Embosphere®

MICROSPHERES

Instructions for use

CE 2797

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ENGLISH

DESCRIPTION

Embosphere® Microspheres are biocompatible, hydrophilic, non-absorbable, precisely calibrated acrylic polymer microspheres impregnated with porcine gelatin and are available in a large range of sizes and concentrations. These spheres are designed to offer controlled, targeted embolization.

IMPLANTABLE DEVICE MATERIALS TABLE

Material	Duration of exposure	Level of patient exposure (maximum solid content by syringe)
Trisacryl Copolymer	Long-Term (> 30days)	159 ± 6 mg
Gelatin	Long-Term (> 30days)	23 ± 1 mg

HOW SUPPLIED

20-mL prefilled syringe with a standard Luer-lock tip, individually packaged in blister tray sealed by a Tyvek® peel-away lid. Plastic screw cap and plunger. Elastomer three-skirt plunger joint.
Contents: 1 mL or 2 mL of microspheres in sterile, pyrogen-free 0.9% NaCl solution.

INTENDED USE/INDICATIONS FOR USE

Embosphere Microspheres are designed to occlude blood vessels, for therapeutic or preoperative purposes, in the following procedures:

- Embolisation of hypervascular tumours and processes, including uterine fibroids, meningiomas, liver tumours.
- Embolisation of the prostate arteries for relief of symptoms related to Benign Prostatic Hyperplasia.
- Embolisation of arteriovenous malformations.
- Haemostatic embolisation.

40-120 µm microspheres are more specifically designed for embolisation of meningiomas and liver tumours.

CLINICAL BENEFITS

Embolisation with Embosphere Microspheres is a minimally invasive treatment that is effective:

- For women with uterine fibroids for relief of related symptoms including heavy menstrual bleeding, pelvic pain or pressure, and/or urinary dysfunction, and for improvement of quality of life.
- For patients with hypervascular tumours, including liver tumours, for relief of related symptoms and for delay of the disease progression.
- For patients with meningioma, for reduction of intraoperative blood loss during resection procedure.
- For men with benign prostatic hyperplasia (BPH) for relief of related lower urinary tract symptoms (LUTS), such as urinary frequency, inability to urinate, incomplete emptying of bladder, difficulty starting urination, and straining to urinate or weak urine stream, and for improvement of quality of life.
- For patients with arteriovenous malformations for relief of related symptoms.
- For patients with haemorrhage for immediate and long-term bleeding control.

For a copy of this device's current European Summary of Safety and Clinical Performance (SSCP), please go to the European database on medical devices (Eudamed), where it is linked to the basic UDI-DI. https://ec.europa.eu/tools/eudamed. Basic UDI-DI: 08844504856SE2.
Alternatively, download a copy of the SSCP from:
https://www.merit.com/sscp

MAGNETIC RESONANCE IMAGING

Embosphere Microspheres are made of tris-acryl polymer impregnated with porcine gelatin and are magnetic resonance (MR) compatible.

CONTRAINDICATIONS

All indications

- Patients unable to tolerate vascular occlusion procedures.
- Vascular anatomy or blood flow precluding correct catheter placement or embolic agent injection.
- Presence of arteries supplying the lesion not large enough to accept Embosphere Microspheres
- Presence of collateral vessel pathways potentially endangering normal territories during embolization
- Presence or likely onset of vasospasm.
- Vascular resistance peripheral to the feeding arteries precluding passage of Embosphere Microspheres into the lesion
- In large diameter arteriovenous shunts (i.e., where the blood does not pass through an arterial/capillary/venous transition but directly from an artery to a vein)
- High-flow arteriovenous shunts or with a diameter greater than the selected microspheres
- Presence of severe atheromatous disease
- Patients with known allergy to gelatin.

50-100 µm, 40-120 µm and 100-300 µm microspheres are not recommended for use in the bronchial circulation.

UFE Specific Contraindications

- Pregnant women
- Suspected pelvic inflammatory disease or any other active pelvic infection
- Any malignancy of the pelvic region
- Endometrial neoplasia or hyperplasia
- Presence of one or more submucosal fibroid(s) with more than 50% growth into the uterine cavity
- Presence of pedunculated serosal fibroid as the dominant fibroid(s)
- Fibroids with significant collateral feeding by vessels other than the uterine arteries

PAE Specific Contraindications

- Active urinary tract infection or prostatitis
- Prostate cancer
- Bladder cancer
- Chronic renal failure
- Bladder atonia, neurogenic bladder disorder, or other neurological disorder impacting bladder function
- Bladder stones
- Urinary obstruction due to causes other than BPH, including urethral stricture
- Excessive vessel tortuosity or severe atherosclerosis

