# EMBOZENE® Microspheres
Instructions for Use

CE 0086

## 1. Product Description

Embozene® Microspheres are spherical, tightly calibrated, biocompatible, non-resorbable, hydrogel microspheres coated with an inorganic perfluorinated polymer (Polyzene®-F). They are available in a range of sizes suitable for embolic therapy. Embozene® Microspheres are available as colored and opaque (non-colored) microspheres. Colored microspheres are color-coded by size.

Embozene® Microspheres are available in ten sizes. They are presented in prefilled syringes or vials with a choice 1 ml or 2 ml of product. Embozene® Microspheres may be ordered using the product reference numbers listed in Tables A and B.

Table A. Product Specifications and Ordering Information for Color-Advanced Microspheres

| Nominal Size | Label & Microspheres Color | Design Specifications | Minimum Inner Diameter Required for Catheter | Ref Numbers 1ml Vial with Colored Microspheres | Ref Numbers 2ml Vial with Colored Microspheres | Ref Numbers 1ml Syringe with Colored Microspheres | Ref Numbers 2ml Syringe with Colored Microspheres |
|---|---|---|---|---|---|---|---|
| **40 µm** | Black | 40 µm ± 10 µm | 0.002 inches | 10401-V1 | 10402-V1 | 10410-S1 | 10420-S1 |
| **75 µm** | Burgundy | 75 µm ± 15 µm | 0.003 inches | 10701-V1 | 10702-V1 | 10710-S1 | 10720-S1 |
| **100 µm** | Orange | 100 µm ± 25 µm | 0.004 inches | 11001-V1 | 11002-V1 | 11010-S1 | 11020-S1 |
| **250 µm** | Yellow | 250 µm ± 50 µm | 0.009 inches | 12001-V1 | 12002-V1 | 12010-S1 | 12020-S1 |
| **400 µm** | Blue | 400 µm ± 50 µm | 0.013 inches | 14001-V1 | 14002-V1 | 14010-S1 | 14020-S1 |
| **500 µm** | Red | 530 µm ± 50 µm | 0.016 inches | 15001-V1 | 15002-V1 | 15010-S1 | 15020-S1 |
| **700 µm** | Green | 700 µm ± 50 µm | 0.021 inches | 17001-V1 | 17002-V1 | 17010-S1 | 17020-S1 |
| **900 µm** | Purple | 900 µm ± 75 µm | 0.027 inches | 19001-V1 | 19002-V1 | 19010-S1 | 19020-S1 |
| **1100 µm** | Gray | 1100 µm ± 75 µm | 0.033 inches | 111001-V1 | 111002-V1 | 111010-S1 | 111020-S1 |
| **1300 µm** | Pink | 1300 µm ± 75 µm | 0.038 inches | 113001-V1 | 113002-V1 | 113010-S1 | 113020-S1 |

Table B. Product Specifications and Ordering Information for Opaque (Non-Colored) Microspheres

| Nominal Size | Label Color | Design Specifications | Minimum Inner Diameter Required for Catheter | Ref Numbers 1ml Vial with Opaque Microspheres | Ref Numbers 2ml Vial with Opaque Microspheres | Ref Numbers 1ml Syringe with Opaque Microspheres | Ref Numbers 2ml Syringe with Opaque Microspheres |
|---|---|---|---|---|---|---|---|
| **40 µm** | Black | 40 µm ± 10 µm | 0.002 inches | 10401-V0 | 10402-V0 | 10410-S0 | 10420-S0 |
| **75 µm** | Burgundy | 75 µm ± 15 µm | 0.003 inches | 10701-V0 | 10702-V0 | 10710-S0 | 10720-S0 |
| **100 µm** | Orange | 100 µm ± 25 µm | 0.004 inches | 11001-V0 | 11002-V0 | 11010-S0 | 11020-S0 |
| **250 µm** | Yellow | 250 µm ± 50 µm | 0.009 inches | 12001-V0 | 12002-V0 | 12010-S0 | 12020-S0 |
| **400 µm** | Blue | 400 µm ± 50 µm | 0.013 inches | 14001-V0 | 14002-V0 | 14010-S0 | 14020-S0 |
| **500 µm** | Red | 530 µm ± 50 µm | 0.016 inches | 15001-V0 | 15002-V0 | 15010-S0 | 15020-S0 |
| **700 µm** | Green | 700 µm ± 50 µm | 0.021 inches | 17001-V0 | 17002-V0 | 17010-S0 | 17020-S0 |
| **900 µm** | Purple | 900 µm ± 75 µm | 0.027 inches | 19001-V0 | 19002-V0 | 19010-S0 | 19020-S0 |
| **1100 µm** | Gray | 1100 µm ± 75 µm | 0.033 inches | 111001-V0 | 111002-V0 | 111010-S0 | 111020-S0 |
| **1300 µm** | Pink | 1300 µm ± 75 µm | 0.038 inches | 113001-V0 | 113002-V0 | 113010-S0 | 113020-S0 |

