OncoSil™ System

Instructions for Use

Product Name: OncoSil™ System - Clinical

Product Number: OS01-93

OncoSil MEDICAL

Product Number: OS01-93

⚠ Please read these Instructions for Use in their entirety prior to using OncoSil™

Exclusively for use in a clinical investigation

For the latest version of this Instructions for Use:

https://www.oncosil.com/resource-library/?resource-category=ifu

For the latest version of the Summary of Safety and Clinical Performance (SSCP)

https://www.oncosil.com/resource-library/?resource-category=reports

1. DEVICE DESCRIPTION

OncoSil™, is comprised of **OncoSil Phosphorous-32 Microparticles** (hereafter **Microparticles**) and **OncoSil Diluent** (hereafter **Diluent**).

The Microparticles contain Phosphorous-32, a pure beta-emitter radioisotope with a physical half-life of 14.27 days. The maximum energy of the emitted beta particles is 1.711 MeV. The average energy of the emitted beta particles is 0.6950 MeV. The maximum range of emissions in tissue is 8.2 mm. The average range of emissions in tissue is 2.76 mm. In therapeutic use, 98% of the radiation is delivered within 81 days. The Microparticles are a permanent implant. The Microparticles are manufactured by combining highly pure silicon with phosphorous, to produce grey-black Microparticles.

The Microparticles are provided in individually crimp-sealed vials, containing 250 ±10% MBq at 12:00 CET (CEST) on the reference date. Each vial is moist heat (autoclave) sterilised. Each individual vial of Microparticles is placed inside a Perspex lined lead pot to shield personnel from radiation during shipping and handling.

The Diluent comprises of inactive pharmacopeia grade excipients and performs as a carrier to facilitate implantation of the Microparticles into target treatment tumour.

The Diluent is moist heat (autoclave) sterilised and provided in individually crimp-sealed vials each containing approximately 9 mL of Diluent.

Note: OncoSil™ does not incorporate any material or ingredient derived from medicinal, human, animal or recombinant origin.

2. INTENDED USE

OncoSil™ is intended for intratumoural implantation into a pancreatic tumour per the Clinical Investigation Plan (CIP).

3. INDICATIONS FOR USE

OncoSil™ is indicated for the treatment of patients with pancreatic cancer per the Clinical Investigation Plan (CIP).

4. CERTIFICATION OF TREATMENT FACILITIES AND PERSONNEL

The OncoSil™ System is to be used in a licensed treatment facility. These facilities must hold an appropriate license for the isotope Phosphorous-32 (^{32}P), which mandates that these institutions will have an appointed Radiation Safety Officer (RSO) / Radiation Protection Officer (RPO) who will be the primary contact for all matters related to radiation safety.

The OncoSil™ suspension should be prepared within the Nuclear Medicine Department or within a licensed Radiopharmacy. Only appropriately licensed personnel, who have been trained in the preparation of the OncoSil™ suspension may prepare the product for implantation.

As the implantation and handling of OncoSil™ involves a multi-disciplinary team approach, the following personnel may be expected to undertake the OncoSil Medical Training Programme:

- Nuclear Medicine Personnel (Physician, Physicists, Technologists, Radiopharmacist)
- Radiation Safety Officers (RSO) / Radiation Protection Officer (RPO)
- Radiation, Medical and Surgical Oncologists
- Interventional Radiologists
- Endoscopist

- Procedural staff (nurses, anaesthetists)

OncoSil Medical can only authorise a shipment of the OncoSil™ System after:

1. The license for the treatment facility to receive and hold ^{32}P has been verified by OncoSil Medical.
2. A training visit has been conducted in which relevant individuals permitted to work as an Authorised Dispenser (AD), Authorised User (AU) and surgical/procedural personnel etc. have completed the training and experience set out by OncoSil Medical. Please see below
3. The treatment facility has calibrated their ion chamber using the OncoSil™ Calibration System.

4.1 Authorised Dispenser and Authorised User

Authorised Dispenser (AD)

- **Definition of Authorised Dispenser (AD)** as defined by OncoSil Medical, is the person preparing the OncoSil™ suspension (i.e. Radiopharmacist, Nuclear Medicine Personnel) and must successfully complete additional training on the OncoSil™ device as described below;

  AD Training: The AD attends the OncoSil Medical Training Programme and performs at least one cold dose (i.e., Microparticles are not radioactive) dilution which is supervised by an OncoSil Medical representative (Authorised Trainer).

Authorised User (AU)

- **Definition of Authorised User (AU)** as defined by OncoSil Medical, is the physician physically depressing the syringe containing OncoSil™ during the implantation procedure and must have successfully completed additional training on the OncoSil™ device as outlined below;

AU Training: In order to become a fully accredited Authorised User, the AU attends the OncoSil Medical Training Programme and must perform their first patient implantation supervised by an OncoSil Medical representative (Authorised Trainer).