Neurological Specific Contraindications

- Presence of patent extra-to-intracranial anastomoses or shunts
- Presence of end arteries leading directly to cranial nerves
- In any vasculature where Embosphere Microspheres could pass directly into the internal carotid artery, vertebral artery, intracranial vasculature or the above listed vessels

POTENTIAL COMPLICATIONS

All indications
Vascular embolisation is a high-risk procedure. Complications may occur at any time during or after the procedure, and may include, but are not limited to, the following:

- Complications related to catheterization (e.g. haematoma at the site of entry, clot formation at the tip of the catheter and subsequent dislodgement, nerve and/or circulatory injuries which may result in leg injury, infection)
- Vessel or lesion rupture and haemorrhage
- Occlusion of vessels in healthy territories
- Paralysis resulting from untargeted embolization or ischemic injury from adjacent tissue edema

- Stroke or cerebral infarction
- Ischaemia at an undesirable location, including ischaemic stroke, ischaemic infarction (including myocardial infarction), and tissue necrosis
- Blindness, hearing loss, loss of smell, and/or paralysis
- Capillary bed occlusion and tissue damage
- Death
- Undesirable reflux or passage of Embosphere Microspheres into normal arteries adjacent to the targeted lesion or through the lesion into other arteries or arterial beds, such as the internal carotid artery, pulmonary, or coronary circulations
- Pulmonary embolism due to arterial venous shunting
- Vasospasm
- Recanalisation
- Foreign body reaction necessitating medical intervention
- Infection necessitating medical intervention
- Allergic reaction to medications (e.g. analgesics)
- Allergic reaction due to contrast media or embolic material
- Cutaneous irritations (e.g. rash), possibly delayed from the time of embolization
- Post-embolisation syndrome, such as transient pain, nausea, vomiting, fever, possibly delayed from the time of embolization
- Transient hypertensive episode
- Additional information is found in the Warnings section

UFE Specific Potential Complications

- The most frequently anticipated post procedure complications are abdominal pain, discomfort, fever and/or nausea, collectively known as "Post-embolization Syndrome." Some patients may also experience constipation. This is generally managed with prescription or over-the-counter medications.
- Premature ovarian failure (i.e., menopause)
- Amenorrhea
- Infection of the pelvic region
- Uterine/ovarian necrosis
- Phlebitis
- Deep vein thrombosis with or without pulmonary embolism
- Vaginal discharge
- Tissue passage, fibroid sloughing, or fibroid expulsion post UFE
- Post-UFE intervention to remove necrotic fibroid tissue
- Vagal reaction
- Hysterectomy

PAE Specific Potential Complications

- Non-targeted embolization of the rectum, bladder, scrotum, penis, or other areas
- The most frequent post-procedure complication includes "Post-PAE Syndrome", which includes nausea, vomiting, fever, pelvic pain, burning sensation, dysuria, and frequent or urgent urination
- Skin burn (radiation exposure) from prolonged fluoroscopy time
- Blood in urine, semen, or stool
- Bladder spasm
- Urinary tract infection
- Urinary retention
- Constipation
- Urethral obstruction

Neurological Specific Potential Complications

- Ischemic stroke or ischemic infarction
- Neurological deficits, including cranial nerve palsies

PRECAUTION

All indications

- DO NOT USE THIS PREFILLED SYRINGE TO DIRECTLY INJECT EMBOSPHERE MICROSPHERES. THIS IS A "RESERVOIR" SYRINGE. PLEASE REFER TO INSTRUCTIONS PARAGRAPH.
- Embosphere Microspheres must only be used by specialist physicians trained in vascular embolisation procedures. The size and quantity of microspheres must be carefully selected according to the lesion to be treated, entirely under the physician's responsibility. Only the physician can decide the most appropriate time to stop the injection of microspheres.
- Patients with known allergy to contrast medium may require corticosteroids prior to embolization.
- Additional evaluations or precautions may be necessary in managing periprocedural care for patients with the following conditions:
- Bleeding diathesis or hypercoagulative state
- Immunocompromise
- Do not use if blister tray, peel-away film, screw cap or syringe appear damaged.
- This is a disposable product. Discard opened syringes after use.
- For single patient use only - Contents supplied sterile
- Never reuse, reprocess, or resterilise. Reusing, reprocessing or resterilising may compromise the structural integrity of the device and/ or lead to device failure, which in turn may result in patient injury, illness or death. Reusing, reprocessing or resterilising may also create a risk of contamination of the device and/ or cause patient infection or cross infection including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient. All procedures must be performed according to accepted aseptic technique.
- The syringe is intended for embolic use only. Do not use for any other application.

