Medical Services Advisory Committee (MSAC) Public Summary Document

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

Applicant: **Oncobeta Therapeutics Pty Ltd**

Date of MSAC consideration: **1 April 2026**

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) brachytherapy for basal cell carcinoma (BCC) or cutaneous squamous cell carcinoma (SCC) was received from Oncobeta Therapeutics Pty Ltd by the Department of Health, Disability and Ageing.

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 supported the creation of new Medicare Benefit Schedule (MBS) items for the use of Re-188 brachytherapy for treatment of non-melanoma skin cancer (NMSC).

MSAC considered Re-188 brachytherapy had comparable safety and clinical effectiveness outcomes to external beam radiation therapy (EBRT) based on 2-year follow-up data from the key single-arm study[1]. MSAC considered that Re-188 brachytherapy had a clinical role for a defined population of patients with lesions unsuitable for surgery and who would otherwise be suitable candidates for EBRT. MSAC considered Re-188 brachytherapy is an important treatment option for patients in rural and remote areas as it can be administered in a single session, unlike EBRT which requires multiple treatment sessions. Re-188 brachytherapy uses an unsealed radioactive source which may restrict the locations and providers able to offer the service, depending on state and territory based regulatory requirements.

MSAC considered that dermatologists, plastic surgeons and general practitioners (GPs) are appropriate referring practitioners for patients being considered for Re-188 brachytherapy. MSAC considered it appropriate to enable GPs with expertise in skin cancer to refer patients, as many GPs have the clinical expertise to assess and refer patients with NMSCs. MSAC considered that limiting referral to dermatologists or plastic surgeons may inappropriately restrict access in rural and remote areas where availability of these specialists may be limited. MSAC considered the financial impact of Re-188 brachytherapy to the MBS was likely to be cost-saving compared to EBRT across a range of real-world scenarios, however, noted uncertainty around the rate of Re-

[1] Rhenium-Skin Cancer Therapy (SCT) for the Treatment of Non-Melanoma Skin Cancer. (EPIC-Skin) https://clinicaltrials.gov/study/NCT05135052

188 brachytherapy substitution of EBRT, and the risk that the availability of publicly funded Re-188 brachytherapy could increase demand for treatment.

MSAC considered that the department should review the service utilisation and patient out-of-pocket costs 2 years after MBS-listing. MSAC considered that there may be circumstances where involvement of a multidisciplinary team (MDT) may be required for treatment planning and recommended that MBS item's explanatory note specify MDT involvement where appropriate. MSAC considered that the planning item should be 'applicable once per treatment session' and the treatment items should be 'applicable once per lesion per lifetime'. MSAC considered that Re-188 brachytherapy should exclude patients with previously treated NMSCs and the previous treatment types should be clearly specified in the item descriptors.

Consumer summary

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

Non-melanoma skin cancer is the most common form of cancer in Australia. Currently, non-melanoma skin cancers are usually treated with surgery. If a patient cannot have surgery, then the skin cancer is usually treated with a type of radiation therapy called external beam radiotherapy (EBRT). With EBRT, a machine directs radiation beams at the cancer to destroy the cancer cells. Patients need to visit a treatment centre several times over a few days to weeks for the beam radiotherapy.

Re-188 brachytherapy is another form of radiation therapy used to treat non-melanoma skin cancer. It uses a paste containing a radioactive substance called Re-188. With Re 188 brachytherapy, the skin cancer is covered with a sterile protective foil. The Re-188 paste is put onto the foil using a special applicator and left on the affected skin for a pre-set amount of time. The paste lets out radiation that destroys the cancer cells. When the time is up, the foil is pulled off the skin. Patients do not need to have any injections or creams to make the skin numb, and the treatment can be done in a single outpatient visit. Re-188 brachytherapy can treat smaller, shallow skin cancers that are less than 3 mm deep and are less than 8cm^2 in size. Studies showed that most skin cancers treated with Re-188 brachytherapy were treated successfully.

MSAC had previously considered this application at its July 2023 meeting. MSAC did not recommend MBS listing of Re-188 brachytherapy then, because there was not a strong, clear case that the Re-188 brachytherapy was safe and effective in comparison to treatments already on the MBS. There were also questions about the claimed cost savings. MSAC considered a reapplication at its April 2025 meeting but deferred its decision, asking for the target population and comparator to be more clearly defined, and for more certainty in the evidence and costing assumptions that informed the proposed MBS item fee.

In this resubmission, the eligible population had been clarified as patients with non-melanoma skin cancer who have lesions:

- located in hard-to-treat areas (such as nose, eyebrow, lip, ear, finger, genitals, shin or collarbone), and
- who are not suitable for surgery, and
- would otherwise be suitable for EBRT.

The resubmission also included extra data from a study that did not have a control group but suggested that Re-188 brachytherapy was safe and effective over at least 2 years. More information about costs was provided. MSAC considered Re-188 was likely to be cost-saving to the MBS compared with EBRT, for this defined group of patients. However, MSAC noted

Consumer summary
uncertainty about this, because adding Re-188 brachytherapy to the MBS could lead to it being chosen as a substitute for EBRT more often, or more broadly, than expected. MSAC also noted that Re-188 brachytherapy uses an unsealed radioactive source. Therefore, treatment would only be provided by licensed experts in approved facilities that can manage radiation safety requirements, including radioactive waste disposal. This may limit where the service can be made available. MSAC also noted that treatment decisions should be made with input from the relevant specialists and involvement of a multidisciplinary team where appropriate. MSAC also recommended safeguards, including a review of service utilisation and any patient out-of-pocket costs approximately 2 years after the service is funded on the MBS, along with clear eligibility criteria to ensure the service is used by the intended patient group. **MSAC's advice to the Commonwealth Minister for Health, Disability and Ageing** MSAC supported MBS listing of Re-188 brachytherapy for selected patients with non-melanoma skin cancer who are not suitable for surgery and would otherwise be treated with EBRT. MSAC considered that dermatologists, plastic surgeons, and suitably skilled GPs can refer patients for Re-188 brachytherapy. Allowing experienced GPs to refer patients supports access to care, especially in rural and remote areas where specialist services may be limited.

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

MSAC noted that this was a resubmission from Oncobeta Therapeutics Pty Ltd requesting Medicare Benefits Schedule (MBS) listing of Re-188 brachytherapy as an alternative to external beam radiation therapy (EBRT) for the treatment of patients with non-melanoma skin cancer (NMSC) who are not suitable for surgery. MSAC had previously considered this application at its July 2023 and April 2025 meetings.

MSAC did not support MBS listing at its July 2023 meeting because it considered the comparative safety and effectiveness of Re-188 brachytherapy versus EBRT to be uncertain due to limitations in the evidence base, and the economic case (including claimed cost savings) to be highly uncertain due to lack of clarity and variability in the appropriate EBRT comparator modalities and associated costs. At its April 2025 meeting, MSAC deferred advice on public funding for Re-188 brachytherapy, noting the absence of consensus on the standard of care comparator and the limited comparative safety and effectiveness data available to support the economic model. MSAC considered that, despite the low-certainty evidence, Re-188 brachytherapy was likely to have a clinical role for a defined subset of patients. MSAC advised that a resubmission should address key outstanding issues, including:

- clearer definition of the target patient population, detailing those most likely to benefit, and with explicit description of patient and lesion factors
- additional information and justification for the proposed MBS items, covering costs for the Re-188 compound and clinician time, while excluding waste disposal and non-isotope consumables to ensure fees reflect actual service delivery
- further cost analysis, such as cost per treatment success and/or cost per lesion, including consideration of risks and costs associated with managing adverse events from Re-188 brachytherapy.

The applicant was granted a hearing, in which they highlighted the changes that had been made in the resubmission and answered questions from MSAC.

MSAC noted the consultation input received for this resubmission from 2 consumer organisations, 9 medical/other organisations and 2 individuals (further noting that 6 of the 13 inputs were submitted prior to MSAC's previous consideration of the application in April 2025).

MSAC noted ESC's comments on the revised target patient population and considered the most appropriate patients for referral for Re-188 brachytherapy would be those with well-defined low risk NMSC in anatomically challenging locations such as the nasolabial folds, periorbital regions, ear pinna, or other sites where surgery or radiation therapy risks poor cosmetic or functional outcomes. MSAC considered that patients who decline surgery should not be eligible for Re-188 brachytherapy under the MBS, to ensure that eligibility is based on clearly defined clinical, technical or logistical criteria rather than a preference to avoid surgery where surgery is clinically indicated. MSAC noted the importance of clearly specifying the reasons for patients being unsuitable for surgery, to avoid unintended expansion to surgically indicated lesions. MSAC noted that the resubmission retained the restriction to patients with previously untreated lesions (which aligns with the inclusion criteria for the EPIC-Skin study) and had not widened eligibility to patients with previously treated lesions. MSAC considered that this was appropriate but only previous treatment with surgery, EBRT, or brachytherapy should be specified as exclusion criteria for the item descriptors.

MSAC reviewed the revised clinical management algorithm and noted that assessment for surgical suitability would be undertaken by a dermatologist or plastic surgeon, and that referrals for Re-188 brachytherapy may also be made by a general practitioner (GP) where a dermatologist or plastic surgeon is not readily available. MSAC noted that, in practice, GPs will have varying levels of confidence and expertise in referring patients for Re-188 brachytherapy, and those who are less confident in their assessment would be expected to seek consultation from a specialist before referring a patient to Re-188 brachytherapy. MSAC noted ESC's concerns about how a 'skin specialist GP' would be defined given that no formal definition currently exists. MSAC considered that the factors determining whether the patient receives EBRT or Re-188 brachytherapy were not completely clear but considered the definitive decision to choose between different treatment modalities, including EBRT, Re-188 brachytherapy, or other therapies should be made by the treating clinician. This may include an assessment by a multidisciplinary team (MDT) involving the referring skin specialist (dermatologist, plastic surgeon or GP), a radiation oncologist, and a nuclear medicine specialist.

MSAC considered the potential role of an MDT in the initial assessment, treatment planning, and evaluation of patient outcomes. The applicant clarified in the hearing they considered an MDT discussion should be undertaken 'where appropriate', noting that the eviQ criteria recommended MDT review for patients who meet the criteria for definitive EBRT for basal cell carcinoma, and the current application aligns with those criteria. MSAC also noted that requiring a formal MDT for Re-188 brachytherapy may inadvertently restrict access to treatment for patients in rural and remote areas. However, MSAC emphasised that the decisions about the most appropriate care should be informed by review and discussion among all relevant clinicians. MSAC considered that MDT involvement should be recommended for appropriate cases but should not be compulsory, noting that access to an MDT may not be available to all patients. MSAC recommended that this should be reflected in the explanatory note for the treatment items.

MSAC noted the revised MBS item descriptors, including a planning item and several treatment items to be used according to the size of the lesion being treated, were consistent with the approach previously taken by the department for defining MBS items for burns treatment. MSAC noted the treatment items no longer included costs for consumables based on previous MSAC advice. The applicant confirmed in the hearing that the proposed fee covers the full cost of delivering the service, with clinics bearing any additional costs (including consumables, wastage

and waste disposal). The applicant also confirmed that strategies are in place to minimise wastage of the Re-188 carpoule.

Regarding the planning item, the applicant confirmed at the hearing that the lesion mark-up would be performed by the treating clinician. MSAC noted that lesion mark-up may be undertaken by the treating clinician or the referring skin specialist as part of the multidisciplinary team process. MSAC considered that lesion mark-up should only be performed and claimed by a clinician with appropriate competency in skin lesion delineation, and that this should be stated in an explanatory note.

For the treatment items, MSAC confirmed that the planning item should be applicable once per treatment session, and the treatment items should be applicable once per lesion per lifetime. Where multiple lesions are treated in the same attendance, benefits are payable with graded payments according to lesion size.

MSAC noted that the resubmission did not provide new evidence for safety or effectiveness. The preliminary 2-year follow-up data from the EPIC-Skin study (NCT05135052) provided by the applicant in the pre-ESC response were not formally evaluated however, MSAC noted that the 2-year data appeared consistent with the 1-year findings included in the resubmission, with a similar adverse event profile observed up to 24 months. MSAC considered that Re-188 brachytherapy was likely to be cost-effective and cost-saving to the MBS compared with EBRT in most real-world scenarios but noted uncertainty about the extent of substitution for EBRT and the risk that publicly funded access could increase overall utilisation. MSAC supported the MBS listing of Re-188 brachytherapy and advised that the department should review service utilisation, patient out-of-pocket costs, and co-payments 2 years post MBS listing.

MSAC noted that Re-188 represents an unsealed radioactive source and considered that state and territory laws regulating the possession and use of unsealed radioactive sources may limit which providers and locations are able to offer Re-188 brachytherapy.

MSAC confirmed the following MBS item descriptors:

Category 3 – Therapeutic Procedures Group T2 – Radiation Oncology Subgroup 13 – Brachytherapy
MBS item XXXX1 Epidermal radioisotope therapy planning Epidermal radioisotope therapy, using Rhenium-188 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, 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, from tables, charts, or data from a treatment planning system. Applicable once per ~~course of~~ treatment session.
Fee: ~~$206.80~~ $208.60 **Benefit: 75%** = ~~$155.10~~ $156.45 **85%** = ~~$175.78~~ $177.35

Category 3 – Therapeutic Procedures
Group T2 – Radiation Oncology
Subgroup 13 – Brachytherapy

MBS item XXXX2

Delivery of Epidermal radioisotope therapy

Epidermal radioisotope therapy, using Rhenium-188, to 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 area of the lesion/s is no more than 300 mm^2

d) surgery on the lesion is not feasible, due to tumour characteristics, patient factors, or risk of functional loss/unacceptable cosmetic outcomes ~~or for patients declining surgical excision~~; and

e) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and

f) the service is referred by a dermatologist, plastic surgeon, or a ~~skin specialist GP~~ general practitioner if a dermatologist or plastic surgeon is not readily available; and

g) the lesion has not previously been treated with surgery, external beam radiation therapy or brachytherapy~~, cryotherapy, or topical agents~~; and

h) used to implement a plan as described in item XXXX1.

~~Applicable for total surface area of lesion/s treated.~~

Applicable once per lesion per lifetime.

Fee: $2,123.95 **Benefit 75%** = ~~$1,592.96~~ $1,593.00 **85%** = ~~$1,805.36~~ $2,019.45

MBS item XXXX3

Delivery of Epidermal radioisotope therapy

Epidermal radioisotope therapy, using Rhenium-188, to 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 area of the lesion/s is at least 301 mm^2 but no more than 500 mm^2

d) surgery on the lesion is not feasible, due to tumour characteristics, patient factors, or risk of functional loss/unacceptable cosmetic outcomes; and

e) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and

f) the service is referred by a dermatologist, plastic surgeon, or a general practitioner if a dermatologist or plastic surgeon is not readily available; and

g) the lesion has not previously been treated with surgery, external beam radiation therapy or brachytherapy; and

h) used to implement a plan as described in item XXXX1.

Applicable once per lesion per lifetime.

Fee: $3,286.75 **Benefit 75%** = ~~$2,465.06~~ $2,465.10 **85%** = ~~$2,793.74~~ $3,182.25

MBS item XXXX4

Delivery of Epidermal radioisotope therapy

Epidermal radioisotope therapy, using Rhenium-188, to 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 area of the lesion/s is at least 501 mm^2 but no more than 700 mm^2

d) surgery on the lesion is not feasible, due to tumour characteristics, patient factors, or risk of functional loss/unacceptable cosmetic outcomes; and

e) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and

f) the service is referred by a dermatologist, plastic surgeon, or a general practitioner if a dermatologist or plastic surgeon is not readily available; and

g) the lesion has not previously been treated with surgery, external beam radiation therapy or brachytherapy; and

h) used to implement a plan as described in item XXXX*1*.