Note: In some cases, the AD and the AU may be the same person. If so, they will be required to complete both OncoSil Medical Training Programmes in order to be accredited in both roles.

All personnel must be trained by an OncoSil Medical representative (Authorised Trainer). Supplemental training may be required if significant revisions are made to existing procedures by the company.

The AD and AU will each receive accreditation from OncoSil Medical to document that they are authorised to order and handle the OncoSil™ System.

5. STORAGE AND TRANSPORTATION CONDITIONS

Upon receipt of the OncoSil™ System and once incoming inspection requirements are fulfilled, the device should be stored inside the Type A packaging and moved to Nuclear Medicine Department/Radiopharmacy, or other approved location that is able to handle radioactive materials until the OncoSil™ suspension is to be prepared.

The Microparticles and Diluent should be stored at room temperature. **Do not freeze the Diluent.**

6. DEVICE PRESENTATION

Each OncoSil™ System will be labelled with the product code **OS01-93** and will contain the following components:

- 1 sealed can encasing 1 x vial of the Microparticles containing 250±10% MBq at 12:00 CET (CEST) on the reference date. The vial is supplied inside a Perspex lined lead pot.
- 2 vials of approximately 9 mL of OncoSil Diluent.
- 1 empty sterilised P6 vial for dilution of suspension of OncoSil™ (identified with a green stripe on the top of the label).
- 1 empty lead pot for dilution of suspension of OncoSil™ (identified with a green stripe on the top of the label)

7. ACCESSORIES

A number of accessories routinely available in Nuclear Medicine Departments/Radiopharmacy are used to prepare the OncoSil™ suspension. These accessories are not supplied with the OncoSil™ System. Examples include:

- Long forceps/tweezers with rubber tips (preferably 20-25 cm, to minimise radiation finger doses)
- Plastic backed absorbent surface covers
- Sterile Luer lock syringes (3 mL or 5 mL and 10 mL)
- Sterile 16–21-gauge needles, 5-7 cm in length
- Sterile aeration / filtered venting needles
- Sterile Isopropyl Alcohol (IPA) Wipes
- Beta radiation syringe shields (3 mL or 5 mL and 10 mL)
- Lead transport box
- Protective clothing (gloves, coats, goggles etc.)
- Three-way Luer lock tap

8. PATIENT SELECTION AND PRE-TREATMENT TESTING

Patients with pancreatic tumours may be considered for treatment with OncoSil™ on this study. Refer to Clinical Investigation Plan (CIP) for full patient selection details.

In general, the target tumour should be;

- Chosen based on radiological investigation
- Visible on ultrasound imaging
- Judged to be technically accessible

It is recommended that the size of target tumour is under 7cm (longest diameter) and under 110cc volume. There is limited experience implanting tumours of >50cc. In the clinical studies of OncoSil™, the median volume was 24cc.

A number of assessments are recommended prior to treatment with OncoSil™. These are often part of standard patient workup and include:

- Medical assessment of relevant patient's risk characteristics and contraindications (to confirm it is reasonable to undertake the implantation procedure). Refer to PRECAUTIONS in Section 21.
- Histological or cytological confirmation of diagnosis
- Laboratory evaluation to ensure adequate haematological, renal and hepatic function
- Biochemical tests of pancreatic function (e.g. amylase, lipase)
- Coagulation profile
- Radiological investigations include:
  - CT scans of the pancreas, thorax, abdomen, pelvis
  - CT imaging to determine tumour volume

9. CALCULATING DOSE AND IMPLANTATION STRATEGY

Prior to patient implantation, OncoSil™ should be prepared within the Nuclear Medicine Department of the implanting treatment facility, or within a licensed Radiopharmacy. The Microparticles and Diluent are combined in accordance with the pre-defined **DETAILED SUSPENSION PREPARATION PROTOCOL** outlined in Section 10 below.

The OncoSil™ System is supplied sterile and is intended for single-patient, single-use. It is administered by direct implantation into the tumour (avoiding vessels), using the prepared suspension of OncoSil™ with a final radioactive concentration of 6.6 MBq/mL. The dose activity is calculated using the tumour volume and the required absorbed dose to the tumour. To deliver 100 Gy to the tumour an Implanted Volume/Tumour Volume (IV/TV) of 8% is required. In order to achieve 100 Gy, for example, the following steps need to be performed:

Estimation of Tumour Volume (TV)

Baseline tumour volume estimation for patients is the responsibility of the patient's treatment team.