UFE Specific Precautions

- There is an increased chance of retro-migration of Embosphere Microspheres into unintended blood vessels as uterine artery flow diminishes. Embolization should be stopped when the vasculature surrounding the fibroid can no longer be visualized but before complete stasis in the uterine artery.
- UFE should only be performed by specialist physicians who have received appropriate training for treatment of uterine leiomyomata (fibroids).

Liver tumour Specific Precautions

- There is no known incompatibility between Embosphere Microspheres and chemotherapeutics used for the treatment of liver tumours.

PAE Specific Precautions

- The PAE procedure should only be performed by specialist physicians who have received appropriate training.
- Collateral circulation may be present and can dilate and supply adjacent arteries as resistance within the prostatic bed increases. Therefore, there is potential for severe complications with nontargeted embolization.
- There is an increased chance of retro-migration of Embosphere Microspheres into unintended blood vessels as prostatic artery flow diminishes. Embolization should be stopped when the vasculature surrounding the prostate can no longer be visualized but before complete stasis in the prostatic artery.

Haemostatic indication Specific Precautions

- Embolization of the splenic artery may be associated with inferior vena cava thrombus.

WARNINGS

All indications

- Embosphere Microspheres contain gelatin of porcine origin, and therefore, could cause an immune reaction in patients who are hypersensitive to collagen or gelatin. Careful consideration should be given prior to using this product in patients who are suspected to be allergic to injections containing gelatin stabilizers.
- Studies have shown that Embosphere Microspheres do not form aggregates, and, as a result, penetrate deeper into the vasculature as compared to similarly sized PVA particles. Care must be taken to choose larger sized Embosphere Microspheres when embolising arteriovenous malformations with large shunts to avoid passage of the spheres into the pulmonary or coronary circulation.
- Some of the Embosphere Microspheres may be slightly outside of the range, so the physician should be sure to carefully select the size of Embosphere Microspheres according to the

size of the target vessels at the desired level of occlusion in the vasculature and after consideration of the arteriovenous angiographic appearance. Embosphere Microspheres size should be selected to prevent passage from artery to vein.

- Because of the significant complications of misembolisation, extreme caution should be used for any procedures involving the extracranial circulation encompassing the head and neck, and the physician should carefully weigh the potential benefits of using embolisation against the risks and potential complications of the procedure. These complications can include blindness, hearing loss, loss of smell, paralysis and death.
- Serious radiation induced skin injury may occur to the patient due to long periods of fluoroscopic exposure, large patient diameter, angled x-ray projections, and multiple image recording runs or radiographs. Refer to your facility's clinical protocol to ensure the proper radiation dose is applied for each specific type of procedure performed. Physicians should monitor patients that may be at risk.
- Onset of radiation-induced injury to the patient may be delayed. Patients should be counseled on potential radiation side effects and whom they should contact if they show symptoms.
- Pay careful attention for signs of mistargeted embolisation. During injection carefully monitor patient vital signs to include SaO2 (e.g. hypoxia, CNS changes). Consider terminating the procedure, investigating for possible shunting, or increasing microsphere size if any signs of mistargeting occur or patient symptoms develop.
- Consider upsizing the microspheres if angiographic evidence of embolisation does not quickly appear evident during injection of the microspheres.

UFE Specific Warnings

Warnings About UFE and Pregnancy

- The effects of UFE on the ability to become pregnant and carry a fetus to term, and on the development of the fetus, have not been determined. Therefore, this procedure should only be performed on women who do not intend future pregnancy.
- Women who become pregnant following UFE may be at increased risk for postpartum haemorrhage, preterm delivery, cesarean delivery, and malpresentation.
- Devascularization of the uterine myometrium resulting from UFE may theoretically put women who become pregnant following UFE at increased risk of uterine rupture.

Other UFE Warnings

- When using Embosphere Microspheres for uterine fibroid embolization, do not use microspheres smaller than 500 microns.
- An appropriate gynecologic work-up should be performed on all patients presenting for embolization of uterine fibroids (e.g., gynecologic history, fibroid imaging, endometrial sampling to rule out carcinoma in patients with abnormal menstrual bleeding).
- The diagnosis of uterine sarcoma could be delayed by taking a nonsurgical approach (such as UFE) to treating fibroids. It is important to pay close attention to warning signs for sarcoma (e.g., rapid tumour growth, postmenopausal with new uterine enlargement, MRI findings) and to conduct a more thorough work-up of such patients prior to recommending UFE. Recurrent or continued tumour growth following UFE should be considered a potential warning sign for sarcoma and surgery should be considered.

