Australian Government

Department of Health

Application 1657

Rhenium-188 brachytherapy for non-melanoma skin cancer

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant): Oncobeta Therapeutics Australia Pty Ltd
Corporation name: OncoBeta GmbH (Germany)
ABN: Not applicable
Business trading name: OncoBeta®

Primary contact name: REDACTED

Primary contact numbers
Business: **REDACTED**
Mobile: **REDACTED**
Email: **REDACTED**

Alternative contact name: REDACTED

Alternative contact numbers
Business: **REDACTED**
Mobile: **REDACTED**
Email: **REDACTED**

2. (a) Are you a consultant acting on behalf of an Applicant?

☒ Yes
☐ No

3. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☐ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

4. Application title

Rhenium-188 brachytherapy for non-melanoma skin cancer

5. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Non-melanoma skin cancer (NMSC), also known as keratinocyte cancer, includes basal cell carcinoma (BCC) squamous cell carcinoma (SCC) and various other less common lesions. NMSC is the most common form of cancer in Australia, with almost one million cases being diagnosed and treated each year. Although rarely fatal, treatment of NMSC represents a major cost burden to the health system, accounting for around 8% of total spending on cancer treatment and more than $700 million of expenditure through the MBS. The most common cause of NMSC is sun exposure, while other predisposing factors include genetic skin conditions and immunosuppressive diseases or treatments. Although a range of definitive treatment options is currently available in Australia (and funded through the MBS) these are subject to various limitations of effectiveness, safety, tolerability, and acceptability. New, non-invasive, non-scarring treatment options that can be delivered quickly in an outpatient setting would represent a significant improvement in the standard of care.

6. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

The proposed service is a novel form of brachytherapy for NMSC, which uses the Beta emitter radioisotope Rhenium-188. During treatment, the affected area of the skin is covered with the sterile protective foil. The Rhenium-188 is then applied in a matrix on the foil using a special applicator device. The irradiation time required to achieve the desired target dose at the defined penetration depth is calculated based on the radioactivity of the substance being applied and the surface area to be treated. After the calculated irradiation time, the matrix is removed by pulling the foil from the skin. The procedure is highly effective, while also non-invasive, painless, and non-scarring. It can be provided without anaesthesia, over a short period of time in an outpatient setting. As such, the service offers multiple practical, economic, and patient relevant benefits over existing management options, especially surgical removal of larger lesions. It is significant that treatment with Rhenium-188 Brachytherapy will have a positive impact on the quality of life of patients being treated. The reduced scarring and healing time mean patients can return to life sooner than would be expected for a surgical treatment.

7. (a) Is this a request for MBS funding?

☒ Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☐ Amendment to existing MBS item(s)
☒ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

N/A

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

N/A

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☒ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

(g) If yes, please advise:

However, it is anticipated that other public funding would be used in some institutions/instances for the purchase of capital equipment required to provide the service.

8. What is the type of service:

☒ Therapeutic medical service
☐ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☐ Co-dependent technology
☐ Hybrid health technology

9. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

N/A

10. Does your service rely on another medical product to achieve or to enhance its intended effect?

☐ Pharmaceutical / Biological
☐ Prosthesis or device
☒ No

11. If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

N/A

12. If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

N/A

13. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables: The main (and active) single use consumable is the Rhenium-188 compound; a paste that contains radioactive particles in a viscous polymeric matrix. This is supplied in a "Carpoule"; a single use unit comprising a reservoir for the compound, and various other components necessary for its safe application. The compound is applied on to a special protective foil that has been applied over the area needed to treat so that the radioactive compound never comes in direct contact with the skin. This enables an application to several lesions on several patients of up to a total area of 25cm2 per Carpoule. The special protective foil that is also supplied are 15 x 20 cm sheets and may be cut to fit the contours of the area to be treated optimally (including a security margin). The sheets may also be applied overlapping with additional sheets (in the case of larger lesions). While all technically single use items, these can in practice be used to treat more than one patient during the same treatment session. Except for the foil, which is a generic item, these single-use consumables are all OncoBeta® proprietary items.