## 2. Presentation

### 2.1 Syringe

Embozene® Microspheres are offered in a 20 ml syringe prefilled with either 1 ml or 2 ml of product suspended in a non-pyrogenic, sterile transport solution of physiological saline. The total volume of Embozene® Microspheres including transport solution is approximately 7 ml. Prefilled syringes of Embozene® Microspheres are packaged in a sterile, sealed tray with a peel-away lid. A color-coded label indicates the specific size of the microspheres contained in the syringe (see Tables A and B).

### 2.2 Vial

Embozene® Microspheres are offered in vials filled with either 1 ml or 2 ml of product suspended in a non-pyrogenic, sterile transport solution of physiological saline. The total volume of Embozene® Microspheres including transport solution is approximately 7 ml. Prefilled vials of Embozene® Microspheres are packaged in a sterile, sealed, tray with a peel-away lid. A

color-coded label indicates the specific size of the microspheres contained in the vial (see Tables A and B).

## 3. Indications and Contraindications

### 3.1 Indications

Embozene® Microspheres are indicated for embolization of the following conditions:

- Hypervascular tumors.
- Arteriovenous malformations.
- Uterine fibroids.
- Hepatocellular carcinoma.
- Tumors of head, neck, torso, and skeletal system.
- Bleeding and trauma.
- Pre-operative reduction of bleeding other than in the central nervous system.

### 3.2 Contraindications

Embolization procedures shall not be performed if:

- Patient is unable to tolerate vascular occlusion procedures.
- Vascular anatomy precludes correct catheter placement or embolic injection.
- Presence or likely onset of vasospasm.
- Presence of a blood coagulation disorder that would prohibit arterial punctures.
- Presence of severe atheromatous disease that would preclude correct catheter placement.
- Presence of patent extra-to-intra-cranial anastomoses or shunts from the arterial to the venous circulation.
- Presence of collateral vessel pathways which could potentially endanger non-targeted tissue during an embolization procedure.
- Presence of any vasculature where Embozene® Microspheres could pass directly into the central nervous system, central circulatory system or other non-target territories.
- Patient has high-flow arteriovenous shunt with diameter greater than the selected Embozene® Microspheres.
- Patient is pregnant.
- Patient has known allergies to barium sulfate, 3-aminopropyltrialkoxysilane, polyphosphazene or IV radiopaque contrast agent.

## 4. Warnings / Precautions

### 4.1 Warnings

Vascular embolization is a high risk procedure. The procedure should be performed by specialized 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 Embozene® Microspheres into normal arteries adjacent to the targeted lesion or through the lesion into other arteries or arterial beds.
- Embolization of the wrong artery or migration of the microspheres to 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(s).
- Thrombosis of the artery at the incision site for arterial access.
- Pulmonary embolization.
- Ischemia at an undesirable location.
- Capillary bed saturation and tissue damage.

- Ischemic stroke or ischemic infarction.
- Vessel or lesion rupture and hemorrhage.
- Neurological deficits including cranial nerve palsies.
- 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 the blood vessels during embolization, which may include a radiation burn and risks to future fertility.
- Death.
- For gynecological embolizations, including fibroid embolization, risks include expulsion of a fibroid tumor or embolization materials from the uterus through the vagina after the procedure, amenorrhea following the procedure, worsening of fibroid related symptoms or the onset of new symptoms, premature menopause, infection of the endometrium or other structures in the pelvis, which, if severe, could require a hysterectomy, and rupture of the uterus.

Do not use Embozene® Microspheres in conjunction with embolization devices based on organic solvents such as ethyl alcohol or dimethyl sulfoxide (DMSO) at the same embolization site.

