MERIT MEDICAL

Q2
QUADRASPHERE™
MICROSPHERES

CAUTION: Federal (U.S.A.) law restricts this device to sale by or on the order of a physician.

INSTRUCTIONS FOR USE

INTENDED USE:

QuadraSphere Q2 Microspheres are indicated for embolization of hypervascularized tumors including hepatoma, and peripheral arteriovenous malformations.

DESCRIPTION:

QuadraSphere Q2 Microspheres are part of a family of embolic agents based on proprietary technologies. They are designed for controlled, targeted embolization. QuadraSphere Q2 Microspheres are biocompatible, hydrophilic, non-resorbable, expandable, and conformable microspheres. QuadraSphere Q2 Microspheres are supplied as dry particles, and are available in a dry size range of 20-40µm, which expand to approximately 4X their diameter (80-160µm) when reconstituted.

DEVICE PACKAGING:

QuadraSphere Q2 Microspheres are contained in a sterile, 10 mL vial, with a crimped cap, packaged in a sealed pouch.
Contents: 25 mg (nominal) of dry QuadraSphere Q2 Microspheres per vial to be reconstituted in 100% NaCl 0.9% aqueous solution or non-ionic contrast medium, or 50% non-ionic contrast medium and 50% NaCl 0.9% aqueous solution before use.

CONTRAINDICATIONS:

- Patients intolerant to vascular occlusion procedures
- Vascular anatomy or blood flow precluding correct catheter placement or embolic injection
- Presence or suspicion of vasospasm
- Presence or likely onset of hemorrhage
- Presence of severe atheromatous disease
- Feeding arteries too small to accept QuadraSphere Q2 Microspheres
- Presence of collateral vessel pathways potentially endangering normal territories during embolization
- High flow arteriovenous shunts or fistulas with luminal diameter greater than the QuadraSphere Q2 Microspheres
- Vascular resistance peripheral to the feeding arteries precluding passage of QuadraSphere Q2 Microspheres into the lesion
- Do not use in pulmonary vasculature, coronary and central nervous system vasculature
- Known sensitivity to poly vinyl alcohol-co-sodium acrylate

WARNINGS:

- QuadraSphere Q2 Microspheres should only be chosen after careful consideration of the arteriovenous angiographic appearance to prevent passage from any artery to vein.
- Some of the QuadraSphere Q2 Microspheres may be slightly outside of the size range, so the physician should be sure to carefully select QuadraSphere Q2 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.
- Because of the significant complications of misembolization, 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 embolization 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, 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.
- Onset of radiation injury to the patient may be delayed. Patients should be counselled on potential radiation effects, what to look for and whom to contact if symptoms occur.
- QuadraSphere Q2 Microspheres MUST NOT be reconstituted in sterile water for injection. Reconstitution in sterile water results in extensive swelling that renders the injection of QuadraSphere Q2 Microspheres very difficult or may prevent injection.
- Do not reconstitute QuadraSphere Q2 Microspheres with Lipiodol/Ethiodol.
- Pay careful attention for signs of mistargeted embolization. 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 microsphere if angiographic evidence of embolization does not quickly appear evident during injection of the microspheres.

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 embolization can lead to mistargeted embolization 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 ischemic injury results from use of smaller sized microspheres and consideration must be given to the consequence of this injury prior to embolization. Potential consequences include swelling, necrosis, paralysis, abscess and/or stronger post-embolization syndrome.
- Post embolization swelling may result in ischemia to tissue adjacent to target area. Care must be given to avoid ischemia of intolerant, non-targeted tissue such as nervous tissue.