Applicable once per lesion per lifetime.

Fee: $4,973.95 **Benefit 75%** = ~~$3,730.46~~ $3,730.50 **85%** = ~~$4,277.86~~ $4,869.45

MBS item XXXX5

Delivery of Epidermal radioisotope therapy

Epidermal radioisotope therapy, using Rhenium-188, to 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 area of the lesion/s is at least 701 mm^2 but no more than 800 mm^2

d) surgery on the lesion is not feasible, due to tumour characteristics, patient factors, or risk of functional loss/unacceptable cosmetic outcomes; and

e) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and

f) the service is referred by a dermatologist, plastic surgeon, or a general practitioner if a dermatologist or plastic surgeon is not readily available; and

g) the lesion has not previously been treated with surgery, external beam radiation therapy or brachytherapy; and

h) used to implement a plan as described in item XXXX1.

Applicable once per lesion per lifetime.

Fee: $6,113.95 **Benefit 75%** = ~~$4,585.46~~ $4,585.50 **85%** = ~~$5,196.86~~ $6,009.45

MBS Explanatory Note XXXX - Delivery of epidermal radioisotope therapy

Exclusion criteria

- Perineural invasion (PNI)
- Lymphovascular invasion (LVI)
- Bony involvement
- Poorly differentiated
- Melanoma
- Unable to shield sensitive organs from beta radiation
- Positive margins from prior excisions
- Locally advanced or metastatic disease
- >3mm deep or unable to verify depth
- Peripheral Vascular Disease
- Gorlin syndrome.
- Sites of poor vascularity or healing, and wear and tear sites.

Multidisciplinary team consideration

The management of non-melanoma skin cancer using Rhenium-188 epidermal radioisotope therapy can be clinically complex. Where appropriate, the involvement of an appropriately experienced multidisciplinary team (MDT) in the initial assessment, treatment planning, and evaluation of patient outcomes is recommended.

4. Background

The Medical Services Advisory Committee (MSAC) has previously considered the use of epidermal radioisotope therapy using Re-188 (hereafter referred to as Re-188 brachytherapy) for treatment of non-melanoma skin cancer (NMSC) at its July 2023 meeting (MSAC application 1657) and April 2025 meeting (MSAC application 1657.1).

At the April 2025 meeting, MSAC deferred advice on public funding for Re-188 brachytherapy in cases where surgery is not possible due to either lesion location or it being contraindicated, including where there are patient safety concerns. MSAC acknowledged that, despite low-certainty evidence, Re-188 brachytherapy is likely to have a clinical role for a defined subset of patients. However, MSAC noted the absence of consensus on the standard of care comparator and the limited comparative safety and effectiveness data available to support the economic model. MSAC advised that a resubmission should address key outstanding issues, such as:

- clearer definition of the target patient population, detailing those most likely to benefit, and with explicit description of patient and lesion factors
- additional information and justification for the proposed MBS items, covering costs for the Re-188 compound and clinician time, while excluding waste disposal and non-isotope consumables, to ensure fees reflect actual service delivery
- further economic analysis, such as cost per treatment success and/or cost per lesion, including consideration of risks and costs associated with managing adverse events (AEs) from Re-188 brachytherapy.

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

Table 1 Summary of key matters of concern

Component	Matter of concern	How the current assessment report addresses it
Population	MSAC requested clarity around the eligible population, suggesting treatment 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. [PSD, p.6]	Addressed. The population has been redefined using eviQ criteria for definitive EBRT in cutaneous BCC/SCC to ensure that patients considered for Re-188 brachytherapy are drawn only from those for whom radiation therapy is clinically appropriate (i.e. surgery is not feasible or is declined). Additional Re-188–specific eligibility thresholds have been set based on histopathology, geometry and depth. While anatomical location is not specified, the site and surface curvature must allow for Re-188 placement. The commentary noted that the proposed MBS items also restrict the intervention to previously untreated lesions, consistent with the key clinical evidence. The commentary suggested that Re-188 brachytherapy may be most appropriate for a narrower population – patients for whom conventional EBRT is not feasible or practical due to clinical, technical or logistical constraints (see Table 6). These patients are likely to benefit most from Re-188 brachytherapy as an alternative treatment modality; however, clearly defining this subgroup within an item descriptor may prove challenging.
Clinical place in therapy	MSAC requested that an appropriate referral pathway should be defined. [PSD, p.6] MSAC considered that, to improve equity in rural and remote areas, the referrer should be amended to any GP in consultation with a dermatologist or plastic surgeon. [PSD, p.3]	Partially addressed. ADAR Appendix A outlined the referral pathway for patients prior to Re-188 brachytherapy. Although not explicitly stated in Appendix A, where a dermatologist or plastic surgeon is not readily available, a skin-specialist GP would assume responsibility for the 'gating decision' – assessing surgical suitability, discussing surgery as first-line treatment, considering non-surgical options if surgery is inappropriate or declined, and marking lesion borders. The commentary noted that neither the referral pathway nor the clinical management algorithm specifies the need for an MDT review prior to Re-188 brachytherapy, and this requirement is also absent from the proposed MBS items. It further highlighted uncertainty about whether GP referrals are intended to be restricted to regions without specialist access and how such restrictions would be implemented in practice.
Proposal for public funding	MSAC requested 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. [PSD, p.6]	Addressed. Following advice provided at the pre-submission meeting in July 2025, new MBS items have been drafted in consultation with the department. A planning item has been proposed, applicable once per treatment session, with a fee aligned to kilovoltage planning item 15950. In addition, 4 treatment items have been proposed to cover both the cost of Re-188 resin/paste and associated service costs, consistent with brachytherapy item 15982. The 4 treatment items are structured by lesion size: 0-300 mm^2, 301-500 mm^2, 501-700 mm^2 and 701-800 mm^2. Nursing time and non-isotope-related consumables (protective film, nose/ear plugs, patient protection underpads, waste collection bags and containers for disposal) are no longer included in the proposed fees.
Treatment costs	MSAC requested more accurate costings of both Re-188 brachytherapy (including realistic wastage) and EBRT – based on additional stakeholder engagement and feedback and preferably including	Partially addressed. Costings for Re-188 brachytherapy have been updated to reflect the revised MBS items, both with and without consideration of carpoule wastage (estimated at 22%). The commentary raised concerns about the basis of the wastage estimate, the potential for lower carpoule

Component	Matter of concern	How the current assessment report addresses it
	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. [PSD, pp.6-7]	utilisation, and the residual risk that clinics may pass these costs on to patients as out-of-pocket expenses. The ADAR continued to rely on GenesisCare data and an advisory board clinician survey to estimate EBRT utilisation rates and costs for NMSC treatment. The commentary noted that previous concerns regarding these data sources remain relevant. The GenesisCare dataset provides only an approximation of the proposed population, while the advisory board survey – completed by 10 radiation oncologists, only 4 of whom had access to SXRT – showed different EBRT utilisation patterns where SXRT was available (lower use of IMRT/VMAT), reducing comparator costs. Interrogation of the GenesisCare dataset and survey results by the commentary revealed considerable variability in treatment practices across lesion types and sites, although highly fractionated schedules (18–20) were typical.
AE costs	Further examination of the potential costs and consequences of AEs related to Re-188 brachytherapy. [PSD, p.7]	Partially addressed. The economic analysis included costs for managing AEs; however, the commentary noted these may be underestimated, particularly for Grade 4 AEs, which generally require surgical management (e.g. debridement or skin grafting) or hospitalisation. Costs associated with AE management were not considered in the financial analysis.
Economic evaluation	MSAC requested 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). [PSD, p.7]	Partially addressed. A simplified CEA was presented alongside a CCA. The CEA estimated cost per lesion treated/removed, incorporating retreatment and AE management costs. The model assumed the same treatment was applied for both initial treatment and retreatment, which was inconsistent with the proposed MBS items that require that the lesion must not have been previously treated. The ADAR sensitivity analyses were limited to: inclusion of Re-188 wastage; exclusion of retreatment; use of an alternative EBRT source (advisory board clinician survey instead of GenesisCare data); variation in EBRT fractions (5–32); and restricting AEs to Grade 3 only. The CCA included cosmesis outcomes and indirect costs such as patient travel and productivity loss. The commentary proposed an alternative base case using the best available clinical evidence and a refined cut of the GenesisCare data. It was assumed that all retreatment would involve EBRT. The commentary noted that key limitations of the economic evaluation remain, namely: (i) uncertainty in comparator treatment costs, including EBRT modality breakdown; and (ii) the sourcing of clinical inputs from fair- or poor-quality single-arm studies, with differing outcome assessment timepoints between Re-188 brachytherapy and EBRT.
Financial analysis costs	MSAC noted that the ADAR used the full fee in the financial analysis, so did not account for the GPG or an 85% benefit fee when calculating the MBS costs. [PSD, p.6] 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,	Partially addressed. The GPG has been appropriately incorporated into the financial analysis. The updated analysis does not consider costs after treatment delivery.

Component	Matter of concern	How the current assessment report addresses it
	management of adverse effects, etc.). [PSD, p.6]	
Financial analysis scenarios	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 in 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. [PSD, p.6]	Not addressed. Lesion type scenarios have not been presented. However, after extensive analysis of the GenesisCare dataset and advisory board clinician survey results, the commentary did not identify any clear patterns in the use of EBRT modalities or fractionation across different lesion types or sites. ADAR sensitivity analyses tested the impact of changes to EBRT fractions (5 to 22) but not changes to the EBRT modalities likely to be displaced by Re-188 brachytherapy.

ADAR = Applicant-Developed Assessment Report; AE = adverse event; BCC = basal cell carcinoma; CCA = cost-consequence analysis; CEA = cost-effectiveness analysis; EBRT = external beam radiation therapy; GP = general practitioner; GPG = greatest permissible gap; IMRT/VMAT= intensity-modulated radiation therapy/volumetric modulated arc therapy; MBS = Medicare Benefits Schedule; MDT = multidisciplinary team; MSAC = Medical Services Advisory Committee; NMSC = non melanoma skin cancer; PICO = population, intervention, comparator, outcomes; PSD = Public Summary Document; QoL = quality of life; Re-188 = Rhenium-188; SCC = squamous cell carcinoma; SXRT = superficial X-ray radiation therapy.
Source: Derived from Table 1.1.1 and Commentary Table 12 of MSAC 1657.1 ADAR + in-line commentary.

5. Prerequisites to implementation of any funding advice

The Rhenium Skin Cancer Therapy (RSCT) system was registered with the Therapeutic Goods Administration (TGA) as a class IIb medical device in November 2022. The Rhenium-188 compound had already been included in the Australian Register of Therapeutic Goods (ARTG) as a class IIb device since December 2020. Both the compound and the system are intended to treat skin cancer using the radioisotope Re-188.

Table 2 ARTG summary for RSCT

Product name and Sponsor	ARTG summary	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	The Rhenium-SCT is intended to be used to treat skin cancer using the radioisotope Rhenium-188. The main component of the Rhenium-SCT is a radioactive paste (Rhenium-188 compound). In order to put the paste close to the tumour the paste is applied over a protective foil over the tumour and thus only irradiates diseased tissue. The penetration range of its beta-radiation is very shallow in the human tissue (2-3 mm).

ARTG = Australian Register of Therapeutic Goods; GMDN = Global Medical Device Nomenclature; Rhenium-SCT/RSCT = Rhenium Skin Cancer Therapy.
Source: Public Summary on the ARTG website.

6. Proposal for public funding

Re-188 brachytherapy is currently reimbursed on a case-by-case basis in Australia by some health insurers. The ADAR sought public funding via the MBS, and the revised proposal intends to create 5 new MBS items: 1 planning item and 4 treatment items.

The applicant made several adjustments to the ADAR following consultation with the department, where it was discussed how the revised ADAR could address MSAC's previous concerns regarding the proposed MBS items and MBS fees. The adjustments were:

- Removing the costs for non-isotope-related consumables, nursing time and overlapping clinician time for batched patients/lesions, ensuring clinicians are not simultaneously billing for concurrent sessions.
- Combining the cost of the radioisotope paste with the application service across a series of items that cover a range of lesion areas. Bundling these costs simplifies the billing structure, reduces administrative complexity, and reflects the clinical reality that paste application and treatment delivery are inseparable components of the procedure.
- Including a base planning item, which can only be applied once per treatment course per patient.

The possibility of introducing a second planning item with a reduced fee for additional planning required for subsequent lesions treated in the same session was considered but deemed unnecessary by the applicant. This decision reflects the expectation that the incremental planning effort for additional lesions is minimal and does not justify a separate fee, as most planning activities are completed during the initial planning stage and any additional work for subsequent lesions is considered part of the overall treatment process.

The proposed planning item is shown in Table 3. The item is intended to be claimed once per course of treatment, regardless of the number of lesions treated. The fee is benchmarked against MBS item 15950, which covers planning for a single, simple-complexity superficial X-ray radiation therapy (SXRT) treatment and closely aligns with the proposed Re-188 brachytherapy planning service. This planning process includes patient setup, tumour demarcation based on clinical assessment, recording and measuring the treatment surface area, and performing dosimetry planning using data table lookups. The wording of the proposed item descriptor is consistent with that agreed by MSAC (PSD for MSAC application 1657.1, p.10).

The department advised that Re-188 brachytherapy was delivered in a single session, therefore specifying the planning item for 'once per treatment session' rather than 'once per course of treatment' provided greater clarity.

Table 3 Proposed item descriptor for planning *with ESC proposed amendments*

Category 3 – THERAPEUTIC PROCEDURES Group T2 – Radiation Oncology Subgroup 4 – Brachytherapy
MBS item XXXX1 Epidermal radioisotope therapy planning Epidermal radioisotope therapy, using Rhenium-188 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, 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, from tables, charts, or data from a treatment planning system. Applicable once per ~~course of~~ treatment *session*.
Fee: ~~$206.80~~ *$208.60* **Benefit: 75%** = ~~$155.10~~ *$156.45* **85%** = ~~$175.78~~ *$177.35*

Source: Table 1.8.1 of MSAC 1657.1 ADAR + in-line commentary. Commentary amendments are shown in strikethrough and italics. Proposed fee is based on MBS item 15950 for single, simple-complexity kilovoltage planning.

The 4 updated treatment items cover 4 lesion area bands based on the total surface area of lesions, as shown in Table 4. The proposed MBS fees incorporate both the cost of healthcare provider time to administer the Re-188 resin/paste and the cost of the resin/paste itself. Provider time has been benchmarked against MBS item 15982 for brachytherapy treatment.

According to the ADAR, the total production cost of one carpoule of Re-188 resin/paste is approximately $**redacted**, which can treat around 2,500 mm² (25 cm²) of lesion area. This represents an increase in total carpoule cost from the initial MSAC application (1657) in June 2022 to reflect:

- funding for technology transfer from the Australian Nuclear Science and Technology Organisation (ANSTO) to Cyclotek to establish higher-capacity manufacturing for reliable patient access
- inflationary pressures and global increases in radioisotope precursor costs.

However, the commentary noted that the surface area treatable per carpoule also appears to have increased since the initial application:

- ADAR 1657 (June 2022, p.17) – Average transported cost per carpoule was $**redacted**, treating approximately 1,800 mm² (~$**redacted** per mm²)
- ADAR 1657.1 (October 2024, p.29; October 2025, p.31) – Total production cost per carpoule is $**redacted**, treating approximately 2,500 mm² (~$**redacted** per mm²).

The calculation of fees for each surface area band is based on median lesion sizes observed in the EPIC-Skin study. Assuming one lesion is treated per area band per carpoule (Table 4), estimated carpoule utilisation is 78.1% (1,953 mm² of 2,500 mm² capacity), resulting in wastage of approximately 22% ($**redacted**). The ADAR noted that local clinics typically achieve batching efficiencies of 80–90%. Wastage is discussed later in this section.

