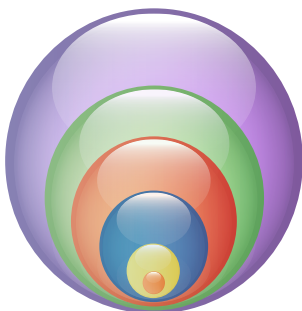


HydroPearl™



 **TERUMO**
HydroPearl™
Microspheres

Instructions For Use

 **TERUMO**

HydroPearl™ Microspheres Instructions for Use
STERILE – SINGLE USE ONLY – NON-PYROGENIC

MR Compatibility: MR Safe

Rx Only: Federal (USA) law restricts this device to sale by or on the order of a physician.

DESCRIPTION:

HydroPearl Microspheres are part of a family of embolic materials based on MicroVention's proprietary microsphere technology. These spheres are designed to offer controlled, targeted embolization. HydroPearl Microspheres are made using Poly-Ethylene Glycol and are precisely calibrated, non-resorbable, hydrophilic, compressible, and biocompatible. HydroPearl Microspheres are available in the following size range:

Microparticle Size	Label Color
75 ± 30 µm	Orange
200 ± 75 µm	Yellow
400 ± 75 µm	Blue
600 ± 75 µm	Red
800 ± 75 µm	Green
1100 ± 75 µm	Purple

PRESENTATION:

- HydroPearl Microspheres are contained in a sterile 20 cc pre-filled syringe and packaged in a pre-formed tray with Tyvek peel-away lid.
- Each syringe contains approximately 2 ml of HydroPearl Microspheres in non-pyrogenic, sterile, transport solution of physiological buffered saline.
- The product is packaged sterile. Do not use if the unit package is opened or damaged.
- Each syringe is intended for a single patient use only. Do not re-sterilize. Discard any unused material.

INTENDED USE:

The HydroPearl Microspheres are intended for the embolization of arteriovenous malformations and hypervascular tumors, including uterine fibroids, and for embolization of prostatic arteries (PAE) for symptomatic benign prostatic hyperplasia (BPH).

CONTRAINDICATIONS

- Targeted embolization of blood vessels belonging to the central nervous system
- Patients intolerant to occlusion procedures
- Vascular anatomy or blood flow that precludes catheter placement of embolic agent injection
- Presence or likely onset of vasospasm
- Presence or likely onset of hemorrhage
- Presence of severe atheromatous disease
- Presence of feeding arteries smaller than distal branches from which they emerge
- Presence of collateral vessel pathways potentially endangering normal territories during embolization
- Presence of arteries supplying the lesion not large enough to accept HydroPearl Microspheres
- Vascular resistance peripheral to the feeding arteries precluding passage of HydroPearl Microspheres into the lesion
- In large diameter, arteriovenous malformations (i.e. where the blood does not pass through an arterial/capillary/venous transition but directly from an artery to vein)
- In the pulmonary vasculature

**Uterine Fibroid Embolization (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.

Prostatic Artery Embolization (PAE) SPECIFIC CONTRAINDICATIONS:

- Evidence of prostatic cancer or bladder cancer
- Urethral stricture
- Prostate size less than 40 grams
- Active urinary tract infection or prostatitis
- Interest in the preservation of fertility
- Patients with renal impairment
- Peak urinary flow rate greater than 12 ml/sec
- Large bladder diverticula or stones
- Neurogenic bladder
- Detrusor failure

WARNINGS:

