



Australian Government

Department of Health

MSAC Application 1648

ONCOSIL™ FOR LOCALLY ADVANCED UNRESECTABLE PANCREATIC CANCER

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

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

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

Email: hta@health.gov.au

Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant):

Corporation name: OncoSil™ Medical Pty Ltd

ABN: 89 113 824 141

Business trading name: OncoSil™ Medical

Primary contact name: REDACTED

Alternative contact numbers

Business: **REDACTED**

Mobile: **REDACTED**

Email: **REDACTED**

Alternative contact name: REDACTED

Primary contact numbers

Business: **REDACTED**

Mobile: **REDACTED**

Email: **REDACTED**

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

Yes

No

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

Yes

No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

OncoSil™ MSAC application for locally advanced unresectable pancreatic cancer.

4. 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)

Pancreatic cancer is an insidious disease. Few symptoms occur in the early stages of the disease and symptoms that are specific enough to suspect pancreatic cancer typically do not develop until the disease has reached an advanced stage (Ryan et al., 2014, Vincent et al., 2011). Therefore, it is common for the disease to have spread beyond the pancreas at the time of diagnosis (Cancer., 2014, Bond-Smith et al., 2012).

The majority of patients (around 85%) present with advanced disease that is not amenable to potentially curative surgery. Out of these 85% patients, approximately 30% of these patients present with unresectable locally advanced (non-metastatic) disease, the remainder (55%) present with overt metastatic disease.

Although pancreatic cancer is typically considered a systemic disease, it is recognized that local progression, even in those with metastases, causes a significant burden of morbidity as well as mortality. 10–25% of patients experience local progression along with distant spread before death. (Iacobuzio-Donahue et al., 2009) Because of close proximity to vital organs, local progression from pancreatic cancer is a cause of significant morbidity, and current treatment options are limited. Based on autopsy study, around 30% of patients die due to consequences of locally destructive tumour growth (Iacobuzio-Donahue et al., 2009). Improving local control is therefore an important clinical objective (Balaban et al., 2017).

5. 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)

OncoSil™ is a device that imparts a pre-determined dose of beta radiation directly into the cancerous tissue. The beta particles emitted by OncoSil™ travel a short distance in tissue causing damage to cancer cell DNA, which renders them incapable of further cell division and proliferation. OncoSil™ in combination with Gemcitabine or FOLFIRINOX proves to be a better treatment option for locally advanced unresectable pancreatic cancer.

There are three proposed medical services:

Nuclear Medicine

- i. Professional attendance and handling for assessment and preparation of OncoSil microparticles for injection of by endoscopic ultrasound (endoscopy with ultrasound imaging).
- ii. SPECT-CT Scan on Day 1 and Day 7 post OncoSil implantation

Endoscopy

- i. Injection of OncoSil by endoscopic ultrasound (endoscopy with ultrasound imaging)

6. (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:

In addition to three new codes requested, two current MBS codes are requested to be amended to accommodate this service and proposed new item codes.

The two codes are: MBS Item 61462 and MBS Item 61505

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

- i. Minor amendments to the item descriptor that does not affect how the service is delivered
- ii. An amendment to an existing specific single consultation item
- iii. An amendment to an existing global consultation item(s)
- iv. 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

7. 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

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

N/A

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

- Pharmaceutical / Biological
- Prosthesis or device
- No

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

N/Ap

(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)?

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

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

Yes

No

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

Billing code(s): N/A

Trade name of prostheses: N/A

Clinical name of prostheses: N/A

Other device components delivered as part of the service: N/A

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

Will be considered in future

Yes

No

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

Yes

No

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

N/A

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

Single use consumables: OncoSil device delivering P-32 micro-particles

Multi-use consumables: Nil

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (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: Brachytherapy device

Manufacturer's name: OncoSil™

Sponsor's name: OncoSil™ Medical

- (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

14. (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: N/A

TGA approved indication(s), if applicable: N/A

TGA approved purpose(s), if applicable: N/A

15. 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

Date of submission to TGA: **REDACTED**

Estimated date by which TGA approval can be expected: **REDACTED**

TGA Application ID: **REDACTED**

TGA approved indication(s): Proposed: OncoSil™ is intended for intratumoural implantation into a pancreatic tumour via injection under endoscopic ultrasound guidance. OncoSil™ is indicated for the treatment of patients with locally advanced unresectable pancreatic cancer.

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

N/A

PART 4 – SUMMARY OF EVIDENCE

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

	Type of study*	Title of research	Short description of research **	Website link to research	Date***
1	PanCO Study Abstracts	<p>PanCO: An Open-Label, Single-Arm Pilot Study of Phosphorus-32 Microparticles in Unresectable Locally Advanced Pancreatic Adenocarcinoma with FOLFIRINOX or Gemcitabine + Nab-Paclitaxel Chemotherapies</p> <p>Paul Ross et al</p> <p>NCRI cancer conference abstracts: 2019</p>	<p>LAPC has a poor prognosis with chemotherapy or chemoradiotherapy being the only standard treatment available. This study abstract reports the initial results of the ongoing pilot study in combination with chemotherapy. The patients received GNP or FOLFIRINOX. The diffusion pattern of P-32 suspension was assessed by EUS and bremsstrahlung SPECT/CT. The response was assessed using RECIST 1.1 with CT scans every 8 weeks and FDG-PET scans at baseline and week 12. Out of the 42 patients implanted with P-32 10 received FOLFIRINOX and 40 received GNP. 39 adverse events were related to study device/procedure of which 2 were grade 3 (abdominal pain, fatigue). No serious device- or radiation-related toxicities reported.</p>	<p>https://abstracts.ncri.org.uk/abstract/panco-an-open-label-single-arm-pilot-study-of-phosphorus-32-microparticles-in-unresectable-locally-advanced-pancreatic-adenocarcinoma-with-folfirinox-or-gemcitabine-nab-paclitaxel-chemotherapies/</p>	June 2019