PRECAUTIONS:

- QuadraSphere Q2 Microspheres must only be used by physicians trained in vascular embolization procedures.
- The size and quantity of microspheres must be carefully selected according to the lesion to be treated and the potential presence of shunts.
- Only the physician can decide the most appropriate time to stop the injection of QuadraSphere Q2 Microspheres. Do not use if the vial, cap, or pouch appear damaged.
- For single patient use only - contents supplied sterile - never reuse, reprocess, or resterilize the contents of a vial that has been opened.
- Reusing, reprocessing or resterilizing 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 resterilizing 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.
- QuadraSphere Q2 Microspheres MUST NOT be used in their original dry state. They must be reconstituted before use.
- QuadraSphere Q2 Microspheres swell in aqueous solution. The magnitude of swelling depends on the ionic concentration of the solution. The microspheres swell to approximately 4X their diameter in 0.9% NaCl aqueous solution and non-ionic contrast media, as compared to their initial dry diameter.
- QuadraSphere Q2 Microspheres are compressible and can be injected easily through microcatheters. However, injection of the QuadraSphere Q2 Microspheres before they are fully expanded could result in failure to reach the intended embolization target and possible embolization of a larger tissue area.
- Patients with known allergies to non-ionic contrast media 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

POTENTIAL COMPLICATIONS:

Vascular embolization 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:

- Paralysis resulting from untargeted embolization or ischemic injury from adjacent tissue oedema
- Undesirable reflux or passage of QuadraSphere Q2 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 circulation
- Pulmonary embolism due to arteriovenous shunting
- Ischemia at an undesired location, including ischemic stroke, ischemic infarction (including myocardial infarction), and tissue necrosis
- Capillary bed occlusion and tissue damage
- Vasospasm
- Recanalization
- Blindness, hearing loss, and loss of smell
- Foreign body reactions necessitating medical intervention
- Infection necessitating medical intervention
- Complications related to catheterization (e.g. hematoma at the incision site, clot formation at the tip of the catheter and subsequent dislodgement, and nerve and/or circulatory injuries which may result in injury)
- Allergic reaction to medications (e.g. analgesics)
- Allergic reaction to non-ionic contrast media or embolic material
- Vessel or lesion rupture and hemorrhage
- Death
- Additional information is found in the Warnings section

SWELLING BEHAVIOR:

QuadraSphere Q2 Microspheres swell during reconstitution with NaCl 0.9% aqueous solution and non-ionic contrast media. When hydrated in 100% NaCl 0.9% aqueous solution or non-ionic contrast medium, or 50% non-ionic contrast and 50% NaCl 0.9% aqueous solution, QuadraSphere Q2 Microspheres swell approximately 4X their original dry diameter in approximately 10 minutes. For example, QuadraSphere Q2 Microspheres with a dry diameter of approximately 20-40 microns in their dry state will expand to approximately 80-160 microns during reconstitution as recommended below. Because of the inherent variability of the swelling process, some of the QuadraSphere Q2 Microspheres will be slightly outside of this size range after reconstitution, so the physician should be sure to carefully select QuadraSphere Q2 Microspheres according to the size of the target vessels at the desired level of occlusion in the vasculature and the nature of the aqueous solution.

CATHETER COMPATIBILITY:

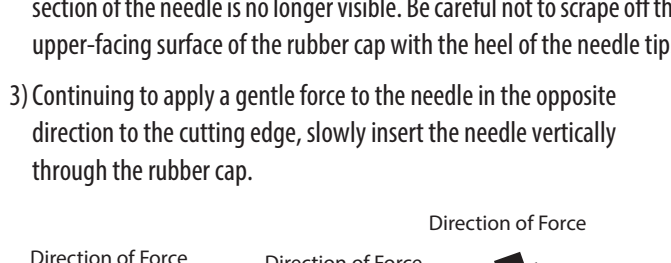
QuadraSphere Q2 Microspheres can be injected with microcatheters with the following specifications:

Dry (µm)	Approximate Reconstituted Size range (µm)	Catheter Size ID (in.)
20-40	80-160	≥ 0.020

INSTRUCTIONS:

QuadraSphere Q2 Microspheres must be reconstituted with 100% NaCl 0.9% aqueous solution or non-ionic contrast medium, or 50% non-ionic contrast medium and 50% NaCl 0.9% aqueous solution.