PAE Specific Warnings

- A thorough clinical evaluation should be performed on all patients presenting for embolization for BPH (e.g., urinalysis, digital rectal exam, symptom scores, prostate imaging, prostate-specific antigen test, transrectal ultrasound) to rule out prostate cancer.
- Because of the tortuous vessels and duplicative feeding arteries in the pelvic area, extreme caution should be used when performing prostatic artery embolization (PAE). Complications of mistargeted embolization include ischemia of the rectum, bladder, scrotum, penis or other areas.
- When using Embosphere Microspheres for prostatic artery embolization, do not use microspheres smaller than 100 microns. It is recommended to use 300-500 microns.

Warnings About PAE and Fertility

- The effects of PAE on fertility have not been determined. Therefore, this procedure should not be performed on men wanting to father a child.

Haemostatic Specific Warnings

- Since Embosphere Microspheres have not been evaluated to control bleeding or haemorrhaging for neurovascular indications, they should not be used for this purpose in the neurovasculature.

Warnings about use of small microspheres

- Careful consideration should be given whenever use is contemplated of embolic agents that are smaller in diameter than the resolution capability of your imaging equipment. The presence of arteriovenous anastomoses, branch vessels leading away from the target area or emergent vessels not evident prior to embolisation can lead to mistargeted embolisation and severe complications.
- Microspheres smaller than 100 microns will generally migrate distal to anastomotic feeders and therefore are more likely to terminate circulation to distal tissue. Greater potential of ischaemic injury results from use of smaller sized microspheres and consideration must be given to the consequence of this injury prior to embolisation. The potential consequences include swelling, necrosis, paralysis, abscess and/or stronger post embolisation syndrome.
- Post embolisation swelling may result in ischaemia to tissue adjacent to target area. Care must be given to avoid ischaemia-intolerant, nontargeted tissue such as nervous tissue.

INSTRUCTIONS FOR USE

- Carefully evaluate the vascular network associated with the lesion using high resolution imaging prior to beginning the embolization procedure.
- Embosphere Microspheres are available in a range of sizes. Because of the potential for misembolisation and the inherent variability in sphere sizes, the physician should be sure to carefully select the size of Embosphere Microspheres according to the size of the target vessels at the desired level of occlusion in the vasculature.
- Carefully select the size of microspheres according to the size of the vessels identified and the catheter used. Embosphere Microspheres are flexible particles that support temporary compression by 20 to 30% to facilitate passage through microcatheters. Studies have shown a direct correlation between the size of microspheres and the size of occluded vessels.
- Choose a delivery catheter based on the size of the target vessel and the microsphere size being used. Refer to below table for catheters and Embosphere Microspheres sizes compatibility.
- Embosphere Microspheres are not radiopaque. It is recommended that the embolization be monitored using fluoroscopic visualization by adding the appropriate amount of non-ionic contrast medium to the physiologic suspension fluid.

To Deliver Embosphere Microspheres

- Inspect packaging and syringe before use to ensure that they are intact. The external surface of the syringe is sterile.
- According to aseptic technique, open the peel-away film beginning at the tip, and peel back the film completely to the base. Gently tip the sterile syringe on the sterile field, avoiding contact with any parts previously sealed.
- Unscrew the cap of the Embosphere Microspheres prefilled syringe.
- It is highly recommended to add non-ionic contrast agent to monitor the injection radiologically. Gently draw non-ionic contrast agent directly into the reservoir syringe. The ideal suspension is usually obtained with a mixture of 50% non-

ionic contrast agent and 50% saline solution. To obtain a homogeneous suspension of Embosphere Microspheres, gently invert the 20mL syringe several times. Non-ionic contrast agent and 0.9% NaCl solution can be added in the same proportions to obtain a more diluted suspension.