Step 1 – First Dilution

The first dilution is to achieve a radioactivity in the range of 35.3 MBq/mL ± 0.59%

1. The initial dilution of the OncoSil Microparticles must be calculated using **Table 1: Volume required for the first Dilution of OncoSil™ Suspension** by adjusting the amount of Diluent added in accordance with the day the implantation will occur with respect to the reference date.
2. After completing the first dilution step as indicated above, the radioactivity of the first dilution should be in the range of 35.3 MBq/mL ± 0.59%.

Note: The reference date and time for OncoSil™ doses is Central European Time (CET or CEST) at 12:00 hrs. The activity referenced to 12:00 CET/CEST is required to be adjusted for different time zones around the world.

Table 1: Volume required for the first Dilution of OncoSil™ Suspension

Day of Implantation (Relative to Reference Date)	Aliquot of Diluent to add (mL)	Vial Total Radioactivity (MBq)
-2	7.7	276
-1	7.3	262
0	7.0	250
+1	6.7	238
+2	6.4	227
+3	6.0	216
+4	5.8	206
+5	5.5	196
+6	5.2	187
+7	5.0	178

Step 2 – Second Dilution

The second dilution is to obtain the standardised concentration of 6.6MBq/mL for administration.

1. Add 7.5 mL of Diluent to the empty P6 vial (identified with a green stripe on the top of the label).
2. Under aseptic conditions, draw up 1.7 mL of the first dilution prepared in step 2 above. Add the 1.7 mL to the P6 vial to give a final volume of 9.2 mL.
3. This now gives an OncoSil™ suspension of 6.6 MBq/mL on the day of implantation. This is the concentration required for administration.

OncoSil™ must be used within 24 hours of preparation, with exception if the preparation was performed +7 days from reference date. If the suspension is made on day +7 it must be used the same day.

Note: Once the day of implantation is chosen and the dilutions above have been performed the implantation date cannot be changed otherwise the concentration of 6.6 MBq/mL required for implantation will not be correct.

Step 3 – Determination of the Volume to be implanted

Use the 2 equations shown below to calculate the actual OncoSil™ activity to be dispensed and then implanted, to achieve 100 Gy in this example.

1. $OncoSil™\ Volume\ to\ be\ Implanted_{ml} = \text{Tumour Volume}_{\text{ml}} \times \frac{8}{100}$
2. $Dose\ to\ be\ Implanted_{MBq} = \text{OncoSil™ Volume to be Implanted}_{\text{ml}} \times 6.6$

Step 4 - Pre-Injection Confirmation

In order to confirm the radioactivity to be implanted into the patient:

1. Measure the total vial radioactivity of the P6 vial using the ionisation chamber.
2. Draw up the required volume of OncoSil™ into the syringe.
3. Post syringe draw-up, measure the residual OncoSil™ suspension in the P6 vial in the ionisation chamber.
4. Subtract the post-draw up activity measurement from the initial activity measurement to confirm the patient dose.

Step 5 - Post-Injection Confirmation

The total radioactivity delivered to the patient (total activity implanted in the tumour) is determined by subtraction of the post-implantation volume (mL) reading in the syringe from the pre-implantation volume (mL) within the syringe (i.e. an ionisation chamber measurement is not required for syringe contents).

10. DETAILED SUSPENSION PREPARATION PROTOCOL

This section provides a detailed instruction for the preparation of OncoSil™ as calculated in Section 9, above.

Note:

- The suspension preparation must be performed by the Authorised Dispenser trained by an OncoSil Medical representative.
- Suspension preparation is the responsibility of the treatment facility.
- Before beginning the procedure, the labelling of all components of the OncoSil™ System should be checked to ensure that the correct materials are available for use. Visually inspect the vials for cracks, breakages, and

incomplete seal **prior** to use. If there is sign of damage, return the damaged component(s) to the radiation shields and contact OncoSil Medical.

- To minimise the risk of microbiological contamination, OncoSil™ should be prepared in a clean environment using standard techniques. For example, operators should wear fresh gloves and treat the gloves with a commercial bactericidal hand wash.
- The suspension procedure is to be performed behind Perspex or Lucite, suitable for shielding from beta particles, under a fume hood.
- This procedure should **not** be performed under a laminar flow hood, which directs airflow towards the operator thereby risking exposure to radioactive material.
- All syringes must be used within an appropriate beta-radiation (Perspex/Lucite) syringe shield.
- All vials within the OncoSil™ System must only be used for a single preparation. All contaminated waste must be placed in a designated radioactive waste container.
- Upon withdrawing needles from vials, be aware of any drips of radioactive suspension from the needle tip that could drop onto the top of the vial or the bench.