- Vascular embolization is a high risk procedure. The procedure should be performed by physicians trained in vascular embolization procedures. Complications can occur at any time during or after the procedure.
- Do not use HydroPearl Microspheres in conjunction with other embolization devices based on organic solvents such as ethyl alcohol or dimethyl sulfoxide (DMSO), at the same embolization site.
- Use only non-ionic contrast agents in accordance with contrast agent labeling. Device compatibility with other contrast agents has not been established.
- Risks of radiation from angiography and fluoroscopy used to visualize the blood vessels during embolization, which may include a radiation burn and risks to future fertility.
- If arteriovenous anastomoses, branch vessels which lead away from the targeted embolization area, or emergent vessels not evident prior to embolization are present, it can lead to mistargeted embolization and cause severe complications for the patient.
- Microspheres smaller than 100 μm can migrate to distal anastomotic feeders and embolize circulation to distal tissue. For this reason, smaller microspheres have a greater likelihood of causing unwanted ischemic injury. This should be considered prior to starting the embolization procedure. Possible consequences include, but are not limited to, paralysis, necrosis, swelling, abscess formation and more severe post embolization syndrome.
- Ischemia of tissue adjacent to the targeted area may result from post-embolization swelling. Therefore, special care should be taken to avoid such ischemia of non-tolerant, non-targeted tissue such as the nervous system.
- Careful consideration should be given when using small microspheres contingent on the resolution of the imaging equipment used. The presence of arteriovenous anastomosis, branch vessel leading away from the target area or emergent vessels not evident prior to embolization can lead to mistargeted embolization and severe complications.
- Smaller microspheres may pose a greater ischemic risk and consideration must be given to the consequence of the injury prior to embolization.
- Consider upsizing HydroPearl Microspheres if angiographic appearance of embolization does not quickly appear during injection of the microspheres.
- If there are any symptoms of undesired embolization during injection, consider stopping the procedure to evaluate patient conditions and actions to be taken.
- HydroPearl Microspheres delivery time and amount. Typically, the artery will accept fewer HydroPearl Microspheres as the treatment progresses. Proximal slowing or termination of flow may indicate that the vessel or the target area is filled with HydroPearl Microspheres. Careful fluoroscopic monitoring is required.
- Microsphere embolization must be performed slowly. The injection speed and manner must be controlled. Excessive injection speed may result in retrograde material transport affecting other and healthy organs.
- Avoid reflux of HydroPearl Microspheres as this can induce immediate ischemia of the tissue or vessel.
- Carefully select microsphere size due to the tighter calibration of HydroPearl Microspheres, it has demonstrated the ability to penetrate deeper when compared to other cleared embolics.

UFE SPECIFIC WARNINGS:

- There is no long-term data on the effect of UFE on the ability to become pregnant and carry a fetus to term, and on the development of the fetus.

- 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 the following:
 - Postpartum hemorrhage
 - Preterm delivery
 - Caesarean delivery
 - Malpresentation
 - Abnormal placentation
- De-vascularization of the uterine myometrium resulting from UFE may increase the risk of uterine rupture of women who subsequently become pregnant following UFE.
- When using HydroPearl Microspheres for uterine fibroid embolization, do not use beads smaller than 500 microns.
- When embolizing uterine fibroids, 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 the microspheres into unintended blood vessels as uterine artery flow diminishes.
- An appropriate gynecologic work-up should be performed on all patients presenting for embolization of uterine fibroids (e.g. gynecologic history, fibroid imaging, and endometrial sampling to rule out carcinoma in patients with abnormal menstrual bleeding).
- The diagnosis of uterine sarcoma could be delayed by taking a non-surgical approach (such as UFE) to treating fibroids. It is important to pay close attention to warning signs for sarcoma (e.g., rapid tumor growth, postmenopausal with new enlargement, MRI findings) and to conduct a more thorough work-up of such patients prior to recommending UFE. Recurrent or continued tumor growth following UFE should be considered a potential warning sign for sarcoma and surgery should be considered.

PAE SPECIFIC WARNINGS:

- An appropriate urological work-up should be performed on all patients (e.g., urological history and appropriate testing, such as Prostate-Specific Antigen test, and, when appropriate, biopsy) to rule out carcinoma.
- The effect of prostatic embolization on male fertility has not been determined. Therefore, this procedure should only be performed on men who are willing to accept the risk of future infertility.
- Three-dimensional planning imaging (e.g., magnetic resonance angiography [MRA], computed tomographic angiography [CTA]) should be performed prior to embolization on patients who have had any previous invasive treatment to the prostate (e.g., surgery, ablation, etc.) or pelvic irradiation.
- Because of the tortuous vessels and duplicative feeding arteries in the pelvic area, extreme caution should be used when performing prostatic artery embolization (PAE). Collateral circulation may be present and can dilate and supply adjacent arteries as resistance within the prostatic bed increases. Complications of mistargeted embolization include ischemia of the rectum, bladder, scrotum, penis, or other areas.
- When using HydroPearl Microspheres for prostatic artery embolization, do not use microspheres smaller than 100 microns. It is recommended to use 400 microns.
- There is an increased chance of retro-migration of HydroPearl 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.

PRECAUTIONS:

- Do not use if the syringe or packaging appears damaged.
- Select the size and quantity of HydroPearl Microspheres appropriate for the pathology to be treated and the microcatheter used.
- Embolization with HydroPearl Microspheres should only be performed by physicians who have received appropriate interventional occlusion training in the region intended to be embolized.
- Patients with known allergy to contrast medium may require corticosteroids prior to embolization.
- For single patient use only – do not reuse, reprocess, or resterilize the device.
- The syringe is intended for embolic use only. Do not use for any other application.
- At the discretion of the physician, pneumatic compression devices may be used for patients currently taking hormone therapy, uterine

volume > 1000 cc, and patients that are overweight to lower the risk of deep vein thrombosis.

