Australian Government

Department of Health

Application Form

(New and Amended Requests for Public Funding)

(Version 2.5)

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 in order 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.

The application form will be disseminated to professional bodies / organisations and consumer organisations that have will be identified in Part 5, and any additional groups that the Department deem should be consulted with. The application form, with relevant material can be redacted if requested by the Applicant.

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

Phone: +61 2 6289 7550
Fax: +61 2 6289 5540
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):
Corporation name: BTG International Asia Limited
ABN: REDACTED
Business trading name: BTG International Asia Limited

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 – REDACTED
☒ No – REDACTED

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

BTG International Asia Limited

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?

Not applicable

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

4. Application title

Transarterial radioembolisation with yttrium-90 (TARE-Y) for the treatment of unresectable hepatocellular carcinoma

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)

Hepatocellular carcinoma (HCC) is a type of primary liver cancer arising from hepatocytes, the main cell type found in the liver. The main risk factors for developing HCC are alcohol abuse and hepatitis B virus (HBV) or C virus (HCV) infection. The causes of HCC vary across countries, with HBV being the main cause in regions where infection is endemic (e.g. parts of Asia) and cirrhosis due to alcohol abuse, HCV or obesity being the main cause in regions where HBV in not endemic (e.g., North America and Europe).[1] HCC is the most common type of liver cancer, and one of the most common types of cancers seen worldwide, being the fifth most common in men and the ninth most common in women. Due to its high mortality to incidence ratio (0.95) it is the third largest contributor to cancer mortality overall.[2]

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)

TARE-Y (also known as selective internal radiation therapy; SIRT) is a medical procedure for the treatment of unresectable HCC. TARE-Y utilises the differential blood supply of the healthy and tumorous liver (80% of the blood supply to the liver is via the portal vein and almost all the blood supply to liver tumours is via the hepatic artery), and involves the delivery of yttrium-90-containing microspheres of 20-60 µm diameter. Two types of microspheres are available: resin (SIR-Spheres/Sirtex Medical Products) and glass (TheraSphere/BTG International Asia). The yttrium-90 (Y-90) emits high energy beta radiation with a mean tissue penetration of 2.5 mm (maximum 11 mm). Thus, the microspheres deliver a cytocidal dose of beta radiation to the cancer cells with minimal irradiation of normal healthy liver tissue. Because of the small size of the microspheres, tumour necrosis is largely caused by radiation, with only a minor contribution from embolisation due to the particles.

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:

Not applicable

[1] Park et al. (2015) Global patterns of hepatocellular carcinoma management from diagnosis to death: the BRIDGE Study. Liver International 35: 2155-2166.
[2] Ferlay et al (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer 136: E359-E386.

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

Not applicable

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)

There are currently interim MBS item numbers relating to the use of resin microspheres (SIR-Spheres) in patients with "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". The item numbers are:

- 35404 – Dosimetry, handling and injection of SIR-Spheres
- 35406 – Trans-femoral catheterisation of the hepatic artery to administer SIR-Spheres
- 35408 – Catheterisation of the hepatic artery via a permanently implanted hepatic artery port to administer SIR-Spheres.

This application is proposing two new MBS item numbers relating to the use of TARE-Y. The two proposed item numbers are similar to MBS 35404 and 35406; the differences being that (i) they are for treatment using resin or glass microspheres and (ii) the indication is for patients with unresectable HCC.

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

☐ Yes
☒ No

(g) If yes, please advise:

Not applicable

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)*:

Not applicable

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?

Not applicable

☐ Yes
☐ No

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

Not applicable

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

Not applicable

☐ Yes (please provide PBAC submission item number below)
☐ No

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

Not applicable

Trade name: Insert trade name here
Generic name: Insert generic name here

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

☒ Yes (resin microspheres/SIR-Spheres)
☒ No (glass microspheres/TheraSphere)

(b) If yes, please provide the following information (where relevant):

Resin microspheres/SIR-Spheres
Billing code(s): SE001
Trade name of prostheses: SIR-Spheres including Delivery Apparatus
Clinical name of prostheses: Biocompatible microspheres 20-60mm (microns) in diameter containing yttrium-90.
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

(c) 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 – glass microspheres/TheraSphere; an application will be made for inclusion of glass microspheres/TheraSphere on the Prostheses List in due course.

(d) 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

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

Not applicable

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

For TARE-Y using resin microspheres/SIR-Spheres
PVC tubing, ABS stopcocks, acrylic holders and stainless steel needles with PE hubs

For TARE-Y using glass microspheres/TheraSphere
TheraSphere is supplied with the following accessories:

- One multi-use non-sterile administration accessory kit (supplied to each site), including an acrylic box base, top shield, removable side shield and bag hook. This kit ensures optimal layout of the administration set and dose vial to facilitate monitoring of the infusion process and provides beta radiation shielding.
- One single-use TheraSphere administration set which includes a gamma radiation-sterilised disposable tubing set and 1 empty sterile vial. The pre-assembled tubing set contains a needle plunger assembly and an integrated 20 ml syringe, used to deliver the microspheres from the dose vial to the patient catheter. The one-way valves incorporated in the administration set control the flow of liquid so that it will only flow in the appropriate direction (one set is needed for each dose vial infused and they are supplied in quantities of five).

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:

Resin microsphere/SIR-Spheres
Type of therapeutic good: Biocompatible microspheres 20-60µm in diameter containing yttrium-90.
Manufacturer's name: Sirtex Medical Products
Sponsor's name: Sirtex Medical Products

Glass microspheres/TheraSphere
Type of therapeutic good: Insoluble glass microspheres where yttrium-90 is an integral constituent of the glass. The mean sphere diameter ranges from 20 to 30 µm. Each milligram contains between 22,000 and 73,000 microspheres. TheraSphere® is supplied in 0.6 ml of sterile, pyrogen-free water contained in a 1.0 ml v-bottom vial secured within a clear acrylic vial shield. TheraSphere® is available in six dose sizes: 3 GBq (81 mCi), 5 GBq (135 mCi), 7 GBq (189 mCi), 10 GBq (270 mCi), 15 GBq (405 mCi) and 20 GBq (540 mCi).
Manufacturer's name: BTG International Asia
Sponsor's name: BTG International Asia

(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?

Resin microsphere/SIR-Spheres
☐ Class III
☒ AIMD
☐ N/A

Glass microsphere/TheraSphere
☐ Class III
☐ AIMD
☒ N/A; not yet registered but would be classified as an AIMD.

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)?

Resin microsphere/SIR-Spheres
☒ Yes (if yes, please provide details below)
☐ No

SIR-Spheres – radionuclide source, therapeutic, brachytherapy, manual, permanent implant
ARTG listing, registration or inclusion number: 149332
TGA approved indication(s), if applicable: Intended for the treatment of inoperable liver cancer

Thus, the current TGA-approved indication encompasses use for unresectable HCC.

Glass microsphere/TheraSphere

☐ Yes (if yes, please provide details below)

☒ No

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?

Glass microsphere/TheraSphere

☒ No

☐ Yes

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?

Glass microsphere/TheraSphere

☒ Yes (please provide details below)

☐ No

Estimated date of submission to TGA: end April 2017

Proposed indication(s), if applicable: TheraSphere is used in the treatment of hepatic neoplasia.

Thus, the proposed TGA indication encompasses use for unresectable HCC.

PART 4 – SUMMARY OF EVIDENCE

The following tables in Q18 and Q19 provide a summary of the RCT (completed and ongoing) and 'higher quality' observational study evidence available for the comparison between TARE-Y, and TACE/DEB-TACE and sorafenib. Higher quality observational evidence refers to non-randomised, comparative studies that have attempted to match on potential confounders, or adjust for potential confounding.

A number of published meta-analyses were also identified by the literature search; however, these are considered to be of poor methodological quality due to inappropriate pooling of studies, and would not be used as the basis of a clinical argument. There is, however, one ongoing prospective, individual patient meta-analysis currently underway; this would be very informative for a comparison between TARE-Y and sorafenib. The identified meta-analyses are summarised following the RCT and observational study tables, as is the ongoing prospective, individual patient data meta-analysis.

