re-188 compound.

The commentary considered that there was substantial uncertainty in the financial estimates presented by the ADAR and tested these uncertainties. Table 22 presents the sensitivity analysis that would affect the MBS budgets and Table 23 presents sensitivity analysis on how the cost of wastage and reduced batching would affect other combined health budgets.

Table 22 Results of sensitivity analysis for net budget impact to MBS

Changes made	Year 2025	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030
Base case (22 fractions per treatment)	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Fractions redacted per treatment	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Fractions redacted per treatment	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Fractions redacted per treatment	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED

Source: Calculated during evaluation using the 85% benefit.

Table 23 Results of sensitivity analysis for net budget impact to all health budgets

Changes made	Year 2025	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030
Modified Base case	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
4 patients per carpoule	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
Only one average patient per carpoule	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED

Source: Calculated during evaluation using the 85% benefit.

The ADAR's base case provides estimated that Re-188 brachytherapy will save the MBS an estimated **redacted** over six years. However, the commentary considered this estimate was not robust. Sensitivity analysis demonstrated that with reasonable modification of the input data listing the MBS items demonstrated a financial budget impact (to combined MBS, State, and territory health budgets) that ranged from a 6 year cost saving of **redacted** (if **redacted** fractions of the comparator treatment was needed) to a cost of **redacted** (if only one carpoule per patient was used). This was based on varying the number of fractions used in the comparator treatment and the amount of wastage of Re-188.

15. Other relevant information

The previous PSD requested that any resubmission of the Re-188 brachytherapy application should present additional research into patient preferences for the treatment. The ADAR presented a brief narrative literature review of seven studies on patient reported outcomes regarding Keratinocyte cancers (KC) and NMSC therapies (Table 24). The commentary considered this was not relevant to the current ADAR as the wrong comparator was used.

Table 24 Publications used in the narrative literature presented in the ADAR

Study	N	Intervention	Condition	Year of Study	Study design
Alam, M., et al. (2011)	982	Mohs micrographic surgery	NMSC	2005	Prospective cohort
D'Hondt, V., et al. (2023)	217	Mohs Micrographic Surgery	facial NMSC	2020 - 2021	Prospective cohort
Dirr, M. A., et al. (2023)	259	Anaesthetic injection preceding each Mohs Micrographic Surgery stage	Facial surgery	NR	Prospective cohort
Krönert, M., et al. (2024)	19	Re-188 brachytherapy (16 with surgery before or after Re-188 brachytherapy)	NMSC	2020 - 2023	Prospective cohort
Lee, E. B., et al. (2021)	226	Mohs Micrographic Surgery	NMSC	NR	Prospective cohort
Nierich, J., et al. (2024)	122	facial reconstruction	after Mohs micrographic surgery for NMSC	Surgery 2006 - 2011 - questionnaire at 10 year follow up	Prospective cohort
Tietze, J. K., et al. (2023)	22	Re-188 brachytherapy	NMSC	2020 -2021 - 12 month follow up	Prospective cohort

Source: compiled during evaluation. NMSC = non-melanoma skin cancer; Re-188 brachytherapy = Rhenium Skin Cancer Therapy.

In summary, patients thought that though Mohs surgery was highly successful, it is often lengthy, painful, and can lead to disfigurement, particularly in sensitive areas like the ears or nose.^{23, 24} Patients may delay surgery due to fear of pain and complications, resulting in prolonged periods of reduced quality of life.^{25, 26} Conversely, Re-188 brachytherapy is perceived as less painful with better aesthetic outcomes. In a survey of patients who underwent both treatments, Re-188 brachytherapy was preferred for its lower pain levels and fewer complications. While both procedures received high aesthetic ratings from patients, dermatologists favored the outcomes of Re-188 brachytherapy. When considering future treatments, a significant portion of patients preferred Re-188 (44%) brachytherapy over surgery (19%).²⁷

In addition, a national NMSC survey by Omnipoll (conducted between November 17-22, 2022), was presented. It is unclear if this study was commissioned by the applicant. The survey included over 1,200 respondents aged 18 and above, revealed that nearly 90% of respondents considered a quick and easy procedure to be very important or extremely important. This indicates that patients are not in favor of a lengthy course of conventional radiation therapy. Additionally, most respondents rated a painless, nonsurgical procedure, good aesthetic results, successful tumor removal, and fast recovery as very or

²³ Lee, E. B., et al. (2021). "Patient Outcomes and Satisfaction After Mohs Micrographic Surgery in Patients with Nonmelanoma Skin Cancer." *Dermatologic Surgery* 47(9).