Table 4 Breakdown of proposed cost per MBS treatment item

Treated area size (mm^2)	Median area treated (mm^2)[a]	Cost of Re-188 per median area treated[b]	Proposed fee for administration time[c]	Proposed MBS fee per item
0–300	225	**$redacted**	**$redacted**	$2,123.95
301–500	378	**$redacted**	**$redacted**	$3,286.75
501–700	600	**$redacted**	**$redacted**	$4,973.95
701–800	750	**$redacted**	**$redacted**	$6,113.95

MBS = Medicare Benefits Schedule; Re-188 = Rhenium-188.
a Median area treated from the EPIC-Skin study, based on a total of 169 lesions (102 sized 0–300 mm^2, 37 sized 301–500 mm^2, 24 sized 501–700 mm^2, 6 sized 701–800 mm^2). The mean area treated was not substantially different from the median.
b Calculated as median area treated x $**redacted** (i.e. cost per mm^2, calculated as cost per carpoule [$**redacted**] divided by the total area that can be treated per carpoule [2,500 mm^2]).
c Administration time per lesion, benchmarked to MBS item 15982.
Source: Table 1.8.6 of MSAC 1657.1 ADAR + in-line commentary.

The 4 proposed treatment items, grouped by lesion size bands, are presented in Table 5. The description of the eligible patient population has been updated using wording sourced directly from eviQ to ensure that patients considered for these services are restricted to those for whom definitive external beam radiation therapy (EBRT) is clinically appropriate, including patients who decline surgical excision. The items do not include Re-188–specific eligibility thresholds beyond surface area and depth. Section 5 outlines additional clinical considerations for identifying patients suitable for Re-188 brachytherapy.

The ADAR proposed that suitability for Re-188 brachytherapy is determined entirely by the referring dermatologist, plastic surgeon, or skin-specialist general practitioner (GP) where access to a dermatologist or plastic surgeon is not readily available.

The commentary noted that the requirement for multidisciplinary team (MDT) discussion is not included in the proposed item descriptors but may be prudent to ensure optimal patient selection and treatment planning. A joint task force of the Groupe Européen de Curiethérapie and the European Society for Radiotherapy and Oncology (GEC-ESTRO) Head and Neck and Skin (HNS) and Brachytherapy Physics Quality Assurance System (BRAPHYQS) Working Groups advises that application of Re-188 requires a highly specialised MDT comprising a radiation oncologist, medical physicist, and nuclear medicine specialist (Lozares et al. 2025).[2]

Consistent with MSAC advice, the descriptor specifies that the lesion must not have been previously treated (i.e. the service applies only to treatment-naïve lesions). This aligns with the key clinical evidence; in the EPIC-Skin study, patients who had received prior treatment (surgery, radiation, or laser therapy) for their target lesion(s) were excluded.

The ADAR proposed treatment items apply to the 'total surface area of lesions treated', which prevents claiming multiple items in a single session for multiple lesions. The commentary noted advice from the department to amend the item description to 'applicable once per lesion per life time', allowing one planning item to be claimed alongside multiple treatment items for patients with multiple lesions. The potential impact of patients with multiple lesions has not been explicitly accounted for in the economic or financial analyses. The commentary noted that 71.2% of patients with recorded tumour information in the EPIC-Skin study had a single lesion, 19.6% had

[2] Lozares S, Tur P, Ballester F, Bundschuh RA, González-Pérez V, Jaberi R, Vijande J, Walter R, Tedgren ÅC, Tagliaferri L, Siebert FA and Rembielak A (2025) 'Head and neck and skin (HNS) GEC-ESTRO and BRAPHYQS working groups joint critical review of the use of Rhenium-188 in dermato-oncology', *Clin Transl Radiat Oncol*, 53:100991, doi:10.1016/j.ctro.2025.100991.

2 lesions, and 9.2% had 3 lesions. The commentary considered the amendment to once per lesion per life time could substantially increase costs compared to the ADAR's approach. For instance, a patient with 2 lesions of 150 mm^2 each would incur $4,247.90 ($2,123.95 x 2) under the department's proposal, versus $2,123.95 using the total area approach. However, the commentary noted the cost implications of the proposed amendment could not be assessed because the GenesisCare dataset does not include information about surface area and number of the lesions at patient-level.

Table 5 Proposed item descriptors for treatment by lesion size band (0–300 mm^2, 301–500 mm^2, 501–700 mm^2, 701–800 mm^2) *with ESC proposed amendments*

Category 3 – THERAPEUTIC PROCEDURES Group T2 – Radiation Oncology Subgroup 4 – Brachytherapy
MBS item XXXX2 *Delivery of* Epidermal radioisotope therapy Epidermal radioisotope therapy, using Rhenium-188, to 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 area of the lesion/s is no more than 300 mm^2 d) surgery on the lesion is not feasible, due to tumour characteristics, patient factors, or risk of functional loss/unacceptable cosmetic outcomes or for patients declining surgical excision; and e) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and f) 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 g) the lesion has not previously been treated h) used to implement a plan as described in item XXXX1. Applicable for total surface area of lesion/s treated. *Applicable once per lesion per lifetime.*
Fee: $2,123.95 **Benefit 75%** = ~~$1,592.96~~ *$1,593.00* **85%** = ~~$1,805.36~~ *$2,019.45*
MBS item XXXX3 *Delivery of* Epidermal radioisotope therapy Epidermal radioisotope therapy, using Rhenium-188, to 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 area of the lesion/s is at least 301 mm^2 but no more than 500 mm^2 d) surgery on the lesion is not feasible, due to tumour characteristics, patient factors, or risk of functional loss/unacceptable cosmetic outcomes or for patients declining surgical excision; and e) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and f) 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 g) the lesion has not previously been treated h) used to implement a plan as described in item XXXX1. Applicable for total surface area of lesion/s treated. *Applicable once per lesion per lifetime.*

Category 3 – THERAPEUTIC PROCEDURES Group T2 – Radiation Oncology Subgroup 4 – Brachytherapy
Fee: $3,286.75 **Benefit 75%** = ~~$2,465.06~~ *$2,465.10* **85%** = ~~$2,793.74~~ *$3,182.25*
MBS item XXXX4 *Delivery of* Epidermal radioisotope therapy Epidermal radioisotope therapy, using Rhenium-188, to 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 area of the lesion/s is at least 501 mm^2 but no more than 700 mm^2 d) surgery on the lesion is not feasible, due to tumour characteristics, patient factors, or risk of functional loss/unacceptable cosmetic outcomes or for patients declining surgical excision; and e) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and f) 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 g) the lesion has not previously been treated h) used to implement a plan as described in item XXXX*1*. Applicable for total surface area of lesion/s treated. *Applicable once per lesion per lifetime.*
Fee: $4,973.95 **Benefit 75%** = ~~$3,730.46~~ *$3,730.50* **85%** = ~~$4,277.86~~ *$4,869.45*
MBS item XXXX5 *Delivery of* Epidermal radioisotope therapy Epidermal radioisotope therapy, using Rhenium-188, to 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 area of the lesion/s is at least 701 mm^2 but no more than 800 mm^2 d) surgery on the lesion is not feasible, due to tumour characteristics, patient factors, or risk of functional loss/unacceptable cosmetic outcomes or for patients declining surgical excision; and e) the service is provided by a suitably trained nuclear medicine physician or radiation oncologist in an approved facility; and f) 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 g) the lesion has not previously been treated h) used to implement a plan as described in item XXXX*1*. Applicable for total surface area of lesion/s treated. *Applicable once per lesion per lifetime.*
Fee: $6,113.95 **Benefit 75%** = ~~$4,585.46~~ *$4,585.50* **85%** = ~~$5,196.86~~ *$6,009.45*

Source: Tables 1.8.2, 1.8.3, 1.8.4 and 1.8.5 of MSAC 1657.1 ADAR + in-line commentary. Commentary amendments are shown in strikethrough and italics. The greatest permissible gap (GPG) from 01 November 2025 is $104.50. As per GN.10.26, the calculated benefit has been rounded to the nearest higher 5 cents. The department suggested the items should apply 'once per lesion' rather than for the total surface area of lesion/s treated – this suggested amendment has not been implemented above.

Wastage

According to the PSD for MSAC application 1657.1 (p.3), representatives of the applicant acknowledged in the hearing that achieving 100% batching efficiency is not feasible in practice.

The applicant stated that private Australian clinics currently report an average utilisation of 65%, typically achieved with an average of 4 patients per session (PSD, p.36). Carpoules must be used within an hour of opening, cannot be stored, and have a 17-hour half-life, making timely batching essential.

The current ADAR reiterated that clinics bear the cost of wastage because carpoules are purchased upfront. To minimise wastage, clinics often delay sessions until sufficient patients can be scheduled, prompting some patients to travel to other clinics for expedited treatment. International experience (e.g. South Africa, Spain, Austria) indicates that reimbursement improves batching efficiency and reduces delays.

The commentary reiterated MSAC's concerns that, despite batching strategies, residual risks such as patient non-attendance at appointments can lead to unavoidable wastage. This uncertainty may impose financial pressures on state and territory hospital budgets in the public setting and result in clinics passing costs to patients in the private setting. Furthermore, patient out-of-pocket expenses may rise if they are required to travel longer distances to enable greater efficiency in carpoule batching.

7. Population

The proposed population has been redefined using eviQ criteria for definitive EBRT in patients with BCC or SCC.[3] This approach is intended to limit consideration of Re-188 brachytherapy to patients for whom radiation therapy is regarded as appropriate and clinically justified. The population comprises adults with histologically confirmed cutaneous BCC or SCC who are eligible for definitive radiation therapy under eviQ criteria – that is, patients for whom surgery is not feasible due to tumour characteristics, patient factors, or the risk of functional loss or unacceptable cosmetic outcomes, or who decline surgery after informed counselling. Within this group, patients must also meet additional Re-188-specific suitability requirements, assessed by a dermatologist or plastic surgeon (or a skin-specialist GP where specialist access is limited). These requirements include:

- low-risk histology without features necessitating margin-controlled surgery or deep-tissue radiation
- lesions no deeper than 3 mm and no larger than 8 cm^2 in surface area, confirmed clinically and by pathology (or, in rare cases, by high-frequency ultrasound)
- anatomical sites where applicator conformity is achievable without jeopardising critical structures.

Both absolute and relative contraindications for Re-188 brachytherapy should be considered when determining suitability. Absolute contraindications include lesions with bony involvement, inability to shield critical organs from beta radiation, and locally advanced or metastatic disease. Relative contraindications or precautions include perineural or lymphovascular invasion, positive margins from prior excisions, poorly differentiated histology, prior radiation to the site, sites of poor vascularity or healing, areas subject to mechanical stress, peripheral vascular disease, and genetic conditions such as Gorlin syndrome.

The population potentially eligible for Re-188 brachytherapy represents a subset of the eviQ EBRT-eligible cohort, limited to patients who have undergone surgical assessment, entered the non-surgical radiation therapy pathway, and subsequently been evaluated for suitability for Re-

[3] Note that skin brachytherapy is currently outside the scope of eviQ protocols for BCC and SCC.

188 brachytherapy (see referral and management pathway below). Importantly, this refinement to the population does not expand the denominator used in the financial analyses, because:

- all patient allocation remains within EBRT eligibility bounds
- selection is more stringent than for conventional EBRT
- no patients are captured from a surgery-indicated pathway.

Clinical rationale for Re-188 brachytherapy preference

Re-188 brachytherapy may be preferred over conventional EBRT when its technical characteristics offer distinct clinical advantages. This includes cases where lesion geometry or anatomical site makes highly conformal applicator placement beneficial – such as on curved or irregular surfaces – allowing clinicians to exploit the steep dose fall-off to better spare adjacent healthy tissue. It is particularly well suited to lesions that meet its defined size and depth thresholds, where superficial targeted dose delivery is more appropriate than deeper-penetrating EBRT. Its use may also be advantageous when treating lesions close to sensitive, cosmetically important, or functionally critical structures, where the sharper dose gradient of brachytherapy can reduce collateral exposure.

Patient-related factors also influence selection. Individuals who are frail, have mobility limitations, or face difficulty attending multiple EBRT sessions may benefit from the shorter treatment schedule offered by Re-188 brachytherapy. This is especially relevant for patients living in remote areas or those for whom repeated hospital visits are impractical. MSAC has noted that Re-188 brachytherapy may be particularly advantageous for older patients, given concerns about radiation exposure in younger populations (PSD for MSAC application 1657.1, p.3). In clinical practice, clinicians have also reported a preference for Re-188 brachytherapy when EBRT is technically challenging or when patient-specific factors – such as anxiety related to immobilisation devices or cognitive impairment – limit the feasibility of conventional fractionated therapy.

MSAC considered that Re-188 brachytherapy may be a suitable option for a well-defined population in circumstances where EBRT is difficult to deliver, such as when lesion location or the need for multiple visits creates practical barriers (PSD for MSAC application 1657.1, p.4). The ADAR did not outline further criteria to restrict the population to circumstances where Re-188 brachytherapy offers a more suitable radiation delivery approach than conventional EBRT. The commentary summarised potential considerations (Table 6), including absolute and relative contraindications, while acknowledging that these may be challenging to operationalise within an MBS item descriptor. The commentary noted that clinical studies of Re-188 brachytherapy included patients outside of this defined population, so these criteria reflect a funding framework rather than limitations imposed by the evidence base.

Table 6 Commentary proposed population restrictions for Re-188 brachytherapy

Parameter	Specific requirements
Histology/cancer subtype	• Histologically confirmed superficial NMSC, limited to superficial BCC, nodular BCC without high-risk features, SCC in situ (Bowen's disease), or minimally invasive cutaneous SCC without high-risk features; excludes other high-risk, aggressive, deeply invasive, or rare subtypes[a]
Lesion characteristics	• Lesion depth ≤3 mm (confirmed clinically or via imaging when required) • Lesion area ≤8 cm² (or as per item size bands) • Located on cosmetically or functionally sensitive sites (e.g. face, ear, periorbital region, nasal ala/tip, lip, finger), excluding involvement of the medial canthus, eyelid margin, or vermillion lip[b] • No high-risk histology[a], perineural or lymphovascular invasion[b] • No prior treatment with surgery or RT[b]

Treatment setting	• Definitive (curative) intent only; not intended for palliative, adjuvant, neoadjuvant, or prophylactic treatment, or recurrent disease within previously irradiated fields
	• Surgery is unsuitable due to anatomical constraints, expected functional loss, poor cosmetic outcome, need for complex reconstruction, or patient declining surgery after counselling
	• Conventional EBRT is not feasible or practical for the patient due to clinical, technical or logistical reasons:
	  ○ severe frailty or mobility impairment that prevents completion of a multi-fraction EBRT schedule
	  ○ comorbidities or cognitive impairment making repeated attendance unsafe or impossible
	  ○ demonstrable geographic/logistical barriers (e.g. no reasonable access to radiation therapy services, preventing completion of a multi-fraction EBRT schedule)
	  ○ lesion location or anatomical factors that impede adequate immobilisation or shielding (e.g. periocular region), or complex skin curvature/contour that makes accurate EBRT planning and reproducible setup unreliable.

BCC = basal cell carcinoma; EBRT = external beam radiation therapy; NMSC = non-melanoma skin cancer; Re-188 = Rhenium-188; RT = radiation therapy; SCC = squamous cell carcinoma.
a EPIC-Skin included subjects with confirmed histology and stage I or II BCC or SCC (SCC well to moderately differentiated), and clinically node negative disease.
b EPIC-Skin excluded lesions located on the medial canthus, eyelid margin (upper and lower) or vermillion lip, lesions with perineural or lymphovascular invasion, and lesions treated previously with surgery or radiation therapy.
Source: Commentary Table 3 of MSAC 1657.1 ADAR + in-line commentary.

