Australian Government

Department of Health

Application Form

(New and Amended Requests for Public Funding)

SIR-Spheres Y-90 resin microspheres for the treatment of other indications outside of primary liver cancers (hepatocellular carcinoma (HCC) and cholangiocarcinoma) and hepatic metastases which are secondary to colorectal cancer and are not suitable for resection or ablation, used in combination with systemic chemotherapy using 5-fluorouracil (5FU) and the current MBS interim listed hepatic metastases which are secondary to colorectal cancer and are not suitable for resection or ablation, used in combination with systemic chemotherapy using 5-fluorouracil (5FU) and leucovorin.

- **liver dominant tumours (incl. breast cancer)**
- **neuroendocrine tumours (NETs)**

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant):
Corporation name: Sirtex Medical Limited
ABN: REDACTED
Business trading name: REDACTED

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

(b) If yes, what is the Applicant(s) name that you are acting on behalf of?

Insert relevant Applicant(s) name here.

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
☒ n/a

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

4. Application title

SIR-Spheres Y-90 resin microspheres for the treatment of other indications outside of primary liver cancers (hepatocellular carcinoma (HCC) and cholangiocarcinoma) and hepatic metastases which are secondary to colorectal cancer and are not suitable for resection or ablation, used in combination with systemic chemotherapy using 5-fluorouracil (5FU) and the current MBS interim listed hepatic metastases which are secondary to colorectal cancer and are not suitable for resection or ablation, used in combination with systemic chemotherapy using 5-fluorouracil (5FU) and leucovorin.

- liver dominant tumours (eg breast cancer) – unresectable, chemoresistant liver-only metastases from primary breast cancer
- neuroendocrine tumours (NETs) – unresectable, metastatic NETs confined to the liver (second line to chemotherapy)

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)

Unresectable metastatic NETs confined to the liver (second line to chemotherapy)

Neuroendocrine tumours (NETs) are a genetically diverse spectrum of malignant solid tumours arising from the secretory cells of the neuroendocrine system that produce peptides causing characteristic hormonal syndromes. NETs can be clinically symptomatic (i.e., 'functioning'), or silent, (i.e., 'nonfunctioning'). The most frequently diagnosed NETs are small intestine tumours, lung and rectum.

Most patients with NETs have metastatic disease at diagnosis, with regional or distant metastasis observed in 50% of patients. Initial metastases are usually noted in regional lymph nodes, then in the liver and finally in distant sites such as bone. Large proportions of NETs are nonfunctioning and are diagnosed incidentally during an unrelated procedure. The clinical symptoms of functioning NETs generally arise after the tumour has metastasized to the liver.

Unresectable, chemoresistant liver-only metastases from primary breast cancer

Breast cancer is the most common malignancy in females, with an estimated lifetime risk of 10–15 %. Despite advances in adjuvant therapies, approximately 20 % of patients develop metastatic disease. These patients have a poor prognosis, with a 5-year survival of only 20–25 %. Breast cancer most frequently metastasizes to the skeleton, liver, lungs, and brain.

Liver metastases are present in approximately 15 % of patients with metastatic breast cancer; metastatic deposits confined to the liver occur in approximately 4–5 % of patients with metastatic breast cancer.

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)

SIR-Spheres Y-90 resin microspheres (Selective Internal Radiation Spheres) are yttrium-90 microspheres that are implanted into malignant liver tumours for the purpose of selectively delivering high doses of ionising radiation to the tumour. They are injected into the hepatic artery by means of a trans-femoral catheter or a permanently implanted hepatic artery port with a catheter. Following injection, the SIR-Spheres Y-90 resin microspheres become concentrated in the microvasculature of the liver cancer, where they have a local radiotherapeutic effect. As tumours within the liver derive their blood supply almost exclusively from the hepatic artery, the SIR-Spheres Y-90 resin microspheres are preferentially delivered in greater amounts to the tumour rather than to the normal liver parenchyma, which is supplied by both the hepatic artery and the portal vein. Following decay of the yttrium-90, the inert resin microspheres remain implanted in the tissue.