Figure 1: The OncoSil™ System

Step-by-step procedure:

Contents: 1 sealed can encasing 1 x vial containing Microparticles @ 250 ±10% MBq supplied inside a Perspex lined lead pot, 2 vials of approximately 9 mL of OncoSil Diluent, 1 empty sterilised P6 vial for dilution of suspension of OncoSil™ (identified with a green stripe on the top of the label), 1 empty lead pot for dilution of suspension of OncoSil™ (identified with a green stripe on the top of the label).

1. Remove the components from the Styrofoam insert in the Type A package.
2. Hold the sealed can securely.
3. Pull ring and remove lid from the can.
4. Remove the packing material and the Perspex lined lead pot containing the Microparticles vial from the tin.
5. Place the can, lid and packing material in appropriate waste after checking for radioactive contamination.

Note: The initial preparation and the dilution to the standardised concentration of 6.6MBq/mL for administration should be done consecutively.

Note: A filtered/aeration venting needle should be used to assist with all steps of the dose preparation procedure.

Step 1 – First Dilution

6. **Microparticles Vial:** Take the Perspex lined lead pot that encloses the vial of Microparticles.
7. Remove the tape that's securing the top and bottom segments of the Perspex lead pot and CAREFULLY AND SLOWLY remove ONLY the lead lid from the pot.
   Note: that the lid is the larger lead segment.
8. The vial containing the Microparticles is itself contained within a further Perspex lined shield.
9. Using long forceps/tweezers remove Perspex lid only.
10. Using long tweezers, wipe the rubber stopper of the Microparticles vial with a sterile IPA wipe.
11. Using long forceps/tweezers replace Perspex lid.
12. **Diluent Vial:** Invert Diluent vial until the suspension is homogeneous.
13. Remove the plastic cap to expose the rubber stopper and wipe with a sterile IPA wipe.
14. Using a sterile 10 mL syringe with needle, draw up the required volume of Diluent (as per **Table 1: Volume required for the first Dilution of OncoSil™ Suspension**) and dispense through the small hole in the top of the Perspex lid into the Microparticles vial via its rubber stopper.
15. With the needle tip above the suspension, withdraw the air from the vial containing the Microparticles suspension, and expel any remaining diluent remaining in the needle. This step can be repeated if not all the Diluent is cleared from the syringe and needle.
16. With the needle tip above the suspension, pull back the syringe plunger to minimise the risk of drips from the needle tip, before CAREFULLY removing the needle from the vial.
17. Dispose syringes and needles in appropriate/radioactive waste.
18. Replace the lead lid of the pot.
19. **To assist mixing:** Firmly hold the top and bottom segments of the Perspex lined lead pot in a closed position and invert the suspension to obtain a homogeneous mixture. Do this 20-30 times.
20. Remove the lead lid of the pot and using long forceps/tweezers remove the Perspex lid.
21. Using long forceps/tweezers remove the Microparticles vial from the Perspex lined shield to check if suspension is homogeneous.
22. If the suspension is not homogeneous, replace Microparticles vial into Perspex lined shield, replace both the Perspex lid and lead lid of pot and repeat the inversion step until the suspension is homogeneous. Again, remove the lead lid from the pot and using long forceps/tweezers remove the Perspex lid and Microparticles vial to re-check if suspension is homogeneous.
23. Once homogeneous, using long forceps/tweezers, place the Microparticles vial into an OncoSil™ calibrated ionisation chamber to verify the total vial radioactivity of the Microparticles from the first dilution. Refer to **Table 1: Volume required for the first Dilution of OncoSil™ Suspension** to verify the diluted vial total radioactivity (MBq) relative to the reference date.
24. Return the Microparticles vial back into the Perspex lined lead shield and replace the Perspex lid using long forceps/tweezers. Replace the lead lid of the pot.
25. Immediately prepare the second stage of the dilution process (see below).