Clinical referral pathway

The ADAR outlined a clinical referral and management pathway, which included the following steps:

1. GP/skin-specialist GP consult and standard workup
2. Dermatologist or plastic surgeon specialist consult (gating decision – clinical assessment, informed discussion and documentation)
3. Referral to radiation oncology/nuclear medicine
4. Radiation oncology/nuclear medicine intake (eligibility and treatment planning)
5. Treatment, aftercare and surveillance

Patients with suspected NMSC typically present first to a GP, who may perform a biopsy, initiate treatment such as excision or topical therapy, and refer complex or high-risk cases to a specialist. Referral should include histology, lesion photographs with scale, relevant comorbidities, prior treatments, and patient preferences.

Specialist consultation with a dermatologist and/or plastic surgeon determines surgical suitability. Surgery remains the standard of care for eligible lesions, and patients are counselled on technique, cure rates, and cosmetic outcomes. If surgery is unsuitable (due to anatomical

constraints, comorbidities, or expected poor cosmetic or functional results), or is declined after informed discussion, non-surgical options are considered.

Non-surgical options include but are not limited to conventional EBRT or Re-188 brachytherapy. EBRT can treat both superficial lesions and deeper or larger lesions, including high-risk pathology or when complex margins are required. Re-188 brachytherapy is also suitable for superficial lesions (≤3 mm depth, ≤8 cm^2 area, low-risk histology) and is preferred in situations when EBRT is impractical due to factors such as frailty, cognitive impairment, geographic barriers, or technical challenges such as difficulties with immobilisation or complex skin contours. Referral for Re-188 brachytherapy should include pathology reports confirming depth, lesion demarcation, and documentation of surgical unsuitability or patient refusal.

Radiation oncology or nuclear medicine teams confirm eligibility, plan treatment, and provide patient education on procedure, aftercare, and expected outcomes. Following treatment, patients receive written aftercare instructions and enter a structured follow-up schedule, typically at 1–3 weeks, 6 months, 12 months, and annually thereafter, coordinated by dermatology, radiation oncology, or the GP, depending on location and patient needs.

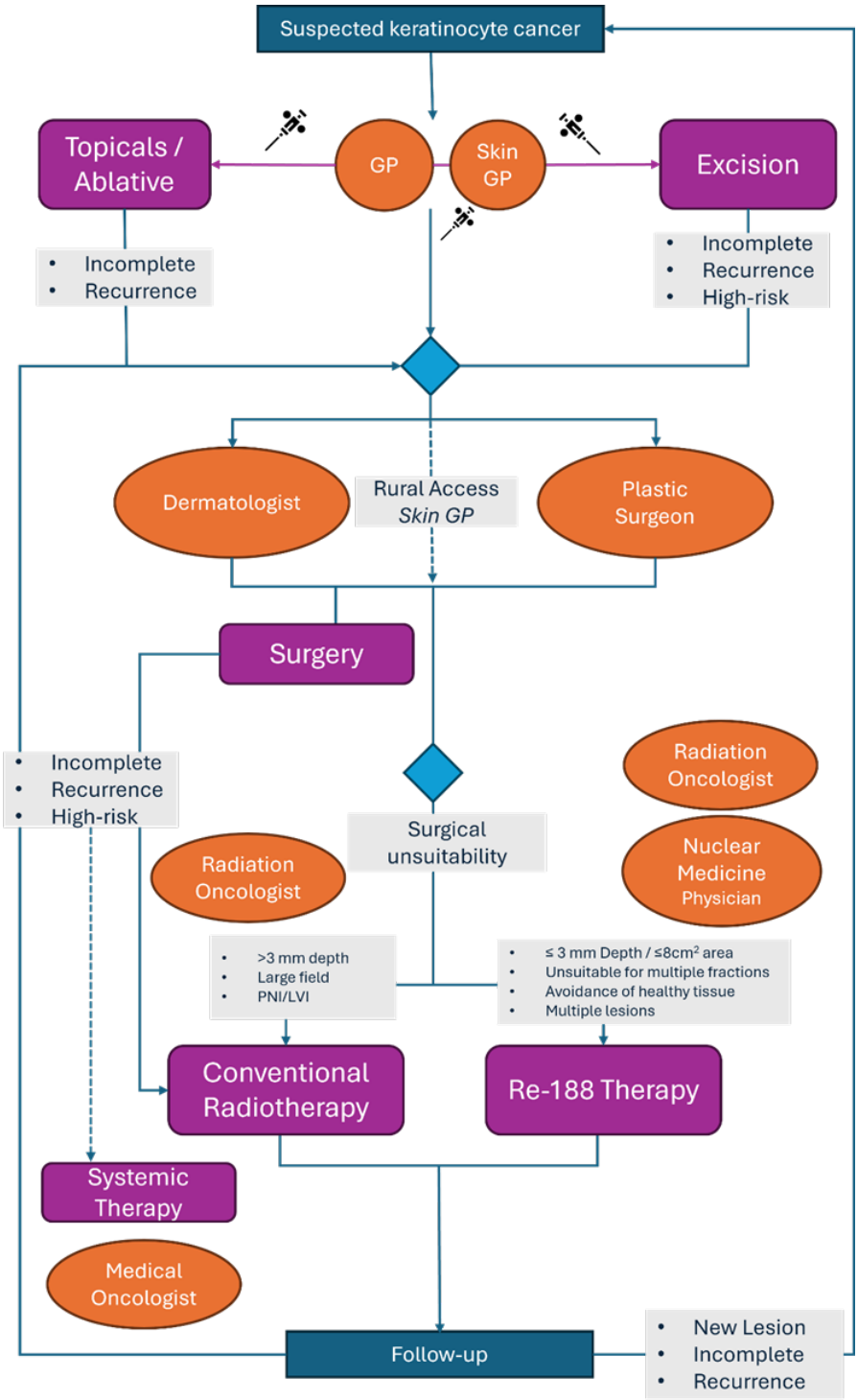
The commentary noted that the referral pathway does not address situations where a dermatologist or plastic surgeon is unavailable, requiring skin-specialist GPs to assume responsibility for the gating decision. This involves assessing surgical suitability, discussing surgery as a first-line option, considering non-surgical alternatives if surgery is inappropriate or declined, and marking lesion borders before referral to radiation oncology or nuclear medicine. It remains unclear whether the GP must consult a dermatologist or plastic surgeon before proceeding, or whether they can independently complete Step 2 – clinical assessment, informed discussion, and documentation – and refer the patient directly to radiation oncology or nuclear medicine.

Clinical management algorithm

The proposed clinical management algorithm, illustrating the positioning of Re-188 brachytherapy in relation to conventional radiation therapy, is presented in Figure 1. This version represents a minor revision of the algorithm included in the previous ADAR. Notably, the term ‘surgical contraindication’ has been replaced with ‘surgical unsuitability’ to more comprehensively encompass tumour characteristics, patient-specific factors, risks of functional impairment or unacceptable cosmetic outcomes, and instances where patients decline surgical excision. The updated algorithm also incorporates factors – such as lesion characteristics – that may influence the selection between conventional radiation therapy and Re-188 brachytherapy.

The updated algorithm explicitly addresses rural access considerations by incorporating skin-specialist GPs into the referral pathway when dermatologists or plastic surgeons are unavailable. This inclusion is consistent with established referral practices for conventional radiation therapy. However, the commentary noted that it remains unclear whether GP referrals are intended to be restricted to regions without specialist access and how such restrictions would be operationalised in practice. In addition, neither the referral pathway nor the clinical management algorithm specifies the requirement for MDT review prior to Re-188 brachytherapy. Current eviQ guidelines recommend MDT review for definitive EBRT treatment of BCC/SCC where appropriate, and similar consideration may be warranted for Re-188 brachytherapy to ensure optimal patient selection and treatment planning.

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



GP = general practitioner; LVI = lymphovascular invasion; PNI = perineural invasion; Re-188 = Rhenium-188.
Note: The figure outlines several factors (e.g. lesion depth, suitability for multiple fractions) that may influence the choice between conventional radiation therapy and Re-188 brachytherapy. These factors are not intended as strict eligibility criteria. Conventional radiation therapy can be used in patients with multiple lesions and those with lesion depth ≤3 mm, and it can be delivered in a way that minimises exposure to healthy tissue. Similarly, Re-188 brachytherapy is suitable for patients with single lesions.
Source: Figure 1 of MSAC 1657.1 ADAR + in-line commentary.

8. Comparator

EBRT remained the comparator in the ADAR resubmission. The modality split and fractionation schedule were broadly consistent with the previous submission, although a different method was used to derive the data.

To support the comparator modality split and fractionation schedule, data were sourced from GenesisCare, which the ADAR claims is the largest private provider of skin cancer care in Australia. The GenesisCare dataset comprised all radiation therapy prescriptions generated between 1 July 2022 and 30 June 2023, initially covering redacted cases (patients) across all tumour streams. The dataset was systematically filtered using ICD codes related to NMSC, histopathology confirming BCC or SCC, and TNM classification to approximate the patient population suitable for Re-188 brachytherapy.[4] After filtering, redacted cases remained and were used to calculate the proportional split between electrons, photons, intensity modulated radiation therapy/volumetric modulated arc therapy (IMRT/VMAT), and SXRT, as well as the mean number of fractions. These results were then adjusted using data from a survey of the sponsor's advisory board clinicians to reflect technique-specific usage.

In contrast, the previous ADAR (1657.1, October 2024) relied primarily on advisory board survey data to determine the modality split and fractionation schedule for patients with NMSC lesions suitable for Re-188 brachytherapy. The survey included 10 radiation oncologists from across Australia; however, it is unclear whether they practiced exclusively in the private sector or also in public hospitals. Clinicians were asked how they would treat representative Re-188-indicated patient vignettes based on resources available in their clinics, and how their practices might change if Re-188 brachytherapy were available without cost considerations. The commentary noted uncertainty as to whether these vignettes reflected the broader population eligible for Re-188 brachytherapy.

Of the 8 vignettes considered, 7 related to lesions on the face/head and one was a lesion of the finger knuckle. By comparison, the EPIC-Skin study reported that 67.3% of lesions treated with Re-188 brachytherapy were located on the head or neck, while 32.7% were located elsewhere (9.1% upper limbs, 11.8% lower limbs, and 11.8% torso).

All surveyed clinicians reported access to IMRT/VMAT, electron EBRT, and photon EBRT at least at one practice location. Only 4 had access to SXRT, likely reflecting the shift in Australian clinics toward linear accelerators (Linacs), which offer versatile treatment options – including skin cancer – using electrons or photons. The previous ADAR (1657.1, October 2024, p.15) noted that SXRT machines incur high capital and operational costs, making them less cost-effective in many settings and contributing to the transition to Linacs.

Table 7 compares EBRT usage results from the GenesisCare dataset (redacted cases) and the advisory board survey (10 radiation oncologists who assessed 8 representative vignettes). Both sources show a similar distribution of electrons and photons; however, the GenesisCare data indicates lower SXRT usage and higher IMRT/VMAT usage compared to the advisory board clinician survey.

The commentary also analysed survey responses from the 4 radiation oncologists with access to SXRT. Among these clinicians, electron EBRT (megavoltage) remained the most commonly used modality, followed closely by SXRT. The advisory board report (dated March 2024) noted that

[4] The **redacted** cases in the economic analysis workbook included ICD-10 codes C44.0–C44.9, and tumours staged Tis, T0, T1, T2, or TX, with N0, NX, M0 or MX. However, the commentary noted inconsistency in documentation of the filtering process throughout the ADAR. Furthermore, the 1,827 cases included lesions with high-risk pathology.

several members without access to SXRT often recommend patients travel to a satellite clinic where the technology is available. The report further highlighted that for patients with reduced cognitive or physical ability, or those unable to remain still during treatment, SXRT is generally considered the preferred option.

Table 7 Comparator EBRT modalities derived from the GenesisCare dataset and advisory board survey

EBRT modality	Description	GenesisCare (redacted cases)	Advisory board (n=10)	Advisory board with access to SXRT (n=4)
Electrons	No CT / 2D Calc	0.0%	0.0%	0.0%
	CT scan - No OARs	14.7%	15.4%	21.8%
	CT scan- CTV/PTV & OARs marked & DVH produced	28.3%	29.6%	17.0%
Total electrons	**-**	**43.0%**	**45.0%**	**38.8%**
Photons	CT scan - No OARs	0.5%	0.3%	1.3%
	CT scan- CTV/PTV & OARs marked & DVH produced	0.5%	0.3%	1.3%
Total photons	**-**	**1.0%**	**0.5%**	**2.5%**
IMRT/VMAT	CT scan- CTV/PTV & OARs marked & DVH produced, no motion management	42.0%	49.9%	23.8%
Total IMRT/VMAT	**-**	**42.0%**	**49.9%**	**23.8%**
SXRT/DXRT	SXRT single (without eye shielding)	5.7%	1.9%	14.3%
	SXRT multiple (without eye shielding)	8.0%	2.6%	20.0%
	SXRT single (with eye shielding)	0.0%	0.0%	0.0%
	SXRT multiple (with eye shielding)	0.3%	0.1%	0.8%
Total SXRT/DXRT	**-**	**14.0%**	**4.6%**	**35.0%**

2D = two-dimensional; CT = computed tomography; CTV = clinical target volume; DVH = dose volume histogram; DXRT = deep X-ray radiation therapy (orthovoltage); EBRT = external beam radiation therapy; IMRT/VMAT= intensity modulated radiation therapy/volumetric modulated arc therapy (megavoltage); OAR = organs at risk; PTV = planned target volume; SXRT = superficial X-ray radiation therapy (kilovoltage).
Note: No advisory board survey respondents indicated use of DXRT/orthovoltage.
Source: Tables 1.5.1 and 1.5.2 of MSAC 1657.1 ADAR + in-line commentary.

The average number of fractions in the GenesisCare dataset was 18. For patients receiving EBRT to multiple lesions, fractions were recorded separately for each lesion to calculate the overall mean.

In the advisory board clinician survey, the average number of fractions was 22 across the 8 vignettes (range 6–30 fractions per patient). The commentary noted that for vignettes where superficial EBRT was selected as the primary modality, proposed fractions ranged from 9 to 30, with a mean of 23.

The ADAR acknowledged that the primary limitation of the GenesisCare dataset is that it represents a single provider group and therefore largely reflects private-sector practice. While GenesisCare maintains a substantial footprint across metropolitan and regional Australia, providing a reasonable proxy for private radiation therapy utilisation, it does not fully capture patterns of care in the public system. This distinction is particularly relevant for SXRT, where

utilisation differs between private and public settings and may vary between individual clinicians and centres within the network.

The commentary noted that SXRT (kilovoltage) has traditionally been the standard modality for very superficial NMSC, typically for lesions ≤3 mm in depth. In some cases, anatomical complexity or the need to protect adjacent critical structures may require megavoltage techniques. Lesions on the ear, eyelid, nose, or lip often benefit from greater precision in dose shaping and normal tissue sparing than kilovoltage beams can provide. Megavoltage EBRT – including IMRT or VMAT – may therefore be selected for detailed contouring, complex surface geometry, or proximity to sensitive organs, and is also used in re-irradiation settings where cumulative tissue tolerance is limited. While SXRT remains a conventional approach for superficial NMSC, megavoltage EBRT represents an alternative for cases requiring higher conformality. Access to megavoltage EBRT is generally more widespread than SXRT, and advisory board survey results suggest SXRT use may be influenced by the technology availability.

Beyond the applicability of the GenesisCare dataset, the commentary noted concerns regarding its generalisability to patients who would be candidates for Re-188 brachytherapy under the MBS. The dataset lacks key lesion characteristics such as depth, surface area, geometry, and precise location. Consequently, despite efforts to exclude lesions unlikely to be suitable for Re-188 brachytherapy, the resulting subset may not accurately represent the proposed population.