POTENTIAL COMPLICATIONS:

Vascular embolization is a high-risk procedure. The procedure should be performed by physicians trained in vascular embolization procedures. Complications can occur at any time during or after the procedure and may include, but not limited to:

- Undesirable reflux or passage of HydroPearl Microspheres into normal arteries adjacent to the targeted lesion or through the lesion into other arterial beds or arteries
- Embolization of the wrong artery or migration of the microspheres to the other parts of the body, which may necessitate further treatment.
- Hematoma, or bruising, at the incision site for arterial access
- Arterial aneurysm at the incision site for arterial access
- Deep vein thrombosis, or clotting of a deep vein in patient(s) leg
- Pulmonary Embolization
- Ischemia at an undesired location
- Capillary bed saturation and tissue damage
- Vessel or lesion rupture and hemorrhage
- Vasospasm
- Recanalization
- Foreign body reactions necessitating medical intervention
- Infection necessitating medical intervention
- Clot formation at the tip of the catheter and subsequent dislodgement
- Allergic reaction
- Risks of radiation from angiography and fluoroscopy used to visualize blood vessels during embolization, which may include radiation burn and risks to future fertility
- Death

UFE SPECIFIC POTENTIAL COMPLICATIONS:

Potential post procedure complications include:

- Abdominal pain
- Discomfort
- Fever
- Nausea
- Constipation
- 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
- Transient hypertensive episode
- Hysterectomy
- Rupture of the uterus

PAE SPECIFIC POTENTIAL COMPLICATIONS:

Potential post procedure complications include:

- Non-targeted embolization of the rectum, bladder, scrotum, penis, or other areas
- Nausea
- Vomiting
- Fever
- Pelvic pain
- Acute urinary retention
- Bladder ischemia or necrosis requiring surgical intervention
- Constipation
- Diarrhea
- Hematuria/Hematospermia
- Blood in stool
- Rectal Bleeding
- Rectal or lower colonic strictures
- Sexual dysfunction or impaired fertility

- Urethral or anal burning sensation
- Urethral stricture
- Urinary incontinence
- Urinary tract infection
- Urinary symptoms (e.g. dysuria, urgency, frequency)

INSTRUCTIONS FOR USE:

Preparation

1. Verify that the sterile packaging was not previously compromised.
2. Carefully select the size of the HydroPearl Microspheres according to the size of the target vessels at the desired level of occlusion in the vasculature. When embolizing arteriovenous malformations (AVM), choose a microsphere size that will occlude the nidus without passing through the AVM.
3. Choose a delivery catheter based on the size of the target vessel and the size of the HydroPearl Microspheres to be used. HydroPearl Microspheres can tolerate temporary compression up to 30% in-order to facilitate passage through the delivery catheter.

Microcatheter Compatibility Chart

Microsphere Size	Microcatheter
$\leq 1100 \mu\text{m}$	$\geq 0.041''$ ID
$\leq 800 \mu\text{m}$	$\geq 0.025''$ ID
$\leq 600 \mu\text{m}$	$\geq 0.022''$ ID
$\leq 400 \mu\text{m}$	$\geq 0.017''$ ID

4. HydroPearl Microspheres are not radio-opaque. It is recommended to monitor the embolization under fluoroscopic visualization by adding the desired amount of contrast medium (i.e. Omnipaque) to the suspension fluid. Suspension lifetime and reliability of deployment cannot be predicted with contrast agents which have not been tested.
5. Directly aspirate 4 ml of contrast medium into the syringe to obtain an approximate 50% contrast and approximate 50% saline solution mix. Remove all air from the syringe.
6. To evenly suspend the HydroPearl Microspheres /contrast solution, gently invert the 20 ml syringe several times.
7. Attach the syringe containing the HydroPearl Microspheres to a 1, 3 or a 10-ml syringe using a luer-lock 3-way stopcock; and, if desired, a delivery catheter may be attached to the remaining port on the stopcock. Transfer all contents from the 20 ml to the smaller syringe, wait several minutes to allow the HydroPearl to suspend/reach a homogenous state properly. Smaller sizes will achieve a homogenous/suspension state within minutes and larger sizes may take several minutes before a homogenous/suspension state is achieved.

Suspension characteristics of HydroPearl Microspheres are provided in the table below:

Size Range	Time to Suspension	Time in Suspension
$< 400 \mu\text{m}$	< 3 minutes	≥ 5 minutes
$400 \mu\text{m}$ to $600 \mu\text{m}$	< 4 minutes	> 1 minute
$> 600 \mu\text{m}$	≤ 8 minutes	< 1 minute

Once suspension is achieved, visually observe microspheres for suspension prior to deployment. If microspheres have settled, re-agitate the syringe until suspension is re-established. Maintain suspension of microspheres, to provide smooth deployment into the catheter. Gently agitate the microspheres to re-suspend if it appears that the microspheres have fallen out of suspension.