	Type of study*	Title of research	Short description of research **	Website link to research	Date***
2	Open Label, Single Arm Pilot Study	Mo1304 PANCO: An Open Label, Single Arm Pilot Study of ONCOSIL™, administered to study participants with unresectable locally advanced Pancreatic Adenocarcinoma, given in combination with Folfirinox or gemcitabine +Nab paclitaxel chemotherapies Daniel Crough et al. Gastrointestinal Endoscopy Volume 87, Issue 6, Supplement, June 2018, Page AB437	The initial five patients (3 males, 2 females, median age 70 years [range 63-72 years] with inoperable LAPC were implanted with a single dose of P-32, directly into the pancreatic tumor via EUS guidance. CT scans were conducted every 8 weeks. At 16 weeks, the target tumor response rate (PR) was 20% and target tumor control rate (PR, SD) was 80%. At week 16, 124 adverse events (AEs) occurred in the 5 patients. Nineteen AEs (15%) were considered a CTC grading of 3 (severe) and 4 AEs (3%) were grade 4 (life threatening). None of which have been attributed to the device or the implant procedure. Early data indicates EUS-guided implantation of P-32 was technically easy and well tolerated.	https://doi.org/10.1016/j.gie.2018.04.1954	1 June 2018
3	Open Label, Single Arm Pilot Study	PanCO: An open-label, single-arm pilot study of phosphorus-32 (P-32; OncoSil™) microparticles in patients with unresectable locally advanced pancreatic adenocarcinoma (LAPC) in combination with FOLFIRINOX or gemcitabine + nab-paclitaxel (GNP) chemotherapies Paul J. Ross et al. Journal of Clinical Oncology 2019 37:15_suppl, 4125-4125	P-32 Microparticles is a brachytherapy device that implants a predetermined dose of P-32 into pancreatic tumours via endoscopic ultrasound (EUS) guidance. 42 patients were implanted with the device out of which 28 were male and the median age being 65. From the initial reports of the pilot study, the use of EUS-guided implantation of P-32 was found to be feasible, with an acceptable safety profile in combination with first-line chemotherapy for LAPC patients. Encouraging OR and DCR are observed. Further follow-up is necessary to inform results of local progression free survival and progression free survival.	https://ascopubs.org/doi/abs/10.1200/JCO.2019.37.15_suppl.4125	26 May 2019

	Type of study*	Title of research	Short description of research **	Website link to research	Date***
4	Open Label, Single Arm Pilot Study	<p>OncoPaC-1: An Open-label, Single-Arm Pilot Study of Phosphorus-32 Microparticles Brachytherapy in Combination with Gemcitabine +/- Nab-Paclitaxel in Unresectable Locally Advanced Pancreatic Cancer</p> <p>Bhutani, M.S. et al.</p> <p>International Journal of Radiation Oncology • Biology • Physics, Volume 105, Issue 1, E236 - E237</p>	<p>The aim is to assess the feasibility, safety, and efficacy of P-32 brachytherapy in conjunction with standard chemotherapy in patients with unresectable LAPC. A total of 9 patients with a median age of 65 years (range 57-87) were enrolled in the study. The initial results showed local disease control rate at week 16 to be 88%, with PR or SD reported in 7/8 patients.</p> <p>Early results from the OncoPaC-1 pilot study shows that P-32 brachytherapy in conjunction with standard chemotherapy is technically feasible and has an acceptable safety profile in patients with unresectable LAPC.</p>	<p>https://www.sciencedirect.com/science/article/pii/S0360301619328457</p>	<p>14 September 2019</p>

* 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.

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

	Type of study*	Title of research	Short description of research **	Website link to research	Date***
1	Single arm open label multi institutional research study	A Pilot Study of OncoSil™ Given to Patients with Pancreatic Cancer Treated with FOLFIRINOX or Gemcitabine+Abraxane (PanCO) Clinical trial identifier- NCT03003078 Study status- active and not recruiting.	Study aims to evaluate the safety of OncoSil™ in a patient population undertaking standard chemotherapy for locally advanced unresectable pancreatic cancer. Study being conducted in about 15 sites across Australia, the United Kingdom and Europe (Belgium) involving 40 patients.	https://clinicaltrials.gov/ct2/show/NCT03003078	June 2020
2	Multi center, interventional, Single arm pilot study	A Pilot Study of OncoSil™™ Given to Patients with Pancreatic Cancer Treated with Gemcitabine +/- Nab-paclitaxel. (OncoPaC-1) Clinical trial identifier- NCT03076216 Study status- active and not recruiting.	This Study is designed to meet FDA requirements. Study intends to evaluate the safety of OncoSil™ in a patient population undertaking standard chemotherapy for locally advanced unresectable pancreatic cancer. The clinical investigation will be conducted at approximately 5 sites in the United States involving 20 patients.	https://clinicaltrials.gov/ct2/show/NCT03076216	Jan 2021

