



**Australian Government**

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**Department of Health**

# **Application Form**

**(New and Amended Requests for Public Funding)**

**SIR-Spheres Y-90 resin microspheres for the treatment of primary liver cancers:**

- **Non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC)**
- **Unresectable intrahepatic cholangiocarcinoma (ICC)**

# 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 primary liver cancers:

- Non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC)
- Unresectable intrahepatic cholangiocarcinoma (ICC)

### 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)

Primary liver cancer is one of the less common cancers in Australia. About 1600 people are diagnosed with it every year. It is more than twice as common in men, and the average age at diagnosis is 67.3. HCC and ICC are a subset of the primary liver cancer population.

Primary non-resectable, non-ablatable hepatocellular carcinoma (HCC) and unresectable intrahepatic cholangiocarcinoma (ICC) are not as common as colorectal liver metastases (CLM) in Australia.

#### Non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC)

Hepatocellular carcinoma (HCC) is a primary tumour of the liver that usually develops in the setting of chronic liver disease, particularly in patients with chronic hepatitis B and C. Hepatocellular carcinoma (HCC) – starts in the hepatocytes, the main cell type in the liver. HCC, also called hepatoma, is the most common type of primary liver cancer.

Patients with advanced HCC (Primary non-resectable, non-ablatable hepatocellular carcinoma) that would be suitable for SIRT would have a life expectancy of >3 months, Eastern Cooperative Oncology Group (ECOG) performance status  $\leq 1$ , and: advanced HCC according to the Barcelona criteria (stage C) or recurrent HCC after surgical or thermoablative treatment who are not eligible for surgical resection, liver transplantation or thermal ablation; or two rounds of failed chemoembolisation.

#### Unresectable intrahepatic cholangiocarcinoma (ICC)

Cholangiocarcinoma – starts in the cells lining the bile duct, which connects the liver to the bowel and the gall bladder. It is also called bile duct cancer.

Patients with unresectable intrahepatic cholangiocarcinoma (ICC) have a malignant transformation of cholangiocytes within the hepatic parenchyma. Intrahepatic lesions are often asymptomatic and, therefore, present as an incidental mass lesion without jaundice or other stigmata of biliary obstruction. Given the asymptomatic nature of many ICCs, patients often present with locally advanced tumours. Although surgery offers the highest curative potential, many tumours are deemed unresectable at the time of diagnosis. Patients with unresectable ICC have a median survival of less than eight months.

### 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 non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC) 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.	A multicentre analysis	Sangro B, Carpanese L, Cianni R et al on behalf of European Network on Radioembolization with yttrium-90 resin microspheres (ENRY). Survival after 90Y resin microsphere radioembolization of hepatocellular carcinoma across BCLC stages: A European evaluation. Hepatology 2011; 54: 868–878.	An evaluation of the main prognostic factors driving survival after radioembolization using yttrium-90-labeled resin microspheres in patients with hepatocellular carcinoma at eight European centres covering 325 patients. This analysis provides robust evidence of the survival achieved with radioembolization, including those with advanced disease and few treatment options.	Listed on Pubmed <a href="https://www.ncbi.nlm.nih.gov/pubmed/21618574">https://www.ncbi.nlm.nih.gov/pubmed/21618574</a>	2011

\* 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.

Probably the best evidence for the use of SIR-Spheres Y-90 resin microspheres for unresectable intrahepatic cholangiocarcinoma (ICC) 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***
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	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 analysis	Hoffmann RT, Paprottka PM, Schön A et al. Transarterial hepatic yttrium-90 radioembolization in patients with unresectable intrahepatic cholangiocarcinoma: Factors associated with prolonged survival. Cardiovascular and Interventional Radiology 2012; 35: 105–116.	33 patients with unresectable ICC were treated with (90)Y resin-microspheres and assessed at 3-monthly intervals. Radiologic response was evaluated by using Response Criteria in Solid Tumours (RECIST). Baseline characteristics, biochemical/clinical toxicities, and response were examined for impact on TTP and OS.  Radioembolization is an effective and safe option for patients with unresectable ICC.	Listed on Pubmed  <a href="https://www.ncbi.nlm.nih.gov/pubmed/21431970">https://www.ncbi.nlm.nih.gov/pubmed/21431970</a>	2012

**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 Australia

- 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:**

Primary non-resectable, non-ablatable hepatocellular carcinoma (HCC) and unresectable intrahepatic cholangiocarcinoma (ICC) are not as common as colorectal liver metastases (CLM) in Australia.