8. Draw the HydroPearl Microspheres/contrast solution into the injection syringe slowly and gently to minimize the potential of introducing air into the system. Purge all air from the system prior to injection.
9. Position the catheter at the desired site and carefully evaluate the vascular network associated with the lesion using high resolution imaging prior to beginning the embolization procedure angiography to evaluate the blood supply to the lesion.
10. 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.
11. Inject the HydroPearl Microspheres/contrast solution from the injection syringe under fluoroscopic visualization using a slow pulsatile action, while observing the contrast flow rate.
12. Always inject HydroPearl Microspheres under free flow conditions.
13. If there is no effect on the flow rate, repeat the delivery process with additional injections of HydroPearl Microspheres/contrast solution or larger size HydroPearl Microspheres may be considered. If the

HydroPearl Microspheres/contrast solution requires re-suspension, gently invert the 20 ml syringe several times.

WARNING: Avoid reflux of HydroPearl Microspheres as this can induce immediate ischemia of the tissue or the vessel.

14. Exercise conservative judgment in determining the embolization endpoint.

WARNING: When embolizing uterine fibroids, 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 the microspheres into unintended blood vessels as uterine artery flow diminishes.

WARNING: When embolizing the prostatic artery, embolization should be stopped when the vasculature surrounding the prostate can no longer be visualized but before complete stasis in the prostatic artery. There is an increased chance of retro-migration of the microspheres into unintended blood vessels as prostatic artery flow diminishes.

15. Once the endpoint is reached wait 2-3 minutes to observe whether the beads redistribute themselves and re-establish flow to the target. If flow is re-established re-inject the microspheres till the desired end-point is achieved.

Additional UFE Specific Instructions

16. When embolizing uterine fibroids, choose a microsphere size of 500 µm or greater. An endpoint of stasis or near stasis is recommended with the main uterine artery remaining patent, but with negligible residual flow toward the uterus.
17. This endpoint corresponds to an angiographic image of a patent horizontal segment with absent flow in the ascending segment of the uterine artery.

Additional PAE Specific Instructions

18. A Foley catheter, with its balloon inflated with a mixture of contrast and saline, may be placed prior to PAE for use as a landmark during the embolization procedure.
19. PAE can be performed by either radial or femoral access.

PRECAUTION: At the discretion of the physician, pneumatic compression devices may be used for patients currently taking hormone therapy, uterine volume > 1000 cc, and patients that are overweight to lower the risk of deep vein thrombosis.

Post Procedure

20. Once the desired clinical endpoint is achieved, remove the catheter while maintaining gentle aspiration suction so as not to dislodge HydroPearl Microspheres still within the catheter lumen.
21. Discard any open, unused HydroPearl Microspheres.
22. Do not reprocess open, unused HydroPearl Microsphere syringes. Reprocessing may compromise sterility, biocompatibility and functional integrity of the device.
23. Apply pressure to the puncture site until hemostasis is complete.

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.

CONSERVATION AND STORAGE:


















- HydroPearl Microspheres must be stored in a cool, dry and dark place in its original packaging.
- Use by the date indicated on the device label.
- Do not freeze.

WARRANTY

MicroVention, Inc. warrants that reasonable care has been used in the design and manufacture of this device. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness. Handling, storage, cleaning and sterilization of the device as well as factors relating to the patient, diagnosis, treatment, surgical procedure and other matters beyond MicroVention's control directly affect the device and the results obtained from its use. MicroVention's obligation under this warranty is limited to the repair or replacement of this device through its expiration date. MicroVention Inc. shall not be liable for any incidental or consequential loss, damage or expense directly or indirectly arising from

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EXPLANATION OF SYMBOLS USED ON PRODUCT LABELING:

	Catalog number
	Lot number
	Do not reuse
	Contents
	Caution
	Sterilized using steam or dry heat
	Use-by Date
	Keep away from sunlight
	Keep dry
	Do not freeze
	Date of Manufacture
	Manufacturer
	Consult instructions for use
	Do not use if package is damaged
	For Prescription Use Only
	MR Safe
	Non-Pyrogenic



Manufacturer:

MicroVention, Inc.

35 Enterprise
Aliso Viejo, CA 92656 USA
Tel: 714-247-8000
www.microvention.com

Distributed by:

Terumo Medical Corporation

2101 Cottontail Ln
Somerset, NJ 08873
Tel: (800) 283-7866

Prices, specifications and model
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