Step 2 – Second Dilution

26. Take the empty Perspex lined lead pot.

27. Remove the tape that's securing the top and bottom segments of the lead lined pot and CAREFULLY AND SLOWLY remove ONLY the lead lid from the pot.
    Note: that the lid is the larger lead segment.
28. Remove Perspex lid.
29. Take the empty P6 vial (identified with a green stripe on the top of the label) and place into the Perspex shield within the empty lead pot.
30. Remove the plastic cap of the empty P6 vial to expose the rubber stopper and wipe with a sterile IPA wipe.
31. Replace the Perspex lid.
32. **SECOND Diluent Vial:** Invert second Diluent vial until suspension is homogeneous.
33. Remove the plastic cap of the empty vial to expose the rubber stopper and wipe with a sterile IPA wipe.
34. Using a sterile 10 mL syringe with needle, draw up 7.5 mL of Diluent and dispense into the empty P6 vial (identified with a green stripe on the top of the label) via the Perspex lid and rubber stopper.
35. With the needle tip above the suspension, withdraw the air from the vial, and expel any Diluent remaining in the needle.
    Note: this step can be repeated if not all the Diluent is cleared from the syringe and needle.
36. With the needle tip above the suspension, pull back the syringe plunger to minimise the risk of drips from the needle tip, before CAREFULLY removing the needle from the vial.
37. Dispose the syringes and needles in appropriate/radioactive waste.
38. **First Dilution:** Ensure suspension is homogeneous. If not, with both the Perspex lid and lead lid in place invert suspension 10-20 times or until homogeneous.
39. CAREFULLY and SLOWLY remove lead lid leaving the Perspex top in place.
40. Using a 3- or 5-mL beta-shielded syringe with a 5 cm long needle, remove 1.7 mL of the Microparticles suspension and transfer into the P6 vial which already contains 7.5 mL of Diluent, through the small hole in the top of the Perspex lid via the rubber stopper.
41. With the needle tip above the OncoSil™ suspension, withdraw the air from the vial, and expel any suspension remaining in the needle.
    Note: this step can be repeated if not all the OncoSil™ suspension is cleared from the syringe and needle.
42. With the needle tip above the suspension, pull back the syringe plunger to minimise the risk of drips from the needle tip, before CAREFULLY removing the needle from the vial.
43. Dispose the syringes and needles as radioactive waste.
44. Replace the lead lid of the pot.
45. **To assist mixing:** Firmly hold the top and bottom segments of the Perspex lined lead pot in a closed position and invert the suspension to obtain a homogeneous mixture. Do this 20-30 times.
46. Remove the lead lid of the pot and using long forceps/tweezers carefully remove the Perspex lid.
47. Using long forceps/tweezers remove the P6 vial containing OncoSil™ from the Perspex shield to check if suspension is homogeneous.
48. If the suspension is not homogeneous, replace the P6 vial containing OncoSil™ into the Perspex lined shield, replace both the Perspex lid and lead lid of pot and repeat the inversion step until the suspension is homogeneous. Again, remove the lead lid from the pot and using long forceps/tweezers remove the Perspex lid and the P6 vial containing the OncoSil™ to re-check if the suspension is homogeneous.
49. Once homogeneous, using long forceps/tweezers, place the P6 vial containing OncoSil™ into an OncoSil™ calibrated ionisation chamber, to verify the total vial radioactivity of the Microparticles from the final dilution is 60 MBq per vial. Therefore, the final standardised concentration for administration is designed to be 6.6 MBq/mL on the day of implantation.
50. If the OncoSil™ suspension will not be immediately drawn up into the syringe used for implantation, return the OncoSil™ suspension vial back into the Perspex lined shield and replace the Perspex lid (using long forceps) and lead lid. Move the OncoSil™ suspension and store it in a suitable shielded location, until the suspension is ready to be administered.

Following preparation, the OncoSil™ suspension should be stored within the glass vial, inside the Perspex lined lead pot, at room temperature.

OncoSil™ must be used within 24 hours of preparation, with exception if the preparation was performed +7 days from reference date. If the suspension is made on day +7, it must be used the same day.

Dispose of all vials, Perspex lined lead pots, and packaging materials into appropriate radioactive waste and according to the treatment facility's radiation safety policy.

11. PREPARING THE BETA-SHIELDED SYRINGE AND DISPENSING OF THE ONCOSIL™ SUSPENSION

1. To ensure OncoSil™ is homogeneous, firmly hold the top and bottom segments of the Perspex lined lead pot in a closed position and invert the suspension to obtain an even mixture. Do this 10-20 times, or until homogeneous.
2. Label the empty beta-shielded syringe / transport box with a minimum of the following:
   a. Patient identifiers (initials)
   b. Name of the Radioactive Material (OncoSil Phosphorous-32 Microparticles)
   c. Syringe Volume (mL)
   d. Syringe calculated radioactivity (MBq)
   e. OncoSil™ expiry date and time
3. Place the empty syringe in an appropriate beta-shielded syringe and lock in place.
4. Attach a 7 cm long needle to the syringe within the beta-shielded syringe.
5. SLOWLY and CAREFULLY remove the lead lid (leaving the Perspex lid in place) from the Perspex lined lead pot containing the final OncoSil™ suspension.
6. If not already in place, insert a filtered aeration/venting needle through the hole in the top of the Perspex lid, into the rubber stopper of the P6 vial containing the final OncoSil™ suspension.
7. Using a 7 cm long needle, penetrate the P6 vial containing the final OncoSil™ suspension through the small hole in the Perspex lid and rubber stopper and draw up the required volume estimated from the tumour volume (from **Step 3 Determination of the Volume to be Implanted, in Section 9**) into the beta-shielded syringe.
8. Once the OncoSil™ suspension is within the syringe, detach the needle and attach a three-way Luer tap to seal the end of the syringe.