- Use QuadraSphere Q2 Microspheres according to the size of the target vessels at the desired level of occlusion in the vasculature and the nature of the aqueous solution. See the description of "Swelling Behavior."
- QuadraSphere Q2 Microspheres may be present outside the vial. Therefore, the vial must be aseptically handled away from the main sterile field.
- Ensure the compatibility of QuadraSphere Q2 Microspheres with the intended size of catheter to be used. See the table above.
- Inspect the packaging to confirm that it is intact. Remove the vial from the pouch. The external surface of the vial is sterile.
- To prevent coring the rubber stopper, insert the injection needle as follows:
  1) Hold the needle so that the cutting edge faces upwards and position the tip diagonally to the insertion site. Press the tip against the center of the insertion site.
  2) Apply a gentle force to the needle in the opposite direction to the cutting edge to ease the needle into the insertion site until the heel section of the needle is no longer visible. Be careful not to scrape off the upper-facing surface of the rubber cap with the heel of the needle tip.
  3) Continuing to apply a gentle force to the needle in the opposite direction to the cutting edge, slowly insert the needle vertically through the rubber cap.



  4) After preparation, carefully examine the solution to determine if there are any rubber impurities present. If the solution appears contaminated, do not use it.

PREPARATION FOR EMBOLIZATION:

The approximate reconstitution time is 10 minutes.

- Fill a 10 mL syringe with 100% NaCl 0.9% aqueous solution or non-ionic contrast medium (or 50% NaCl 0.9% aqueous solution and 50% contrast). Connect the syringe to a needle of 20 gauge diameter or larger.
- To ensure proper reconstitution of the QuadraSphere Q2 Microspheres, grasp the vial horizontally in your fingertips and roll the vial several times. This will transfer the dry contents of the vial to the sidewall.
  Note: Pull back only the flip-top cap; do not remove the crimp ring or the stopper from the vial.
- Carefully insert the needle from the syringe through the stopper of the vial. Continue rolling the vial in your fingertips and inject the full amount (10 mL) of reconstitution medium into the vial, then place the vial vertically and carefully remove the syringe with the needle attached.
  Note: The vial is hermetically closed. If aspiration from the syringe into the vial does not automatically occur, then, using caution, manually aspirate air from the vial into the syringe prior to injecting the reconstitution fluid. Proper aspiration and/or venting techniques, as approved by the healthcare facility, may be used for easier injection of reconstitution medium into vial. If aspiration of air from the vial is performed prior to reconstitution, exercise caution not to remove the spheres from the vial.
- To ensure a homogeneous reconstitution of the QuadraSphere Q2 Microspheres, gently invert the vial back and forth so that the liquid contacts the stopper 5-10 times.
  Note: Vigorous shaking may introduce micro bubbles, which can cause the microspheres to aggregate.
- Wait a minimum of 10 minutes to allow the QuadraSphere Q2 Microspheres to reconstitute and expand fully.
- Use a 30 mL syringe and 20 gauge or larger needle to aspirate the contents of the vial. Rotate the vial to a vertical position with the bottom of the vial facing upward. Pull the needle back so that it is submerged in the liquid but not occluded by the stopper. Gently aspirate the entire contents of the vial into the syringe.
  Note: If the air was previously aspirated from the vial, gentle injection of air using the syringe prior to aspirating the contents of the vial will ensure an easier aspiration of vial contents into the syringe. If all contents are not withdrawn, introduce an additional volume of air and repeat the aspiration process. It is possible to add an additional amount of non-ionic contrast or NaCl 0.9% aqueous solution into the syringe in order to get a higher dispersion of microspheres.
- If microspheres were reconstituted using 100% NaCl 0.9%, non-ionic contrast medium must be added to the syringe containing the QuadraSphere Q2 Microspheres for visualization under fluoroscopy. If non-ionic contrast medium was used to reconstitute the microspheres, additional non-ionic contrast medium may be added.