Commentary analysis of treatment patterns

The commentary noted that the filtering process in the ADAR appeared to be inconsistently applied across different sections, and the dataset included some lesions with high-risk histopathology. To better align with lesion types suitable for Re-188 brachytherapy, the commentary applied additional refinements to the ADAR dataset by excluding cases with high-risk histopathology and EBRT treatments where the intent was not curative or radical (i.e. excluding palliative, adjuvant, neoadjuvant, or prophylactic treatments). This further filtering reduced the dataset from **redacted** to **redacted** patient records, which was then analysed for treatment patterns.

Table 8 presents the characteristics of this refined dataset, including the number of fractions and the proportion of treatment modalities across various subsets. The average number of fractions for the full commentary analysis set was 18.6, with minimal variation across subsets. The most notable differences were an increase to 22 fractions for leg lesions and a reduction to 15 fractions for cheek lesions. SXRT was used in 5.6% of all cases, with site-specific variation ranging from 0% to 16.7%; however, small sample sizes for some sites may account for this variance rather than true differences in clinical practice.

Slightly more fractions were used for SCC lesions (19.0) compared to BCC lesions (17.9). These subsets also differed in SXRT utilisation, with BCC lesions nearly twice as likely to be treated with SXRT compared to SCC lesions (7.6% versus 4.4%, respectively). These patterns persisted when the dataset was filtered for single-lesion treatments only.

For a subset of sites considered more sensitive to cosmetic impact, the average number of fractions was 19.5, similar to the overall average for all single-lesion cases (19.6). SXRT use was only slightly higher for these sites (6.7% versus 5.9% for all single-lesion cases).

Table 8 EBRT fractions and treatment modality by lesion type and site – GenesisCare commentary analysis set

Analysis set	Total no. of lesions	Mean fractions	Electrons (%)	Conformal photons (%)	IMRT/VMAT (%)	SXRT (%)
Single and multiple lesions[a]						
All sites	**redacted**	18.6	38.9	0.3	55.3	5.6
SCC	**redacted**	19.0	34.1	0.0	61.5	4.4
BCC	**redacted**	17.9	47.2	0.8	44.4	7.6
Single lesions[a]						
All sites	**redacted**	19.6	36.5	0.4	57.2	5.9
SCC	**redacted**	20.2	30.7	0.0	64.6	4.7
BCC	**redacted**	18.7	45.8	0.9	45.3	7.9
Single lesions by site						
Arm	**redacted**	22.0	14.3	0.0	85.7	0.0
Hand	**redacted**	21.0	44.4	0.0	55.6	0.0
Ear	**redacted**	20.6	34.0	0.0	62.0	4.0
Neck	**redacted**	20.6	42.9	0.0	57.1	0.0
Scalp	**redacted**	20.3	27.2	0.0	67.9	4.9
Nose	**redacted**	20.1	27.7	1.3	62.6	8.4
Leg	**redacted**	19.7	43.3	0.0	52.9	3.8
Potentially cosmesis-sensitive sites[b]	**redacted**	19.5	34.7	0.9	58.1	6.7
Torso	**redacted**	18.3	42.9	0.0	50.0	7.1
Lip	**redacted**	17.5	50.0	0.0	33.3	16.7
Forehead	**redacted**	16.9	52.0	0.0	40.0	8.0
Face	**redacted**	16.3	25.0	0.0	75.0	0.0
Temple	**redacted**	15.4	75.0	0.0	12.5	12.5
Cheek	**redacted**	15.0	66.7	0.0	27.8	5.6

BCC = basal cell carcinoma; EBRT = external beam radiation therapy; IMRT/VMAT = intensity modulated radiation therapy/volumetric modulated arc therapy; SCC = squamous cell carcinoma; SXRT = superficial X-ray radiation therapy.
a The data for multiple lesion treatments do not identify the sites for each dose, so the site-of-treatment subsets were generated only for those patients having treatment for a single lesion. Furthermore, the reliability of these data for single lesion sites is uncertain as lesion site information was coded by the applicant and is not internally consistent for all cases.
b Combined lesion sites: face, cheek, ear, forehead, lip, nose, temple, neck, scalp.
Source: Commentary Table 6 of MSAC 1657.1 ADAR + in-line commentary.

The commentary also analysed advisory board clinician survey results by vignette. These included BCCs located on the basal ala, scalp, ear helix, nose, and finger knuckle, and SCCs on the upper cheek, ear concha, and upper lip. Overall, recommended treatment modalities and protocols varied considerably among radiation oncologists across all case studies. Differences were observed not only in modality choice but also in prescribed dose and fractionation schedules for the same modality. No absolute consensus was reached for any scenario.

9. Summary of public consultation input

Consultation input was welcomed from:

1657.1 – Rhenium-188 brachytherapy for non-melanoma skin cancer	No. of Inputs Received
Organisations (11)	
I am providing input on behalf of a consumer group or organisation. Consumer organisations are not-for-profit organisations representing the interests of healthcare consumers, their families and carers.	2
I am providing input on behalf of a medical, health, or other (non-consumer) organisation. For example, input on behalf of a group of clinicians, research organisation, professional college, or from an organisation that produces a similar service or technology.	9
Health Professionals (1)	
I am a health professional or health academic working in the area.	1
Consumers (1)	
I have the health condition that this health service or technology is for.	1
Grand Total	**13**

MSAC received a total of thirteen consultation submissions for this application, with six of them submitted to the department before MSAC reviewed the application in April 2025. MSAC received consultation input from the following organisations:

- 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) (3 inputs)
- Australasian Association of Nuclear Medicine Specialists (AANMS) (3 inputs)
- Australian and New Zealand Society of Nuclear Medicine (ANZSNM)
- Rare Cancers Australia (RCA)

Level of support for public funding

Consultation input showed differing levels of support for public funding of Re-188 brachytherapy for non-melanoma skin cancer. ACD, RCA and the individual with lived experience were supportive of public funding. AANMS supported public funding subject to specific criteria being met. The remaining organisations and the health professional did not support public funding or did not indicate either way. Those who did not support public funding expressed concerns about safety and efficacy, citing the poor-quality evidence and the absence of longer-term follow-up.

Comments on the PICO

The health professional raised concerns that the proposed population was too broad and would include people for whom the intervention was unsuitable. For example, young patients with a long life-expectancy, in which the risk of radiation-induced second cancers could occur; or people with large area skin cancers increasingly prone to unhealing acute toxicity or long-term late cosmetic or radiation ulcer toxicity. They also stated that an additional necessary (but not sufficient) criteria is that the patient's circumstances and co-morbidities, and the cancer characteristics, must be suitable for a single fraction radiation therapy treatment. The AANMS

supports eligibility criteria that ensure Re-188 is used only when standard treatments (surgery, external beam radiotherapy, superficial X-ray therapy) have been considered and found to be suboptimal or inappropriate for the individual patient.

Consultation input expressed mixed views about the comparator, with some agreeing it was broadly appropriate (PHA, ACD and AANMS) while the RANZCR and the health professional asserted the comparator should be radiation treatment with a single dose or fraction of radiation. RANZCR also recommended that 15902 be considered as a comparator. ASPS stated that the best comparator would be local anaesthetic excision with direct closure by suturing.

The ASPS indicated that certain clinical claims lacked support from the articles referenced in the application and expressed the view that the cited studies had issues with their design, including length of follow-up. AANMS expressed concerns regarding the certainty of outcomes observed in the studies, at this stage. They noted that while preliminary results of the EPIC trial are encouraging, supporting evidence remains limited at this time and a minimum of 2-5 years of follow-up is required to properly assess local control, recurrence, and late toxicity.

Perceived Advantages

Consultation input noted that Re--188 brachytherapy is a non-invasive treatment that can be delivered in an outpatient setting.

ACD, RCA and PHA noted that Re-188 brachytherapy offers a further treatment approach for people with non-melanoma skin cancer. ACD described the proposed service as having a limited but definite role in the management of non-melanoma skin cancers, as an alternative to surgery or conventional radiotherapy, particularly for superficial and smaller lesions (e.g. less than 3mm thick, less than 8cm^2); or where surgery is not appropriate because of various patient (e.g. frail elderly patients who are unable to tolerate radiation therapy) and tumour factors. AANMS stated that Re-188 would be most beneficial for patients who have lesions where surgical reconstruction would be inherently complex or cosmetically suboptimal, such as lesions at anatomically irregular or complex sites (e.g. nasolabial fold, periorbital region). AANMS stated because Re-188 is applied in liquid form, it can conform to anatomically complex sites and could provide reduced risk of scarring, wound breakdown, and nerve injury which may be associated with surgery or less conformable radiation therapy modalities.

The individual with a history of skin cancers described the multiple treatments they experienced (including both radiation therapy and surgical interventions) as very painful, stressful, invasive, and emotionally tiring. They expressed the view that the proposed intervention would improve their life. RCA noted that the relatively quick, single application with little preparation time is extremely attractive for patients.

Perceived Disadvantages

The consultation input identified numerous disadvantages of the proposed treatment including:

- 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.
- The proposed treatment may exceed recommended single-fraction radiation doses.
- The patient follow up in the cited studies was poor and the duration was insufficient to establish recurrence rates and late toxicity.
- Unknown long-term effects of treatment and risk of secondary cancers or other adverse events. Late radiation effects and carcinogenesis are the most worrisome potential

complications, and these occur years to decades after treatment and can be very disfiguring and costly to manage.

- 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 out-of-pocket costs to patients.
- Limited availability to patients, particularly in regional, rural, and remote locations, as the service will only be delivered through accredited nuclear medicine facilities in specialist public and private hospitals (non-admitted patients).
- The 17-hour half-life and the consequent need to transport the radioactive paste quickly and safely may limit availability to patients and/or increase the time needed for the treatment. It is likely to be associated with tightly scheduled timing (as paste delivery and specialist availability must be coordinated).
- The proposed treatment incurs a high financial cost for superficial BCC/SCC <3mm depth where surgery is contraindicated. Most lesions deemed suitable for single fraction of rhenium treatment would also be appropriate for SXRT.
- It is unlikely to reduce linac-related capital costs as only a small proportion of linac treatment time is devoted to skin cancer.

Support for Implementation and Issues

AANMS considered that there would need to be some training of specialists and that practical experience with unsealed radioactive sources, such as Re-188, is imperative to support safe implementation of the service. There is the potential for contamination of patients, therapy surfaces, equipment and staff. They expressed the view that the MBS item descriptor should clearly specify that Re-188 must be applied by a nuclear medicine specialist with appropriate training and expertise in radiation safety and working with unsealed radioactive sources. AANMS also stated that patient education regarding radiation safety is essential, although if patients are selected and managed appropriately, contamination should not be a major concern.

AANMS suggested that cross-referencing with relevant nuclear medicine and radiation oncology MBS items should be considered to ensure appropriate gatekeeping and to avoid inappropriate substitution.

In respect of the MBS fee, AANMS noted that remuneration should reflect the complexity of the service, including the radiation safety requirements and the direct hands-on involvement of the nuclear medicine specialist in material applications, without proposing a specific fee.

AANMS also raised concerns that the referral pathway excludes skin-specialist GPs from directly referring patients for Re-188 assessment, unlike referral pathways for radiation oncology, which

may limit access and increase adding patient costs through the need for an additional specialist consultation.

In response to additional questions relating to clinical practice, ACD, AANMS and ANZSNM provided detailed advice on factors taken into consideration when determining the appropriate treatment options. ACD cited the Cancer Council *Australia Clinical Practice Guidelines for Keratinocyte cancer*. This input also outlined who makes such decisions, when, and how patient preferences are taken into consideration. In this response, ACD noted that since its last submission, additional significant published information is available around the use of Rhenium-188 SCT, including indications, cure rates, side effects, long term cosmesis and patients' acceptability. Some dermatologists now also have experience of referring patients for this treatment and therefore a greater personal understanding of its potential risks and benefits.

AANMS and ACD stated that decisions regarding treatment choice (i.e. choosing between Re-188 and other treatment options such as surgery) are ideally made via multidisciplinary teams which may include the referring skin specialist (e.g. dermatologist or plastic surgeon), radiation oncologist and nuclear medicine specialist.

10. Characteristics of the evidence base

MSAC did not request that the resubmission ADAR address the clinical evaluation, and no updates were provided. MSAC previously considered the clinical evidence for comparative safety and effectiveness presented in the previous ADAR to be low certainty but acknowledged that higher certainty evidence was unlikely to become available (PSD for MSAC application 1657.1, p.5).

The key evidence presented in the previous ADAR was the EPIC-Skin study (NCT05135052), a prospective, multicentre, single-arm study involving 189 adults with BCC or SCC lesions, including 37 from Australian sites. Data presented were from a 12-month interim analysis; the primary endpoint is complete response at 24 months.

The commentary for the resubmission did not identify any new published, planned or ongoing randomised controlled trials or non-randomised studies directly comparing the safety and effectiveness of Re-188 brachytherapy with EBRT in patients with BCC and SCC. EPIC-Skin remains the main ongoing prospective study of Re-188 brachytherapy; it is active but not recruiting, with a primary completion date of July 2026 and estimated study completion in May 2027.

The commentary identified a new single-arm case series (Chessa et al. 2025),[9] which retrospectively analysed 64 consecutive patients with 82 histologically confirmed, difficult-to-treat[5] cutaneous BCCs treated with Re-188 brachytherapy. The mean patient age was 81.6 years, and the mean follow-up duration was 24 months (range 2–24 months). Of the 82 lesions, 13 were superficial BCCs, 60 nodular BCCs, and 9 sclerodermiform BCCs (an aggressive subtype prone to recurrence). Nineteen (23.2%) were recurrent following prior treatment. AEs were not reported in the publication. Effectiveness findings are summarised in Section 9.

[5] Difficult-to-treat BCCs were defined as the presence of one or more criteria determined by the European Association of Dermato-Oncology (EADO): (i) technical difficulty of maintaining function and aesthetics due to the size or location (eyes, nose, lips, and ears) of the tumour; (ii) poorly defined borders often associated with the sclerodermiform subtype or with a recurrence; (iii) multiple recurrences on the face (often requiring much larger excision); (iv) prior radiation therapy; (v) patient's reluctance to accept the consequences of surgery; (vi) patient's comorbidities interfering with surgery.

11. Comparative safety

No updates were made to the clinical safety evaluation. The ADAR emphasised that no Grade 3 or 4 toxicities were reported at the 12-month follow-up visit in EPIC-Skin. However, the commentary pointed out that 9 Grade 3 and 2 Grade 4 events occurred at earlier time points.

In consideration of the evidence presented in the previous ADAR (PSD for MSAC application 1657.1, p.4), 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+ AEs occurred more frequently in Re-188 brachytherapy studies than in EBRT studies. MSAC considered that Re-188 brachytherapy appears to be safe but has a different safety profile to EBRT.

12. Comparative effectiveness

No updates were made to the clinical effectiveness evaluation.

In light of the evidence presented in the previous ADAR (PSD for MSAC application 1657.1, p.4), 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 certainty 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. 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.

As a retrospective case series, the new study by Chessa et al. (2025), does not alter MSAC's conclusions regarding the effectiveness of Re-188 brachytherapy. A complete response was observed in 93% (76/82) of BCC lesions, consistent with the rate reported in EPIC-Skin. The study found no statistically significant differences in response based on anatomical location, tumour size, or prior treatment status. Six recurrences (7.3%) occurred during follow-up (including one previously treated lesion), with a mean time to recurrence of 102 weeks.

However, the study highlights two important considerations:

- follow-up beyond 2 years – ideally 5 years or more – is necessary to accurately assess recurrence
- recurrences observed in sclerodermiform BCCs raise questions about the suitability of Re-188 for aggressive subtypes.