9. Place the beta-shielded syringe in a lead transport box and transport to the procedure area.
10. Once the transport box reaches the procedure area, the beta-shielded syringe containing the OncoSil™ suspension should remain in the lead transport box until required for implantation.

Note: To ensure that the OncoSil™ suspension is homogeneous prior to implantation in the patient, hold the syringe at the body of the shield, being careful not to depress the syringe plunger, mix the OncoSil™ suspension by inverting the beta-shielded syringe three times, or until homogeneous.

12. IMPLANTATION PROCEDURE FOR ONCOSIL™ USING ENDOSCOPIC ULTRASOUND (EUS) GUIDANCE

The OncoSil™ implantation procedure must be performed in a suitable treatment facility environment and by a suitably qualified Endoscopist and the Authorised User (i.e. an OncoSil Medical trained Nuclear Medicine Physician/Radiation Oncologist/Interventional Radiologist).

A number of additional commercially available products are needed to implant OncoSil™ under endoscopic ultrasound (EUS) guidance. They do not form part of the OncoSil™ System and are not supplied by OncoSil Medical. They include:

- Echoendoscope
- A 22-gauge EUS guided FNA needle loaded through the biopsy channel of the echoendoscope or other equivalent device
- [Optional] A catheter extension set
- Syringes filled with saline
- Clinical waste-disposal bag lined with enough gauze to soak 50 mL of fluid
- Clinical waste-disposal bags for disposable accessories and protective clothing of procedure room staff
- Protective clothing (gloves, coats, goggles etc.)

If required, an extension set may be used, as shown below:

- Remove the beta-shielded syringe containing the OncoSil™ suspension from the lead transport box.
- Without depressing the syringe plunger, hold the beta-shielded syringe by its mid portion and mix the OncoSil™ suspension by inverting the beta-shielded syringe three times, or until homogeneous.
- [If using a optional catheter extension set] Remove the protecting Luer cap and attach a catheter extension set to the beta-shielded syringe with the three-way Luer lock tap to the distal end of the catheter extension set.
- Set the three-way Luer lock tap to the 'OPEN ' position.
- HOLDING THE BETA-SHIELDED SYRINGE BY ITS SIDES, KEEPING FINGERS AWAY FROM THE ENDS, position the syringe vertically, void ALL air remaining in the syringe by gently allowing the beta-shielded syringe plunger to press against a horizontal surface until the OncoSil™ suspension appears in the extension set tubing.
- Set the three-way Luer lock tap to the 'CLOSED' position.

Note: Whilst performing the above steps ensure that at all times the beta-shielded syringe is held by its mid portion. Throughout the procedure the operator should restrict exposure to axial radiation from the ends of the beta-shielded syringe.

Implantation Procedure:

1. The endoscope should be used in accordance with the detail guidance provided in the manufacturer's instruction manual (provided with the Endoscope).
2. EUS machine to be set to 'recording mode'.
3. Patient should be prepared in line with routine clinical practice.
4. **Note**: Antibiotic prophylaxis to cover the OncoSil™ implantation procedure is advised. The selection and duration of antimicrobial regimen is based on local guidelines and practice.
5. The target pancreatic tumour is identified on the ultrasound screen.
6. A 22-gauge EUS guided FNA needle is loaded through the biopsy channel of the echoendoscope and slowly advanced through the gastric wall or duodenal wall into the target pancreatic tumour (avoiding damage to surrounding organs).
7. Once the FNA needle is in a satisfactory position within the tumour and avoiding vessels, the stylet is removed and a Luer tap is attached to the FNA needle.
8. To ensure the OncoSil™ suspension is homogeneous, hold the beta-shielded syringe by its mid portion and being careful not to depress the syringe plunger, mix the OncoSil™ suspension by inverting the beta-shielded syringe three times, or until homogeneous.
9. Remove the protecting Luer cap from the beta-shielded syringe containing the OncoSil™ suspension and attach the syringe to the FNA needle via the three-way Luer lock tap before setting the Luer tap to the 'open' position. Ensure that the syringe is securely attached to the three-way Luer lock tap.
10. The required amount of OncoSil™ suspension is then implanted manually by slowly depressing the plunger of the beta-shielded syringe.
11. **Note**: If the resistance met prevents further OncoSil™ suspension from being expelled from the syringe, the needle should be slowly withdrawn within the tumour to a point where the syringe plunger can continue to be depressed (*see note below on backpressure).
12. Once the syringe is empty and the contents have been implanted into the tumour the three-way Luer lock tap is set to the 'closed' position.
13. The beta-shielded syringe containing the OncoSil™ suspension is removed from the three-way Luer lock tap and is re-capped and placed back into the lead transport box.
14. A 5 mL syringe containing saline should now be attached to the FNA needle via the three-way Luer lock tap and the tap re-set to the open position.
15. The remaining contents in the lumen of the FNA needle is then flushed with 1.5 mL of saline in order to flush any remaining OncoSil™ suspension from the needle lumen into the tumour.
16. Prior to removal of the scope from the patient, pull the endoscope back into the stomach, extend the needle sheath beyond the scope tip by about 3cm and flush with the remains of the saline syringe.
17. Recording can be stopped at this point.
18. The tap is then set to 'closed'.
19. Re-sheath the needle, but do not remove the needle assembly from the scope.
20. Remove the scope with the FNA needle assembly in place and the needle sheath still extended beyond the scope tip.