DELIVERY INSTRUCTIONS:

- Carefully evaluate the vascular network associated with the target lesion utilizing high resolution imaging.
  Note: It is important to determine if any arteriovenous shunts are present before beginning embolization.
- Using standard techniques, position the delivery catheter within the target vessel and the catheter tip as close as possible to the embolization target.
- Use an injection syringe no larger than 3 mL for the delivery of QuadraSphere Q2 Microspheres. Use of a 1 mL injection syringe is recommended.
- Aspirate the QuadraSphere Q2 Microspheres mixture into the injection syringe.
- Two methods for embolic aliquot sequestering for injection may be used:
  - **Option1:** Connect a 3-way stopcock to the 30 mL syringe containing the QuadraSphere Q2 Microspheres to the infusion microcatheter and use a 1 mL syringe for injection through the open port of the 3-way stopcock.
  - **Option 2:** Serial aliquots of QuadraSphere Q2 Microspheres can be drawn from the 30 mL syringe into a 1 mL injection syringe through a 3-way stopcock that is not attached to the infusion catheter. The 1 mL syringe containing each aliquot can be attached independently to the infusion microcatheter and injected.
- Invert the 30 mL syringe back and forth to maintain the homogenous suspension of the QuadraSphere Q2 Microspheres mixture.
- Under continuous fluoroscopic guidance, inject the aliquot of QuadraSphere Q2 Microspheres in a slow, nonforceful, pulsatile manner over a time period of approximately 1 minute per mL of microspheres solution. Always inject under free-flow conditions and monitor for reflux.
  Note: Reflux of embolic spheres can induce immediate ischemia of nontargeted tissues and vessels.
- When stasis in the feeding pedicle occurs while delivering the QuadraSphere Q2 Microspheres, wait a minimum of 5 minutes then perform a selective angiogram after the full 5 minute wait to verify the cessation of antegrade flow.
- If cessation of antegrade flow has not occurred, continue infusion under fluoroscopic guidance until the desired devascularization is obtained.
- After the QuadraSphere Q2 Microspheres infusion is completed, remove the catheter while maintaining gentle aspiration to avoid dislodging any residual QuadraSphere Q2 Microspheres that may still be in the catheter lumen. Discard the catheter after removal and do not reuse.
- Discard any open vial or unused QuadraSphere Q2 Microspheres.

CAUTION:

In the event that the catheter becomes obstructed or significant infusion resistance is encountered during injection, do not attempt to flush the catheter with excessive pressure because reflux of embolic material may occur resulting in untargeted embolization. Remove the catheter while applying gentle aspiration and discard.

CONSERVATION AND STORAGE:

QuadraSphere Q2 Microspheres must be stored in a dry, dark place in their original vials and packaging. Use by the date indicated on the labeling. When the procedure of reconstitution is completed, store the solution of QuadraSphere Q2 Microspheres in 35° F to 46° F (2° C to 8° C) conditions and use within 24 hours, IF not used immediately. Do not store QuadraSphere Q2 Microspheres after contrast medium has been added.

Symbol	
	Manufacturer: Name & Address
	Use by date: year-month-day
LOT	Batch code
REF	Catalog number
	Do not resterilize
	Do not use if package is damaged
	Keep away from sunlight
	Keep dry
	Do not re-use
	Caution – Refer to Instructions For Use
	Non-pyrogenic
STERILE R	Sterilized using irradiation
•/●	Size of dry microspheres / Size of hydrated microspheres

INFORMATION ON PACKAGING:

All serious or life-threatening adverse events or deaths associated with use of QuadraSphere Q2 Microspheres should be reported to the U.S. Food and Drug Administration under the MedWatch program and to the device manufacturer. Information about the MedWatch program and forms for reporting adverse events can be obtained at www.fda.gov/safety/medwatch/howtoreport/ucm053074.htm or by calling toll free 888-463-6332. Reports to Merit Medical, Inc. can be made by calling toll free 800-394-0295.

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