It should be noted there are also a number of single-arm case series that provide additional supportive evidence of the efficacy and safety of TARE-Y in HCC that have not been included here.

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 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 cohort study[3] Hong Kong/Queen Elizabeth Hospital 2006-2012	Kwok et al. (2014). "Survival benefit of radioembolization for inoperable hepatocellular carcinoma using yttrium-90 microspheres." J Gastroenterol Hepatol 29(11): 1897-1904.	*Population:* inoperable HCC; N=46 *Comparison:* TARE-Y (SIR-Spheres) versus no TARE-Y *Outcomes:* overall survival; tumour response; adverse events	http://onlinelibrary.wiley.com/doi/10.1111/jgh.12621/abstract;jsessionid=099F60D1CEE0DC86CC9114714EFAE542.f04t04	2014
2.	Retrospective cohort study Spain/ Clinica Universitaria, Pamplona 1996-2008	D'Avola et al. (2009). "A retrospective comparative analysis of the effect of Y90-radioembolization on the survival of patients with unresectable hepatocellular carcinoma." Hepatogastroenterology 56(96): 1683-1688.	*Population:* unresectable HCC; N=35 *Comparison:* TARE-Y (SIR-Spheres) versus conventional care (active treatment or supportive care) *Outcomes:* overall survival	https://www.ncbi.nlm.nih.gov/pubmed/20214218	2009

[3] Observational studies were only eligible for inclusion in this list if they were comparative, and used appropriate methodology to control for potential confounding (eg, multivariate analysis and/or matching).

	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
3.	RCT – phase II Single-centre US	Salem et al. (2016). "Y90 Radioembolization Significantly Prolongs Time to Progression Compared with Chemoembolization in Patients with Hepatocellular Carcinoma." Gastroenterology. *Trial ID:* PREMIERE *Registration no.:* NCT00956930	*Population:* HCC; N=43 *Comparison:* TARE-Y (TheraSphere) versus TACE *Outcomes:* overall survival; time to progression; tumour response *Status:* Completed	http://www.gastrojournal.org/article/S0016-5085(16)34971-X/abstract?referrer=https%3A%2F%2Fwww.ncbi.nlm.nih.gov%2Fpubmed%2F27575820	2016
4.	RCT – pilot study 2 centres France/Spain	Kolligs et al. (2015). "Pilot randomized trial of selective internal radiation therapy vs. chemoembolization in unresectable hepatocellular carcinoma." Liver Int 35(6): 1715-1721. *Trial ID:* SIRTACE *Registration no.:* EUCTR2006-006478-79-DE/NCT00867750	Population: unresectable HCC; N=28 *Comparison:* TARE-Y (SIR-Spheres) versus TACE *Outcomes:* progression-free survival; tumour response; time to response; health-related quality of life; downstaging; adverse events *Status:* completed	http://onlinelibrary.wiley.com/doi/10.1111/liv.12750/abstract	2015
5.	RCT – pilot study Single-centre Germany	Pitton et al. (2015). "Randomized comparison of selective internal radiotherapy (SIRT) versus drug-eluting bead transarterial chemoembolization (DEB-TACE) for the treatment of hepatocellular carcinoma." Cardiovasc Intervent Radiol 38(2): 352-360. *Trial ID:* SIRT-TACE-HCC-Mainz-1 *Registration no.:* NCT01798160	*Population:* HCC; N=24 *Comparison:* TARE-Y (SIR-Spheres) versus DEB-TACE *Outcomes:* overall survival; progression-free survival; time to progression; adverse events *Status:* completed	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4355443/pdf/270_2014_Article_1012.pdf	2015
6.	Retrospective cohort study US/SEER database 2004-2009	Massani et al. (2016). "Yttrium-90 radioembolization versus transarterial chemoembolization for unresectable hepatocellular carcinoma: A comparative analysis." HPB 18: e200-e201.	*Population:* unresectable HCC; N=73 *Comparison:* TARE-Y (not stated) versus TACE in patients with unresectable HCC Outcomes: overall survival	http://www.hpbonline.org/article/S1365-182X(16)30506-8/pdf	2016

	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
7.	Retrospective cohort study US/SEER database 2004-2009	Sanoff et al. (2015). "Effectiveness of Initial Transarterial Chemoembolization for Hepatocellular Carcinoma Among Medicare Beneficiaries." J Natl Compr Canc Netw 13(9): 1102-1110.	*Population:* HCC; N=NR *Comparison:* TARE-Y (not stated) versus TACE *Outcomes:* overall survival; 90-day mortality	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4861995/pdf/nihms781895.pdf	2015
8.	Case-control study US/Mayo Clinic 2005-2008	Moreno-Luna et al. (2013). "Efficacy and safety of transarterial radioembolization versus chemoembolization in patients with hepatocellular carcinoma." Cardiovasc Intervent Radiol 36(3): 714-723.	*Population:* unresectable HCC without PVT; N=116 *Comparison:* TARE-Y (TheraSphere) versus TACE *Outcomes:* overall survival; tumour response; hospitalisation; treatment days; adverse events	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3594060/pdf/nihms417150.pdf	2013
9	Prospective cohort study Hong Kong/Queen Mary Hospital 2009-2013	She et al. (2014). "Survival analysis of transarterial radioembolization with yttrium-90 for hepatocellular carcinoma patients with HBV infection." Hepatobiliary Surg Nutr 3(4): 185-193.	*Population:* HCC with HBV infection; N=32 *Comparison:* TARE-Y (SIR-Spheres) versus TACE *Outcomes:* overall survival; treatment response	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4141294/pdf/hbsn-03-04-185.pdf	2014
10.	Prospective cohort study Italy/NR NR	Carr, (2013). "Repeated chemoembolizations and single hepatic artery 90Yttrium particle therapy confer similar benefits for unresectable HCC." Hepatology International 7: S584.	*Population:* unresectable HCC; N=932 *Comparison:* TARE-Y (TheraSphere) versus TACE *Outcomes:* overall survival; tumour response; adverse events	Not available (conference abstract only)	2013
11.	Retrospective cohort study South Korea/St Mary's Hospital 2009-2012	Yang et al. (2013). "Comparative analysis of treatment response for unresectable hepatocellular carcinoma: Radioembolization versus 3D-CRT combined with TACE." Hepatology 58(4 SUPPL. 1): 1275A.	*Population:* Intermediate to advanced HCC; N=38 *Comparison:* TARE-Y (not stated) versus TACE + 3D-CRT *Outcomes:* overall survival; treatment response	Not available (conference abstract only)	2013

	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
12.	Retrospective cohort study US/Case Western Reserve University School of Medicine 2007 -2010	Lance et al. (2011). "Comparative analysis of the safety and efficacy of transcatheter arterial chemoembolization and yttrium-90 radioembolization in patients with unresectable hepatocellular carcinoma." J Vasc Interv Radiol 22(12): 1697-1705.	*Population:* unresectable HCC; N=73 *Comparison:* TARE-Y (any) with TACE *Outcomes:* overall survival; tumour response; adverse events	http://www.jvir.org/article/S1051-0443(11)01180-8/abstract	2011
13.	Retrospective cohort study US/Northwestern University 9-year period	Salem et al. (2011). "Radioembolization results in longer time-to-progression and reduced toxicity compared with chemoembolization in patients with hepatocellular carcinoma." Gastroenterology 140(2): 497-507.e492.	*Population:* unresectable HCC; N=245 *Comparison:* TARE-Y (TheraSphere) versus TACE *Outcomes:* overall survival; time to progression; tumour response, adverse events	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3129335/pdf/nihms250487.pdf	2011
14.	Retrospective cohort study US/Emory University 1996-2006	Kooby et al. (2010). "Comparison of yttrium-90 radioembolization and transcatheter arterial chemoembolization for the treatment of unresectable hepatocellular carcinoma." J Vasc Interv Radiol 21(2): 224-230.	*Population:* unresectable HCC; N=71 *Comparison:* TARE-Y (SIR-Spheres) with TACE *Outcomes:* overall survival; tumour response; adverse events	http://www.jvir.org/article/S1051-0443(09)01049-5/abstract	2010