**Non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC)**

Hepatocellular carcinoma (HCC, also called malignant hepatoma) is a primary malignancy of the liver and occurs predominantly in patients with underlying chronic liver disease and cirrhosis. Most cases of HCC are secondary to either a viral hepatitis infection (hepatitis B or C) or cirrhosis (alcoholism being the most common cause of liver cirrhosis).

**Unresectable intrahepatic cholangiocarcinoma (ICC)**

Patients with unresectable ICC have a median survival of less than eight months

**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:**

*See answer to Q27 for investigative tests for both primary liver cancers.*

**Non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC)**

Patients with advanced HCC (Primary non-resectable, non-ablatable hepatocellular carcinoma) that would be suitable for SIRT would have:

- a life expectancy of >3 months, Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1, and
- advanced HCC according to the Barcelona criteria (stage C) or recurrent HCC after surgical or thermoablative treatment who are not eligible for surgical resection, liver transplantation or thermal ablation; or two rounds of failed chemoembolisation.

**Unresectable intrahepatic cholangiocarcinoma (ICC)**

Very similar to HCC.

**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 - patients with hepatic metastases secondary to colorectal cancer which are not suitable for resection or ablation.

**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 at the same time as the proposed medical service:**

In the case of ICC used in combination with systemic chemotherapy.

**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):**

Non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC)

The current main treatments for HCC use thermal ablation or deliver chemotherapy directly into the cancer (transarterial chemoembolisation or TACE). Transarterial chemoembolization (TACE) is one of the standard treatments recommended for intermediate stage hepatocellular carcinoma (HCC). Surgery is used for about 5% of people. However:

- Sorafenib 400 mg twice daily (PBS listed pharmaceutical) is the current recommended treatment for advanced HCC.

Unresectable intrahepatic cholangiocarcinoma (ICC)

Systemic chemotherapy with gemcitabine and cisplatin is the currently recommended treatment for unresectable intrahepatic cholangiocarcinoma (ICC) and is thus the comparator. Selective internal radiation therapy (SIRT), using yttrium-90 resin microspheres, is intended to be used in addition to this treatment.

**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):**

The challenges in developing effective therapies for HCC include the inherent chemoresistance of HCC, the pharmacologic challenges presented by a diseased liver, the presentation of most patients at advanced stages, and the difficulty in adequately measuring radiological response.

**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:**

Non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC)

Selective internal radiation therapy (SIRT) using yttrium-90 resin microspheres is intended to be used as an alternative to Sorafenib 400 mg twice daily (PBS listed pharmaceutical), the current recommended treatment for advanced HCC.

Unresectable intrahepatic cholangiocarcinoma (ICC)

Selective internal radiation therapy (SIRT) using yttrium-90 resin microspheres is intended to be used in addition to systemic chemotherapy with gemcitabine and cisplatin, the current recommended treatment for unresectable intrahepatic cholangiocarcinoma (ICC).

**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 also refer to the first column in the answer to Q47.*



Selective internal radiation therapy (SIRT) using yttrium-90 resin microspheres is intended to be used as an alternative to Sorafenib 400 mg twice daily (PBS listed pharmaceutical), the current recommended treatment for advanced HCC.

Selective internal radiation therapy (SIRT) using yttrium-90 resin microspheres is intended to be used in addition to systemic chemotherapy with gemcitabine and cisplatin, the current recommended treatment for unresectable intrahepatic cholangiocarcinoma (ICC).

**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  $\geq 3$  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 non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC) is:

Hepatocellular Carcinoma (HCC)	N	Reference
Incidence of primary liver cancer in Australia	1,658	Globocan 2012
71.2–80.3% of primary liver cancers are HCC (assumes 75.8%)	1,257	Altekruse SF <i>et al. J Registry Manag</i> 2011; <b>38</b> :201–205.
Approx. 55% of HCC patients present with Child-Pugh class A (excludes patients with Child-Pugh class B or C cirrhosis as these are poor candidates for SIRT)	691	GlobalData. Hepatocellular Carcinoma – Opportunity Analysis and Forecasts to 2024. 2015.
Approx. 30% of HCC patients present with BCLC stage A disease; of these, approx. 50% have unresectable or unablutable lesions, have unresectable or unablutable recurrence following ablation or resection, or require a bridge to liver transplantation	116	GlobalData. 2015. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. <i>J Hepatol</i> 2012; <b>56</b> :908–943. Roayaie S <i>et al. Gastroenterol</i> 2009; <b>137</b> :850–855. Nishikawa H <i>et al. Anticancer Res</i> 2012; <b>32</b> :5059–5065. D'Avola D <i>et al. Ann Surg Oncol</i> 2011; <b>18</b> :1964–1971.
Of these BCLC stage A patients, it is estimated that 67% would receive TACE and the remaining 33% are suitable for/receive SIRT	38	GlobalData. 2015. D'Avola D <i>et al. Ann Surg Oncol</i> 2011; <b>18</b> :1964–1971.
Approx. 20% of HCC patients present with BCLC stage B disease; of these, approx. 70% are suitable for intra-arterial therapies at presentation or after recurrence following ablation or resection	97	GlobalData. 2015. D'Avola D <i>et al. Ann Surg Oncol</i> 2011; <b>18</b> :1964–1971.
Of these BCLC stage B patients, it is estimated that 70% would receive TACE and the remaining 30% are suitable for/receive SIRT	32	GlobalData. 2015. D'Avola D <i>et al. Ann Surg Oncol</i> 2011; <b>18</b> :1964–1971.
Approx. 40% of HCC patients present with BCLC stage C disease; of these, approx. 45% have good ECOG performance status (ECOG 0), 45% have branch/segmental portal vein involvement and/or 25% have limited extra-hepatic disease,	87	GlobalData. 2015. D'Avola D <i>et al. Ann Surg Oncol</i> 2011; <b>18</b> :1964–1971. Bruix J <i>et al. J Hepatol</i> 2012; <b>57</b> :821–829. Sinn DH <i>et al. PLoS One</i> 2015;10:e0124434.
Of these BCLC stage C patients, it is estimated that 50% would receive sorafenib and the remaining 50% are suitable for/receive SIRT	44	GlobalData. 2015. D'Avola D <i>et al. Ann Surg Oncol</i> 2011; <b>18</b> :1964–1971.
Estimated patient population	114	

A rough estimate of the number of patients eligible for SIR-Spheres Y-90 resin microspheres for unresectable intrahepatic cholangiocarcinoma (ICC) is:

Cholangiocarcinoma	N	Reference
Incidence of primary liver cancer in Australia	1,658	Globocan 2012
10–15% of primary liver cancers are intra-hepatic cholangiocarcinoma (assume 12.5%)	207	Altekruse SF <i>et al. J Registry Manag</i> 2011; <b>38</b> :201–205. Eckel F <i>et al. Ann Oncol</i> 2011; <b>22</b> (Suppl 6): vi40–vi44.
Approx. 30% of these are resectable; however, the recurrence rate is ~55%	34	Seidensticker R <i>et al. Best Pract Res Clin Gastroenterol</i> 2015; <b>29</b> :319–332. Hyder O <i>et al. Surgery</i> 2013; <b>153</b> :811–818.
The remaining 70% of intra-hepatic cholangiocarcinoma are unresectable	145	Seidensticker R <i>et al. Best Pract Res Clin Gastroenterol</i> 2015; <b>29</b> :319–332.
Total estimated with unresectable or recurrent intra-hepatic cholangiocarcinoma	179	
Assuming 80% of these patients receive first-line chemotherapy, and 50% of these are eligible for SIRT at second-line	72	Estimated, based on published studies e.g. Hoffmann RT <i>et al. Cardiovasc Intervent Radiol</i> 2012; <b>35</b> :105–116.
63.6% of patients are estimated to be suitable for SIR-Spheres Y-90 resin microspheres	46	Sirtex. MSAC submission. 2004
Maximum estimated patient population	46	

**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:**

HCC = 35? ICC = 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	HCC Services	ICC 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 non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC)

MBS 35xxx

Trans-femoral catheterisation of the hepatic artery to administer SIR-Spheres Y-90 resin microspheres to embolise the microvasculature of non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC), 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 non-resectable, non-ablatable hepatocellular carcinoma (advanced HCC), 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 intrahepatic cholangiocarcinoma (ICC)

MBS 35406

Trans-femoral catheterisation of the hepatic artery to administer SIR-Spheres Y-90 resin microspheres to embolise the microvasculature of unresectable intrahepatic cholangiocarcinoma (ICC), for selective internal radiation therapy, used in combination with systemic chemotherapy using gemcitabine and cisplatin and 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 35408

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 intrahepatic cholangiocarcinoma (ICC), for selective internal radiation therapy, used in combination with systemic chemotherapy using gemcitabine and cisplatin and 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?**

Are we missing 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.