Advantages of the use of these intra-arterial radioactive compounds are the ability to deliver high doses of radiation to small target volumes, the relatively low toxicity profile, the possibility to treat the whole liver including microscopic disease and the feasibility of combination with other therapy modalities.

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)?

i. ☐ An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)
iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☐ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)
ix. ☐ Other (please describe below):

(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:

n/a

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)*:

i. ☐ To be used as a screening tool in asymptomatic populations
ii. ☐ Assists in establishing a diagnosis in symptomatic patients
iii. ☐ Provides information about prognosis
iv. ☐ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☐ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions
vi. ☐ Is for genetic testing for heritable mutations in clinically affected individuals and, when also appropriate, in family members of those individuals who test positive for one or more relevant mutations (and thus for which the Clinical Utility Card proforma might apply)

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

☐ Pharmaceutical / Biological
☒ Prosthesis or device
☐ No

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

☐ Yes
☐ No
☒ n/a

(b) If yes, please list the relevant PBS item code(s):

n/a

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

☐ Yes (please provide PBAC submission item number below)
☐ No
☒ n/a

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Trade name: n/a
Generic name: n/a

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

☒ Yes
☐ No

If yes, please provide the following information (where relevant):
Billing code(s): SE001
Trade name of prostheses: SIR-Spheres Y-90 resin microspheres
Clinical name of prostheses: yttrium-90 microspheres
Other device components delivered as part of the service: Delivery apparatus is PVC tubing, ABS stopcocks, acrylic holders and stainless steel needles with PE hubs.

(b) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

☐ Yes
☐ No
☒ n/a

(c) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

☐ Yes
☒ No

(d) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

n/a

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

Single use consumables: Biocompatible microspheres 20-60mm (microns) in diameter containing yttrium-90. Delivery apparatus is PVC tubing, ABS stopcocks, acrylic holders and stainless steel needles with PE hubs.
Multi-use consumables: n/a

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: Medical device
Manufacturer's name: Sirtex Medical Limited
Sponsor's name: Sirtex Medical Limited

(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 III
☒ 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)
☐ No

ARTG listing, registration or inclusion number: 149332
TGA approved indication(s), if applicable: For the treatment of malignant liver tumours of primary or secondary origin that are not suitable for resection or ablation.
TGA approved purpose(s), if applicable: Intended for the treatment of inoperable liver cancer.

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?

☐ Yes (please provide details below)
☐ No
☒ n/a

Date of submission to TGA: n/a
Estimated date by which TGA approval can be expected: n/a
TGA Application ID: n/a
TGA approved indication(s), if applicable: n/a
TGA approved purpose(s), if applicable: 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?

☐ Yes (please provide details below)
☐ No
☒ n/a

Estimated date of submission to TGA: n/a

Proposed indication(s), if applicable: n/a
Proposed purpose(s), if applicable: 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.***

Probably the best evidence for the use of SIR-Spheres Y-90 resin microspheres for Metastatic Breast Cancer is:

	Type of study design*	**Title of journal article or research project (including any trial identifier or study lead if relevant)**	**Short description of research (max 50 words)****	**Website link to journal article or research (if available)**	**Date of publication*****
1.	Single-centre experience	Saxena A, Kapoor J, Meteling B et al. Yttrium-90 radioembolization for unresectable, chemoresistant breast cancer liver metastases: A large single-center experience of 40 patients. Annals of Surgical Oncology 2014; 21: 1296–1303.	Forty patients underwent resin-based Y90 radioembolization for unresectable, chemoresistant BRCLM in a single institution. All patients were followed up with imaging studies at regular intervals as clinically indicated until death. Radiologic response was evaluated with the Response Criteria in Solid Tumors criteria. Clinical toxicities were prospectively recorded. Survival was calculated by the Kaplan-Meier method. This study provides supportive evidence of the safety and efficacy.	Listed on Pubmed https://www.ncbi.nlm.nih.gov/pubmed/24337647	2014

Probably the best evidence for the use of SIR-Spheres Y-90 resin microspheres for Metastatic Neuroendocrine Tumours (NETs) is:

	Type of study design*	**Title of journal article or research project (including any trial identifier or study lead if relevant)**	**Short description of research (max 50 words)****	**Website link to journal article or research (if available)**	**Date of publication*****

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
1.	Retrospective review from 10 institutions.	Kennedy A, Dezarn W, McNeillie P et al. Radioembolization for unresectable neuroendocrine hepatic metastases using resin 90Y-microspheres: Early results in 148 patients; Am J Clin Oncol 2008; 31: 271–279.	Physical, radiographic, biochemical, and clinical factors associated with treatment and response were examined. All patients were followed with laboratory and imaging studies at regular intervals until death, or censured whether other therapy was given after brachytherapy. Toxicities (acute and late) were recorded, and survival of the group determined.	Listed on Pubmed https://www.ncbi.nlm.nih.gov/pubmed/18525307	2008

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes.*

**** If the publication is a follow-up to an initial publication, please advise.*

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 design*	**Title of research (including any trial identifier if relevant)**	**Short description of research (max 50 words)****	**Website link to research (if available)**	**Date*****
1.	n/a				

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment.*

****Date of when results will be made available (to the best of your knowledge).*

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):

The Royal Australian and New Zealand College of Radiologists (RANZCR). Please see web site http://www.insideradiology.com.au/sirt-hp/

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

The Royal Australian and New Zealand College of Radiologists (RANZCR).

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

Cancer Council

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

None

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

Name of expert 1: REDACTED

Telephone number(s): REDACTED

Email address: REDACTED

Justification of expertise: REDACTED

Name of expert 2: REDACTED

Telephone number(s): REDACTED

Email address: REDACTED

Justification of expertise: REDACTED

Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INDICATION, 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:

Neuroendocrine tumours (NETs) - unresectable metastatic NETs confined to the liver (second line to chemotherapy)

Neuroendocrine tumours (NETs) are a heterogeneous group of neoplasms which take origin from the neuroendocrine cell system and are characterized by embryological, biological and histopathological differences. They are considered to be a rare and "niche" pathology. Neuroendocrine tumours may occur at any site in the gastrointestinal system. Neuroendocrine tumours (NETs) are a genetically diverse group of malignancies that sometimes produce peptides that cause characteristic hormonal syndromes. NETs can be clinically symptomatic (functioning) or silent (non-functioning); both types frequently synthesize more than one peptide, although often these are not associated with specific syndromes.

Although NETs comprise less than two percent of GI malignancies, these tumours are actually more prevalent than combined stomach and pancreatic cancers. The presence of hepatic metastases is the most important factor affecting the survival of patients with gastroenteropancreatic neuroendocrine tumours (GEP NETs).

Because of the portal venous drainage of the gastrointestinal tract and pancreas where most NETs arise, hematogenous spread to the liver is quite common, to the extent that dissemination from a primary GEP NET to the liver parenchyma will occur in at least 40% of patients, with some estimates ranging up to 85%. Among these patients with hepatic metastases, about 75% are synchronous and evident at presentation, whereas 25% are metachronous and develop during the disease course. The median overall survival in patients with hepatic metastases is 2–4 years, and estimates for 5-year survival with untreated liver involvement range from 13 to 54%.[1]

Unresectable, chemoresistant liver-only metastases from primary breast cancer

Breast cancer is the most common malignancy in females, with an estimated lifetime risk of 10–15 %. Despite advances in adjuvant therapies, approximately 20 % of patients develop metastatic disease. These patients have a poor prognosis, with a 5-year survival of only 20–25 %. Breast cancer most frequently metastasizes to the skeleton, liver, lungs, and brain.

Liver metastases are present in approximately 15 % of patients with metastatic breast cancer; metastatic deposits confined to the liver occur in approximately 4–5 % of patients with metastatic breast cancer. Breast cancer liver metastases (BRCLM) are associated with considerable mortality and morbidity. Surgical extirpation offers the only opportunity to cure BRCLM but is only possible in 10–20 % of patients. Moreover, the majority of patients of isolated liver BRCLM will still develop recurrent disease. The treatment of unresectable, chemoresistant BRCLM, however, remains a clinical dilemma.