Longer-term data are needed to determine true recurrence rates beyond the 12-month window, as well as durable cosmetic and functional outcomes and late toxicity rates.

Clinical claim

The resubmission retained the previous clinical claim that on the balance of probability, the use of Re-188 brachytherapy is non-inferior in terms safety and effectiveness compared with EBRT.

As noted by the Evaluation Subcommittee (ESC), heterogeneity in the demographics, tumour staging and lack of standard comparator treatment made statistical comparison difficult and the clinical claim uncertain (PSD for MSAC application, p.34).

MSAC noted the non-inferiority claim was not substantiated by the evidence for safety and effectiveness (PSD for MSAC application, p.5).

13. Economic evaluation

In consideration of the economic evaluation presented in the previous ADAR (PSD for MSAC application 1657.1, pp.5-6), MSAC noted that the cost-minimisation approach was not appropriate, while acknowledging that developing a more complex economic model is challenging due to limited comparative data. MSAC advised that a resubmission should include a fit-for-purpose economic evaluation, expressed as cost per treatment and/or cost per lesion treated, and incorporate the costs of retreatment, complications, and service delivery.

A simplified cost-effectiveness analysis (CEA) was presented alongside a cost-consequence analysis (CCA) in the current ADAR. The main CEA estimated cost per lesion treated/removed (i.e. complete response to treatment), incorporating retreatment and Grade ≥2 AE management costs. The CCA additionally included cosmesis outcomes and indirect costs such as patient travel and productivity loss.

A summary of the economic evaluation is presented in Table 9. The analyses used a 12-month time horizon, consistent with the follow-up in the interim analysis available from the EPIC-Skin study. The commentary noted that 12 months may be insufficient to capture recurrence events and late toxicity.

Table 9 Summary of the economic evaluation

Component	Description
Perspective	Health care system perspective
Population	Patients with lesions on any anatomic zone that are contraindicated for surgical excision, including where there are clinician concerns for the patient outcomes from surgery, provided the lesions are within the depth and area specifications of ≤3 mm and ≤8 cm^2, respectively. The commentary noted that although this population description differs from the proposed MBS population, it does not affect the economic model's findings.
Comparator	EBRT
Type(s) of analysis	Cost-effectiveness analysis; cost-consequence analysis
Outcomes	Complete lesion removal; partial lesion removal; adverse event rates; cosmesis; treatment burden (travel to treatment clinic, productivity loss)
Time horizon	12 months
Computational method	Decision tree
Generation of the base case	Within-study economic evaluation
Health states	Complete response; partial response; no response
Cycle length	12 months
Transition probabilities	The lesion is treated with either Re-188 brachytherapy or EBRT and patients either experience a complete response, partial response or no response to treatment. Patients can also experience AEs from treatment. No mortality is included.
Discount rate	No discount rate applied
Software	Microsoft Excel

AE = adverse event; EBRT = external beam radiation therapy; Re-188 = Rhenium-188.
Source: Table 11 of MSAC 1657.1 ADAR + in-line commentary.

Cost-effectiveness analysis

The main outcome assessed in the CEA was treatment response. For both the intervention and the comparator, weighted-average rates for complete, partial, and no response were calculated from the included studies, with 'no response' defined as either progressive or stable disease. The commentary noted that using a weighted average may be inappropriate because studies varied in quality and follow-up duration, and few clearly defined complete or partial responses. EBRT studies were particularly heterogeneous, with follow-up ranging from 3 to 60 months and none assessing response at 12 months.

The ADAR assumed that non-responders (patients who did not achieve complete or partial response) were retreated with the same modality as for initial treatment and achieved the same efficacy outcomes. The commentary noted that this was inconsistent with the proposed MBS items for Re-188 brachytherapy, which specify that the lesion must not have been previously treated, and therefore all retreatment should involve EBRT. In practice, re-irradiation for NMSC unresponsive to initial radiation therapy is uncommon due to the risk of late toxicity and limited benefit, though it may be considered on a case-by-case basis using localised techniques (e.g. superficial or conformal EBRT) to deliver an additional dose while minimising normal tissue exposure.

AE rates were derived from EPIC-Skin and Ferro et al. (2015), the only EBRT study explicitly reporting AEs by grade. Ferro et al., a prospective Phase II study of 31 patients aged ≥70 years treated with short-course EBRT (6 fractions), reported no Grade ≥2 acute or late toxicity during a median follow-up of 30 months. In contrast, EPIC-Skin reported safety outcomes for 187 patients treated with Re-188 brachytherapy, including 11 Grade 3 or 4 events at any timepoint: 7 radiation dermatitis events (5 Grade 3 and 1 Grade 4 at day 14, and 1 Grade 3 at 6 months), 3 ulceration events (1 Grade 4 at day 14 and 2 Grade 3 at 6 months), and 1 Grade 3 induration at 6 months. The commentary noted that the economic model did not fully account for these events over the 12-month horizon.

The ADAR assumed that patients with Grade ≥2 radiation dermatitis or ulceration and Grade ≥3 fibrosis would seek medical attention and receive further treatment, estimated as 2 GP or specialist visits plus topical ointment. The commentary considered these costs were underestimated, particularly for Grade 4 toxicity, which requires urgent hospital-based multidisciplinary management.

In the model, patients could experience AEs from initial treatment but not from retreatment in either group. The commentary noted this assumption may lack clinical validity but becomes irrelevant if EBRT is used exclusively for retreatment, given Ferro et al. reported no Grade ≥2 AEs. The economic evaluation also did not address management of partial responders (defined in EPIC-Skin as ≥30% reduction in lesion diameter). The primary EPIC-Skin publication noted that partial response may allow salvage surgery that is less complex or disfiguring than initially required. In practice, partial responders may also receive EBRT retreatment or another modality on a case-by-case basis.

Four main settings were applied in the model: Re-188 brachytherapy wastage costs, EBRT fraction count, consideration of retreatment results, and EBRT modality source. For the base case, settings included no wastage costs (previous ADAR also excluded these), 18 EBRT fractions (previously 22), inclusion of retreatment results (previously excluded), and use of GenesisCare data for EBRT modality breakdown (previously advisory board clinician survey). Sensitivity analyses tested the effect of each setting. The commentary considered the ADAR's method for

accounting for Re-188 carpoule wastage may be unrealistic[6] and exclusion of wastage costs from the base case is unreasonable, as 100% batching efficiency is not achievable in practice.

The CEA results from the ADAR are presented in Table 10.

Table 10 Results of the stepped economic analysis – cost per lesion treated/removed

Economic analysis steps	Re-188 brachytherapy	EBRT	Incremental
Cost per complete lesion removal (cost per complete responder)			
Step 1 – Study data only (no retreatment)			
Cost of treatment	$3,152.36	$6,195.06	-$3,042.71
Outcomes	0.951	0.913	0.038
Cost per lesion removed – complete removal	$3,314.34	$6,782.89	-$3,468.56
Step 2 – Incorporating retreatment of non-responders			
Cost of treatment	$3,223.04	$6,507.01	-$3,283.97
Outcomes	0.973	0.959	0.013
Cost per lesion removed – complete removal	**$3,313.90**	**$6,782.89**	**-$3,468.99**
Cost per partial/complete lesion removal (cost per partial or complete responder)			
Step 1 – Study data only (no retreatment)			
Cost of treatment	$3,152.36	$6,195.06	-$3,042.71
Outcomes	0.977	0.950	0.028
Cost per lesion removed – complete removal	$3,225.10	$6,523.55	-$3,298.45
Step 2 – Incorporating retreatment of non-responders			
Cost of treatment	$3,223.04	$6,507.01	-$3,283.97
Outcomes	0.999	0.997	0.002
Cost per lesion removed – complete removal	$3,224.68	$6,523.55	-$3,298.87

EBRT = external beam radiation therapy; Re-188 = Rhenium-188.
Source: Tables 31, 32, 34 and 35 of MSAC 1657.1 ADAR + in-line commentary.

An alternative scenario was presented in the commentary using the best available clinical evidence and real-world data. This alternative scenario incorporated:

- Re-188 brachytherapy response rates at 12-month follow-up from the largest of the prospective studies, EPIC-Skin (fair quality); this was the only study to clearly define complete and partial response

[6] The ADAR's approach of assuming one lesion per band does not reflect a clinical scenario, as lesion sizes are not evenly distributed across bands. While this method produced a 22% wastage estimate – reflecting the conservative end of observed batching efficiency – it inflates wastage by repeatedly attributing most of it to small lesions, which are most common. The commentary considered that a more appropriate approach to approximate the true cost of wastage would be to allocate the estimated wastage evenly across all size bands before applying incidence weighting.

- EBRT response rates from the only prospective EBRT study, Ferro 2015 (fair quality); this was the only study that mentioned criteria for complete and partial response (at 3-month follow-up)[7]
- EBRT modality breakdown (Table 11) and fraction number from a subset (n=**redacted** cases) of the GenesisCare dataset that excluded tumour types that are not suitable for Re-188 brachytherapy (based on histology and staging data) and excluded treatment intent other than curative/radical
- retreatment of all non-responders with EBRT
- management of all Grade 3 and Grade 4 AEs
- 22% Re-188 carpoule wastage (consistent with ADAR wastage assumption).

Table 11 Comparator EBRT modalities used in ADAR base case versus commentary alternative scenario

EBRT modality	Description	ADAR base case[a]	Commentary alternative scenario[b]
Electrons	No CT scan	0.0%	0.0%
	CT scan: Clinical markup	15.4%	13.3%
	CT scan: CTV/PTV & OARs marked & DVH produced	29.6%	25.6%
Photons	CT scan: Clinical markup	0.3%	0.1%
	CT scan: CTV/PTV & OARs marked & DVH produced	0.3%	0.1%
IMRT/VMAT	CT scan: CTV/PTV & OARs marked & DVH produced, no motion management	49.9%	55.3%
SXRT	Single fraction	1.9%	2.3%
	Single fraction with eye shielding	0.0%	0.0%
	Multiple fractions	2.6%	3.2%
	Multiple fractions with eye shielding	0.1%	0.1%

CT = computed tomography; CTV = clinical target volume; DVH = dose volume histogram; EBRT = external beam radiation therapy; IMRT/VMAT= intensity modulated radiation therapy/volumetric modulated arc therapy (megavoltage); OAR = organs at risk; PTV = planned target volume; SXRT = superficial X-ray radiation therapy (kilovoltage).
a Based on GenesisCare dataset with **redacted** patients.
b Based on GenesisCare commentary refined dataset with **redacted** patients.
Note: GenesisCare data for each modality have been adjusted by the specific technique usage from the advisory board clinician survey.
Source: Commentary Table 8 of MSAC 1657.1 ADAR + in-line commentary.

The CEA results from the commentary alternative scenario are shown in Table 12. Using a 12-month time horizon, Re-188 brachytherapy was found to be cost-saving compared with EBRT while achieving a similar response rate. Complete response rates after initial treatment were high for both modalities (>94%) and remained very high following EBRT retreatment (~97%), based on the assumption that retreated lesions respond similarly to those initially treated with EBRT – a premise that may not be clinically valid and is tested in sensitivity analysis.

[7] The ADAR used a weighted EBRT response rate based on data from Ferro 2015 (fair quality), Schulte 2005 (poor quality) and Tighe 2021 (poor quality). Schulte 2005 assessed response at 60 months and therefore included recurrence. The publication did not define partial response, which was derived from the following comment: "In 47 cases (3.7%) residual tumour could not be excluded at the end of the treatment." Tighe 2021 reported complete responders only at median 4 months follow-up.

Table 12 Results of the stepped economic analysis – commentary alternative scenario

Economic analysis steps	Re-188 brachytherapy	EBRT	Incremental
Cost per complete lesion removal (cost per complete responder)			
Step 1 – Study data only (no retreatment)			
Cost of treatment	$4,185.95	$6,511.62	-$2,325.67
Outcomes	0.941	0.968	-0.027
Cost per lesion removed – complete removal	$4,450.58	$6,728.67	-$2,278.09
Step 2 – Incorporating retreatment of non-responders			
Cost of treatment	$4,361.94	$6,511.62	-$2,149.68
Outcomes	0.967	0.968	-0.001
Cost per lesion removed – complete removal	**$4,512.22**	**$6,728.67**	**-$2,216.46**
Cost per partial/complete lesion removal (cost per partial or complete responder)			
Step 1 – Study data only (no retreatment)			
Cost of treatment	$4,185.95	$6,511.62	-$2,325.67
Outcomes	0.973	1.000	-0.027
Cost per lesion removed – complete removal	$4,302.23	$6,511.62	-$2,209.39
Step 2 – Incorporating retreatment of non-responders			
Cost of treatment	$4,361.94	$6,511.62	-$2,149.68
Outcomes	1.000	1.000	0.000
Cost per lesion removed – complete removal	$4,361.94	$6,511.62	-$2,149.68

EBRT = external beam radiation therapy; Re-188 = Rhenium-188.
Source: Commentary Table 9 of MSAC 1657.1 ADAR + in-line commentary.

The alternative scenario used the best available evidence but had limitations:

- Response and AE data for Re-188 brachytherapy and EBRT came from single-arm studies with different follow-up periods.
- The 12-month time horizon aligned with follow-up duration available for the EPIC-Skin study but may be insufficient to capture recurrence events and late toxicity.
- EBRT response rates were sourced from Ferro et al. (2015), which examined short-course EBRT (6 fractions) using electron or photon beams – a regimen not reflective of current practice (per GenesisCare data).

A broad set of sensitivity analyses was conducted to address uncertainty in key parameters within the commentary's alternative scenario, focusing on the primary base-case outcome: cost per complete lesion removal.

Analyses explored variations in response rates, Grade ≥3 adverse event rates and associated costs, Re-188 carpoule wastage, EBRT fraction numbers, and EBRT modality distribution.

Re-188 brachytherapy remained cost-saving in nearly all analyses, except when:

- EBRT fraction count was reduced from 18 to the lower bound of 1 (based on the GenesisCare dataset)
- GenesisCare EBRT modality distribution was replaced with advisory board survey data for 4 of the 10 radiation oncologists who had access to SXRT (see Table 7)

- the weighted comparator was replaced with single-modality electrons only or SXRT only.

The economic advantage of Re-188 brachytherapy depends on using a weighted comparator that reflects real-world GenesisCare treatment patterns rather than a simplified single-modality assumption.

As expected, increasing EBRT fractions increased Re-188 brachytherapy savings, while reducing fractions lowered EBRT costs and Re-188 brachytherapy savings. For the weighted comparator, the break-even point for cost neutrality was 6–7 fractions.

Using the average number of fractions for each modality in the weighted comparator, rather than a uniform average of 18 fractions, increased the cost savings for Re-188 brachytherapy because the highest cost modality (IMRT/VMAT) also had the highest average fraction count (22).

Increasing carpoule wastage had a marked impact on the total cost of Re-188 brachytherapy. In a scenario assuming batching of 4 patients, each with a lesion surface area of <300 mm^2 (resulting in 64% carpoule wastage), treatment remained cost saving compared with EBRT, but only by $147. The break-even point for cost neutrality was reached at approximately 67% carpoule wastage (i.e. 33% carpoule utilisation), which equates to treating only 2 patients – one with a lesion measuring 0–300 mm^2 and another with a lesion measuring 501–700 mm^2.