	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
15.	Prospective cohort study US/multicentre 2007-2013	Akinwande et al. (2016). "Radioembolization Versus Chemoembolization (DEBDOX) for the Treatment of Unresectable Hepatocellular Carcinoma: A Propensity Matched Study." Anticancer Res 36(1): 239-246.	*Population:* unresectable HCC; N=358 (96 matched) *Comparison:* TARE-Y (TheraSphere) with DEB-TACE *Outcomes:* overall survival; progression-free survival; tumour response; adverse events	http://ar.iiarjournals.org/content/36/1/239.long	2016
16.	Retrospective cohort study[4] US/multicentre 2007-2013	Akinwande et al. (2015). "Is radioembolization (^{90}Y) better than doxorubicin drug-eluting beads (DEBDOX) for hepatocellular carcinoma with portal vein thrombosis? A retrospective analysis." Surg Oncol 24(3): 270-275.	*Population:* HCC and PVT; N=48 *Comparison:* TARE-Y (TheraSphere) versus DEB-TACE *Outcomes:* overall survival; tumour response; adverse events	http://www.so-online.net/article/S0960-7404(15)30008-6/abstract	2015
17.	RCT 28 centres France	Vilgrain et al. (2014). "Radioembolisation with yttrium90 microspheres versus sorafenib for treatment of advanced hepatocellular carcinoma (SARAH): study protocol for a randomised controlled trial." Trials 15: 474. *Trial ID:* SARAH[5] *Registration no.:* NCT01482442	*Population:* advanced HCC; N~440 *Comparison:* TARE-Y (SIR-Spheres) versus sorafenib *Outcomes:* overall survival; progression-free survival; tumour response; general or liver disease-specific quality of life; adverse events *Status:* completed[6]	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4265525/pdf/13063_2014_Article_2333.pdf	2014

[4] Likely represents a subset of the patients included in Akinwande 2016.
[5] Data from SIRveNIB and SARAH will be used in the prospective individual patient meta-analysis study, VESPRO. See page 24.
[6] No results available as yet. Results will be presented at the European Association for the Study of the Liver, International Liver Congress (EASL/ILC) in Amsterdam, the Netherlands from 19th-23rd April 2017. If not embargoed, the study abstract will be released on 5 April, 2017.

	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
18.	RCT Single-centre Germany	Ricke et al. (2015). "Safety and toxicity of radioembolization plus Sorafenib in advanced hepatocellular carcinoma: analysis of the European multicentre trial SORAMIC." Liver Int 35(2): 620-626. *Trial ID:* SORAMIC *Registration no.:* NCT01126645	*Population:* inoperable HCC ± PVT; N~375 (interim analysis = 40) *Comparison:* TARE-Y (SIR-Spheres) + sorafenib versus sorafenib alone *Outcomes:* adverse events *Status:* still recruiting. Interim safety results published. EDC = March 2018	http://onlinelibrary.wiley.com/doi/10.1111/liv.12622/abstract	2015
19.	Retrospective cohort study Korea/6 centres 2008-2013	Cho et al. (2016). "Radioembolization Is a Safe and Effective Treatment for Hepatocellular Carcinoma with Portal Vein Thrombosis: A Propensity Score Analysis." PLoS One 11(5): e0154986.	*Population:* HCC with PVT; N=63 *Comparison:* TARE-Y (SIR-Spheres) versus sorafenib *Outcomes:* overall survival; time to progression; tumour response; adverse events	http://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0154986&type=printable	2016
20.	Retrospective cohort study Spain/4 centres 2005-2013	de la Torre et al. (2016). "A comparison of survival in patients with hepatocellular carcinoma and portal vein invasion treated by radioembolization or sorafenib." Liver Int 36(8): 1206-1212.	*Population:* HCC with PVT; N=73 *Comparison:* TARE-Y (SIR-Spheres) versus sorafenib *Outcomes:* overall survival	http://onlinelibrary.wiley.com/doi/10.1111/liv.13098/abstract	2016
21.	Retrospective cohort study France/2 centres 2005-2013	Edeline et al. (2016). "Selective internal radiation therapy compared with sorafenib for hepatocellular carcinoma with portal vein thrombosis." Eur J Nucl Med Mol Imaging 43(4): 635-643.	*Population:* HCC with PVT; N = 151 (48 matched) *Comparison:* TARE-Y (TheraSphere) versus sorafenib *Outcomes:* overall survival; tumour response; adverse events	http://link.springer.com/article/10.1007%2Fs00259-015-3210-7	2016

	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
22.	Retrospective cohort study Italy/University of Bologna 2005-NR	Gramenzi et al. (2015). "Yttrium-90 radioembolization vs sorafenib for intermediate-locally advanced hepatocellular carcinoma: a cohort study with propensity score analysis." Liver Int 35(3): 1036-1047.	*Population:* HCC with PVT, very large intermediate HCC or where previous therapies had failed; N=137 (64 matched) *Comparison:* TARE-Y (SIR-Spheres) versus sorafenib *Outcomes:* overall survival; time to progression; tumour response; adverse events	http://onlinelibrary.wiley.com/doi/10.1111/liv.12574/abstract	2015

Abbreviations: 3D-CRT, three-dimensional conformal radiotherapy; DEB, drug-eluting beads; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; NR, not reported; PVT, portal vein thrombosis; RCT, randomised controlled trial; TACE, transarterial chemoembolisation; TARE-Y, transarterial radioembolisation with yttrium-90.

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)	Estimated date of completion
1.	RCT Belgium; The Netherlands	Seinstra et al. (2012). "Transarterial radioembolization versus chemoembolization for the treatment of hepatocellular carcinoma (TRACE): study protocol for a randomized controlled trial." Trials 13: 144. *Trial ID:* TRACE *Registration no:* NCT01381211	*Population:* HCC; N~140 *Comparison:* TARE-Y (TheraSphere) versus DEB-TACE *Outcomes:* overall survival; time to progression; tumour response; quality of life; adverse events *Status:* Recruiting	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3493260/pdf/1745-6215-13-144.pdf	Dec 2016
2.	RCT Saudi Arabia	Transarterial radioembolization versus chemoembolization for the treatment of advanced hepatocellular carcinoma *Trial ID:* RAC#2131 134 *Registration no:* NCT02729506	*Population:* advanced HCC; N~150 *Comparison:* TARE-Y (any) versus DEB-TACE *Outcomes:* overall survival; time to progression; tumour response; quality of life; adverse events *Status:* Recruiting	https://clinicaltrials.gov/ct2/show/NCT02729506	Dec 2017
3.	RCT US, Belgium, France, Italy, Spain, UK	Sinclair (2014). "A prospective randomized clinical trial on 90yttruim transarterial radioembolization (TheraSphere) vs standard of care (sorafenib) for the treatment of advanced hepatocellular carcinoma with portal vein thrombosis." Journal of Vascular and Interventional Radiology 25(5): 817. *Trial ID:* YES-P *Registration no.:* NCT01887717/ EUCTR2012-005375-14-GB/EUCTR2012-005375-14-BE	*Population:* advanced HCC with PVT; N~328 *Comparison:* TARE-Y (TheraSphere) versus sorafenib *Outcomes:* overall survival; time to progression; tumour response; quality of life; adverse events *Status:* ongoing	https://clinicaltrials.gov/ct2/show/NCT01887717	Dec 2019