Multi-use consumables: Multi-use consumables required to provide the service include separate transport and logistics units which are used to safely transport up to five Carpoules of the Rhenium-188 compound. Suitable personal protective equipment must also be used, for both medical professionals and patients, including glasses/goggles, masks, aprons, gloves and mats, some of which will be singe-use and some more multi-use in nature. These additional consumables are all generic items.

Capital equipment: In addition to the single- and multi-use consumables outlined above, the service requires a proprietary OncoBeta® Base Station, Applicator and Measurement Station, and a suitable waste container for radioactive substances, of which the proprietary OncoBeta® Waste Station is an example.

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

14. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Type of therapeutic good: The service involves the use of a multi-component medical device, as described above. Additional detailed information on the device and its components can be provided upon request.
Manufacturer's name: OncoBeta GmbH
Sponsor's name: OncoBeta Therapeutics Australia Pty Ltd

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

☒ Class IIb
☐ AIMD
☐ N/A

15. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
☒ No

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

☒ Yes (if yes, please provide details below)

Rhenium-SCT was included on the ARTG on 9th December 2020 (Entry 351390).

Intended purpose: The Rhenium Skin Cancer Therapy (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 (2-3mm).

Specific conditions: This medical device ARTG inclusion is limited to some medical device of the kind. These devices of the kind are medical devices identified by the manufacturer as - Rhenium-188 paste for the treatment of skin cancer lesions and skin tumours. Other devices of the kind must not be supplied under this ARTG entry in Australia until and unless evidence of the application of appropriate conformity assessment procedure to those devices is provided and accepted by the TGA.

16. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

N/A

17. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

N/A

PART 4 – SUMMARY OF EVIDENCE

18. **Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study	Title / Identifier	Short description	Website link	Year
1.	Retrospective cohort study	Cipriani et al, 2020: Personalized irradiation therapy for NMSC by rhenium-188 skin cancer therapy: a long term retrospective study	Enrolled 52 patients with 55 confirmed NMSC lesions and included 12 months follow up. All lesions showed complete remission and no complications were reported.	pubmed.ncbi.nlm.nih.gov/32648530/	2020
2.	Prospective observational cohort study	Castellucci et al, 2021: High dose brachytherapy with non sealed 188 Re (rhenium) resin in patients with non-melanoma skin cancers (NMSCs): single center preliminary results	Enrolled 50 patients with 60 confirmed NMSC lesions and included 24 months follow up. At 1 year all lesions were free from relapse and at 2 years a single relapse had occurred. Reported side effects were early, mild and resolved.	pubmed.ncbi.nlm.nih.gov/33140131/	2021
3.	Retrospective cohort study	Carrozzo et al, 2014: Dermo Beta Brachytherapy with 188Re in extramammary Paget's disease	Enrolled 5 patients with EMPD and included 34 months of follow up. All lesions were healed after 1 or 2 treatment sessions. Reported side effects were early, mild and quickly resolved.	pubmed.ncbi.nlm.nih.gov/24566572/	2014
4.	Prospective observational cohort study	Carrozzo et al, 2013: Dermo beta brachytherapy with 188-Re in squamous cell carcinoma of the penis: a new therapy	Enrolled 15 patients with SCCP and included 51 months of follow up. Two patients (13%) did not respond to therapy.	pubmed.ncbi.nlm.nih.gov/23557628/	2013
5.	Prospective observational cohort study	Sedda et al, 2008: Dermatological high-dose-rate brachytherapy for the treatment of basal and squamous cell carcinoma	Enrolled 53 patients with confirmed NMSC and included 51 months of follow up. All patients were in remission at 3 months and no relapses or other side effects were observed.	pubmed.ncbi.nlm.nih.gov/18681873/	2008
6.	Retrospective cohort study	Cipriani et al, 2017: Personalized high-dose-rate brachytherapy with non-sealed Rhenium-188 in NMSC	Enrolled 43 patients with confirmed NMSC lesions and included 9.5 months follow up. All patients achieved and maintained remission.	www.cosmosscholars.com/special-issues-ijnmr/46-abstracts/ijnmr/737-abstract-	2017

19. Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only). ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study	Title / Location	Short description	Website link	Date
1.	Retrospective	Sathegke / South Africa	40 NMSC patients, local experience	NA	2021
2.	Prospective	Sathegke / South Africa	20 NMSC patients, material costs	NA	2021
3.	Retrospective	Cardaci / Australia	30 NMSC patients, local experience	NA	2021
4.	Prospective	Krause / Germany	20 NMSC patients, clinical efficacy	NA	2022

OncoBeta is also finalising arrangements for a sponsor-initiated, prospective, single-arm, open-label, multi-centre, multi-national (including Australia) 2-year follow-up trial in approximately 180+ adult patients with histologically confirmed, Stage I or II BCC or SCC of any differentiation, with maximum depth of 3mm and diameter of $8cm^2$. This study is expected to commence recruitment in the 2nd half of 2021 and to have interim results available for a subset of patients in the 2nd half of 2022. A draft protocol for this study is attached to the application for reference.

OncoBeta is also establishing an international registry, which will include an Australian component, that will provide a better understanding of NMSC epidemiology as well the utility of Rhenium-188 Brachytherapy in its treatment. The registry will also allow for long term reportable data and collection on patients with NMSC. It is also planned that this Registry will commence in the 2nd half of 2021.

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

20. List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):

Australian and New Zealand Society of Nuclear Medicine

Australasian Association of Nuclear Medicine Specialists

Royal Australian and New Zealand College of Radiologists

Australasian College of Dermatologists

Australasian Society of Cosmetic Dermatologists

Australian Dermatology Nurses Association

21. List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):

Australasian College of Dermatologists

Australasian Society of Cosmetic Dermatologists

Australian Dermatology Nurses Association

Australasian Dermatopathology Society

Australian Society of Plastic Surgeons

22. List the consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):

The Cancer Council (Australia and States/Territories)

23. List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:

Elekta Pty Ltd

Varian Medical Systems Australasia Pty Ltd

24. Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):

REDACTED

PART 6 – POPULATION, INTERVENTION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

25. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

NMSC comprises predominantly BCC and SCC, although there are other rare subtypes including Morbus Bowen, Queyrat Erythroplasie and extramammary Paget's disease (EMPD). NMSC is the most common form of cancer in humans and Australia has one of the highest incidence rates in the world. Despite (or possibly because of) this high incidence, the local epidemiology is not well characterised: unlike other cancers NMSC is not reportable or captured in national cancer registries; while incidence and prevalence studies are multiple and heterogeneous. Notwithstanding these limitations, available evidence suggests a national incidence of around 300,000 to 500,000 patients, and between 500,000 and 1 million NMSC lesions, each year.

The most common cause of NMSC is sun exposure, while other predisposing factors include genetic skin conditions and immunosuppressive diseases or treatments and other environmental exposures. Incidence increases with age but not linearly and is higher in men than women up to approximately 50 year of age, and similar thereafter. Around 50% of cases present on the head or approximately, 25% on the trunk and approximately 10% each on the upper and lower limbs. Although extremely common, NMSC is very rarely fatal, accounting for less than 1,000 deaths in Australia each year. This reflects the relatively slow and benign course of the disease, high rates of awareness, detection and diagnosis, and the availability of multiple, typically definitive, treatment options.

Detailed, recent and locally specific guidelines are available, which provide an overview of the condition and its prevention, diagnosis and treatment in the Australian setting (Cancer Council Australia, 2019).

26. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:

The vast majority of NMSC in Australia is diagnosed and managed in a primary healthcare setting. The proposed service, by contrast, would be offered exclusively in highly specialised (nuclear medicine) settings, upon referral by a specialist dermatologist or plastic surgeon.