²⁴ Nierich, J., et al. (2024). "Long-Term Patient-Reported Outcomes following Oncological Facial Reconstructive Surgery using the FACE-Q Skin Cancer Module." 39: 262-270.

²⁵ Alam, M., et al. (2011). "Delayed treatment and continued growth of nonmelanoma skin cancer." 64(5): 839-848.

²⁶ Dirr, M. A., et al. (2023). "Pain of local anesthetic injection of lidocaine during subsequent stages of Mohs micrographic surgery: A multicenter prospective cohort study." 89(1): 114-118.

²⁷ Krönert, M.I.C.; Schwarzenböck, S.M.; Kurth, J.; Heuschkel, M.; Krause, B.J.; Emmert, S.; Tietze, J.K. Patient-Orientated Evaluation of Treatment of Non-Melanoma Skin Cancer with Rhenium-188 Compared to Surgery. *Healthcare* 2024, 12, 921. <https://doi.org/10.3390/healthcare12090921>

extremely important. The ADAR stated that these findings suggest broad support for Re-188 brachytherapy treatment if it were indicated.

Rhenium-SCT patient advisory board

In 2024, a consumer advisory board was formed with patient advocates from the Melanoma and Skin Cancer Advocacy Network (MSCAN) to investigate patient preferences for Re-188 brachytherapy. Six participants with skin cancer experience shared their treatment journeys and discussed the importance of broad access to Re-188 brachytherapy, touching on their experiences with skin cancer diagnosis and treatments, desired attributes in new treatments, current burdens with skin cancer treatment, and the impact of having access to Re-188 brachytherapy.

Participants generally described Re-188 brachytherapy as painless and preferable to other treatments like surgery, radiation, or chemotherapy, due to better aesthetic outcomes and fewer painful procedures and clinic visits. They supported reimbursement for Re-188 brachytherapy to ensure equitable access, expressing concerns about costs without reimbursement, especially for multiple lesions. They also favoured shorter treatment durations to manage personal and professional commitments and reduce associated costs.

A follow-up questionnaire completed by additional patients revealed a range of experiences with treatments including excision, surgery, cryotherapy, Re-188 brachytherapy, topical creams, and immunotherapy. Participants highlighted the advantages of Re-188 brachytherapy over other methods in terms of pain, aesthetics, and convenience.

Most participants highlighted efficacy, wait time, downtime, and cosmesis as crucial factors when choosing treatments for KC/NMSC. Cost, pain, and non-invasive options were also important. Those with experience in conventional radiation therapy appreciated its effectiveness but cited negatives like long treatment times, side effects, fatigue, discomfort, radiation burns, ongoing complications, and income loss due to the procedure's length and recovery time.

Conversely, participants with experience in Re-188 brachytherapy had positive views, praising its quick, nonsurgical nature, minimal downtime, favourable toxicity profile, and better functional and cosmetic outcomes. They also noted reduced risks of secondary infections and extended hospital stays compared to surgical procedures.

Given a choice, most participants would have preferred Re-188 brachytherapy for past NMSC lesions. However, they expressed concerns about cost and availability, especially for rural and remote patients. If listed on the MBS, most indicated a strong preference for Re-188 brachytherapy over conventional radiation therapy, if suitable for their lesion.

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Clinical issues:

- ESC considered that the evidence presented does not support the claim of non-inferior safety and clinical effectiveness of Rhenium Skin Cancer Therapy (Re-188 brachytherapy) compared with EBRT. Heterogeneity in the demographics, tumour staging and lack of standard comparator treatment made statistical comparison difficult and the clinical claim uncertain.
- The proposed MBS item for the agent appears appropriate to address the issue of carpoules sharing to maximise use across patients with smaller lesions. However, greater clarification is required regarding how the fees were derived for the proposed planning and delivery items. In addition, it is unclear whether the proposed planning item includes a mark-up of the tumour(s) prior to Re-188 brachytherapy by the referring doctor.
- The Faculty of Radiation Oncology of the Royal Australian & NZ College of Radiologists (RANZCR) advised that the majority of BCC/SCC lesions suitable for Re-188 are appropriate for treatment with superficial radiation therapy (SXRT) using a kilovoltage machine. Hence ESC considered that kilovoltage EBRT, rather than megavoltage EBRT as presented in the ADAR, should be the main comparator.
- The eligible population has been expanded by the applicant to include patients with “safety concerns,” and clarification is required to better define this term, to ensure Re-188 brachytherapy is targeted to those with the highest clinical need for the service, and to reduce use outside the proposed MBS indication.
- ESC noted that the additional benefits of Re-188 brachytherapy related to receiving treatment at a single visit versus multiple visits over a period of weeks were not considered and may potentially underestimate the QoL associated with the intervention.
- ESC noted that it was unclear which centres would be able to provide RSCT. ESC also considered that given Rhenium 188 has a short half-life of 17 hours, this is likely to limit the geographic location of centres to those with sufficient proximity to the source of the Re-188 product and would likely have access implications for patients living in regional or remote areas.