21. Hold the scope tip with the extended needle sheath angled downwards over a clinical waste bag within which there is enough gauze to catch and hold any remaining fluid. Rinse the tip of the scope and sheath with the contents of a 50 mL syringe of water.
22. Once this is complete, remove the needle assembly from the scope and dispose of it in an appropriate radiation waste container.
23. Place the scope in an appropriate receptacle for transport for decontamination and cleaning.
24. The echoendoscope should be checked for radioactive decontamination prior to and after cleaning.
25. Wash and sterilise the echoendoscope using the standard method for cleaning the equipment at site.

Note: Regarding backpressure: If the resistance is too great on the subsequent implant attempt and it is not possible to empty the syringe contents into the tumour, the implantation procedure should be aborted. The syringe containing the OncoSil™ suspension should be removed as described above and the cap replaced before the syringe is placed back into the lead transport box for return to the Nuclear Medicine Department/ Radiopharmacy to measure the volume to calculate the radioactivity remaining in the syringe. In these circumstances where the entire contents of the syringe were not implanted, this needs to be reported to OncoSil Medical (complaints@oncosil.com)

13. DISASSEMBLY OF THE SYRINGE AND SHIELD

THIS IS VERY IMPORTANT FOR RECONCILLIATION OF THE PATIENT DOSE BY THE NUCLEAR MEDICINE PERSONNEL

1. After completion of the implantation, the syringe containing any residual OncoSil™ suspension should be re-capped and then placed into the lead transport box.
2. Transfer to Nuclear Medicine Department/Radiopharmacy for measurement, and then decay.
3. The total radioactivity delivered to the patient (total activity implanted in the tumour) is determined by subtraction of the post-implantation volume (mL) reading in the syringe from the pre-implantation volume (mL) within the syringe (i.e., an ionisation chamber measurement is not required for post-implantation syringe contents).

14. DISPOSAL OF EXCESS ONCOSIL™ SUSPENSION AND ACCESSORIES

Following dilution and implantation, any disposable needles/tubing, syringes with any remaining OncoSil™ suspension, gauzes, gloves, aprons and other protective clothing, must be disposed of as radioactive waste and in accordance with treatment facility policies.

15. STERILISATION OF THE ENDOSCOPE

Following the implantation procedure, the endoscope must be cleaned, washed and sterilised in accordance with local procedures.

The echoendoscope should be checked for radioactive contamination prior to and after cleaning.

16. POST PROCEDURE RECOVERY

- The patient should be carefully monitored, through observation and recording of vital signs, as clinically indicated.
- The patient should be discharged from the department when they have recovered from the procedure.
- Depending on the patient's condition and the physician's assessment, they may be required to stay overnight at the treatment facility.
- SPECT-CT Bremsstrahlung imaging is advised following the implantation period prior to patient discharge to confirm satisfactory localisation of radioactivity.

17. RADIATION SAFETY GUIDELINES FOR ONCOSIL™

All person's handling, dispensing and implanting OncoSil™ must be familiar with and abide by all Local, State and Federal regulatory requirements governing therapeutic radioactive materials. Standard approved radiation protection techniques should be used to protect staff when handling both OncoSil™ and the patient. For more specific guidance on radiation safety as it relates to the OncoSil™ System, refer to the OncoSil™ System Radiation Safety Guidelines.

17.1 General Precautions

- Adequate shielding from beta radiation must be effected during storage, handling and use of OncoSil™.
- Standard procedures and practices used to minimise occupational radiation doses must be effected during storage, handling and use of OncoSil™.
- Unshielded vials and syringes must be handled with forceps that set the fingers away from the unshielded radioactive source by a minimum of 20 cm.
- Care must be taken to ensure minimum radiation exposure to the patient extraneous to the therapeutic objective.
- Care must be taken to ensure minimum radiation exposure to all staff and other personnel who come into contact with the patient.
- Radiation safety practices must be implemented in accordance with Local, State and Federal, regulatory requirements. Any loss of containment (spills and/or leakages) of OncoSil™ must be isolated, contained and cleaned up immediately. Area contamination monitoring practices should then be followed to ensure the isolation, containment and cleaning has been effective.
- Standard clinical practice should be implemented with respect to the implantation delivery method used for OncoSil™.
- OncoSil™ must be prepared behind a screen suitable for shielding from beta particles e.g. Perspex or Lucite.
- OncoSil™ must be stored inside adequate shielding at all times pre-and post-implantation.
- All contaminated waste must be placed in a designated radioactive waste container and disposed of in accordance with treatment facilities policies.