Moreover, it is proposed that eligibility would be limited to patients with more difficult to treat lesions, for which malignancy has been confirmed, melanoma has been excluded, and suitability for treatment with Rhenium-188 clearly established. Indicative criteria are provided in a draft MBS item descriptor, in answer to Question 54.

27. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart depicting the current clinical management pathway up to this point):

Clinical management pathways for NMSC are defined by various factors, including number, size and location of suspicious lesions, clinical and histological assessment of risk, relevant comorbidities, and other individual patient characteristics. All patients generally present first to a General Practitioner. Those with high risk, large, multiple and/or difficult to treat lesions, or comorbidities, would typically be referred to a Dermatologist for further assessment and treatment. Multiple management options are available in this secondary care setting, including surgical excision (inpatient or outpatient) radiotherapy, brachytherapy and/or chemotherapy (where there is confirmation of metastatic disease). In most cases, patient care would be multidisciplinary, involving different specialties and/or institutions. Rhenium-188 brachytherapy would represent a novel addition to the existing suite of options available in this setting, most suitable for a small subset of patients with difficult to treat lesions, uptake of which is expected to be limited by local experience and availability of necessary capital equipment. A simplified flowchart is provided as an attachment to the application.

PART 6b – INFORMATION ABOUT THE INTERVENTION

28. Describe the key components and clinical steps involved in delivering the proposed medical service:

Histological confirmation of malignancy, exclusion of melanoma, determination of suitability for Rhenium-188 therapy and definition of the lesion borders would be performed by a dermatologist or specialist plastic surgeon, who would work closely with a specialist nuclear medicine physician or radiation oncologist to determine the area to be treated and manage the procedure and follow up.

For the procedure itself, in an appropriately equipped nuclear medicine facility, a technician or nurse would typically cover the region to be treated (and an appropriate surrounding area) with the special protective foil, measure the area of the lesion and, as necessary deploy radiation protection accessories to cover sensitive body parts. At the commencement of each treatment session, the technician would also load carpoule containing the Rhenium-188 compound into the applicator and measure/record the value of the radioactivity using the measurement station.

A nuclear medicine physician or specialist radiation oncologist would then apply the compound over the protective foil following the border. A timer would then be started, and the compound measured, with the remaining activity recorded. A medical physicist would then calculate the time the compound must remain on the protective foil to reach the dose at the target depth.

At the elapse of the calculated time, a technician would remove the protective foil including the applied compound and dispose of it safely in an appropriate waste station. If radiation protection accessories were used, they would also be removed, and the patient discharged.

The referring dermatologist or plastic surgeon would follow up the wound healing process with regular controls and later potential remissions as per other methods of treatment for NMSC.

29. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

Yes, the service includes a proprietary Rhenium-188 compound is only approved for use in conjunction with other proprietary equipment, as described in answer to Question 13.

30. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

Yes, the service represents a novel approach to treatment of NMSC. Other forms of brachytherapy are sometimes used in NMSC, however these are not directly comparable to Rhenium-188 treatment.

31. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

The main limitation here will be availability and accessibility of the service, given its relative novelty, requisite capital equipment, and lack of experience among Australian clinicians. This is expected to be a very significant limitation during the first few years following MBS listing.

There are also some limitations based on radiation exposure for healthcare providers and patients. These are complex and dependent upon use of appropriate protective measures and equipment. Detailed information regarding such limits will be provided in the proposed submission based assessment.

32. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

Not applicable.

33. If applicable, advise which health professionals will primarily deliver the proposed service:

Nuclear medicine physicians in collaboration with dermatologists, radiologists and/or plastic surgeons.

34. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

No, however elements of the procedure would usually be performed by a nurse or technician as described in answer to Question 28.

35. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

The service should only be provided by suitably qualified nuclear medicine physicians or radiation oncologists working in accredited facilities with appropriate capital equipment and training in the procedure. Referral would be limited to specialist dermatologists or plastic surgeons.

36. If applicable, advise what type of training or qualifications would be required to perform the proposed service, as well as any accreditation requirements to support service delivery:

Training for nuclear medicine department staff is conducted in person by OncoBeta. Training videos are also available, as well as healthcare professional written information. A certificate of training completion is provided, once training has been completed.

37. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select ALL relevant settings):

☒ Accredited nuclear medicine facilities in specialist public and private hospitals (non-admitted patients)

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

The proposed service incorporates a complex and completely new health technology, that is initially expected to be provided only through a limited number of specialist nuclear medicine facilities in major public/private hospitals, on a non-admitted/outpatient basis.

38. Is the proposed medical service intended to be entirely rendered in Australia?

☒ Yes
☐ No – please specify below

All aspects of the service would be provided in Australia. Most components of the requisite medical device would be imported. However, arrangements are currently being finalised with the Australian Nuclear Science and Technology Organisation (ANSTO) to manufacture and supply the Rhenium-188 compound locally, from late 2021 onwards.

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

39. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

Potential comparators for the proposed medical service, within the target MBS population, include:

- Surgery, encompassing conventional excision or Mohs technique, performed in a mix of inpatient and outpatient settings, under either general or local anaesthesia (local anaesthesia) settings
- External beam radiotherapy (EBRT), frequently delivered over a number of sessions, usually in an outpatient setting
- Other modes of brachytherapy, including superficial, interstitial and electronic approaches, also usually provided in an outpatient setting.

Surgery is by far the most commonly used treatment for NMSC in Australia and would be substituted to a limited extent by Rhenium-188 brachytherapy. Targeted feedback elicited from local specialist colleges and societies has also suggested that Rhenium-188 therapy would be considered in situations where surgery is contraindicated or inappropriate, in which case other radiotherapy approaches, such as EBRT or brachytherapy, may represent a more relevant comparator.

Multiple other treatment options are also used in NMSC, including cryotherapy, electrodessication and curettage, photodynamic therapy, or topical creams and gels including active agents such as imiquimod, diclofenac, or 5-fluroracil. However, these would not typically be considered appropriate in the context of the target population with difficult to treat and specialised secondary treatment setting and are therefore not considered to be relevant comparators for the current application.

40. Does the medical service (that has been nominated as the comparator) have an existing MBS item number(s)?

☒ Yes (please list all relevant MBS item numbers below)

Conventional excision: 31356, 31358, 31359, 31361, 31363, 31365, 31367, 31369 (See Note TN.8.22).

Mohs surgery: 31000, 31001, 31002, 31003, 31004, 31005 (See Note TN.8.151)

Radiotherapy: 15006, 15513, 15112, 15115, 15224, 15254 (See Note TN.2.3)

Brachytherapy: 15536, 15539, 15800, 15850 (See Note TN.8.56)

41. Define and summarise the current clinical management pathway/s that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards, including health care resources):

Management of NMSC patients after treatment may include further histopathologic assessment of the tumour sample, infection control, pain management, infection control, cosmetic repair of the lesion site, individually tailored follow-up to monitor healing and remission, and appropriate re-treatment in the event of recurrence.

42. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

☐ In addition to (i.e. it is an add-on service)
☒ Instead of (i.e. it is a replacement or alternative)

(b) If instead of (i.e. alternative service), please outline the extent to which the current service/comparator is expected to be substituted:

Substitution is expected to be extremely cautious and gradual, reaching only around 1% NMSC treatments within the first five years of listing on the MBS. This gradual predicted uptake is due to a combination of the novelty of the procedure, limited current awareness and experience of it in Australian practice, training and capital equipment requirements, established clinical place, effectiveness and safety of the comparator service and the proposed highly restricted MBS eligibility criteria.

43. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service, including variation in health care resources (Refer to Question 39 as baseline):

The only significant changes to clinical management would be substitution of Rhenium-188 brachytherapy for other surgical and radiotherapy approaches in a small minority of patients. Subsequent follow up requirements and recurrence rates are expected to be broadly similar across the interventions.