Economic issues:

- ESC advised the lack of evidence to support the clinical claim made the cost-minimisation approach inappropriate.
- ESC considered the cost-saving estimates uncertain due to the lack of evidence underpinning the assumptions of clinical equivalence and uncertainty regarding the modality of the comparator EBRT. ESC considered that Re-188 may be more costly under different assumptions, in terms of the proportion of patients using each modality, the number of EBRT fractions, and Re-188 batching. ESC noted the cost per fraction for kilovoltage EBRT is significantly less than for the megavoltage EBRT comparator used in the economic evaluation. On that basis ESC noted that the cost-effectiveness claims of Re-188 brachytherapy over EBRT have likely been overestimated.

Financial issues:

- The ADAR lacks justification for uptake rate estimates, potentially underestimating the adoption of Re-188 brachytherapy. Additional factors such as travel costs, patient preference for Re-188 brachytherapy, and perceived productivity benefits may increase uptake.

- The costs applied in the calculations may underestimate the cost to all health budgets, as batching would need to be 100% efficient to achieve the proposed costs in clinical practice. The excluded costs are also unclear.
- The management of batching and wastage issues would likely be handled by the private clinics (so that health budgets are not affected). However, ESC considered there was a risk of costs being passed to patients. It is unclear how batching and wastage would be addressed in public hospitals.

ESC discussion

ESC noted that this was a resubmission from Oncobeta Therapeutics requesting public funding for Re-188 brachytherapy as an alternative to radiation therapy (RT) for treatment of patients with non-melanoma skin cancer (NMSC) that is not suitable for surgery or when the patient is not suitable for surgery.

ESC noted that MSAC considered this application at its July 2023 meeting. MSAC did not support public funding at the time, advising that a resubmission should address several issues pertaining to the evidence base, EBRT modality for comparator and costs, eligible population, patient preference, wastage, proposed MBS items (descriptors and fees) and radiation safety (including disposal).

ESC noted the consultation feedback stated that patients prefer Re-188 brachytherapy over other treatments as Re-188 brachytherapy may be more convenient (single visit versus multiple visits for EBRT). Feedback from Private Healthcare Australia was also supportive, stating that the proposed treatment is appropriate for difficult lesion locations or lesions that are difficult to treat surgically or with conventional radiotherapy. However, feedback noted the limited evidence and high out-of-pocket costs for Re-188 brachytherapy. Feedback from the Royal Australian and New Zealand College of Radiologists (RANZCR) was not supportive. It stated that the dosage can exceed safe levels, and that the cost of this treatment is high for superficial NMSC, and high compared to other treatments overall. RANZCR also stated that Re-188 brachytherapy can only be provided in nuclear medicine facilities, so may not be easily available in rural and remote areas, and there is insufficient evidence for safety and effectiveness.

ESC noted that the resubmission expanded the population to patients unsuitable for surgery due to clinician concerns for patient safety, not just lesion location that was confirmed as the main population criteria by PASC in December 2021. ESC considered that whilst this expanded population may be clinically appropriate it was difficult to define and estimate the population, which raised concerns regarding the potential for use of the technology outside the intended population. Regarding the proposed population, ESC queried whether patients with multiple lesions who would normally receive field therapy would be suitable for Re-188 brachytherapy and suggested that advice on this be sought from RANZCR.

ESC noted that the proposed clinical management algorithm suggests Re-188 brachytherapy as an alternative therapy to external beam RT (EBRT), not as an additional line of therapy.