Naïve Indirect comparison studies					
	Type of study*	Title of research	Short description of research **	Website link to research	Date***
1	Naïve Indirect Treatment Comparison of PanCO, a Pilot Study of OncoSil P-32 Microparticles Combined with Gemcitabine + Nab-Paclitaxel or FOLFIRINOX Chemotherapy, Versus Standard-of-Care Treatment in Unresectable Locally Advanced Pancreatic Cancer	PanCO Study Results and Naïve indirect treatment comparison which were presented at the ESMO conference on 1 July 2020. Internal Report	In the absence of a head-to-head randomised controlled trial, a naïve indirect treatment comparison (a universally accepted method to provide a valid categorical and statistical comparison of reported outcomes) was used to assess the results of the PanCO study against 'state-of-the-art' (SOTA) therapy obtained from a systematic literature review (SLR) of published scientific literature from prospective Phase II and III clinical studies. • This enabled a robust determination as to whether the improvements observed in the PanCO study were due to CT alone or the combination of CT with OncoSil	ESMO World Congress on Gastrointestinal Cancer, 1-4 July 2020 Abstract P-260 https://www.worldgicancer.com/sites/2020v2.worldgicancer.com/files/2020-05/All_Abstracts_with_categories_website_v2.pdf	1 July 2020

* 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

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

Australian and New Zealand Society of Nuclear Medicine (ANZSNM): <https://www.anzsnm.org.au/>

Gastroenterological Society of Australia (GESA): <https://www.gesa.org.au/>

Statement of clinical relevance has been requested from both nominated groups and will be forthcoming shortly.

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

None

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

PANCARE: <https://www.pancare.org.au/>

Letter of support has been requested from and will be forthcoming shortly.

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

No sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service

- 23. 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), INTERVENTION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. 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:

Pancreas is a gland located behind the stomach, and a part of the digestive system. It is vastly made of exocrine cells that produces enzymes which helps in food digestion process. Pancreas also contains other types of cells such as the endocrine cells which produces blood sugar levelling hormones like insulin. (ACRF, 2017).

Pancreatic cancer occurs when the malignant (cancerous) cells multiplies in the tissues of the gland. It often begins within the cells of pancreatic ducts, and subsequently spreading to the rest of the gland and surrounding regions. The cancer that begins in the ducts of pancreas affecting exocrine cells are called pancreatic adenocarcinoma or pancreatic exocrine cancer. Approximately 70% of the pancreatic cancer arises in the head of the pancreas. Rarely, the cancer initiates in the neuroendocrine cells of pancreas, called the islet cell carcinoma or pancreatic endocrine cancer (AIHW, 2017)

Based on the spread and severity of the disease, pancreatic cancers can be grouped into resectable, borderline resectable, Locally advanced, and metastatic stages.

Locally advanced unresectable pancreatic cancer (LAPC):

Locally advanced unresectable pancreatic cancer is the unresectable stage of pancreatic cancer with tumour extended to major blood vessels and/or adjacent organs, where surgical excision is not a possible treatment option. The cause of pancreatic cancer is complex and multifactorial, arising from a mutation/DNA damage in the pancreatic cell which initiates rapid growth resulting into a tumour. Smoking, age, and genetic lineage are noted to be the dominant factors causing the cancer. (Ruarus, 2018)

- Pancreatic cancer was the 8th most diagnosed cancers in Australia in 2016 and is estimated to remain the same in 2020. (AIHW, 2020)
- The estimated age standardised incidence rates for 2020 is 13 cases per 100000 individuals (13 for males and 12 for females) which is larger than the estimates of 2019 (12 cases per 100000 individuals). The incidence rate is noted to increase with age. (AIHW, 2020)
- Owing to the delay in occurrence of significant symptoms, pancreatic cancers are mostly detected in advanced stage with 30-40% of patients having locally advanced unresectable cancer at the time of diagnosis. (Malik, 2012)
- Subsequently, pancreatic cancer has the highest mortality rate among other cancer types, being the fourth leading cause of cancer deaths in Australia in 2018. (AIHW, 2020)
- The prognosis of pancreatic cancer is poor, with the five-year survival chance being 11% for the period between 2012-2016 in Australia. (AIHW, 2020).

25. 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:

Initially upon a clinical suspicion, the patients showing pancreatic cancer symptoms or with inherited cancer risk are requested to consult an oncologist by their GP. The oncologist then suggests various investigative tests to confirm the presence of cancer. The common tests performed to diagnose pancreatic cancer in Australia include:

- Blood tests to identify and assess liver function, tumour markers and pancreatic hormones.
- Imaging tests such as computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, ultrasound tests (including endoscopic ultrasound), somatostatin receptor scintigraphy, positron emission tomography (PET), and angiography.
- Biopsy of a tissue from the pancreatic gland. (NCCN, 2019)

Based on the results of the diagnostic tests, pancreatic cancer can be classified into five stages (Stage 0 - Stage IV) depending on the size of the tumour and extent of its spread in the patient. The stages 0 - II denotes early to advanced stage cancer where surgical treatment is possible.