	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)	Estimated date of completion
4.	RCT Asia, New Zealand Australia	Gandhi et al. (2016). "Single administration of Selective Internal Radiation Therapy versus continuous treatment with sorafeNIB in locally advanced hepatocellular carcinoma (SIRveNIB): Study protocol for a phase iii randomized controlled trial." BMC Cancer 16(1): no pagination. *Trial ID:* SIRveNIB[7] *Registration no.:* NCT 01135056	*Population:* locally advanced HCC; N~360 *Comparison:* TARE-Y (SIR-Spheres) versus sorafenib *Outcomes:* overall survival; time to progression; tumour response; quality of life; adverse events *Status:* ongoing	http://www.biomedcentral.com/bmccancer/	Recruitment ended in May 2016. The final analysis will be triggered after mortality reaches 266.
5.	RCT United States; Belgium; Canada; China; France; Germany; Italy; Korea, Republic of Singapore; Spain; United Kingdom	Karpf (2015). "A phase III clinical trial of intra-arterial yttrium-90 glass microspheres in the treatment of patients with unresectable hepatocellular carcinoma." Journal of Clinical Oncology 33(3 SUPPL. 1): 477. *Trial ID:* STOP-HCC *Registration no:* NCT01556490	*Population:* unresectable HCC; N~390 *Comparison:* TARE-Y (TheraSphere) + sorafenib versus sorafenib alone *Outcomes:* overall survival; time to progression; tumour response; quality of life *Status:* recruiting	http://ascopubs.org/doi/abs/10.1200/jco.2015.33.3_suppl.477	Oct 2019

Abbreviations: DEB, drug-eluting beads; HCC, hepatocellular carcinoma; PVT, portal vein thrombosis; RCT, randomised controlled trial; TACE, transarterial chemoembolisation; TARE-Y, transarterial radioembolisation with yttrium-90.

[7] Data from SIRveNIB and SARAH will be used in the prospective individual patient meta-analysis study, VESPRO. See page 24.

Supplementary information 1: completed meta-analyses

	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.	Head-to-head meta-analysis of RCTs • Kolligs 2015 • Ricke 2015	Abdel-Rahman and Elsayed (2016). "Yttrium-90 microsphere radioembolisation for unresectable hepatocellular carcinoma." Cochrane Database Syst Rev 2: Cd011313.	*Population:* unresectable HCC *Comparison:* TARE-Y (any) versus any comparator *Outcomes:* none (insufficient evidence)	http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011313.pub2/full	2016
2.	Head-to-head meta-analysis of RCTs (2)/OBS (8) • Pitton 2015 • Kolligs 2015 • Ahmad 2005 • Kooby 2010 • Carr 2010 • Salem 2011 • Lance 2011 • Morena-Luna 2013 • El Fouly 2015 • Akinwande 2015	Facciorusso et al. (2016). "Transarterial radioembolization vs chemoembolization for hepatocarcinoma patients: A systematic review and meta-analysis." World J Hepatol 8(18): 770-778.	*Population:* HCC *Comparison:* TARE-Y (any) versus TACE *Outcomes:* overall survival; 1-yr survival rate; 2-y survival rate; 3-yr survival rate	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4921799/pdf/WJH-8-770.pdf	2016

	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
3.	Head-to-head meta-analysis of OBS • Akinwande 2015 • Morena-Luna 2013 • Lance 2011 • Salem 2011 • Kooby 2010	Lobo et al. (2016). "Unresectable Hepatocellular Carcinoma: Radioembolization Versus Chemoembolization: A Systematic Review and Meta-analysis." Cardiovasc Intervent Radiol 39(11): 1580-1588.	*Population:* unresectable HCC *Comparison:* TARE-Y versus TACE *Outcomes:* 1-yr survival rate; 2-yr survival rate; 3-yr survival rate; 4-yr survival rate; tumour response; complications	http://link.springer.com/article/10.1007%2Fs00270-016-1426-y	2016
4.	RCT Asia, New Zealand Australia	Gandhi et al. (2016). "Single administration of Selective Internal Radiation Therapy versus continuous treatment with sorafeNIB in locally advanced hepatocellular carcinoma (SIRveNIB): Study protocol for a phase iii randomized controlled trial." BMC Cancer 16(1): no pagination. *Trial ID:* SIRveNIB[8] *Registration no.:* NCT 01135056	*Population:* locally advanced HCC; N~360 *Comparison:* TARE-Y (SIR-Spheres) versus sorafenib *Outcomes:* overall survival; time to progression; tumour response; quality of life; adverse events *Status:* ongoing	http://www.biomedcentral.com/bmccancer/	Recruitment ended in May 2016. The final analysis will be triggered after mortality reaches 266.
5.	RCT United States; Belgium; Canada; China; France; Germany; Italy; Korea, Republic of Singapore; Spain; United Kingdom	Karpf (2015). "A phase III clinical trial of intra-arterial yttrium-90 glass microspheres in the treatment of patients with unresectable hepatocellular carcinoma." Journal of Clinical Oncology 33(3 SUPPL. 1): 477. *Trial ID:* STOP-HCC *Registration no:* NCT01556490	*Population:* unresectable HCC; N~390 *Comparison:* TARE-Y (TheraSphere) + sorafenib versus sorafenib alone *Outcomes:* overall survival; time to progression; tumour response; quality of life *Status:* recruiting	http://ascopubs.org/doi/abs/10.1200/jco.2015.33.3_suppl.477	Oct 2019

[8] Data from SIRveNIB and SARAH will be used in the prospective individual patient meta-analysis study, VESPRO. See page 24.

	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
6.	Network meta-analysis of 16 RCTs/OBS including 4 OBS related to TARE-Y • Moreno-Luna 2013 • Kooby 2010 • Carr 2001 • Lewandowski 2009	Tao et al (2016). "A mixed analysis comparing nine minimally invasive surgeries for unresectable hepatocellular carcinoma patients." Oncotarget.	*Population:* unresectable HCC *Comparison:* TARE-Y versus eight other treatments (TACE, DEB-TACE, TACE+EBRT, TACE+HIFU, TACE+PEI, TEA) *Outcomes:* tumour response	http://www.impactjournals.com/oncotarget/index.php?journal=oncotarget&page=article&op=download&path%5B%5D=12348&path%5B%5D=39117	2016
7.	Head-to-head meta-analysis of OBS: • Carr 2010 • She 2014 • El Fouly 2014 • Moreno-Luna 2013 • Salem 2011 • Lance 2011 • Kooby 2010 • Lewandowski 2009	Zhang et al. (2015). "Transarterial Y90 radioembolization versus chemoembolization for patients with hepatocellular carcinoma: A meta-analysis." Biosci Trends 9(5): 289-298.	*Population:* HCC *Comparison:* TARE-Y versus TACE *Outcomes:* overall survival; 1-yr survival rate; 2-yr survival rate; 3-yr survival rate; time-to-progression; hospitalisation-time days; tumour response; complications	https://www.jstage.jst.go.jp/article/bst/9/5/9_2015.01089/_pdf	2015

	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
8.	Head-to-head meta-analysis of 13 OBS with 5 relating to TARE-Y: • Salem 2011 • Carr 2010 • Kooby 2009 • Lewandowski 2009 • Ahmad 2005	Xie et al. (2012). "Comparison of transcatheter arterial chemoembolization and microsphere embolization for treatment of unresectable hepatocellular carcinoma: a meta-analysis." J Cancer Res Clin Oncol 138(3): 455-462.	*Population:* unresectable HCC *Comparison:* microsphere embolisation (including TARE-Y) versus TACE *Outcomes:* overall survival; 1-yr survival; complete response	http://link.springer.com/article/10.1007%2Fs00432-011-1117-7	2012

Abbreviations: DEB, drug-eluting beads; EBRT, external beam radiotherapy; HCC, hepatocellular carcinoma; HIFU, high intensity focused ultrasound; OBS, observational studies; PEI, percutaneous ethanol injections; RCT, randomised controlled trial; TACE, transarterial chemoembolisation; TARE-Y, transarterial radioembolisation with yttium-90; TEA, transarterial ethanol ablation.