ESC noted that 3 new MBS items have been proposed for this service. The first item relates to planning and is based on existing [MBS item 15950](#) (proposed with the same fee of \$203.70) for single complexity single-field radiation therapy. This item includes set-up, tumour demarcation, transcription and measurement of the treatment surface area, and dosimetry planning. ESC questioned whether a visit to a referring practitioner is also required for mark-up of the lesion and, if so, this should be included in the economic evaluation. In addition, ESC queried whether this first item would only be used once per use of the second and third items.

The second MBS item is for the agent and is adjusted to enable multiple lesions per treatment session. The fee (\$393.90) is based upon the use of an aliquot of the carpool of Re-188

resin/paste for each 0.5cm² treatment area. The total cost of the carpoule (approximately **redacted**), which can treat a total surface area of **redacted** cm² would be distributed across multiple patients according to the surface area of their lesions. ESC noted that, due to the 17-hour half-life for Re-188, timely batching of patients is required to address wastage. The pre-ESC response from the applicant noted that at private Australian clinics currently treating patients with Re-188 brachytherapy, there is an average of 65% carpoule utilisation, with an average of 4 patients treated per session

The third MBS item is for delivery, estimated to last 80 minutes. The fee (\$1,733.77 in the ADAR, although this was proposed to be reduced to \$592.92 in the pre-ESC response but the impact of this change in the proposed fee has not been evaluated) is based on 4 times the fee for [MBS item 15982](#) for brachytherapy (estimated to last 20 minutes) and includes the services of radiation therapists, medical physicists and a radiation oncologist (who are required to administer Re-188 brachytherapy), plus nurse time and single-use consumables (including for disposal). ESC considered the basis for the proposed fee to be unclear.

ESC noted that, while the applicant-developed assessment report (ADAR) provided additional information on batching and minimising wastage, considerable uncertainty remained, including who will fund wastage or disposal and the average use per carpoule. ESC noted that batching relies on facilities booking an adequate number of patients. ESC also considered that batching may impact on wait times for therapy, and there was a risk of patients not attending their appointment (due to frailty, forgetting to attend or being unable to make it), which would result in wastage despite the best efforts of the treating clinic. ESC considered that costs from batching or wastage issues will be incurred by the providers.

ESC noted that no studies have been published directly comparing Re-188 brachytherapy and EBRT, and the application does not include either a direct or indirect comparison of the modalities. ESC noted that the resubmission includes a new single-arm study for Re-188 brachytherapy (EPIC study) that includes 24 months of follow-up from 7 international sites, including 4 in Australia, and data from a 12-month interim analysis of response rates, patient-reported outcomes, and patient and clinician assessments of cosmetic outcome.

ESC noted the clinical claim of non-inferior safety and effectiveness compared with conventional EBRT. However, ESC noted that the main comparator modality of EBRT used in the ADAR was megavoltage, based on the applicant's clinical advisory board advice. However, ESC considered that this was not consistent with advice from RANZCR which stated that the main comparative modality in Australian practice was superficial radiation therapy (SXRT) using a kilovoltage machine. ESC also noted that kilovoltage EBRT is significantly less expensive than megavoltage EBRT. ESC advised that the comparator modality and number of required fractions are fundamental points of uncertainty. ESC noted the studies in the evidence base used an inconsistent approach to RT, and the expert opinion provided in the ADAR to clarify the current approach to RT (including type and cycles) in the modelling is inconsistent with advice from RANZCR. On this, ESC noted that there are differing opinions within the clinical community on the most appropriate comparator. The pre-ESC response suggested that estimates could be potentially improved by incorporating data from Services Australia following HW061 registration of kilovoltage treatment machines alongside new Medicare billing codes (which were being sought). ESC noted that EBRT usage data supplied by the applicant from **redacted** could not be verified. ESC considered that additional information from RANZCR and formal consultation feedback from **redacted** with additional details regarding the modalities, fractions of EBRT, treatment intent (curative vs. palliative), completion rates and geographic distribution could be useful to inform decision making and address the uncertainty around the EBRT usage assumptions.

ESC noted that comparative safety was based on a comparison of the proportion of lesions with a Grade 1–3 adverse event following treatment with either Re-188 brachytherapy or EBRT. However, ESC noted that Grade 3+ toxicities occurred in a higher proportion of patients in the Re-188 brachytherapy studies compared to the EBRT studies, ESC noted that there were other important limitations of the comparative assessment. There was heterogeneity between the studies' results, varying sample sizes across all studies, and very small sample sizes for the EBRT studies. There was also lack of uniformity in the timepoint at which study participants were assessed for adverse events following treatment. ESC considered that these limitations made it difficult to draw conclusions with regards to comparative safety.