Table 13 Sensitivity analyses on the commentary alternative scenario

Analysis	Incremental cost	Incremental outcomes	Incremental cost per complete lesion removal	Difference from base case
Base case	**-$2,149.68**	**-0.001**	**-$2,216.46**	**-**
Clinical outcomes				
Re-188 response rate (base case: 94.1% CR, 3.2% PR, 2.7% NR)				
No difference between groups (EPIC-Skin results applied to both groups)	-$2,325.67	0.000	-$2,407.62	-$191.17
Retreatment response rate (base case: 96.8% CR)				
70% (assumption)[a]	-$2,149.68	-0.008	-$2,182.43	$34.03
Grade 3+ AE rate (base case: 5.9% Re-188, 0% EBRT)				
0% (no Grade 3+ AEs for either modality)	-$2,162.81	-0.001	-$2,230.04	-$13.59
Costs				
Re-188 Grade 3+ AE treatment cost (base case: $13.13)				
Hospitalisation for Grade 4 AEs ($171.14)[b]	-$1,991.67	-0.001	-$2,053.01	$163.45
Re-188 carpoule wastage (base case: 22%)				
0% (no wastage, 100% carpoule utilisation)	-$3,188.98	-0.001	-$3,291.56	-$1,075.11
35% (65% carpoule utilisation)	-$1,526.48	-0.001	-$1,571.79	$644.67
64% (assumed 4 patients with 0–300 mm^2 lesions, median 225 mm^2)	-$148.98	-0.001	-$146.83	$2,069.63
Source of EBRT modality breakdown (base case: GenesisCare, n=**redacted** patients)				
GenesisCare – BCC only (n= **redacted**)[c]	-$1,469.83	-0.001	-$1,513.97	$702.49
GenesisCare – SCC only (n= **redacted**)[c]	-$2,541.30	-0.001	-$2,621.12	-$404.66
Ad Board survey, all respondents (n=10)	-$1,230.91	-0.001	-$1,267.09	$949.37
Ad Board survey, access to SXRT (n=4)	$203.39	-0.001	$214.97	$2,431.43
Mean no. of EBRT fractions (base case: 18)				
Lower limit 1 fraction (GenesisCare)	$1,131.43	-0.001	$1,173.92	$3,390.38
Upper limit 34 fractions (GenesisCare)	-$5,237.78	-0.001	-$5,407.40	-$3,190.95
Fractions adjusted for EBRT modality – Electrons 15, Photons 18, IMRT/VMAT 22, SXRT 16 (GenesisCare n= **redacted**)	-$2,649.17	-0.001	-$2,732.58	-$516.12
Single unweighted EBRT comparator[d]				
Electrons only – 15 fractions	$1,385.54	-0.001	$1,436.49	$3,652.95
Photons only – 18 fractions	-$474.30	-0.001	-$485.28	$1,731.18
IMRT/VMAT only – 22 fractions	-$6,044.18	-0.001	-$6,240.65	-$4,024.20
SXRT only – 16 fractions	$2,764.91	-0.001	$2,861.80	$5,078.25

AE = adverse event; BCC = basal cell carcinoma; CR = complete response; EBRT = external beam radiation therapy; IMRT/VMAT = intensity-modulated radiation therapy / volumetric modulated arc therapy; NR = non-responder; PR = partial response; Re-188 = Rhenium-188 brachytherapy; SCC = squamous cell carcinoma; SXRT = superficial X-ray radiation therapy.
a Assumes retreatment may not be as effective as initial treatment. This applies to Re-188 brachytherapy only because there were no non-responders to initial EBRT.
b Assumes treatment/hospitalisation cost of $15,000 for 2/187 (1.1%) patients who had Grade 4 AEs and $222.60 for 9/187 (4.8%) patients who had Grade 3 AEs.
c Analysis does not account for response rates by lesion type, as EBRT results from Ferro et al. (2015) were not reported separately for BCCs and SCCs. EPIC-Skin reported similar complete response rates for BCCs and SCCs (93.9% versus 94.6%).
d Analyses incorporate costs and mean fractions for single modalities instead of assuming a weighted comparator.
Source: Commentary Table 11 of MSAC 1657.1 ADAR + in-line commentary.

Cost-consequence analysis

The ADAR assumed a travel cost of $10 per trip, with one trip for Re-188 brachytherapy and 18 trips for EBRT. The commentary noted this cost estimate is likely too low, as it excludes long-distance travel and accommodation expenses. Instead, the commentary applied Modified Monash categories and Australian Taxation Office (ATO) travel rates, also incorporating one night's accommodation for some remote patients. Using this approach, the estimated average cost was $79.20 for travel alone and $85.05 when accommodation was included, weighted by residential location. These figures may still underestimate costs if Re-188 brachytherapy is only available in metropolitan areas.

While MSAC based its advice on the CCA results that exclude productivity losses, MSAC noted the ADAR assumed productivity losses of $208.32 per treatment, based on half a day off work. The commentary noted that this estimate was likely overstated, as more than half of EPIC-Skin participants were aged 70 or older and likely retired. For those still in the workforce, however, assuming only half a day off per treatment may underestimate losses for rural patients, where a full day per treatment could be more realistic. Time lost for managing adverse events was not considered.

Cosmesis outcomes were calculated as weighted averages across studies, but the commentary noted variability in evaluation timepoints and reliance on patient-reported outcomes, often without standardised scales.

The results of the CCA, incorporating commentary adjustments, are shown in Table 14.

Table 14 Results of the commentary cost-consequence analysis

Costs and outcomes	Re-188 brachytherapy	EBRT	Incremental
Costs			
Treatment (cost per partial or complete lesion removal)	$4,361.94	$6,511.62	-$2,149.68
Travel[a]	$85.05	$1,530.90	-$1,445.85
Productivity loss[b]	$185.82	$3,344.79	-$3,158.97
Outcomes			
Treatment			
Complete lesion removal	0.967	0.968	-0.001
Partial lesion removal	1.000	1.000	0.000
Adverse events			
All Grade 3+ events	0.059	0.000	0.059
Cosmesis[c]			
Poor	0.038	0.018	0.020
Acceptable	0.126	0.005	0.121
Good	0.404	0.333	0.071
Excellent	0.432	0.644	-0.212

EBRT = external beam radiation therapy; Re-188 = Rhenium-188.
a Estimate per treatment assumes combined travel and accommodation costs of $13.20 for individuals living in metropolitan areas and regional centres (representing 80% of the population), $264.00 for those in large and medium rural towns (11%), and $505.00 for residents of small rural towns and remote or very remote communities (9%).
b Estimate assumes an average daily earning loss of $416.64 for 44.6% of patients who are in the workforce.
c Based on weighted average results from all studies with clinician-reported cosmesis outcomes. The ADAR incorporated patient scores.
Source: Commentary Table 10 of MSAC 1657.1 ADAR + in-line commentary.

MSAC noted the commentary's alternative scenario and sensitivity analyses generally indicate Re-188 brachytherapy is cost-saving compared with EBRT, these findings should be interpreted with caution. The economic model relies on limited and heterogeneous clinical evidence, and EBRT cost estimates are subject to uncertainty. GenesisCare data suggest that EBRT for NMSC is predominantly (86.0% of cases) delivered using Linac-based, highly fractionated regimens (megavoltage EBRT), which increases costs. However, when kilovoltage SXRT is available, it is sometimes preferred over other EBRT modalities for NMSC, which lowers overall EBRT costs and reduces the cost advantage of Re-188 brachytherapy.

14. Financial/budgetary impacts

A market share approach was again applied in the resubmission to estimate the expected uptake of the proposed technology. The market share was derived from the utilisation of EBRT modalities most commonly employed in the treatment of NMSC, namely electron therapy, IMRT and SXRT. Re-188 brachytherapy is not expected to increase the overall number of NMSC cases treated following MBS listing; rather, it is anticipated to substitute for existing MBS-listed services.

The size of the current EBRT market was estimated by applying GenesisCare data to MBS utilisation figures. This approach was necessary because EBRT is used to treat a wide range of cancers, and disease-specific granularity is not available within MBS item descriptors, making it difficult to isolate services for NMSC. The commentary noted inconsistencies in the description of the GenesisCare dataset and indicated that the data could not be independently verified, introducing uncertainty into the estimates. The sponsor previously sought additional information from Services Australia regarding radiation therapy usage patterns; however, they were advised that data relating to diagnosis or ICD-10 codes could not be provided for MBS item numbers.

Table 15 summarises the key assumptions used in the utilisation and financial estimates.

Table 15 Data sources and parameter values applied in the utilisation and financial estimates

Data	Value/input	Source and justification
Size of the current comparator market	MBS services for 2018-2023[a] by EBRT modality	Medicare Australia Statistics for relevant EBRT simulation/dosimetry items.
EBRT average annual growth rate	Electrons – 10% IMRT – 6% SXRT – 0%	MBS services data (7 simulation items only) from 2018 to 2023[a]; logarithmic equation. Relates to all use of each EBRT modality, not specific to NMSC.
Average rate of replacement/ substitution of EBRT by Re-188 brachytherapy – base case	Electrons – 17.7% IMRT – 9.7% SXRT – 4.7%	Switch rates from advisory board clinician survey (10 radiation oncologists) based on 8 vignettes. Gradual replacement of EBRT market assumed, reaching switch rates by Year 6.
Maximal rate of replacement/ substitution of EBRT by Re-188 brachytherapy – sensitivity analysis	Electrons – 30% IMRT – 40% SXRT – 25%	Advisory board clinician survey (10 radiation oncologists) – highest of the individual responses. Gradual replacement of EBRT market assumed, reaching switch rates by Year 6.
Proportion of EBRT MBS services used to treat Re-188 eligible NMSCs	Electrons – 69% IMRT – 7% SXRT – 82%	GenesisCare dataset of **redacted** NMSC cases from total **redacted** cases collected over a 12-month period from July 2022 to June 2023.
Average number of EBRT fractions per NMSC patient	18	GenesisCare dataset used for the economic analysis (**redacted** NMSC cases).
Treatment costs for Re-188 brachytherapy	Proposed fees for 5 new MBS items	Assumed 1 planning item per treatment item. Does not incorporate wastage.
Relative usage of proposed MBS items for Re-188 brachytherapy by treatment area band	0–300 mm^2 – 60.4% 301–500 mm^2 – 21.9% 501–700 mm^2 – 14.2% 701–800 mm^2 – 3.6%	Utilisation weighted by proportion of lesions in each treatment area band taken from EPIC-Skin.
Treatment costs for EBRT	Fees for current MBS items for planning and treatment	Historical MBS items for electron therapy, IMRT and SXRT translated to MBS items and fees starting July 2024.

EBRT = external beam radiation therapy; IMRT = intensity modulated radiation therapy (megavoltage); MBS = Medicare Benefits Schedule; NMSC = non-melanoma skin cancer; Re-188 = Rhenium-188; SXRT = superficial X-ray radiation therapy (kilovoltage).
a Services data from the 2024 calendar year were considered unreliable because the entire MBS item code structure for all radiation therapy services were revised in July 2024.
Source: Derived from Table 51 of MSAC 1657.1 ADAR + in-line commentary.

The commentary noted that switching and uptake of Re-188 brachytherapy may exceed advisory board projections due to patient-centred factors such as the convenience of a single treatment visit, reduced travel-related costs, and perceived benefits in terms of time efficiency and productivity. The overall switch rate among the 4 radiation oncologists with access to SXRT was comparable to the average across all survey participants (26.8% for those with SXRT access versus 32.1% across all 10 radiation oncologists); however, the switch rate varied by modality.

The financial implications to the MBS resulting from the proposed listing of Re-188 brachytherapy are summarised in Table 16. Calculation of MBS costs were based on the 85% benefit incorporating the greatest permissible gap (GPG). The ADAR acknowledged that the financial impact may be underestimated due to the exclusion of out-of-pocket costs and the potential effect of the Extended Medicare Safety Net (EMSN).

Table 16 Net financial implications of Re-188 brachytherapy to the MBS

Parameter	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030	Year 2031
Estimated use and cost of the proposed health technology						
Total number of services of Re-188 brachytherapy	800	921	1,542	2,158	2,573	3,104
Planning	400	460	771	1,079	1,286	1,552
Treatment: 0–300 mm^2	242	278	465	651	776	937
Treatment: 301–500 mm^2	88	101	169	236	282	340
Treatment: 501–700 mm^2	57	65	109	153	183	220
Treatment: 701–800 mm^2	14	16	27	38	46	55
Total cost to the MBS	$1,200,363	$1,380,949	$2,312,307	$3,237,516	$3,858,674	$4,655,157
Change in use and cost of other health technologies						
Change in use of number of services of EBRT	7,603	8,747	14,645	20,505	24,440	29,484
Simulation/dosimetry	400	460	771	1,079	1,286	1,552
Treatment	7,203	8,286	13,875	19,426	23,153	27,933
Net change in costs to the MBS	-$1,778,486	-$1,955,056	-$4,025,594	-$5,977,986	-$6,743,789	-$8,682,116
Net financial impact to the MBS	**-$578,123**	**-$574,107**	**-$1,713,288**	**-$2,740,470**	**-$2,885,115**	**-$4,026,959**

EBRT = external beam radiation therapy; MBS = Medicare Benefits Schedule; Re-188 = Rhenium-188.
Note: Costs incorporate 85% benefit with greatest permissible gap (GPG).
Source: Tables 52, 53, 54 and 58 of MSAC 1657.1 ADAR + in-line commentary.

The ADAR stated that listing Re-188 brachytherapy on the MBS is not expected to impact other health budgets during the first 6 years of implementation. However, the commentary noted that costs associated with non-isotope-related consumables – such as protective film, nose and ear plugs, patient protection underpads, and waste collection bags and disposal containers – which were previously included in the proposed MBS fees for Re-188 brachytherapy, are not accounted for in the financial analyses and would represent an additional cost to treatment clinics.

Furthermore, the financial analysis does not consider costs beyond the initial treatment. In the EPIC-Skin Study, Grade 3 adverse events occurred in 4.8% of patients and Grade 4 events in 1.1% within 12 months of treatment. Grade 3 events typically require outpatient management, including wound care, infection control, pain relief, and possible specialist referral. Grade 4 events necessitate urgent hospital-based, multidisciplinary care, often involving surgical intervention (e.g. debridement, grafting) and inpatient treatment, resulting in significantly higher costs. However, the Grade 4 events only occurred in 1.1% of patients at 12-months follow-up.

Re-188 brachytherapy wastage has also not been considered in the financial estimates. However, this omission does not affect MBS costs. If treatment is delivered in a public hospital, costs associated with carpoule wastage are likely to be absorbed by state or territory health budgets. Conversely, if treatment is provided in a private hospital, wastage costs may be passed on to patients.

Finally, because Re-188 brachytherapy involves a single treatment session rather than multiple EBRT fractions, it offers potential cost savings for patients and for state-funded patient travel budgets.

The commentary noted that the vignettes did not clearly describe patients who decline or are unsuitable for surgery and for whom EBRT is not feasible or practical, making the switching rate assumptions unlikely to reflect restrictions limiting Re-188 brachytherapy to such patients. If MBS access is confined to this subset, the actual number of Re-188 brachytherapy services delivered would be lower than current estimates.

Table 17 summarises the sensitivity analyses presented in the ADAR, which examined variations in the rate of EBRT replacement/substitution and the average number of EBRT fractions per patient. The commentary conducted an additional sensitivity analysis using switching rates reported by the 4 radiation oncologists with access to SXRT, assuming gradual uptake through Year 6 (consistent with ADAR assumptions). Under this scenario, cost savings associated with Re-188 brachytherapy were substantially reduced due to minimal displacement of IMRT.

Table 17 Results of sensitivity analysis for net financial impact of Re-188 brachytherapy to the MBS

Parameter	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030	Year 2031
Base case	-$578,123	-$574,107	-$1,713,288	-$2,740,470	-$2,885,115	-$4,026,959
EBRT displacement						
Maximum from Ad Board survey[a]	-$1,508,671	-$3,191,811	-$6,873,916	-$11,044,181	-$13,658,331	-$16,588,770
Ad Board with access to SXRT[b]	$5,901	-$5,133	-$33,605	-$80,209	-$145,828	-$248,205
EBRT fractions						
22	-$780,001	-$797,348	-$2,171,659	-$3,423,012	-$3,654,210	-$5,017,769
5	$77,979	$151,426	-$223,581	-$522,209	-$385,556	-$806,828

EBRT = external beam radiation therapy; MBS = Medicare Benefits Schedule; SXRT = superficial X-ray radiation therapy (kilovoltage).
a Switching rates: electron therapy 30%, IMRT 40%, SXRT 25%.
b Switching rates: electron therapy 13.3%, IMRT 1.8%, SXRT 11.8%.
Source: Tables 60 and 61 of MSAC 1657.1 ADAR + in-line commentary.