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:

Patients with unresectable metastatic NETs confined to the liver (second line to chemotherapy)

Patients with unresectable, chemoresistant liver-only metastases from primary breast cancer.

[1] Lewis MA, Hobday TJ. Treatment of Neuroendocrine Tumor Liver Metastases. International Journal of Hepatology Volume 2012 (2012). http://dx.doi.org/10.1155/2012/973946

See answer to Q27 for investigative tests.

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 [as an attachment to the Application Form] depicting the current clinical management pathway up to this point):

- Blood test samples ('liver function tests') can be taken to see how well the liver is working and can be used to monitor patients for the early detection of secondary cancer
- A chest x-ray may be taken to determine if the cancer has spread to the lungs
- A CT scan to create a cross sectional, 3D image of the tumour(s) and surrounding tissues and organs.
- Liver biopsy
- A CT scan can be combined with a PET scan to show where there are any cell changes in the body, and whether the cancer has spread
- Magnetic resonance imaging (MRI) to show the tumour(s) in great detail and look at the blood supply to the liver
- Ultrasound

PART 6b – INFORMATION ABOUT THE INTERVENTION

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

Selective Internal Radiation Therapy (SIRT) normally comprises two procedures:

Preparation or "work-up"

In preparation for the angiogram: blood tests to evaluate the kidney function and blood clotting.

Angiogram to prepare the liver for SIRT. During the angiogram a small amount of dye (or contrast medium) is injected through a catheter (a thin plastic tube) inserted into an artery. The dye travels down the catheter into the liver and highlights the vessels.

The work-up procedure for SIRT is normally done on an outpatient basis.

Implant of SIR-Spheres Y-90 resin microspheres®

A second angiogram is performed to implant the SIR-Spheres Y-90 resin microspheres® (SIRT). The catheter used during the angiogram is then guided by the interventional radiologist through the artery and placed close to the tumours in the liver. The purpose of the angiogram this time is to implant the SIR-Spheres Y-90 resin microspheres®. SIR-Spheres Y-90 resin microspheres® are then infused through a catheter into the liver. This whole procedure may take about 60 minutes.

For this procedure, the patient is admitted to hospital.

Source: http://www.insideradiology.com.au/

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

SIR-Spheres Y-90 resin microspheres (Selective Internal Radiation Spheres) are yttrium-90 microspheres that are implanted into malignant liver tumours for the purpose of selectively delivering high doses of ionising radiation to the tumour.

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?

A new approach for this patient sub-group.

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):

To be claimed once in the patient's lifetime only.

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:

n/a

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

The service must be performed by a specialist or consultant physician recognised in the specialties of nuclear medicine or radiation oncology.

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

n/a

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 must be performed by a specialist or consultant physician recognised in the specialties of nuclear medicine or radiation oncology.

Patients must have a referral from an oncologist to the interventional radiologist.

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:

The service must be performed by a specialist or consultant physician recognised in the specialties of nuclear medicine or radiation oncology.

Sirtex provides a robust training programme, the SIR-Spheres Microspheres Training, Evaluation and Certification (TEC) Programme, for institutions or new users that want to start or re-start a SIR-Spheres Y-90 resin microspheres service. The training programme is designed to instruct new physicians and healthcare professionals in the clinical use of SIR-Spheres Y-90 resin microspheres and to help an institution to build a sustainable, high-quality SIR-Spheres Y-90 resin microspheres programme.

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

- ☒ Inpatient private hospital
- ☒ Inpatient public hospital
- ☒ Outpatient clinic
- ☐ Emergency Department
- ☐ Consulting rooms
- ☐ Day surgery centre
- ☐ Residential aged care facility
- ☐ Patient's home
- ☐ Laboratory
- ☐ Other – please specify below

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

See answer to Q28 - Preparation or “work-up” carried out in outpatient setting. Implant of SIR-Spheres Y-90 resin microspheres® carried out in inpatient setting.