Supplementary information 2: ongoing meta-analyses

	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.	Prospective individual patient meta-analysis • SARAH - RCT • SIRveNIB - RCT	Individual Patient Data Prospective Meta-analysis (IPD PMA) of Selective Internal Radiation Therapy (SIRT) versus Sorafenib for Locally Advanced or Recurrent Hepatocellular Carcinoma (HCC) Including SARAH and SIRveNIB Trials Study ID: VESPRO	*Population:* locally advanced or recurrent HCC *Comparison:* TARE-Y (any) versus sorafenib *Outcomes:* overall survival, tumour response, progression-free survival, progression in liver, disease control in liver, toxicity	http://www.researchprotocols.org/2017/2/e17/	Not reported. The SARAH results are due to be released in April 2017.

Abbreviations: IPD, individual patient data; HCC, hepatocellular carcinoma; PMA, prospective meta-analysis; RCT, randomised controlled trial; TARE-Y, transarterial radioembolisation with yttrium-90.

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):

Professional bodies/organisations representing health professionals who provide the specific service include:

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

Interventional Radiology Society of Australasia (IRSA)

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)

Interventional Radiology Society of Australasia (IRSA)

The Gastroenterological Society of Australia (GESA)

The Australian Liver Association

Australian New Zealand Hepatic, Pancreatic and Biliary Association (ANZHPBA)

The Medical Oncology Group of Australia (MOGA)

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

BTG International has contacted a number of consumer organisations; however, they have either not yet responded, or have stated they do not represent HCC. There is currently no consumer organisation that specifically represents patients with HCC, a group of patients who experience a disease with the highest rate of increasing mortality and the second highest rate of increasing incidence in Australia, and who are often migrants from hepatitis B-endemic countries and experience challenges in communicating with medical professionals.[9]

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

Sirtex Medical Limited

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

[9] Robotin et al. (2016) Listening to the consumer voice: developing multilingual cancer information resources for people affected by liver cancer. Health Expectations 20: 171-182.

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:

Hepatocellular carcinoma is a type of primary liver cancer arising from hepatocytes, the main cell type found in the liver. HCC is one of the most common types of cancers seen worldwide, being the fifth most common in men and the ninth most common in women, and is the third largest contributor to cancer mortality overall. Liver cancer has a very poor prognosis – the mortality to incidence ratio of liver cancer is 0.95.[10]

The most commonly used staging system for HCC is the Barcelona Clinic Liver Cancer (BCLC) algorithm, shown in **Table 1**. Classification into stages 0 (very early stage), A (early stage), B (intermediate stage), C (advanced stage) and D (terminal stage) is dependent on (i) the number, size and extent of spread of the tumour/s, (ii) the Child-Pugh score (which measures the extent of liver disease) and (iii) and the patient's performance status. When the patient with HCC has decompensated liver disease and poor performance status, this is considered to be the terminal stage and treatment is palliative only. In BCLC 0 and A HCC, the patient has few tumours, reasonable liver function and good performance status; as such potentially curative treatment such as ablation, resection or transplant are indicated. It should be noted that in some cases of BCLC stage A disease, patients are not considered eligible for these treatments due to lesion size, multifocality or portal hypertension/poor liver function, and so alternative treatments such as transarterial chemoembolisation (TACE) may be indicated. Intermediate and advanced HCC (BCLC-B and C) is characterised by multinodular tumours, portal invasion or extrahepatic spread, and may include moderately reduced liver function and performance status. First-line treatments for BCLC stage B and C are TACE and sorafenib, respectively. While treatments with survival benefit are available, these tumours are considered unresectable and the primary aim of treatment in these patients is palliative. *Patients with unresectable disease (unresectable stage A disease, and stage B and C disease) would be eligible for treatment with TARE-Y; however, a decision around whether to request reimbursement for TARE-Y in the total population, or a subgroup of this population, is yet to be made. This decision will be informed by feedback from appropriate clinician groups and discussion of this application with the department.*

Table 1 also summarises the prognosis of untreated and treated patients with HCC for each of the BCLC stages, and shows that the earlier HCC is detected, the better the prognosis. Unfortunately, most HCCs are diagnosed at stage B or higher.[11]

[10] Ferlay et al (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer 136: E359-E386.
[11] Park et al (2015) Global patterns of hepatocellular carcinoma management from diagnosis to death: the BRIDGE Study. Liver International 35: 2155-2166.

Table 1 Prognosis of HCC by BCLC staging system

BCLC Stage	Description	Tumour burden and invasiveness	Child-Pugh score[12]	Performance status[13]	Natural history	Recommended therapy	Expected survival with recommended therapy
Potentially curative							
0	Very early	Single < 2 cm	A	0	> 36 months	Ablation Resection Transplant	70–90% 5-year survival with ablation, transplant, resection
A	Early	Single < 5 cm or 3 nodules < 3 cm each	A and B	0	36 months	Ablation Resection Transplant **TACE in some**	50–70% 5-year survival with ablation, transplant, resection
Palliative							
B	Intermediate	Large/multinodular	A and B	0	16 months	TACE	20 months median survival
C	Advanced	Vascular invasion and/or extrahepatic spread	A and B	1-2	4-8 months	Sorafenib	6–11 months median survival
D	End stage	Any of the above	C	3-4	< 3 months	Best supportive care	-

Source: Adapted from Lau et al. (2016).[12] The populations of interest to this application are shown in bold.
Abbreviations: BCLC, Barcelona Clinic Staging System; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolisation.

There are a number of risk factors associated with the development of HCC. Most notably these include alcohol abuse, and hepatitis B (HBV) or C (HCV) infection. The causes of HCC vary across countries, with HBV being the main cause in regions where infection is endemic, and cirrhosis due to alcohol abuse, hepatitis C or obesity being the main cause in regions where HBV in not endemic. The results of the BRIDGE study, a large retrospective chart review of more than 18,000 HCC patients at 42 sites in 14 countries, show that there are a number of differences in the characteristics of patients and disease seen at diagnosis between Asian countries, and compared with Western regions.[13] The prevalence of HBV in patients diagnosed with HCC is substantially higher in China, Taiwan and South Korea (63-77%) compared with North America, Europe and Japan (10-23%), while HCV is most prevalent in this population in North America, Europe, Taiwan and Japan (31-64%), and least prevalent in China and South Korea (3-10%). Alcoholic liver disease and non-alcoholic steatohepatitis is most prevalent in this population in North America (21% and 12%, respectively) and Europe (37% and 10%, respectively) compared with Asia (4-13% and 1-6%, respectively). A recent study by Choo and colleagues (2016)[14] investigated in detail the differences in epidemiology, genetics, treatment approaches and clinical outcomes for Asian and non-Asian patients, and concludes that there are inherent differences between HCCs from Eastern and Western populations, and that this creates challenges in terms of devising a standard treatment approach. This is of particular relevance to Australia where there is substantial immigration from parts of Asia where HBV is endemic (China and India currently provide the highest number of permanent migrants to Australia),[15] and liver cancer has the highest rate of increasing mortality of all cancers – from 2.3 per 100,000 persons in 1982 to 6.0 per 100,000 in 2014, and the second highest rate of increasing incidence of all cancers (behind thyroid cancer) – 1.8 per 100,000 persons in 1982 to 6.4 per 100,000 in 2014 (AIHW, 2014).

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:

TARE-Y would be most appropriate for particular groups of patients with unresectable HCC, including:

[12] Lau et al. (2016) Current role of selective internal radiation with yttrium-90 in liver tumours. Future Oncology 12(9): 1193-1204.
[13] Park et al. (2015) Global patterns of hepatocellular carcinoma management from diagnosis to death: the BRIDGE Study. Liver International 35: 2155-2166.
[14] Choo et al. (2016) Comparison of hepatocellular carcinoma in Eastern versus Western populations. Cancer [Epub ahead of print].
[15] http://parlinfo.aph.gov.au/parlInfo/download/library/prspub/3165114/upload_binary/3165114.pdf;fileType=application%2Fpdf#search=%22migration%20%20a%20quick%20guide%22

- patients with unresectable BCLC stage A, or BCLC stage B disease who cannot tolerate TACE
- patients with BCLC stage C disease, particularly those with portal vein invasion/thrombosis (PVI/PVT) who cannot tolerate sorafenib;
- patients whose disease has previously not responded to TACE or sorafenib.
- candidates for downstaging to resection or transplantation, or who require a bridge to transplantation, who cannot tolerate other treatments.