Do not use ionic contrast agent with this product. Ionic contrast agents could alter the microsphere characteristics resulting in microsphere deformation and procedure failure.

**4.2 Precautions**

To maintain safety, the following precautions shall be considered:

- Each package of Embozene® Microspheres is intended for single patient use only. Discard any unused material. Do not resterilize.
- Physicians using Embozene® Microspheres should have appropriate training and experience in a related interventional procedure.
- The physician should carefully select the size and quantity of Embozene® Microspheres according to the lesion to be treated based on the physician's education and training and currently available scientific evidence.
- Physicians must decide the most appropriate time to stop the infusion of Embozene® Microspheres. Typically the artery will accept fewer Embozene® Microspheres as the treatment progresses. Proximal slowing or termination of flow may indicate that the vessel or the target area is occluded by Embozene® Microspheres. Careful fluoroscopic monitoring is required.
- Microparticle embolization must be performed slowly. The injection speed and manner must be controlled. Excessive injection rate may result in retrograde flow in the vessel leading to embolization of other non-target healthy tissue or organs.
- Do not use Embozene® Microspheres if the sterile barrier, the vial, the cap, the syringe or the package appears to be opened or damaged prior to use.
- Do not use Embozene® Microspheres that have been improperly stored or mishandled.
- The color of the Embozene® Microspheres may be visible through the skin if injected into superficial arteries.
- 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 non-targeted embolization and cause severe complications for the patient.
- Particles smaller than 100 µm can migrate to distal anastomotic feeders and embolize circulation to distal tissue. For this reason, smaller particles 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.

- Consider upsizing Embozene® Microspheres if angiographic appearance of embolization does not quickly appear during injection of the microspheres.
- If there are any symptoms of unwanted embolization during injection, consider stopping the procedure to evaluate the possibility of shunting. Such symptoms may include changes in patient vital signs, such as hypoxia or central nervous system changes.

**5. Interaction with Pharmaceuticals**

There are no known chemical interactions between Embozene® Microspheres and pharmaceuticals.

**6. Instructions for Use**

**6.1 Catheter Selection**

Embozene® Microspheres are designed to be used with a variety of catheters and microcatheters. Select a delivery catheter of appropriate size, suitable for the dimensions of the target vessels. Embozene® Microspheres can tolerate temporary compression to facilitate passage through the delivery catheter. Utilize the catheter's minimum inner diameter measurement to determine catheter-to-microsphere compatibility. You may use Table A and B as a reference.

**6.2 Procedure Preparation**

1. Position the catheter at the desired site and perform baseline angiography to evaluate the blood supply to the lesion.
2. Carefully select the size of Embozene® Microspheres according to the size of the vessel identified and catheter used.
3. Verify that the sterile packaging was not previously compromised.

**6.3 Instructions for Use of Prefilled Syringe**

1. Gently swirl the contents before opening the syringe.
2. Use only non-ionic contrast agent in accordance with the contrast agent labeling with respect to dosage. Add an appropriate amount of contrast agent to the product to obtain homogeneous suspension and fluoroscopic visibility. For recommendations on specific contrast agents, refer to the *Contrast Agent Mixing Chart*. Recommended contrast agent volume is expressed in ml per syringe and is intended as guidance only.
3. Add the appropriate amount of contrast medium into the syringe.
4. Rotate or gently shake the syringe every 30 seconds to agitate the microspheres and contrast agent until a homogeneous suspension is achieved. For the smaller sizes, a homogenous suspension may be achieved in less than a minute. For the larger sizes, this may take several minutes. Once suspension is achieved, visually observe microspheres for suspension prior to deployment. If microspheres have settled, re-shake before deploying.
5. Purge all air from the syringe.
6. Attach the 20 ml syringe to one port of the luer-lock 3-way stopcock and a 1 ml injection syringe to another port of the stopcock. Attach a delivery catheter to the remaining port on the stopcock.
7. Draw the Embozene® Microsphere mixture slowly and gently into the injection syringe to minimize the potential of introducing air into the system.
8. Under continuous fluoroscopic control, slowly infuse Embozene® Microspheres into the blood stream. Always inject under free flow conditions. To optimize injection through the catheter, it is recommended that the syringe remains in a horizontal position during injection.