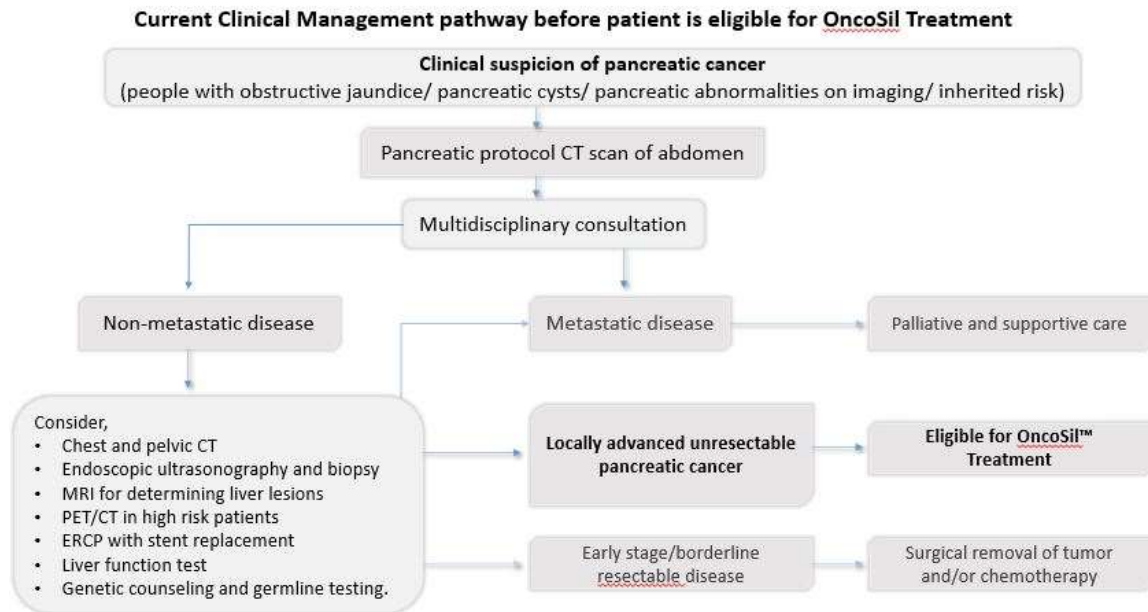
The stage III pancreatic cancer represents the unresectable stage where the cancer has spread deeply into the tissues affecting major blood vessels and lymph nodes nearby. Locally advanced unresectable pancreatic cancer is the third stage of cancer with target tumour growth being 2-6 cm in size and no distant metastases. Stage IV represents the metastatic stage of the cancer. (APGI, 2016)

A multidisciplinary team of health professionals is consulted for the treatment and care of pancreatic cancer patients. Treatment for this cancer is recommended based on the stage, location, severity, age, and other health issues of the patient. As resection is not considered possible in locally advanced pancreatic cancers, chemotherapy or chemoradiotherapy and palliative care is the standard treatment recommended for LAPC in Australia. (M. Ducreux, 2015)

Cancer Patients diagnosed with locally advanced unresectable pancreatic cancer are eligible to avail OncoSil™ treatment.

26. 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):

Before being eligible for OncoSil™ treatment, patients are advised to take a series of diagnostic tests to confirm the presence of pancreatic tumour. Patients suspected for pancreatic cancer showing symptoms such as jaundice, pancreatic cysts, abdomen pain, pancreatic abnormalities and inherited genetic risk are initially subjected to take a pancreatic protocol CT scan of the abdomen by their GP/Oncologist. Once the tumour is identified, a multidisciplinary team of health and allied health oncology professionals are consulted for analysing the stage of the cancer (M. Ducreux, 2015). Further investigative tests are then recommended by the oncologist to determine the cancer size, location, spread and severity of the disease. A series of tests including chest and pelvic CT, endoscopic sonography, biopsy, PET/CT in high-risk patients, MRI for identifying liver lesions, liver function tests and genetic counselling are done to confirm the presence LAPC with no metastases (NCCN, 2019). Patients are advised to the standard chemotherapy regimen before being eligible for OncoSil™ implantation.



NCCN guidelines for patients, Pancreatic cancer 2019.

PART 6b – INFORMATION ABOUT THE INTERVENTION

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

- OncoSil™ is intended for intra-tumoral implantation into the pancreatic tumour in patients diagnosed with Locally advanced unresectable pancreatic cancer.
- Before implantation, the patients are subjected to a full blood count, liver function tests, Alpha-fetoprotein test and a CT scan of pancreas.
- After the endoscopic diagnosis, patients are advised to a standard chemotherapy regimen (FOLFIRINOX or gemcitabine + nab-paclitaxel) for three weeks. OncoSil™ is implanted in the fourth week of the treatment schedule with a 48-hour window between the chemotherapy sessions. (Previous chemotherapy - 48 hours – OncoSil™ Implantation – 48 hours - next chemotherapy session).
- Prior to implantation, patients are subjected to a standard anaesthesia practice that is followed for upper gastrointestinal endoscopic procedures. OncoSil™ is injected into the target pancreatic tumour via an Endoscopic Ultrasound guided needle.
- The OncoSil™ system comes with a sealed vial of microparticles (250±10% MBq), two vials of OncoSil™ diluent (apprx 9 mL), a P6 vial and an empty lead pot. The OncoSil™ microparticles are suspended in a rheological Diluent in accordance to the pre-defined suspension protocol. The suspension intends to deliver an average absorbed radiation dose of 100 Gy (±20%) to the target treatment tumour.

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

OncoSil™ is a device containing phosphorus (³²P) micro-particles. It delivers greater radiation dose in a highly targeted manner directly into a tumour in a single implantation whilst sparing surrounding healthy tissue and critical organs. OncoSil™ in combination with standard chemotherapy provides higher survival advantage.

29. 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?

OncoSil™ device is implanted intratumorally in patients diagnosed with Locally advanced unresectable pancreatic cancer using Endoscopic Ultrasonography. The OncoSil™ suspension is prepared by combining the ³²P microparticles and OncoSil™ Diluent by trained professionals following the preparation protocols provided by OncoSil™. Using endoscopic guidance, the needle containing OncoSil™ suspension is injected into the target lesion following standard EUS procedure.