Regarding tumour response, ESC noted that overall response rates were similar for Re-188 brachytherapy and EBRT, and rates of relapse were low. However, ESC considered that the evidence presented in the ADAR was inadequate to accurately assess the comparative effectiveness, due to all studies being single arm cohort studies, of fair to poor quality, with considerable heterogeneity between the different treatment studies. Due to these factors a formal statistical comparison could not be conducted.

ESC noted that the evidence for cosmesis (which is an important patient consideration) was limited by considerable heterogeneity in the outcome measures between studies, and lack of uniformity in the follow-up periods across studies. This made it difficult to draw conclusions around the comparison of Re-188 brachytherapy to EBRT for this outcome.

ESC noted that patient-reported outcomes were considered in terms of patient preference and quality of life. For patient preference, ESC noted that this was informed by a survey of a small patient advisory board comprising 6 patients (3 had previous Re-188 brachytherapy exposure). Participants were broadly supportive of reimbursement of Re-188 brachytherapy for equitable access. Participants generally preferred a short duration of treatment to better manage work and family commitments, and to mitigate the compounding costs associated with treatment, travel and time off work.

ESC noted that QoL was reported using the Skin Cancer Index, which is a validated disease-specific QoL instrument with 3 distinct subscales: emotion, social, and appearance. At 12 months, patients in the EPIC study reported continuing improvements over baseline and 6-month QoL scores. Parallel outcomes could not be found in EBRT studies. ESC considered that the conclusion of non-inferiority with regards to QoL was likely conservative given the single-visit nature of Re-188 brachytherapy.

ESC considered that there is still uncertainty around the cost of the comparator, the size of the proposed population and uptake rates, which MSAC had identified during its previous consideration of this application. ESC considered that the proportion of patients receiving different EBRT modalities is uncertain, and that the varying estimates of EBRT modality use impact the weighted average cost. Additionally, the data provided by **redacted** did not account for how BCC/SCC cancer cases compare to the general population receiving EBRT.

Regarding the ADAR's reliance on data from **redacted** (and anecdotal/informal evidence), ESC noted that the pre-ESC response stated that the applicant was unable to obtain requested information from Services Australia regarding radiotherapy usage patterns, stating that Services Australia 'cannot provide information relating to diagnostics or ICD-10 codes for MBS item numbers'.

ESC noted that the economic evaluation was a cost-minimisation approach (CMA) based on the assumption of equivalence between Re-188 brachytherapy and EBRT. ESC noted that no model was developed for the economic evaluation – only a direct comparison of MBS costs was presented. ESC noted that the MSAC Guidelines recommended a health care system perspective,

which includes health and health-related resource use (costs and cost offsets), and health-related outcomes. ESC considered that assuming identical costs for some therapies risks underestimating differences, masking true resource use, leading to misleading conclusions in the analysis. Additionally, ESC considered that the potential for wastage was not considered and may underestimate total costs.

ESC noted the cost-minimisation approach estimated the average cost of Re-188 brachytherapy is \$4,694.77/patient, the average cost of EBRT is \$5,952.33/patient, and the average cost saving per course of treatment is \$1,257.76. ESC noted that the ADAR claimed no other costs or cost offsets, but ESC considered that a more transparent breakdown of all cost components may be necessary, including the costs of managing adverse events (especially Grade 3 and 4 events). ESC noted that if batching is not achieved and inefficiencies arise due to uncertainties around carpoule usage, additional costs, and feasibility in the Australian setting, the cost of Re-188 brachytherapy could increase to **\$redacted** per patient. Sensitivity analyses from the commentary showed that changes in the number of fractions used per treatment and the carpoule usage each impacted the cost difference between Re-188 brachytherapy and EBRT. ESC noted that the sensitivity analyses indicated that Re-188 brachytherapy is cost-saving for EBRT fractions greater than 10 within the assessed range (9–30), although greater transparency is needed for the calculations. ESC considered that a sensitivity analysis using the number of fractions per treatment from the **redacted** data (18), and a sensitivity analysis on the percentage utilisation of the carpoule would be useful for MSAC decision-making.

ESC considered that the conclusion that Re-188 (RSTC) was cost-saving compared to EBRT was uncertain due to lack of evidence underpinning the assumptions of clinical equivalence and the costing of megavoltage rather than kilovoltage EBRT. ESC considered that Re-188 may also be more costly under different assumptions regarding the proportion of patients using each EBRT modality, the number of EBRT fractions required, and Re-188 batching.