   Avoid reflux of Embozene® Microspheres as this can lead to embolization of other non-target, healthy tissue, or organs and induce immediate ischemia of the tissue or vessel.
9. Continue infusion until the desired devascularization is achieved.
10. Once the procedural endpoint is reached, wait for 5 minutes to observe whether the microspheres redistribute themselves and re-establish flow to the target. If flow is re-established, inject an additional volume of microspheres until the final procedural endpoint is achieved.
11. At the end of the infusion, remove the catheter while maintaining gentle aspiration to avoid dislodging any residual Embozene® Microspheres still inside the catheter.
12. Discard any opened Embozene® Microspheres prefilled syringe units.

### 6.4 Instructions for Use of Vials

1. Gently swirl the contents before opening the vial.
2. Pour the contents into a sterile basin that is labeled for this purpose.
3. Use only non-ionic contrast agent in accordance with the contrast agent labeling with respect to dosage. Add an appropriate amount of contrast agent to the product to obtain homogeneous suspension and fluoroscopic visibility. For recommendations on specific contrast agents, refer to the *Contrast Agent Mixing Chart*. Recommended contrast agent volume is expressed in ml per vial and is intended as guidance only.
4. Rotate or gently shake the sterile basin every 30 seconds to agitate the microspheres and contrast agent until a homogeneous suspension is achieved. For the smaller sizes, a homogenous suspension may be achieved in less than a minute. For the larger sizes, this may take several minutes. Once suspension is achieved, visually observe microspheres for suspension prior to deployment. If microspheres have settled, re-shake before deploying.

   Do not use any tool, such as a syringe or medical instrument, to promote the suspension, as this could damage the Embozene® Microspheres.
5. Transfer Embozene microspheres suspension from the sterile basin to an appropriately sized reservoir syringe.
6. Purge all air from the syringe.
7. Attach this reservoir syringe to one port of the luer-lock 3-way stopcock and a 1 ml injection syringe to another port of the stopcock. Attach a delivery catheter to the remaining port on the stopcock.
8. Draw the Embozene® Microsphere mixture slowly and gently into the injection syringe to minimize the potential of introducing air into the system.
9. Under continuous fluoroscopic control, slowly infuse Embozene® Microspheres into the blood stream. Always inject under free flow conditions. To optimize injection through the catheter, it is recommended that the syringe remains in a horizontal position during injection.

   Avoid reflux of Embozene® Microspheres as this can lead to embolization of other non-target, healthy tissue, or organs and induce immediate ischemia of the tissue or vessel.
10. Continue infusion until the desired devascularization is achieved.
11. Once the procedural endpoint is reached, wait for 5 minutes to observe whether the microspheres redistribute themselves and re-establish flow to the target. If flow is re-established, inject an additional volume of microspheres until the final procedural endpoint is achieved.
12. At the end of the infusion, remove the catheter while maintaining gentle aspiration to avoid dislodging any residual Embozene® Microspheres still inside the catheter.
13. Discard any opened vials or unused Embozene® Microspheres.

## 7. Storage Conditions

- Embozene® Microspheres should be stored in a dry, dark and cool place.
- Contents of inner peel-package are sterile and non-pyrogenic provided that the peel-package has not been opened or damaged.
- Product must be used prior to expiration date on label.
- Do not freeze.

## 8. Limited Warranty

Descriptions or specifications in this document are intended to provide physicians with information relating to the Embozene microspheres' product description, safe handling procedures, and potential risks inherent to embolization procedures, and do not constitute a guarantee. There is no express or implied warranty, including without limitation, any implied warranty of merchantability or fitness for a particular purpose. Under no circumstances shall CeloNova BioSciences, Inc. be liable for any direct, incidental, or consequential damages. No person has the authority to bind CeloNova BioSciences, Inc. to any representation or warranty except as specifically set forth herein.

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## 9. Definitions

| | | | |
|---|---|---|---|
| Do Not Resterilize |  | Expiration Date |  |
| Keep Dry |  | Lot Number |  |
| Keep Away from Sunlight |  | Sterilized by Steam |  |
| Authorized Representative in The European Union |  | Single Use |  |
| Do not Use if Package is Damaged |  | Temperature Lower Limit |  |
| Manufacturer |  | Catalog Number |  |
| Consult Instructions for Use |  | | |



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