30. 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):

OncoSil™ is intended to be prepared specifically in a Nuclear Medicine department of the treatment facility or in a licensed Radiopharmacy by appropriately licensed professionals trained in OncoSil™ preparation. The treatment facility should hold an appropriate license for isotope Phosphorous ³²P.

The OncoSil™ implant solution volume should be calculated equal to 8% of the determined target volume of tumour. The concentration of injected OncoSil should be 6.6MBq/ml imparting an absorbed dose of 100 Gy to the target tissue. OncoSil™ is intended as a single patient single use device lasting for 16 weeks.

31. 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:

Patients diagnosed with LAPC are subjected to the standard chemotherapy regimen (FOLFIRINOX or gemcitabine + nab-paclitaxel). OncoSil™ is implanted in week 4 with a mandatory 48-hour lapse between the previous chemotherapy session and implantation and between the implantation to the next therapy session. Post OncoSil™ implantation a 4-hour observation period is recommended to monitor consciousness and vital signs. Blood sampling for assessing radioactivity is to be done once prior to implantation and once within the 4-hour observation period. Urine sampling for radioactivity is done within the 4-hr observation period post implantation. Bremsstrahlung Imaging for visualising the implanted microparticles is also to be done within the 4-hr period post implantation.

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

The proposed service will be performed by a qualified endoscopist and the OncoSil™ trained authorised User.

The implantation and handling of OncoSil™ involves a multi-disciplinary team approach, the following type of users are expected:

Nuclear Medicine (Personnel Physician, Physicists, Technologists, Radiopharmacist)

Radiation Safety Officers (RSO) / Radiation Protection Officer (RPO)

Nuclear Medicine Specialist licensed to administer unsealed sources, in an EPA or equivalent registered facility with radiation safety, waste management and safety capability.

Endoscopist at EUS injection

Procedural staff (nurses, anaesthetists, technologist).

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

Not applicable.

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

The proposed service must be performed in a licensed treatment facility having the license for isotope Phosphorous ³²P. OncoSil should be prepared within the Nuclear Medicine department of the treatment facility or in a licensed radiopharmacy, who have an appointed Radiation safety officer/ Radiation Protection Officer (RPO). A licensed professional trained in OncoSil™ preparation should prepare the product for implantation. A trained endoscopist should perform the EUS guided implantation of the device. Patients are referred to OncoSil™ treatment by an oncologist.

35. 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:

OncoSil™ provides the Instructions for Use (IFU) and the Institution Training Manual (ITM) to guide and prepare the users in the procedures for using OncoSil™ system.

A OncoSil™ usage trained authorised professional from the Nuclear Medicine department of the treatment facility should perform OncoSil™ preparation. The device implantation must be performed by specialists qualified and trained in endoscopic ultrasonography and Nuclear Medicine.

A Nuclear Medicine Specialist licensed to administer unsealed sources, in an EPA or equivalent registered facility with radiation safety, waste management and safety capability.

At EUS injection there is an Endoscopist and the Nuclear Medicine specialist (who injects) and either a medical physicist (scientist) or technologist to check the instrument and surrounds for any contamination post injection.

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

- Inpatient private hospital (admitted patient)
- Inpatient public hospital (admitted patient)
- Private outpatient clinic
- Public outpatient clinic
- Emergency Department
- Private consulting rooms - GP
- Private consulting rooms – specialist
- Private consulting rooms – other health practitioner (nurse or allied health)
- Private day surgery clinic (admitted patient)
- Private day surgery clinic (non-admitted patient)
- Public day surgery clinic (admitted patient)
- Public day surgery clinic (non-admitted patient)
- 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:

OncoSil™ is implanted in the fourth week of the treatment series, with a 48-hour gap between the previous chemotherapy session, implantation, and the next chemotherapy session.

Patients are admitted to the private/public hospital and monitored both before and after implantation. The device is implanted via EUS guidance by specialist endoscopists and nuclear medicine specialist in a single day, which can be carried out in a public/private day surgery clinic. An oncologist consultation is required before and after implantation.

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

- Yes
- No – please specify below

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

38. 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):

Current standard-of-care for patients with unresectable LAPC (i.e. ‘state-of-the-art’ therapy) i.e. chemotherapy (CT) alone or induction chemotherapy (ICT) with consolidative chemoradiotherapy (CCRT) will be included as comparators.

CT alone was considered as comparator for the base case analysis, as it was the regimen that OncoSil™ was added to in the key clinical trial PanCO and is the main regimen for treatment of pancreatic cancer.

The comparison of OncoSil™ plus CT with ICT + CCRT will be presented as well.