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

44. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

Rhenium-188 brachytherapy offers a new modality for management of difficult to treat NMSC lesions, which is non-invasive, painless, can usually be delivered in a single session, over a short period of time, without the need for anaesthesia, in an outpatient setting. It will be particularly beneficial for lesions located on areas such as the nose, eyebrow, lip, ear, digit, genitalia, shin or collarbone, or for patients who are otherwise deemed unsuitable for treatment by surgery and/or EBRT.

Clinical trials have shown the procedure to deliver remission rates similar those reported for surgery and radiotherapy, up to 3 years after treatment, in a single outpatient treatment, without functional mutilation or scarring and associated need for cosmetic repair. The net impact of these benefits for patients, in terms anaesthesia and infection risk, procedural and post-operative pain, disfiguration and scarring, health related quality of life, healthcare costs, and functional and economic wellbeing are very significant.

45. Please advise if the overall clinical claim is for:

☒ Superiority (in terms of patient reported outcomes and health related quality of life)
☒ Non-inferiority (in terms of remission and recurrence rates)

46. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes: Adverse reactions to the respective procedures, post-procedure infections, scarring and functional mutilation, secondary corrective procedures

Clinical Effectiveness Outcomes: Remission and recurrence, pain and discomfort, scarring and disfiguration, health related quality of life, other healthcare resource use

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

47. Estimate the prevalence and/or incidence of the proposed population:

The epidemiology of NMSC in Australia is incompletely understood, as these lesions are not generally reported in State/Territory or National cancer registries. However, both incidence and prevalence are universally recognised as being high, and age specific rates to be among the highest in the world. Multiple published studies are available, which have used different methodologies and report unsurprisingly heterogeneous results (Perera et al, 2015). A recent analysis of Medicare sample data estimated a person-based incidence of 1,531 and a lesion based incidence of 3,155 per 100,000 persons aged over 20 years (i.e. ≈300,000 and ≈600,000 cases per year); (Pandeya et al, 2017). Using different source studies, Cancer Council Australia guidelines attributed 939,000 treatment episodes to NMSC during 2015. It is unknown at this stage what proportion of cases might meet the proposed MBS eligibility criteria. It is the intention of Oncobeta to commence a national Registry for NMSC. This will allow a better understanding of disease epidemiology as well the utility of Rhenium-188 Brachytherapy.

48. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year:

The majority of patients would receive only one session of treatment per lifetime and very few would receive more than two sessions per lifetime.

49. How many years would the proposed medical service(s) be required for the patient?

A single treatment session will be definitive in most cases, however patients may present subsequently with new lesions, while the possibility of recurrence also cannot be excluded.

50. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

Approximately 500

51. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

Year 2 ≈ 1,000; Year 3 ≈ 2,000; Year 4 ≈ 4,000.

In addition to proposed eligibility criteria for the MBS item, the main constraints on uptake will be awareness of and experience/training in the new procedure and availability of the capital equipment.

PART 8 – COST INFORMATION

52. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

It is proposed that the MBS item would include the acquisition cost for the single use consumable items, and the healthcare practitioner time involved in delivering the service. Costs for the capital equipment and multi-use consumables and more general clinic infrastructure would presumably be excluded.

The cost of one carpoule containing the Rhenium-188 compound will be approximately REDACTED. This carpoule contains sufficient material for a treatment area of approximately 25 cm^2. Depending on the specific caseload on a given day, that could encompass 25 patients each with 1 cm^2 lesions or 3 patients each with lesions totalling 8.3 cm^2. However, on average one carpoule treats approximately 4-6 patients. The cost of one 15 x 20 cm sheet of protective foil (300 cm^2) will be approximately $AU 6.23.

Defining appropriate local costs for the healthcare practitioner time involved in delivering the service in Australia will require further consultation with relevant clinical groups. However in Europe these are around REDACTED for the first lesion treated and REDACTED for each additional lesion treated on a given day.

53. Specify how long the proposed medical service typically takes to perform:

Treatment time varies based on the number and size of lesions being treated, however the average is around 45 minutes and maximum around 180 minutes. Some additional time is required for preparation of the patient and any post-procedure monitoring. The clinical workflow typically involves a dermatologist, specialist nurse/technician and nuclear medicine physician or radiation oncologist.

54. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

Indicative draft MBS item descriptors are provided below, noting that these will inevitably require subsequent revision and refinement during the PICO confirmation process.

The intent here is:

- To limit eligibility to the target population of patients with more difficult to treat lesions, for which malignancy has been confirmed, melanoma has been excluded, and suitability for treatment with Rhenium-188 is clearly established on the basis of size, location and/or comorbidities; and
- To limit treatment to appropriately trained nuclear medicine physicians or radiation oncologists, working from accredited facilities, using appropriate capital equipment, and treating only upon referral from specialist dermatologists and plastic surgeons.

Three discrete but similarly structured item numbers have been proposed for lesions of different size as it is anticipated that the cost of treating lesions will be predominantly determined by this parameter.

The item describes treatment of a single NMSC lesion, with recognition that a multiple operation rule will likely be required in circumstances where patients have multiple lesions treated in a single session.

The item will need to encompass both the medical practitioner and single use consumable components of the service, and has not been defined at this stage, pending further consultation.

Category 3 - Therapeutic Procedures – Group T2 - Radiation Oncology; Subgroup 4 - Brachytherapy
Proposed item descriptor: Epidermal radioisotope therapy, using rheuium-188, of a malignant non-melanoma skin lesion, if: a) malignancy has been confirmed and melanoma excluded by histological examination; and b) the maximum depth of the lesion is less than 3 mm; and c) the necessary excision diameter is between 15 mm and 30 mm; and d) the lesion is excised from nose, eyebrow, lip, ear, digit, genitalia, shin or collarbone, or a contiguous area; or e) the patient has comorbidities that prevent surgical excision or external beam radiotherapy; and f) the service is provided by a suitably trained nuclear medicine physician in an approved facility; and g) the service is referred by a specialist dermatologist or plastic surgeon Multiple Operation Rule (the detail of which will need to be confirmed) Fee: $To be determined subject to clinical consultation and cost effectiveness assessment

Category 3 - Therapeutic Procedures – Group T2 - Radiation Oncology; Subgroup 4 - Brachytherapy
Proposed item descriptor: Epidermal radioisotope therapy, using rheuium-188, of a malignant non-melanoma skin lesion, if: a) malignancy has been confirmed and melanoma excluded by histological examination; and b) the maximum depth of the lesion is less than 3 mm; and c) the necessary excision diameter is between 30 mm and 50 mm; and d) the lesion is excised from nose, eyebrow, lip, ear, digit, genitalia, shin or collarbone, or a contiguous area; or e) the patient has comorbidities that prevent surgical excision or external beam radiotherapy; and f) the service is provided by a suitably trained nuclear medicine physician in an approved facility; and g) the service is referred by a specialist dermatologist or plastic surgeon Multiple Operation Rule (the detail of which will need to be confirmed) Fee: $To be determined subject to clinical consultation and cost effectiveness assessment

Category 3 - Therapeutic Procedures – Group T2 - Radiation Oncology; Subgroup 4 - Brachytherapy
Proposed item descriptor: Epidermal radioisotope therapy, using rheuium-188, of a malignant non-melanoma skin lesion, if: a) malignancy has been confirmed and melanoma excluded by histological examination; and b) the maximum depth of the lesion is less than 3 mm; and c) the necessary excision diameter is between 50 mm and 80 mm; and d) the lesion is excised from nose, eyebrow, lip, ear, digit, genitalia, shin or collarbone, or a contiguous area; or e) the patient has comorbidities that prevent surgical excision or external beam radiotherapy; and f) the service is provided by a suitably trained nuclear medicine physician in an approved facility; and g) the service is referred by a specialist dermatologist or plastic surgeon Multiple Operation Rule (the detail of which will need to be confirmed) Fee: $To be determined subject to clinical consultation and cost effectiveness assessment

Attachment: Clinical management pathway for NMSC in Australia