General practitioners are usually the first point of contact for a patient. If they are diagnosed with HCC, they will then be referred to a surgeon who will determine whether the disease is resectable. If it is not, they will refer the patient to a medical oncologist or hepatologist, who may refer the patient to an interventional radiologist if they think the patient is a suitable candidate for TARE-Y. The interventional radiologist then determines the patient's suitability for TARE-Y by performing imaging, angiography and a technetium 99m macroaggregated albumin (MAA) scan to determine the extent of any lung shunting. If it is deemed safe to proceed with treatment, on treatment day the interventional radiologist will site the microcatheter in the hepatic artery and the microspheres will be prepared and injected.[16]

[16] The dose for the proposed medical service is calculated in the Nuclear Medicine department by a nuclear physicist/nuclear medicine physician or by Radiation Oncology. The dose is customised for each patient.

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):

Based on the interim results of a survey of clinicians who treat HCC, current treatment for unresectable HCC in Australia is consistent with the BCLC management pathway, in which TACE and sorafenib are the main first-line treatments: TACE for intermediate (BCLC B) disease and sorafenib for advanced (BCLC C) disease. The BCLC management pathway also states that in cases where the proposed first-line treatment is contraindicated owing to a patient's clinical status, the treatment approach recommended for the subsequent disease stage should be considered. As such, a patient with early stage HCC (BCLC stage A) might benefit from TACE.

See **Attachment 1** for a clinical management pathway flowchart. This flowchart has been developed based on the BCLC management pathway and the pathway included in the 2012 protocol for MSAC Application number 1242 (Yttrium-90 microspheres/Sirtology Pty Ltd).

PART 6b – INFORMATION ABOUT THE INTERVENTION

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

Prior to treatment

All patients undergoing TARE-Y require the following investigations, regardless of which microsphere is being used (i.e. resin or glass):

1. History, physical examination, assessment of performance status
2. Clinical laboratory tests (complete blood count with differential, blood urea nitrogen, serum creatinine, serum electrolytes, liver function, albumin, lactate dehydrogenase, prothrombin time)
3. Chest X-ray, tumour marker assay, carcinoembryonic antigen [CEA], α-fetoprotein)
4. Computed tomography (CT)/magnetic resonance imaging (MRI) scan of the abdomen and pelvis with assessment of portal vein patency
5. Arteriography/lung shunting study.

Treatment

If a patient meets the treatment requirements, and treatment occurs, a catheter is inserted into the femoral artery and then guided to the hepatic artery. The radioactive microspheres (glass or resin) are then infused, a procedure that takes several minutes. The entire procedure takes 1-1.5 hours. Following infusion, the patient remains in the recovery area or Nuclear Medicine Department for 2-6 hours. The patient may be required to remain in hospital overnight.

Medications the patient may receive on the day of treatment include:

- A sedative and pain medication (in preparation for the procedure)
- A low-dose steroid to help combat fatigue
- An anti-ulcer medication to help protect the stomach
- An antibiotic to reduce potential for infection.

Follow-up

Follow-up imaging to determine treatment response is conducted using CT or MRI. There is no standard protocol for timing of imaging; however, the first scan should be approximately 1-2 months' post-treatment, with follow-up at 3-6 months thereafter. During follow-up visits patients are also assessed for treatment-related adverse events including abdominal pain, nausea, vomiting and fatigue, as well as specific rare side effects including hepatic abscess, perihepatic ascites, pleural effusion, radiation cholecystitis and radiation pneumonitis.

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

It should be noted that this application is for TARE-Y the procedure, and not limited to a specific microsphere type. TARE-Y can be delivered using either of the two currently commercially available Y-90 emitting microsphere products – TheraSphere (glass microspheres) or SIR-Spheres (resin microspheres) – both of which have registered trademarks. The main characteristic that distinguishes these microspheres from others is the fact they contain Y-90. There are some differences between the glass and resin Y-90 microspheres as summarised in **Table 1**, with the main difference being the lower density of Y-90 per sphere for resin compared with glass microspheres. This means that more resin spheres are required to administer a given dose, thus resulting in a higher embolic effect.

If the item descriptor specifies the use of Y-90 emitting microspheres, then any new Y-90-emitting microspheres, should they become available, would also be able to be used.

Table 1 Characteristics of commercially available Y-90 microspheres

Characteristic	TheraSphere (BTG International)	SIR-Spheres (Sirtex Medical)
Isotope	Yttrium-90	Yttrium-90
Half-life; h	64.2	64.2
Material	Glass with yttrium in matrix	Resin bound with yttrium
Diameter; mean µm (range)	25 (20-30)	35 (20-60)
Activity per particle; Bq	2500	50
Spheres per 3 Bq	1.2 million	40-80 million
Spheres per dose	4 million	30-60 million
Specific gravity; g/mL	3.2	1.6
Embolic effect	Negligible	Mild
Contrast injection	No	During infusion
FDA approved indication	HCC	CLM with intrahepatic floxuridine
Australian approved indication	Not yet registered	Inoperable liver cancer

Source: adapted from Mahnken (2016)[17]
Abbreviations: CLM, colorectal liver metastases; HCC, hepatocellular carcinoma.

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, TARE-Y represents a new approach to treating a specific type of patient – those with unresectable HCC. While pharmacological agents are currently available for this patient group (chemotherapy delivered transarterially [TACE] and sorafenib), this localised radiotherapy technique offers an alternative mode of treatment for these patients, as well as providing a new treatment option for patients who fail or are contraindicated for treatment with TACE or sorafenib, but who are still eligible for further 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):

Yes, as follows:

- Accessibility – access to the proposed service may be limited by the number of approved facilities and the number of certified specialists available.

[17] Mahnken (2016) Current status of transarterial radioembolisation. World Journal of Radiology 8(5): 449-459.

- Dosage –lung exposure to radiation should not be greater than 30 Gy per treatment and 50 Gy cumulatively. Patients who require more than two treatments to achieve tumour coverage, or patients being treated repeatedly in the same target volume after progression, may require repeat Tc-99m MAA lung shunting fraction assessment.
- Quantity – In many cases, the service will be delivered once only in a lifetime. However, there may be occasions when the service is delivered twice. This may occur when the service is delivered in separate administrations to individual lobes of the liver, or in the case where a patient responds well and upon disease recurrence or new tumours, treatment is repeated. Patients receive on average 1.8 treatments per lifetime.
- Frequency – follow-up occurs no earlier than 30 days after initial treatment and at this stage administration to another lobe, or a subsequent administration, may be considered and planned. Reasons for not continuing with treatment may include: (i) progression in the treated area implying radiation resistance; (ii) development of significant extrahepatic disease; (iii) worsening of liver function; (iv) worsening of performance status.

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:

Other resources/services required at the same time as proposed medical services include:

- Drugs including a pre-treatment H2 antagonist or proton pump inhibitor and pain medication
- Hospitalisation during and after the implantation of the Y-90 microspheres
- The Y-90 microspheres.

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

Interventional radiologist

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

Not applicable. The service cannot be delegated or referred to another professional; only the interventional radiologist can conduct the implant of microspheres.

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

As noted in the current MBS item (35406) for administration of SIR-Spheres in patients with hepatic metastases secondary to colorectal cancer, and the proposed MBS item for administration of TARE-Y using resin or glass microspheres, “the procedure must be performed by a specialist or consultant physician recognised in the specialties of nuclear medicine or radiation oncology on an admitted patient in a hospital.”

Referral for this service would be limited to specialist physicians including gastroenterologists, hepatologists, medical oncologists and 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:

Interventional radiologists are required to be trained in the use of TheraSphere and SIR-Spheres. Training covers patient selection via clinical outcomes review, dosimetry/treatment planning, infusion techniques and radiation safety. The training is supplied by the relevant company (BTG and Sirtex) and no cost to the hospital is incurred. No capital purchase is required by the hospital.