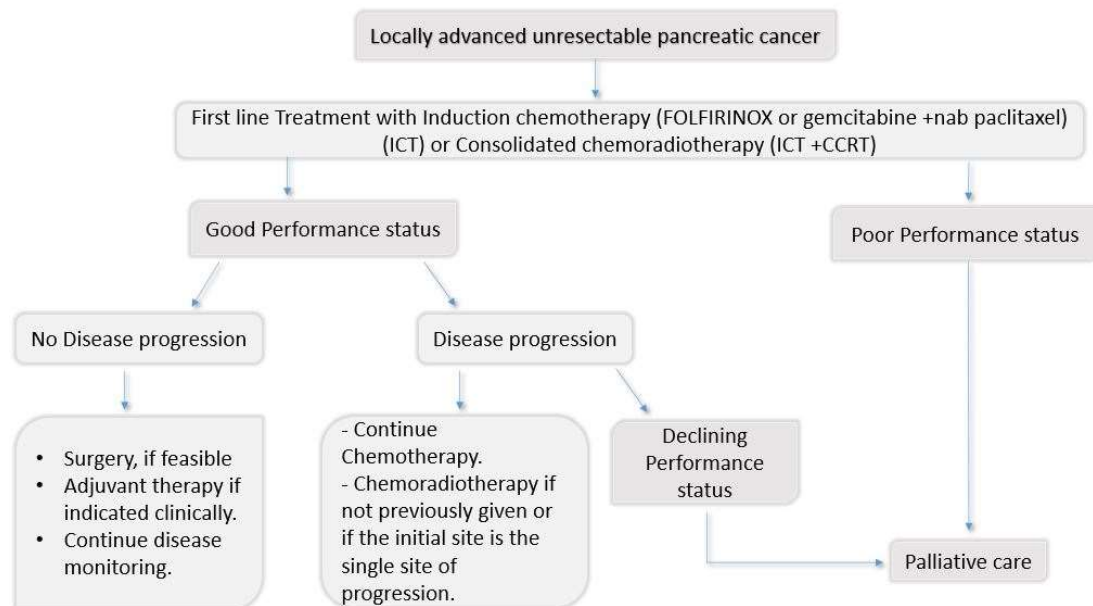
39. Does the medical service (that has been nominated as the comparator) have an existing MBS item number(s)?

- Yes (please list all relevant MBS item numbers below)
 No

40. Define and summarise the current clinical management pathway/s that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [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):

In patients showing promising outcomes and good performance, surgical resection is considered if the chemotherapy or chemoradiotherapy treatment is successful in concentrating the tumour. For the patients showing poor performance status and/or sustained disease progression, palliative care is the only available option.

Current Clinical Management pathway after comparator treatment



NCCN Clinical Practice Guidelines in Oncology, Pancreatic Adenocarcinoma, version.1 2019

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

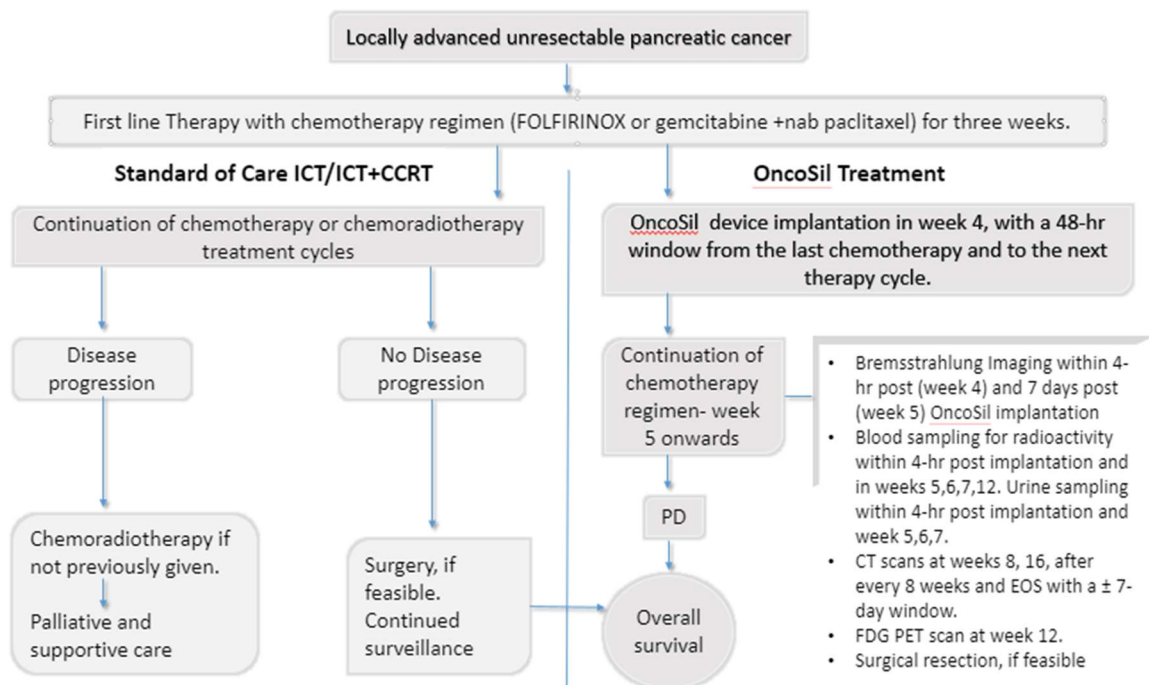
- In addition to (i.e. it is an add-on service)
- Instead of (i.e. it is a replacement or alternative)

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

N/A

42. 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):

OncoSil™ is to be used in addition to the gemcitabine or FOLFIRINOX chemotherapy. Therefore, after implantation of the device, chemotherapy sessions are expected to continue until the expected clinical outcomes achieved.



PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. 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):

PanCo study shows a satisfactory safety profile for OncoSil™ with no evidence of significant safety concerns or unexpected safety outcomes attributed specifically to the device and/or implantation procedure. There were relatively few Adverse Events/Serious Adverse events associated with OncoSil device and implantation compared to chemotherapy (4.1% vs 61% of total AE/SAEs reported).