17.2 Patient & Visitors Precautions

- For vulnerable groups such as pregnant women, infants and children, the patient should avoid unnecessary contact for 2 weeks.

17.3 Staff Precautions

- Individual monitoring of personnel in accredited treatment facilities is a general requirement. There are no special requirements for personnel handling OncoSil™ in relation to radiation dose monitoring. General film badges or some form of personal dosimeter are acceptable.
- Nursing care and ward cleaning requirements will be at the discretion of the treatment facility's radiation safety

procedures.

18. ADVERSE EVENTS

In the previous clinical studies, the following adverse events were considered to have a probable or definite causal relationship with OncoSil™:

- Procedure-related pain
- Abdominal pain and discomfort
- Nausea
- Vomiting
- Lethargy
- Fever
- Abnormal liver function tests

19. WARNINGS

- If any signs of damage or ineffective sterile barrier integrity are observed for the OncoSil™ System, DO NOT USE the system and contact OncoSil Medical. Signs of damage and/or ineffective sterile barrier integrity may include, for example, broken vial, cracked vial, broken ring pull, non-intact tamper evident seals, missing vial caps etc.
- OncoSil™ System is supplied sterile. There is no data to support the sterility or functionality of OncoSil™ past its expiration date.

20. CONTRAINDICATIONS

- OncoSil™ is contraindicated in patients who have a known history of hypersensitivity to silicon or phosphorous.
- OncoSil™ is contraindicated where endoscopic ultrasound (EUS) directed implantation is considered hazardous (refer to PRECAUTIONS.

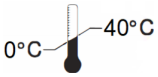
21. PRECAUTIONS

- Implantation of OncoSil™ should not occur in the following special situations:
  - Presence of multiple collateral vessels surrounding or adjacent to the target tumour
  - Presence (or significant risk) of varices near the target tumour
- Caution is advised where previous EUS (e.g., diagnostic EUS-FNA) was considered technically too difficult.
- Caution is strongly advised in the setting of recent, clinically significant pancreatitis. Implantation is not recommended.
- Caution is advised if administering chemotherapy within 48 hours either side of the OncoSil™ implantation.
- OncoSil™ has not been studied in patients who have previously received radiotherapy to the target organ.
- Since the combination of standard radiotherapy and OncoSil™ has not been investigated, additional radiotherapy is not recommended following OncoSil™ treatment.
- Antibiotic prophylaxis to cover the OncoSil™ implantation procedure is advised. The selection and duration of antimicrobial regimen is based on local guidelines and practice.
- Pain relief may be required to treat abdominal pain experienced immediately following implantation of OncoSil™.
- Gastro-protection e.g. with a proton-pump inhibitor or similar therapy, starting just prior to or at the time of implantation, and continued for up to 6 months post-implantation is considered reasonable.
- The safety of OncoSil™ has not been established in patients who are pregnant or who, within twelve months of implantation, become pregnant.
- The safety of OncoSil™ has not been established for future children of patients who are pregnant at the time of implantation, or who, within twelve months of implantation, become pregnant.
- The safety of OncoSil™ has not been established for children being breastfed by patients at the time of implantation or subsequent to implantation.
- The safety of OncoSil™ has not been established in patients who are < 18 years of age and is therefore not indicated for use in this population group.
- Due to limited clinical experience, caution is advised when treating tumours with volumes in excess of 50cc with OncoSil™. A risk-benefit assessment by the implanting physician is strongly advised.

22. SERIOUS INCIDENTS

Any serious incident that has occurred in relation to the OncoSil™ device must be reported to OncoSil Medical IMMEDIATELY, and without delay to complaints@oncosil.com as well as the competent authority of the Member State in which the user is established.

23. APPLICABLE SYMBOLS

	Do Not Re-Use		Use By Date
	Caution		This way up
	Radioactive Hazard		Temperature Limitation (upper and lower)
	Do not use if package is damaged	 	Consult Instructions For Use (QR Code link)
	Manufacturer combined with Date of Manufacture		Sterile Using Steam or Dry Heat
	Catalogue number		Authorised representative in the European Community
	Serial Number		UK Responsible Person (UKRP)
	Medical Device		

OncoSil™ is a Registered Trademark of OncoSil Medical Ltd

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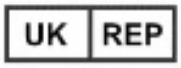

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