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

☒ Yes
☐ No – please specify below

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):

Since this patient population has unresectable, chemoresistant liver metastases, the only true comparator is palliative care only.

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

☐ Yes (please provide all relevant MBS item numbers below)
☒ No

41. Define and summarise the current clinical management pathways 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 [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards including health care resources):

Nothing after palliative care.

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

☒ Yes
☐ No

(b) If yes, please outline the extent of which the current service/comparator is expected to be substituted:

Selective internal radiation therapy (SIRT) using yttrium-90 resin microspheres is intended to be used prior to palliative care only.

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):

Please refer to the first column in the answer to Q47.

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):

Treatment goals of SIRT with SIR-Spheres Y-90 resin microspheres are to: extend overall survival (OS); increase time to progression (TTP) or increase progression-free survival (PFS); downsize liver tumours to potentially curative resection or bridge to transplantation; and relieve symptoms to improve quality of life (QoL) relative to current best standard of care.

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

☒ Superiority
☐ Non-inferiority

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:

Clinical Effectiveness Outcomes: Delayed disease progression in the liver.

Safety Outcomes: Common grade ≥ 3 AEs associated with chemotherapy such as neutropenia, febrile neutropenia, and thrombocytopenia

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

47. Estimate the prevalence and/or incidence of the proposed population:
A rough estimate of the number of patients eligible for SIR-Spheres Y-90 resin microspheres for unresectable metastatic NETs confined to the liver (second line to chemotherapy) is:

Metastatic Neuroendocrine Tumours (mNET)	N	Reference
Incidence of neuroendocrine tumours in Australia	1,500	Unicorn Foundation. 2016
Approx. 67% of neuroendocrine tumours are of gastrointestinal or pancreatic (GEP) origin (*vs.* lung or thymus)	1,000	Garcia-Carbonero R. *Cancer Metastasis Rev* 2014; 33:343–344.
40-80% of GEP-NET patients develop metastases (assume 60%)	600	Vilchez *et al*. *Best Pract Res Clin Endocrinol Metab* 2016;30:141−147.
40-93% of mNET patients have liver metastases (assume 50%)	300	Vilchez *et al*. *Best Pract Res Clin Endocrinol Metab* 2016;30:141−147.
30-40% of patients with mNET confined to the liver are resectable (assume 35%); however, the recurrence rate is ~50%	52	Pavel M *et al*. *Neuroendocrinology* 2012;95:157–176.
The remaining 70% of mNET liver metastases are unresectable	196	Pavel M *et al*. *Neuroendocrinology* 2012;95:157–176.
Total estimated with unresectable mNET liver metastases	248	
Assuming 80% of these receive first-line chemotherapy, and may be eligible for SIRT at second-line or later	198	Pavel M *et al*. *Neuroendocrinology* 2016;103:172–185. Estimated, based on published studies
63.6% of patients are estimated to be suitable for SIR-Spheres Y-90 resin microspheres	126	Sirtex. MSAC submission. 2004
Maximum estimated patient population	126	

A rough estimate of the number of patients eligible for SIR-Spheres Y-90 resin microspheres therapy for unresectable, chemoresistant liver-only metastases from primary breast cancer is:

Breast Cancer	N	Reference
Incidence of women with breast cancer in Australia	14,710	Globocan 2012
6% of breast cancer patients have metastases at presentation	883	Cardoso F *et al. Ann Oncol* 2011;22:vi 25-vi30.
~30% of early stage breast cancer develop metastases	4413	EBCTCG. *Lancet* 2012;379:432-444.
Total estimated with metastatic breast cancer	5296	
Approx. 4-5% of metastatic breast cancer patients have liver-only metastases (assume 5%)	265	Cianni R *et al. Future Oncol* 2014;10(Suppl):93–95.
82% of breast cancer patients with liver-only metastases are unresectable	217	Eichbaum MH *et al*. *Breast Cancer Res Treat* 2006;96:53-62.
An estimated 50% of patients with unresectable mBCa may be eligible for SIRT	109	Estimated, based on published studies
63.6% of patients are estimated to be suitable for SIR-Spheres Y-90 resin microspheres	54	Sirtex. MSAC submission. 2004

Maximum estimated patient population	54	

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

Once

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

Once per lifetime

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

NETS = 35? Breast Cancer = 8?