Treatment objectives of OncoSil™ are- prolonged overall survival, increased local disease control rates, prolonged progression free survival and higher disease control and overall response rates.

The median overall survival of OncoSil™ as depicted by the PanCo study is 15.5 months which is superior than the median overall survival of all standard therapies (12.7 months) as identified from the meta-analysis.

LDCR16 weeks – achieving stable disease (SD), partial response (PR) or complete response (CR) by RECIST v1.1 on imaging across consecutive (i.e. confirmatory) imaging assessments – was the primary

performance endpoint for the PanCO study. Previous studies of radiotherapy and chemotherapy in LAPC have demonstrated disease control rates in the range of 72.2–87.0% with lower confidence limits ranging from 46.5–70.5%. The PanCO study LDCR_{16 weeks} convincingly demonstrates with statistical significance that OncoSil™ plus CT is better than CT alone.

The median progression free survival of OncoSil™ as depicted by the PanCo study is 9.3 months which is greater than the median progression free survival of all standard therapies (7.6 months) as identified from the meta-analysis.

The DCR for study participants in the PanCO study is 95.7% while the DCR of standard care calculated from the meta-analysis was just 71.3%.

The ORR for study participants in the PanCO study is 29.8% while the ORR of standard care calculated from the meta-analysis was mere 18.2%.

The clinical outcomes for unresectable LAPC patients receiving OncoSil™ in addition to standard chemotherapy are found to be greater than the outcomes from standard of care therapies.

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

- Superiority
- Non-inferiority

45. 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:

- 1 Median overall survival
- 2 Median progression free survival
- 3 Resection Rate
- 5 Disease control rates
- 6 Overall response rates

Safety Outcomes:

- 1 Device/procedure related adverse events,
- 2 serious adverse events

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

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

As per AIHW 2020 Cancer Data, the estimated number of new pancreatic cancer cases diagnosed in 2020 is 3933 (2015 males + 1918 females). Pancreatic cancer accounts for an estimate of 2.7% of all new cancers diagnosed in 2020. In 2016, 3,378 new cases of pancreatic cancer were diagnosed in Australia (1,745 males and 1,633 females). In 2016, the age-standardised incidence rate was 12 cases per 100,000 persons (13 for males and 11 for females). In 2020, it is estimated that the age-standardised incidence rate will be 13 cases per 100,000 persons (14 for males and 11 for females). The incidence rate is expected to increase with age (AIHW, 2020).

By the end of 2015, there were 3866 people living, diagnosed with pancreatic cancer between the period 2011 to 2015. The chance of survival accounted for 11% in the period 2012-2016. (AIHW, 2020)

The estimated number of deaths due to pancreatic cancer in 2020 is 3300 (1716 males+ 1584 females) which is significantly higher than the estimates in 2019 - 3051 (1590 males+ 1460 females). (AIHW, 2019)

Approximately 30% of pancreatic cancer patients are diagnosed with unresectable LAPC (Benjamin, 2019), which would equate to approximately 1,180 patients.

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

OncoSil™ is intended as a once off treatment per year.

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

OncoSil™ is intended as a once off treatment, lasting for 16 weeks

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

The number of projected patients who will utilise OncoSil in first full year **REDACTED**. This is based on the number of unresectable LAPC, the availability of OncoSil and the number of centres able to administer OncoSil.

50. 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 number of medical services over the next 5 years is provided in the table below. The constraints in the healthcare system that limit the use of will be the number of accredited centre able to administer OncoSil. OncoSil is an unsealed radioactive source of injection and thus will need to be administered by a Nuclear Medicine specialist who has a radiation license that allows them to administer such radiopharmaceuticals.

Medical oncologists do not have this capability/licensing and most radiation oncologists are licensed for sealed (not unsealed) radioactive sources.

The sites of dose preparation (i.e. the Nuclear Medicine Departments), and the dose administration under EUS administration (that is, endoscopy room) need to also be licensed by the state EPA or equivalent organisation to allow the treatment to be performed.

Nuclear Medicine Departments will need to be EPA licensed for the work with comprehensive radiation safety and waste disposal plans and the EUS room where the injection will take place also has to be licensed.

This is very important because there are hefty fines and also potential prison terms for breach of these laws. Thus, the risk of 'leakage' to populations not targeted by the service, is anticipated to be very low to nil.

	Year 1	Year 2	Year 3	Year 4	Year 5
Number of doses/patients	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED

PART 8 – COST INFORMATION

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

ONCOSIL Service Description	Cost Source	Fee/Cost	Benefit (\$)	Benefit (%)	Annual Frequency	Cost Benefit \$x Annual Frequency
Pre-Implant services						
Attendances					1	
- consultant physician (gastro/med onc)	MBS 110	\$157.95	\$118.46	75%	1	\$118.46
- consultant physician (gastro/med onc) if complex	MBS 132	\$276.25	\$207.19	75%	1	
- consultant physician (gastro/med onc) follow-up	MBS 116	\$79.05	\$59.29	75%	1	
- nuclear medicine physician (not seeing pt)	MBS 110	\$157.95	\$118.46	75%	1	\$118.46
- radiologist (CT Scans)	MBS 104	\$89.55	\$67.16	75%	1	\$67.16
Pathology (of biopsy)						
- Full blood count	MBS 65070	\$16.95	\$14.41	85%	1	\$14.41
- Liver function test	MBS 66512	\$17.70	\$15.05	85%	1	\$15.05
- Alpha-fetoprotein test	MBS 66653	\$44.60	\$37.91	85%	1	\$37.91
Radiology						
- CT Pancreas	MBS 61505	\$100.00	\$85.00	85%	1	\$85.00
Diagnosis						
- Diagnostic Upper GI endoscopy	MBS 30473	\$182.65	\$155.25	85%	1	\$155.25
Implantation Services						
Nuclear Medicine						
- OncoSil Dilution/Preparation and Implantation of OncoSil	Proposed New MBS Item	REDACTED	REDACTED	85%	1	REDACTED
Endoscopist						
- Implantation of Oncosil	Proposed New MBS Item	REDACTED	REDACTED	85%	1	REDACTED
Anaesthesiologist						
Anaesthesia	MBS 20745	\$142.80	\$107.10	75%	1	\$107.10
Anaesthesia	MBS 23091	\$183.60	\$137.70	75%	1	\$137.70
Post Implantation						
Post-op SPECT Scan (location of implant) Day 1 specific to Oncosil	Proposed New MBS Item Code	REDACTED	REDACTED	85%	1	REDACTED
Post-op SPECT Scan (location of implant) Day 7 - add to existing 61426 to account for new code above	MBS 61426 (need to amend)	\$129.00	\$96.75	75%	1	\$96.75
Post-op CT Scan (location of implant) Day 1 or 7- add to existing 61505 to account for new code above	MBS 61505 (need to amend)	\$100.00	\$75.00	75%	1	\$75.00

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

Nuclear Medicine

- i. Dilution and Preparation of Oncosil will take approximately 2 hours

Endoscopy

- i. Endoscopic implantation will take approximately 45-60minutes

53. 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.

New MBS Item Descriptor

Implantation of OncoSil by Endoscopist

	Category 3 – THERAPEUTIC PROCEDURES
MBS item number XXXX	Group T8 – Surgical Operations Subgroup 1 - General
Injection of OncoSil by endoscopic ultrasound (endoscopy with ultrasound imaging) for selective internal radiation therapy of locally advanced pancreatic cancer not suitable for resection, used in combination with guideline-directed systemic chemotherapy.	
To be claimed once in the patient's lifetime only.	
(Anaes.) (Assist.)	
MBS Fee: REDACTED ; 85% REDACTED ; 75% = REDACTED	

This proposed MBS fee above is based on MBS Item **REDACTED**

New MBS Item Descriptor

Dilution, Preparation and Implantation of OncoSil by Nuclear Medicine

Category 5 – DIAGNOSTIC IMAGING SERVICES	
MBS item number XXXX	Group I4 – Nuclear Medicine Imagine Subgroup 1 - Nuclear Medicine – non PET
Professional attendance and handling by a nuclear medicine specialist, for assessment and preparation of OncoSil microparticles suspended in rheological diluent for injection of OncoSil by endoscopic ultrasound (endoscopy with ultrasound imaging) for selective internal radiation therapy of locally advanced pancreatic cancer, not suitable for resection, and used in combination with guideline-directed systemic chemotherapy.	
Documented radiation safety program and radiation safety committee led by an accredited Radiation Safety Officer is required.	
MBS Fee: REDACTED Benefit: 75% = REDACTED 85% = REDACTED	

This proposed fee is based on the current MBS Item **REDACTED**. The proposed fee encompasses costs of radiopharmaceutical preparation by technologist and the implantation by the nuclear medicine physician.

New MBS Item Descriptor

Proposed MBS Item Fee: use for day 1 OncoSil implantation

Category 5 – DIAGNOSTIC IMAGING SERVICES	
MBS item number XXXX	Group I4 – Nuclear Medicine Imagine Subgroup 1 - Nuclear Medicine – non PET
Single photon emission computed tomography imaging using Oncosil P32.	
MBS Fee: REDACTED Benefit: 75% = REDACTED 85% = REDACTED	

This MBS Code to be used Day 1 of OncoSil implantation and the proposed fee is based on the current MBS item **REDACTED**

Amend MBS Item Code 61462

Proposed MBS Item Fee: use for day 7 post OncoSil implantation

Category 5 – DIAGNOSTIC IMAGING SERVICES	
MBS item number 61462	Group I4 – Nuclear Medicine Imagine Subgroup 1 - Nuclear Medicine – non PET
Repeat planar and single photon emission tomography imaging, or repeat planar imaging or single photon emission tomography imaging on an occasion subsequent to the performance of item 61364, 61426, 61429, 61430, 61442, 61450, 61453, 61469 or 61485 (<u>include new SPECT MBS items above</u>), if there is no additional administration of radiopharmaceutical and if the previous radionuclide scan was abnormal or equivocal (R)	
MBS Fee: \$129.00 Benefit: 75% = \$96.75 85% = \$109.65	

We propose an amendment to MBS code 61462 to include the newly created code for SPECT Day 1 OncoSil

Amend MBS Item Code 61505

Proposed MBS Item Fee: use for day 1 and or 7 post OncoSil implantation

Category 5 – DIAGNOSTIC IMAGING SERVICES	
MBS item number 61505	Group I4 – Nuclear Medicine Imagine Subgroup 1 - Nuclear Medicine – non PET
CT scan performed at the same time and covering the same body area as single photon emission tomography or positron emission tomography for the purpose of anatomic localisation or attenuation correction if no separate diagnostic CT report is issued and only in association with items 61302 to 61647 (R)	
MBS Fee: \$100.00 Benefit: 75% = \$75.00 85% = \$85.00	

We propose an amendment to MBS code 61505 to include the newly created code for SPECT Day 1 and/or 7 post OncoSil.

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