15. Other relevant information

MSAC has previously noted that the half-life of Re-188 (approximately 17 hours) requires timely batching of patients. This characteristic may constrain service locations to those reasonably close to the radiopharmaceutical production facilities, which may create access challenges in regional or remote areas. The applicant previously stated that established infrastructure already supports Re-188 clinics nationally and internationally, and licensed Australian centres handling radioisotopes can be serviced reliably. The current ADAR further clarified that the carpoule must be used within an hour of opening. There is no storage. The carpoule has a 17-hour half-life and also dries out 1-2 hours after opening, implying decay timing is related to carpoule opening. Confirmation by the applicant of the decay time of the carpoule from production as described in the Rhenium-SCT Technical Safety Dossier would be useful to confirm the half-life of the Re-188 carpoule.

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Clinical issues:

- Patient population – The EPIC study excluded patients who had received previous treatment (surgery or EBRT) for their lesion(s). However, other studies identified by the commentary have included patients with lesions that had been previously treated, with response rates similar to those reported in the EPIC study. MSAC may wish to consider the effectiveness and safety in patients with previously treated lesions; alternatively, if restricting the patient population to those with no previous treatment, then 'previous treatment' should be clearly defined.
- Referral pathway – ESC noted several issues with specifying the referrer as a 'dermatologist, plastic surgeon or skin-specialist GP', in terms of limited access to those specialties and difficulties defining a 'skin-specialist GP'. In addition, MSAC may also wish to consider the involvement of a multidisciplinary team in line with current radiation therapy guidelines, ensuring that the policy and cost implications of this are covered.

Economic issues:

- Comparator dataset and time horizon used in model – ESC noted several limitations in the GenesisCare dataset used to populate the EBRT arm of the model, and residual uncertainty regarding population alignment, but considered that this was the best available real-world data.
- Variation in EBRT modality used for the comparator and the characteristics of eligible lesions reduced confidence in the economic analysis and introduced uncertainty regarding the extent to which Re-188 brachytherapy would substitute for EBRT in clinical practice. ESC noted there was a risk that no substitution of EBRT may occur and this was not reflected in the economic analysis.
- Costs for EBRT vary widely in the model due to EBRT modality mix and the number of EBRT fractions. ESC noted that cost neutrality was reached at 6 to 7 fractions of EBRT. ESC assumed that, as most eligible non-melanoma lesions would likely require more than 7 fractions of EBRT (typically 18 to 20 fractions as seen in the GenesisCare dataset), it was likely that Re-188 therapy would be cost-saving under current practice assumptions.
- Clarification from the applicant would be useful around whether patients are required to attend additional mandatory visits with the referring clinician prior to Re-188 treatment for 'lesion mark-up'. If required, these visits have not been included in the economic or financial analyses and may incur additional costs.

Financial issues:

- Substitution rate – Projected cost savings in the financial analysis are driven by Re-188 brachytherapy substituting for EBRT in eligible patients – that is, patients must be candidates for EBRT for those cost savings to be realised. ESC considered there was a risk that some cost offsets from Re-188 brachytherapy may not be realised if Re-188 brachytherapy increased demand, as some EBRT eligible patients may have otherwise opted for no treatment due to factors related to preference or treatment burden.

ESC Discussion

ESC noted this was a resubmission from Oncobeta Therapeutics requesting Medicare Benefits Schedule (MBS) listing of rhenium-188 (Re-188) brachytherapy as an alternative to external beam radiation therapy (EBRT) for treatment of patients with non-melanoma skin cancer (NMSC)

who are not suitable for surgery. MSAC had previously considered this application at its July 2023 and April 2025 meetings.

At the April 2025 meeting, MSAC deferred advice on public funding for Re-188 brachytherapy in cases where surgery is not indicated. MSAC noted the absence of consensus on the standard of care comparator, and the limited comparative safety and effectiveness data available to support the economic model. MSAC considered that, despite the low-certainty evidence, Re-188 brachytherapy is likely to have a clinical role for a defined subset of patients. MSAC advised that a resubmission should address key outstanding issues, including:

- clearer definition of the target patient population, detailing those most likely to benefit, and with explicit description of patient and lesion factors
- additional information and justification for the proposed MBS items, covering costs for the Re-188 compound, waste disposal, consumables and clinician time to ensure fees reflect actual service delivery
- further economic analysis, such as cost per treatment success and/or cost per lesion, including consideration of risks and costs associated with managing adverse events from Re-188 brachytherapy.

ESC noted the consultation input received for this ESC meeting from one individual and one organisation, as well as the input from Oncobeta's consumer advisory board that was included in the applicant-developed assessment report (ADAR). Consumer comments indicated a preference for Re-188 brachytherapy, particularly in relation to the reduced number of visits required and the reduced burden of care. ESC noted that concerns raised in consultation feedback related to the costs of safe disposal of radioactive waste from the treatment were also discussed at PASC. No additional information regarding disposal was provided in the current ADAR.

ESC noted that the applicant's pre-ESC response included updated preliminary 24-month follow-up results from the EPIC-Skin study, the pivotal trial, showing a complete response rate of 94.7% across all tumours. ESC noted this 24-month follow-up data from the EPIC-Skin study indicated a reduction in adverse events at 24 months compared with 12 months, no late toxicities or cosmesis issues, and improved subjective measures of cosmetic appearance.

ESC considered that MSAC's request to clarify the target patient population and lesion characteristics had been partially addressed in the resubmission. ESC noted the proposed lesion characteristics that would determine eligibility for Re-188 brachytherapy were restricted to those lesions which had not previously been treated with surgery or EBRT, lesions without high-risk features, and lesions located on cosmetically or functionally sensitive sites. However, ESC considered that the available evidence was limited in its ability to support exclusion based on prior treatment status. ESC noted that, while the EPIC-Skin study excluded patients with prior surgery or EBRT treatment, other evidence considered by the commentary included patients with previously treated lesions. This evidence, including, the meta-analysis[8] provided in the pre-ESC response and the Chessa et al.[9] study identified by the commentary, reported response rates similar to those reported in the EPIC-Skin study. ESC considered this relevant when determining the appropriate positioning of Re-188 brachytherapy within the Australian clinical context and the potential eligible population. If patients with lesions that had received prior treatment are to be excluded from Re-188 brachytherapy, ESC considered that 'previous treatment' should be clearly

[8] Sadeghpour et al. (2025) Targeted *β*-therapy with rhenium-aided therapy for cutaneous lesions: a systematic review and meta-analysis. *Front. Med.*12:1707729. Doi: 10.3389/fmed.2025.1707729

[9] Chessa MA, Baraldi C, Savoia F, Maltoni L, Clarizio G, Filippi F, Piraccini B, Dika E, Pitino A, Tripepi G, Zagni F, Strigari L, Vetrone L, Fanti S and Castellucci P (2025) 'Unsealed188 rhenium resin brachytherapy in non-surgical candidates with refractory basal cell carcinoma: Clinical outcomes', *Dermatol Pract Concept*, 15(2):4993, doi:10.5826/dpc.1502a4933

defined (for example, surgery, EBRT, cryotherapy, topical agents (e.g. imiquimod)). ESC considered that additional eligibility criteria (such as absolute or relative contraindications including locally advanced or metastatic disease, bony involvement, and others listed in the ADAR) could be included in an explanatory note to the MBS item. ESC raised concerns regarding the appropriateness of the proposed eligibility criteria including patients who declined surgery. ESC considered inclusion of patients who declined surgery could impact estimates for uptake and utilisation.

ESC noted the proposed separate MBS item descriptors for planning and treatment based on lesion size. For the planning item, ESC noted that the lesion and patient factors that affect eligibility for Re-188 brachytherapy were not fully specified in the item descriptor. The ADAR proposed that activities contributing to treatment planning could be undertaken by both the referring clinician (through lesion mark-up) and the treating physician (through formal treatment planning prior the Re-188 brachytherapy application), and that reimbursement for the planning item would be shared between the referrer and the treating physician accordingly. However, ESC noted advice from the department that a single MBS item cannot be split between clinicians. ESC considered that confirmation from the applicant would be useful regarding the role of the referrer in lesion mark-up and the distinction between identifying appropriate lesions (which may be undertaken by the referring clinician and is covered by existing MBS items) and more involved treatment planning undertaken by a radiation oncologist (which would be covered by the proposed planning item). If these additional mandatory visits to the referring clinician are required prior to Re-188 brachytherapy, ESC noted these activities and costs have not been included in the economic or financial analyses. ESC also supported the department's proposed change to the planning item to be 'applicable once per treatment session', as a single planning session could cover multiple lesions that would be treated in a single treatment session from the same carpoule.

ESC noted the proposed MBS item descriptors for the treatment items, which specify that the service must be referred by a dermatologist, plastic surgeon, or a skin-specialist GP if a dermatologist or plastic surgeon is not readily available. ESC noted that there were no specific qualifications to define a 'skin-specialist GP', and also that it would be challenging to limit GP referral to areas where dermatologists or plastic surgeons are unavailable. In addition, requiring the referring practitioner to be a dermatologist or plastic surgeon may lead to inequitable access, even in metropolitan areas. ESC noted it was unclear if 'skin-specialist GPs' can refer a patient directly to a radiation oncologist or if they must first refer the patient to a dermatologist. ESC also noted that the current EviQ guidelines for EBRT in these patients recommend involving a multidisciplinary team (MDT) where appropriate. ESC suggested that MSAC may wish to consider whether similar guidance is warranted for Re-188 brachytherapy, noting that MDT review is not mandated under EviQ guidelines and accessing an MDT may potentially delay treatment.

ESC supported the department's proposed addition to the treatment MBS item descriptor of 'applicable once per lesion per lifetime'.

Noting the uncertainties raised in the commentary regarding the location and number of treatment delivery sites and how this may affect equity of access for rural and remote patients, ESC requested clarification from the applicant for MSAC consideration regarding whether treatment would be limited to existing sites if Re-188 brachytherapy was supported and also what considerations are needed for setting up additional treatment sites. ESC noted that travel costs had been included in the resubmission for both EBRT and Re-188 brachytherapy, however ESC considered the assumed travel cost of $10 per trip was likely to be underestimated. In addition, ESC noted that productivity costs were included in the resubmission's cost-consequence analysis and the incorporation of productivity changes in the model was inconsistent with the MSAC Guidelines, which state that productivity changes may be included in

a supplementary analysis but should not be included in the base case, and when included should address the three underpinning assumptions in Appendix 10 of the MSAC Guidelines.

Regarding wastage, ESC noted that 22% wastage had been included in the base case and the commentary investigated alternative scenarios in the economic evaluation. ESC noted that sensitivity analysis demonstrated cost neutrality would be reached at 67% wastage. However, ESC noted that wastage and non-attendance had not been included in the financial impacts. ESC noted the wastage and batching issues had been extensively discussed at previous ESC and MSAC meetings. ESC noted the pre-ESC response that the wastage risk and batching issues would be borne by clinics and would not be passed onto patients. ESC did not consider it necessary to revisit wastage assumptions in the financial analysis prior to MSAC consideration.

ESC noted the economic evaluation, which was a cost-effectiveness analysis and cost-consequences analysis comparing Re-188 brachytherapy with EBRT, as requested by MSAC. The base case indicated that Re-188 brachytherapy was dominant, and this remained the case in a range of sensitivity analyses.

ESC noted that the economic evaluation assumed that Re-188 brachytherapy would substitute for EBRT in eligible patients, and that uncertainty regarding the real-world substitution rate for EBRT may introduce additional uncertainty into the economic results.

ESC noted that the model results were highly sensitive to assumptions regarding the EBRT comparator, particularly the EBRT modality mix and the number of fractions delivered. ESC noted that cost savings decreased as the number of EBRT fractions declined. ESC agreed with the commentary that Re-188 brachytherapy was cost-saving in most scenarios except when the weighted comparator was replaced with single-modality electrons only or superficial X-Ray (SXRT), which did not reflect the variation in real-world treatment patterns seen in the GenesisCare dataset, or where SXRT was more frequently utilised. ESC advised MSAC that where SXRT is more commonly used, such as in the public sector, the cost advantage of Re-188 brachytherapy would likely be reduced, and in extreme low-fraction scenarios, may be lost.

ESC noted that, within the limits of the data available, cost neutrality was reached at 6 to 7 fractions of EBRT, and therefore, ESC considered that Re-188 brachytherapy was likely to be cost-saving in clinical contexts where EBRT fractionation exceeds this threshold, and noted that most non-melanoma lesions would require more than 7 fractions of EBRT (typically 18 to 20 fractions as seen in the GenesisCare dataset).

ESC considered that the model inputs from the EPIC study and GenesisCare data with a 12-month time horizon, although limited, were the best available data sources. However, ESC noted the residual uncertainty regarding population alignment and suggested that MSAC may wish to consider restricting the MBS item descriptor to clearly defined lesion characteristics consistent with the evidence base. ESC noted the preliminary 24-month EPIC study results did not suggest a material change in the clinical evidence previously considered by MSAC.

ESC noted that the base-case model assumed that non-responders are re-treated with the same modality in both Re-188 brachytherapy or EBRT arms and there are no adverse events from retreatment. ESC considered that this assumption may lack clinical validity, noting that this assumption was also inconsistent with the proposed MBS restriction that lesions must not have been treated prior to Re-188 brachytherapy. ESC noted the commentary tested alternative retreatment pathways and adverse event assumptions, and the cost-saving results were robust to those changes. ESC noted the residual uncertainty in health outcomes given the absence of robust data to validate model parameters but did not consider them to be a major driver of the economic results.

ESC noted the financial and budgetary impact analysis applied a market share approach, given EBRT is currently MBS-listed, and projected net cost savings to the MBS in the base case of $578,123 in year 1 through to $4,026,959 in year 6. ESC considered that short-term cost savings were likely but noted that longer-term financial impacts remained uncertain and were sensitive to assumptions regarding EBRT displacement rates, average EBRT fractions, and the weighted average cost per course of treatment.

ESC noted that costs for managing adverse events were included in the economic analysis but not in the financial analysis. ESC considered that adverse event management costs in the economic analysis were likely to be underestimated, particularly for severe (Grade 4) adverse events that may require hospital-based care rather than management within a single GP consultation and topical agents. However, ESC noted that the commentary sensitivity analyses, which incorporated the costs of managing Grade 4 adverse events, demonstrated that these costs were small and did not materially affect the economic conclusions.

ESC noted that the projected cost savings in the financial analysis were driven by Re-188 brachytherapy substituting for EBRT – that is, patients would need to be candidates for EBRT for cost savings to be realised. ESC considered there was residual uncertainty related to the uptake of Re-188 brachytherapy due to underestimation of patient preference and to the real-world substitution rate for EBRT. ESC considered there was a risk that some cost offsets from Re-188 brachytherapy may not be realised as some EBRT eligible patients may have otherwise opted for no treatment due to factors related to preference or treatment burden.

17. Applicant comments on MSAC's Public Summary Document

OncoBeta welcomes the MSAC's recommendation to support the MBS listing of Rhenium-188 therapy. We are deeply committed to the evidence-based implementation of this therapy. OncoBeta looks forward to working collaboratively with clinical teams across Australia to ensure eligible patients can access this treatment in an efficient and affordable way.

18. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website