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	NETs Services	BC Services
1	35	8
2	50	12
3	60	18
4	75	23

PART 8 – COST INFORMATION

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

MBS Item 35406: Fee: $813.30 Benefit: 75% = $610.00

MBS Item 35408: Fee: $610.10 Benefit: 75% = $457.60

Prostheses List: SE001 benefit $8,230 - SIR-Spheres Y-90 resin microspheres including Delivery Apparatus

Component	SIR-Spheres Y-90 resin microspheres
Work-up	$2,230
Treatment	$14,964
Adverse events	$828
Follow up	$3,157
Total av cost/patient	$21,219

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

Approximately 60 minutes

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.

Proposed MBS Listings for Selective Internal Radiation Therapy (SIRT) for unresectable metastatic NETs confined to the liver (second line to chemotherapy)

MBS 35xxx
Trans-femoral catheterisation of the hepatic artery to administer SIR-Spheres Y-90 resin microspheres to embolise the microvasculature of unresectable metastatic NETs confined to the liver (second line to chemotherapy), for selective internal radiation therapy, not being a service to which item 35317, 35319, 35320 or 35321 applies excluding associated radiological services or preparation, and excluding aftercare
Multiple Services Rule T8.2
(Anaes.) (Assist.)
Fee: $813.30 Benefit: 75% = $610.00

MBS 35xxx
Catheterisation of the hepatic artery via a permanently implanted hepatic artery port to administer SIR-Spheres Y-90 resin microspheres to embolise the microvasculature of unresectable metastatic NETs confined to the liver (second line to chemotherapy), for selective internal radiation therapy, not being a service to which item 35317, 35319, 35320 or 35321 applies excluding associated radiological services or preparation, and excluding aftercare
Multiple Services Rule T8.2
(Anaes.) (Assist.)
Fee: $610.10 Benefit: 75% = $457.60

Proposed MBS Listings for Selective Internal Radiation Therapy (SIRT) for unresectable liver-only metastases from primary breast cancer

MBS 35xxx
Trans-femoral catheterisation of the hepatic artery to administer SIR-Spheres Y-90 resin microspheres to embolise the microvasculature of unresectable, chemoresistant liver-only metastases from primary

breast cancer, for selective internal radiation therapy, not being a service to which item 35317, 35319, 35320 or 35321 applies excluding associated radiological services or preparation, and excluding aftercare
Multiple Services Rule T8.2
(Anaes.) (Assist.)
Fee: $813.30 Benefit: 75% = $610.00

MBS 35xxx
Catheterisation of the hepatic artery via a permanently implanted hepatic artery port to administer SIR-Spheres Y-90 resin microspheres to embolise the microvasculature of unresectable, chemoresistant liver-only metastases from primary breast cancer, for selective internal radiation therapy, not being a service to which item 35317, 35319, 35320 or 35321 applies excluding associated radiological services or preparation, and excluding aftercare
Multiple Services Rule T8.2
(Anaes.) (Assist.)
Fee: $610.10 Benefit: 75% = $457.60

PART 9 – FEEDBACK

The Department is interested in your feedback.

55. How long did it take to complete the Application Form?

Approximately five full days

56. (a) Was the Application Form clear and easy to complete?

☐ Yes
☒ No

(b) If no, provide areas of concern:

Example: Q42 (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)? Answer yes / no. This does not make sense.

57. (a) Are the associated Guidelines to the Application Form useful?

☐ Yes
☒ No

(b) If no, what areas did you find not to be useful?

No Part F?

58. (a) Is there any information that the Department should consider in the future relating to the questions within the Application Form that is not contained in the Application Form?

☒ Yes
☐ No

(b) If yes, please advise:

Example: It's standard to identify published papers using authors. This information is not required in the table for Q18. Also, asking where the paper can be found is unusual since the majority of published papers are on Medline.