A market-share approach was used to estimate the financial impact, which ESC considered to be appropriate. ESC noted the following key assumptions and drivers of rates and growth:

- EBRT replacement estimates were based on a clinical survey and a **redacted** email on NMSC case mix.
- The rate of replacement of EBRT was based on applicant assumption without justification. The ADAR projected market growth based on usage trends for intensity-modulated radiation therapy over the past 5 years.
- The ADAR assumed an average of 22 EBRT fractions per patient. ESC noted that the range of fractions per patients from the advisory board of skin specialist radiation oncologists was 9–30.

ESC noted that the assumptions for the uptake rate estimates were not justified and considered that they may underestimate the uptake of Re-188 brachytherapy. ESC advised that further details regarding how the uptake rates were calculated based on **redacted** data and expert input from skin specialist radiation oncologists may be useful for MSAC decision-making.

ESC noted that the cost to the MBS (85% benefit) for Re-188 brachytherapy is estimated at **redacted** in year 1 to **redacted** in year 6. The net financial impact to the MBS is estimated to be a cost saving of **redacted** in year 1, increasing to a saving of **redacted** in year 6. In addition to calculating EBRT costs on a megavoltage basis rather than a kilovoltage basis, ESC noted that the estimated cost savings are influenced by the number of fractions per treatment and batching; decreasing both the number of fractions per treatment and the number of patients per carpoule reduces the cost savings to the point where Re-188 brachytherapy becomes more costly than EBRT.

ESC considered that the value of a single visit for Re-188 brachytherapy vs multiple visits for EBRT, including the impact of a single visit on QoL, was potentially underestimated. ESC noted that patients in the survey preferred the single visit aspect of Re-188 brachytherapy. ESC also considered that Re-188 brachytherapy provided a significant benefit for rural patients, as some rural patients may decline treatment if multiple trips are required for treatment (as is the case of EBRT), with the travel impacting and causing significant costs to patients and their families. ESC therefore considered that there are potential cost savings for state-funded patient travel budgets, but these have not been included in the costings. ESC considered that additional comparative evidence on both the usage patterns and total costs for both Re-188 brachytherapy and EBRT may be useful for decision making.

ESC noted that the half-life of Rhenium 188 was approximately 17 hours. This suggested that the production of Rhenium 188 and its transport would need to be close to the radiopharmaceutical production centres. This may restrict the geographic availability of Rhenium 188. ESC considered that the short half-life, the need to batch patients and the structure of the MBS items could also create an incentive for service providers to provide Rhenium 188 to a larger number of patients with smaller lesions.

ESC acknowledged the difficulty in identifying relevant studies but considered that issues previously identified by MSAC regarding the lack of good quality comparative evidence remained unresolved. ESC considered the evidence presented in the current ADAR is insufficient to support the clinical claim and more clinical evidence comparing the relationship between Re-188 brachytherapy and EBRT is needed to accurately compare their total costs. Additionally, confirmation of the EBRT modalities and the likely proportion of patients receiving each EBRT modality should be compared with the true usage of Re-188, taking into consideration wastage and batching.

17. Applicant comments on MSAC's Public Summary Document

The applicant appreciates MSAC's acknowledgment of the clinical benefits associated with Rhenium-188 brachytherapy (Re-188) for the treatment of non-melanoma skin cancer (NMSC) in indicated patients. Furthermore, MSAC's recognition of non-inferior effectiveness for certain patient populations and lesions is underscored by the support for public funding by key referring and treating clinical colleges. MSAC has explicitly highlighted patient preference benefits, noting the convenience and improved quality of life associated with the single-session treatment approach of Re-188. The applicant welcomes continued collaboration with the Department to resolve any questions pertaining to batching, referral pathways, and rural patient access, highlighting successful implementation across Europe and Africa. Given MSAC's acceptance of the planning component of the proposed MBS item structure, the applicant is committed to addressing outstanding economic modelling questions to resolve remaining queries around the additional items. The applicant is grateful to MSAC, clinical stakeholders, patient advocacy groups, and the Department for their ongoing engagement, guidance, and support throughout this application process. We remain fully committed to working collaboratively to facilitate timely, publicly funded access to Re-188 brachytherapy for Australian patients.

18. Further information on MSAC

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