- Do not use the 20mL prefilled syringe to inject Embosphere Microspheres through the catheter, as a catheter occlusion may result.
- Remove all air from the syringe and connect it to one hub of the three-way stopcock.
- Wait several minutes to allow the Embosphere Microspheres to suspend in the solution.
- Draw up the suspension using a 1 mL or 3 mL injection syringe connected to another hub of the three-way stopcock. Avoid back and forth movements to reduce the risk of introducing air into the system. Check that the desired quantity and concentration of microspheres are used.
- Remove all air from the syringe.
- Introduce the delivery catheter into the target vessel according to standard techniques. Position the catheter tip as close as possible to the treatment site to avoid inadvertent occlusion of normal vessels.
- Screw the syringe onto the hub of the catheter, using the male Luer-lock connector of the stopcock.
- Open stopcock to connect the injection syringe with the catheter.
- Under continuous fluoroscopic control, slowly infuse microspheres into the blood stream while observing the contrast flow rate. If there is no effect on the flow rate, repeat the delivery process with additional injections of the Embosphere Microspheres/contrast solution. Consider using larger sized Embosphere Microspheres if the initial injections do not alter the contrast flow rate. If the Embosphere Microspheres/contrast solution requires re-suspension, gently invert the 20 mL syringe several times.
- Always inject under free flow conditions. Reflux of microspheres can induce immediate ischaemia of healthy tissues or vessels.
- Continue infusion until the desired devascularisation is obtained. Studies have shown that Embosphere Microspheres penetrate more distally into the lesion than PVA particles of similar size. Reduction of the arterial blood supply to the lesion is therefore more progressive. Exercise conservative judgment in determining the embolization endpoint.
- Femoral puncture can result in arterial spasm. This may predispose to femoral thrombosis (e.g., leg injury). Femoral patency should be re-assessed prior to final catheter removal.
- At the end of the infusion, remove the catheter while maintaining gentle suction to avoid dislodging any residual microspheres still within the catheter lumen, then close the three-way stopcock.
- Apply pressure to the puncture site until haemostasis is complete.
- Discard any remaining Embosphere Microspheres and the used syringes.

Additional UFE Specific Instructions

- When embolizing uterine fibroids, choose an Embosphere Microsphere of 500 microns or greater.
- At the discretion of the physician, pneumatic compression devices may be used for patients currently taking hormone therapy, uterine volume >1000cc, and patients that are overweight to lower the risk of deep vein thrombosis.
- Embolization should be stopped when the vasculature surrounding the fibroid can no longer be visualized but before complete stasis in the uterine artery. There is an increased chance of retro-migration of Embosphere Microsphere into unintended blood vessels as uterine artery flow diminishes.

Additional PAE Specific Instructions

- For prostatic artery embolization, it is recommended to use Embosphere Microspheres 300-500 microns.
- A Foley catheter, with its balloon inflated with a mixture of non-ionic contrast and saline, may be placed prior to PAE for use as a landmark during the embolization procedure.
- PAE can be performed by either radial or femoral access.

Additional AVM Specific Instructions

- When embolizing arteriovenous malformations (AVMs), choose an Embosphere Microsphere size that will occlude the nidus without passing through the AVM.

CONSERVATION / STORAGE / DISPOSAL

- Embosphere Microspheres must be stored in a cool, dry and dark place in their original syringe and packaging.
- Use by the date indicated on the syringe label.
- Do not freeze.
- Do not resterilize.
- After use, Embosphere Microspheres must be disposed as per hospitals contaminated waste circuit.

Size Range (µm)	Minimum Catheter ID	Color Code	1 mL	2 mL
50-100	0.016" (0.41 mm)	Grey	S010GH	S020GH
40-120	0.016" (0.41 mm)	Orange	S110GH	S120GH
100-300	0.017" (0.43 mm)	Yellow	S210GH	S220GH
300-500	0.018" (0.46 mm)	Blue	S410GH	S420GH
500-700	0.020" (0.51 mm)	Red	S610GH	S620GH
700-900	0.027" (0.69 mm)	Green	S810GH	S820GH
900-1200	0.038" (0.97 mm)	Purple	S1010GH	S1020GH

PATIENT COUNSELING INFORMATION

- Patients should have a clear understanding prior to embolization of who will provide their post procedure care and whom to contact in case of an emergency after embolization.
- Embolization patients should have an understanding of the potential benefits, risks, and adverse events associated with embolization. In particular, patients should understand that there is a chance their symptoms will not improve following embolization.

Information on packaging

	Manufacturer
	Date of manufacture: YYYY-MM-DD
	Use by date: YYYY-MM-DD
	Lot number
	Catalog number
	Do not resterilize
	Do not use if package is damaged and consult instruction for use
	Keep away from sunlight

	Keep dry
	Single use
	Caution
	Non-pyrogenic
	Sterilized using steam
	Lower limit of temperature
	Medical Device
	Unique Device Identifier
	Single sterile barrier system with protective packaging inside

	Consult Instructions for Use
	Patient identification
	Healthcare centre or doctor
	Date
	Patient information website
	CE mark - Notified body identification: 2797
	Caution: Federal (USA) law restricts this device to use by or on the order of a licensed physician.

In the European Union, any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the applicable Member State.

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