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

The service can be provided in both the public and private hospital sector. The requirement for an inpatient service is that the pre-treatment screening and treatment itself requires the administration of radioactive substances. The patient will require appropriate monitoring following the procedure and to

ensure that patient and radiation safety requirements are met, the service is most reasonably delivered in an inpatient setting. The facility will require a license to receive, handle, store and manage radioactive waste disposal. The need for overnight versus day-only service is primarily determined by the nuclear medicine requirements of the hospital and regional regulations.

☒ Inpatient private hospital
☒ Inpatient public hospital
☒ Outpatient clinic – but only where they have capacity for nuclear medicine licensing or affiliation with a local hospital, and capacity to perform interventional radiology.
☐ 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:

Not applicable

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

☒ Yes
☐ No – please specify below

Specify further details here

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):

According to the BCLC management pathway, and the interim results of a clinician survey, the most commonly used treatments for unresectable HCC are **TACE** and **sorafenib**, with **drug-eluting bead-TACE (DEB-TACE)** also used (although substantially less than conventional TACE). If TARE-Y is limited to use in patients who cannot tolerate or have failed first-line treatment with TACE/DEB-TACE or sorafenib for unresectable HCC, then **no therapy (or best supportive care)**, is the most appropriate comparator.

While the main comparison will be no therapy/best supportive care, comparisons of TARE-Y against the first-line treatments TACE/DEB-TACE and sorafenib will also be included to provide assurance of its the comparative efficacy and safety.

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

☒ Yes – for TACE
☒ No – for no therapy/best supportive care and sorafenib (although it does have a PBS item number – see below)

TACE

Item 35321 – PERIPHERAL ARTERIAL OR VENOUS CATHETERISATION to administer agents to occlude arteries, veins or arterio-venous fistulae or to arrest haemorrhage, (but not for the treatment of uterine fibroids or varicose veins) percutaneous or by open exposure, excluding associated radiological services or preparation, and excluding aftercare, not being a service associated with photodynamic therapy with verteporfin

Item 35317 - PERIPHERAL ARTERIAL OR VENOUS CATHETERISATION with administration of thrombolytic or chemotherapeutic agents, BY CONTINUOUS INFUSION, using percutaneous approach, excluding associated radiological services or preparation, and excluding aftercare (not being a service associated with a service to which another item in Subgroup 11 of Group T1 or items 35319 or 35320 applies and not being a service associated with photodynamic therapy with verteporfin)

Sorafenib

PBS item number 9380Q

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):

Patients on no therapy/best supportive care would be monitored regularly for signs of disease progression.

Follow-up after treatment with TACE would be the same as that for the proposed medical service TARE-Y. Follow-up imaging to determine treatment response would be conducted using CT or MRI and the timing would be similar (1-2 months post-treatment and then 3-6 months thereafter). Patients on sorafenib would also likely be monitored for treatment response using imaging at similar intervals. During follow-up visits, patients would also be assessed for treatment-related adverse events.

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

☒ Yes – will be used instead of no treatment/best supportive care in patients who cannot tolerate, or have failed, first-line treatment with TACE or sorafenib
☐ No

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

Up to 100%

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 introduction of TARE-Y is not expected to change the current clinical pathway following treatment. Whether receiving no treatment/best supportive care or TARE-Y, patients would undergo periodic clinical and imaging assessments to determine disease progression.

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):

The clinical claim for use in patients who cannot tolerate or who have failed TACE/DEB-TACE or sorafenib would be superior efficacy and inferior harms over no treatment/best supportive care and.

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

☐ Non-inferiority
☒ Superiority over no treatment/best supportive care for use in patients who cannot tolerate or who have failed TACE/DEB-TACE or sorafenib.

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: liver toxicity; lung toxicity; adverse events; others that are identified from the evidence.

Clinical Effectiveness Outcomes: overall survival; progression-free survival; tumour response; quality of life; healthcare resource utilisation; others that are identified from the evidence.

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

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

The following table estimates the total population who might be eligible for treatment with TARE-Y **if it was available for use in all patients with unresectable HCC.** As shown in **Table 2**, the estimated number of patients who could potentially receive treatment with TARE-Y is low, ranging from 76–86 per year over the period examined. Based on the requested indications (i.e. second-line use and for bridge-to-transplant) the numbers will likely be substantially lower.

Table 2 Estimated number of patients who may receive treatment with TARE-Y

	Description	Source	2018	2019	2020	2021	2022
A	Australian Population	AIHW[18]	25,201,001	25,635,818	26,078,139	26,528,090	26,985,806
B	Proportion with liver cancer (C22)	Estimated from AIHW[18]	0.000069	0.000070	0.000071	0.000072	0.000073
C	Number of patients with liver cancer	A*B	1738	1791	1845	1901	1959
D	Adjustment for underreporting to Cancer Registries (C22)	Hong et al. (2016)[19]	1.80	1.80	1.80	1.80	1.80
E	Adjusted number of patients with liver cancer	C*D	3128	3223	3321	3422	3527
F	Proportion with HCC (C22.0)	UKCR[20]	0.50	0.5	0.5	0.5	0.5
G	Number of patients with HCC	E*F	1564	1612	1661	1711	1763
H	Proportion with unresectable tumours	Interim survey analysis	0.44	0.44	0.44	0.44	0.44
I	Number of patients with unresectable HCC	G*H	688	709	731	753	776
J	Proportion potentially eligible for TARE-Y	Interim survey analysis	0.42	0.42	0.42	0.42	0.42
K	Number of patients with who are potentially eligible for TARE-Y	I*J	289	298	307	316	326
L	Proportion of patients put forward for workup	Interim survey analysis	0.5	0.5	0.5	0.5	0.5
M	Number of patients put forward for workup	K*L	145	149	153	158	163
N	Proportion of patients with < 20% lung shunting	Interim survey analysis	0.75	0.75	0.75	0.75	0.75
O	Number of patients eligible for therapy with TARE-Y	M*N	101	104	107	111	114
P	Uptake rate	Interim survey analysis	0.7	0.7	0.7	0.7	0.7
Q	**Expected number of patients receiving TARE-Y**	**O*P**	**76**	**78**	**81**	**83**	**86**

Abbreviations: ABS, Australian Bureau of Statistics; AIHW, Australian Institute of Health and Welfare; CRUK, Cancer Research United Kingdom; HCC, hepatocellular carcinoma; TARE-Y, transarterial radioembolisation with yttrium-90.

[18] Australian Institute of Health and Welfare (AIHW) 2016. Australian Cancer Incidence and Mortality (ACIM) books: Liver Cancer, Canberra: AIHW. http://www.aihw.gov.au/acim-books.

[19] Hong et al. (2016) Novel population-based study finding higher than reported hepatocellular carcinoma incidence suggests an updated approach is needed. Hepatology 63(4): 1205-1212.

[20] Cancer Research UK, http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/liver-cancer, Accessed September 2016.

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

In many cases the service will be delivered once only in a lifetime. However, there may be occasions when the service is delivered twice. This may occur when the service is delivered in separate administrations to individual lobes of the liver, or in the case where a patient responds well and upon disease recurrence or new tumours, treatment is repeated. Patients receive on average 1.8 treatments per lifetime.

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

See above

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

It is estimated that if TARE-Y was available for any treatment, 76 patients with unresectable HCC may utilise TARE-Y in the first full year.

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:

The estimated uptake based on an interim analysis of a clinician survey, as shown in **Table 2**, is 70%. This current estimate seems high, but ultimately results in only a small number of patients receiving TARE-Y each year. The likely uptake of TARE-Y is dependent on which population/s are requested and so will be examined in greater detail when that decision is made.

It is not anticipated that there will be any constraints in meeting the needs of the proposed population. In addition, it is not expected that there would be leakage to another population. TARE-Y is only appropriate for the treatment of liver cancers, the most common of which are HCC and colorectal liver metastases. TARE-Y using SIR-Spheres is already reimbursed on the MBS for colorectal liver metastases.

PART 8 – COST INFORMATION

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

The likely cost to the MBS of providing the proposed medical procedure is approximately $5,151.65.

As described in Part 2, the medical procedure is TARE-Y for the treatment of unresectable HCC. This procedure involves the delivery of yttrium-90-containing microspheres of 20-60 µm diameter to the liver via catheterisation of the hepatic artery.

The key components and clinical steps involved in delivering the proposed medical service were presented in Section 28 and form the basis of the costings. The likely cost to the MBS of providing the proposed medical service is summarised in **Table 3** and has been split by:

- Pre-surgery costs – including attendances, pathology, radiology, angiography and the lung shunting study;
- Surgery costs - including radiology, angiography and catheterisation of the hepatic artery, as well as dosimetry, handling and injection of the microspheres;
- Post-surgery costs – including follow-up investigations such as radiology and associated attendances.

The methodology and assumptions used in the cost calculation are described below:

- The costings provided are for the first treatment only.
- The relevant MBS codes relating to the radiological and angiographic/lung shunting work-up and the interventional procedure were provided by an interventional radiologist.
- For the MBS services included in this costing, the financial unit cost used is the rebate amount, which is 75% of the Schedule Fee for in hospital services and 85% for out of hospital services. Costs are sourced from the February 2017 Medicare Benefits Schedule Book.
- Follow-up imaging to determine treatment response is assumed to be conducted using CT. There is no standard protocol for timing of imaging; however, the first scan should be approximately 1-2 months' post-treatment, and with follow-ups at 3-6 months thereafter. Thus, this costing assumes two follow-up scans per patient.

As the perspective of the costings is from the MBS, PBS services for medications on the day of surgery are not included. Similarly, hospital costs such as overnight stay or a radiation safety officer are not included because they will be paid by the hospital or private health funds.

The Y-90 microspheres will be available on the Prostheses List and as such are not a cost to MBS as they will be paid by private health funds. At present, the only brand of microsphere currently commercially available is SIR-Spheres. An application for inclusion of TheraSphere on the Prostheses List will be made by BTG International in due course.

There will likely be a proportion of patients who undergo pre-surgery work-up (attendances, pathology and radiology) who are unsuitable for delivery of the microspheres due to significant lung shunting; this proportion is estimated to be approximately 25%. Weighting the workup costs to account for these patients increases the average cost per patient for the first treatment to **$5777.58**.

As stated, the costings provided in the table are per patient for the first treatment only. Subsequent treatments (on average an additional 0.8 per patient) are expected to increase the cost (assuming the work-up does not need to be repeated) to **$7764.36**.

The management of adverse events has not been included in the costings. This is because the common events such as abdominal pain, nausea, vomiting and fatigue are generally mild in nature and easily managed. Regarding the specific rare side effects including hepatic abscess, perihepatic ascites, pleural effusion, radiation cholecystitis and radiation pneumonitis, these are reduced by having a thorough pre-

surgery work up. Inclusion of costs relating to both adverse events and the work-up may double count costs to an extent.

Table 3 Likely per patient cost of providing the proposed medical service – first treatment only

Description	Fee	Benefit	Source	Base units per person	Cost
	A	B	C	D	E = B x D
Pre-surgery work-up					
Attendances - History and physical exam					
- consultant physician	$85.55	$72.75	MBS 104	1	$72.75
- haematologist	$85.55	$72.75	MBS 104	1	$72.75
- radiologist	$85.55	$72.75	MBS 104	1	$72.75
Pathology					
- full blood count	$16.95	$14.45	MBS 65070	1	$14.45
- Liver function test	$17.70	$15.05	MBS 66512	1	$15.05
- Alpha-fetoprotein test	$44.60	$37.95	MBS 66653	1	$37.95
- coagulation test	$13.70	$11.65	MBS 65120	1	$11.65
Radiology					
- CT scan with contrast (lungs abdomen)	$560.00	$479.80	MBS 56807	1	$479.80
- Ultrasonic cross-sectional echography	$109.10	$92.75	MBS 55054	1	$92.75
Angiography					
- Selective arteriography or selective venography by DSA technique - 3+ vessels	$144.25	$122.65	MBS 60078	1	$122.65
- DSA - 10+ runs	$1,376.30	$1,296.10	MBS 60033	1	$1,296.10
Nuclear medicine					
- Technetium 99m scan with MAA	$253.00	$215.05	MBS 61499	1	$215.05
Surgery					
Ultrasonic cross-sectional echography	$109.10	$81.85	MBS 55054	1	$81.85
Selective arteriography or selective venography by DSA technique - 3+ vessels	$144.25	$108.20	MBS 60078	1	$108.20
DSA - 10+ runs	$1,376.30	$1,032.25	MBS 60033	1	$1,032.25
Trans-femoral catheterisation of hepatic artery	$813.30	$610.00	**Proposed**	1	$610.00
Injection of Y-90 microspheres	$346.60	$259.95	**Proposed**	1	$259.95
Post-surgery - Year 1					
- CT scan with contrast (lungs abdomen)	$283.85	$241.30	MBS 56847	2	$482.60
- consultant physician (subsequent)	$43.00	$36.55	MBS 105	2	$73.10
TOTAL COSTS					$5,151.65

Abbreviations: CT, computed tomography; DSA, digital subtraction angiography; MAA, macroaggregated albumin; MBS, Medicare Benefits Schedule.

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

The different components of the service typically take the approximately 1-2.25 hours and include the following:

- Transfemoral catheterisation – 0.25 to 1 hour
- Y-90 microsphere dose handling and injection – 0.5 hour
- Y-90 microsphere infusion – 0.25 to 0.75 hour.

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.

The proposed MBS item descriptors are presented below. These are based on the existing descriptors for SIRT using SIR-Spheres in patients with *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*. Please note that an item based on MBS 35408 (catheterisation of the hepatic artery via a permanently implanted hepatic artery port to administer SIR-Spheres) has not been requested as this procedure is no longer used.

These proposed descriptors may be refined depending on the outcome of discussions with the Department, feedback from PASC, and the availability of clinical evidence.

Category 3 – THERAPEUTIC PROCEDURES	
Group	T8 – SURGICAL OPERATIONS
Subgroup	3 – VASCULAR
Subheading	13 – INTERVENTIONAL RADIOLOGY PROCEDURES

Proposed item descriptor:

DOSIMETRY, HANDLING AND INJECTION OF yttrium-90-emitting microspheres for selective internal radiation therapy of hepatocellular carcinoma that is not suitable for resection or ablation [specific population groups to be added as appropriate], not being a service to which item 35317, 35319, 35320 or 35321 applies

The procedure must be performed by a specialist or consultant physician recognised in the specialties of nuclear medicine or radiation oncology on an admitted patient in a hospital.

Fee: $346.60 Benefit: 75% = $259.95

Category 3 – THERAPEUTIC PROCEDURES	
Group	T8 – SURGICAL OPERATIONS
Subgroup	3 – VASCULAR
Subheading	13 – INTERVENTIONAL RADIOLOGY PROCEDURES

Proposed item descriptor:

Trans-femoral catheterisation of the hepatic artery to administer yttrium-90-emitting microspheres to embolise the microvasculature of hepatocellular carcinoma that is not suitable for resection or ablation [specific population groups to be added as appropriate], 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

Fee: $813.30 Benefit: 75% = $610.00

PART 9 – FEEDBACK

The Department is interested in your feedback.

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

~ 15 days

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

☒ Yes, but see below
☐ No

(b) If no, provide areas of concern:

There is a lot of detail required considering all we wanted to do was initiate the discussion with the Department. A mechanism for having a pre-application meeting (similar to the PBAC pre-submission meetings) would have been useful, given that we already know that TARE-Y is definitely eligible for MSAC funding as it is currently funded on an interim basis for another indication.

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?

Not applicable

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:

See comment above.