HepaSphere™

English

Microspheres

INSTRUCTIONS FOR USE

INTENDED USE

HepaSphere™ Microspheres are indicated for use in embolization of blood vessels with or without delivery of doxorubicin HCl for therapeutic or preoperative purposes in the following procedures:

- Embolization of hepatocellular carcinoma
- Embolization of metastases to the liver.

HepaSphere Microspheres loaded with irinotecan are indicated for use in:

- Embolization of metastatic colorectal cancer (mCRC) to the liver.

DESCRIPTION

HepaSphere Microspheres are part of a family of embolic agents based on proprietary technologies. They are designed for controlled, targeted embolization. The HepaSphere Microspheres can be loaded with doxorubicin HCl or irinotecan, and are able to release the drug locally at the embolization site. HepaSphere Microspheres are biocompatible, hydrophilic, non-resorbable, expandable, and conformable microspheres. HepaSphere Microspheres swell upon exposure to aqueous solutions. They are available in a range of sizes.

Dry(µm)	30-60	50-100	100-150	150-200

DEVICE PACKAGING

HepaSphere Microspheres are contained in a sterile, 10 ml vial, with a crimped cap, packaged in a sealed pouch.
Contents: 25 mg or 50 mg of dry HepaSphere Microspheres per vial to be reconstituted 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 haemorrhage
- Presence of severe atheromatous disease
- Presence of collateral vessel pathways potentially endangering normal territories during embolization
- High flow arteriovenous shunts or fistulae with luminal diameter greater than the selected size of HepaSphere Microspheres
- Vascular resistance peripheral to the feeding arteries precluding passage of HepaSphere 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

- HepaSphere Microspheres size must be chosen after consideration of the arteriovenous angiographic appearance. HepaSphere Microspheres size should be selected both to be appropriate for the size of the vessel feeding the target and to prevent passage from artery to vein.
- Some of the HepaSphere Microspheres may be slightly outside of the range, so the physician should be sure to carefully select the size of HepaSphere 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 untargeted embolization, 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.
- HepaSphere Microspheres MUST NOT be reconstituted in sterile water for injection. Reconstitution in sterile

water results in extensive swelling that renders the injection of HepaSphere Microspheres very difficult or may prevent injection.
- Do not reconstitute HepaSphere Microspheres with Lipiodol / Ethiodol.
- Pay careful attention for signs of untargeted embolization. During injection carefully monitor patient vital signs to include SaO_2 (e.g. hypoxia, CNS changes). Consider terminating the procedure, investigating for possible shunting, or increasing Microspheres size if any signs of untargeted embolization occur or patient symptoms develop.
- Consider upsizing the Microspheres 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 untargeted embolization and severe complications.
- Microspheres smaller than 100 microns 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. The 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
HepaSphere 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 HepaSphere 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.

HepaSphere Microspheres MUST NOT be used in their original dry state. They must be reconstituted before use. HepaSphere Microspheres swell in aqueous solution. The magnitude of swelling depends on the ionic concentration of the solution. The microspheres swell to approximately four times their diameter in 0.9% NaCl aqueous solution and nonionic contrast media, as compared to their initial dry diameter. The magnitude of swelling when loaded with doxorubicin HCl is dependent upon the amount of drug with which the product is loaded. Lyophilized doxorubicin HCl must be reconstituted in NaCl 0.9 % solution. HepaSphere Microspheres undergo a size decrease of about 20% when loaded with doxorubicin HCl, and 30% when loaded with irinotecan compared to the size in pure NaCl 0.9 % aqueous solution. HepaSphere Microspheres are compressible and can be injected easily through microcatheters. However, injection of the HepaSphere Microspheres before they are fully expanded could result in failure to reach the intended embolization target and possible embolization of a larger tissue area.
Note: Maximum recommended concentration of doxorubicin HCl is 5mg/ml. Concentrations of doxorubicin HCl above 5mg/ml substantially increase the solution viscosity and make it difficult to handle with HepaSphere Microspheres.
Maximum recommended concentration of irinotecan is 20 mg/ml.

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

Note: If loading HepaSphere Microspheres with doxorubicin HCl or irinotecan, refer to the appropriate drug IFU for information concerning contraindications, warnings, precautions, potential complications, dosage, and patient management before use.

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 HepaSphere 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
- Recanalisation
- Blindness, hearing loss, and loss of smell
- Foreign body reactions necessitating medical intervention
- Infection necessitating medical intervention
- Complications related to catheterization (e.g. haematoma at the site of entry, clot formation at the tip of the catheter and subsequent dislodgement, and nerve and/or circulatory injuries which may result in leg 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

HepaSphere 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, HepaSphere Microspheres swell approximately 4 times their original dry diameter in approximately 10 minutes. For example, HepaSphere Microspheres with a diameter of approximately 50-100 microns in their dry state will expand to approximately 200-400 microns during reconstitution as recommended below. Because of the inherent variability of the swelling process, some of the HepaSphere Microspheres will be slightly outside of this range after reconstitution, so the physician should be sure to carefully select the size of HepaSphere 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.

Note: To expand properly HepaSphere Microspheres need to be exposed to a minimum of 10 ml of solution for doxorubicin HCl or saline and a minimum of 5 ml for irinotecan. The magnitude of swelling when loaded with doxorubicin HCl is dependent upon the amount of drug with which the product is loaded. HepaSphere Microspheres undergo a size decrease of about 20% when loaded with doxorubicin HCl compared to the size in pure NaCl 0.9% aqueous solution and about 30 % when loaded with irinotecan.

CATHETER COMPATIBILITY

HepaSphere Microspheres can be injected with microcatheters with the following specifications:

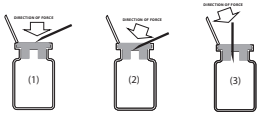
Dry (µm)	Approximate Reconstituted Size range (µm)	Catheter Size ID(in.)
30-60	120-240	≥0.021
50-100	200-400	≥0.021
100-150	400-600	≥0.024
150-200	600-800	≥0.027

INSTRUCTIONS

HepaSphere 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 if using without delivery of doxorubicin HCl or irinotecan, or loaded with doxorubicin HCl solution or irinotecan solution before positioning the catheter.

- Carefully select the size of HepaSphere 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".
- HepaSphere Microspheres may be present outside the vial. Therefore, the vial must be aseptically handled away from the main sterile field.
- Ensure the compatibility of the HepaSphere 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 bevel faces upwards and position the tip diagonally to the insertion site. Press the tip against the centre of the insertion site.
2. Apply a gentle force to the needle in the opposite direction to the bevel 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 bevel, 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.

HEPASPHERE MICROSPHERES CAN BE USED WITH OR WITHOUT LOADING OF DOXORUBICIN HCl OR IRINOTECAN.

OPTION 1: PREPARATION FOR EMBOLIZATION WITHOUT DRUG (BLAND)

The approximate reconstitution time when used without loading of a drug is 10 min.

- Fill a 10ml 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 HepaSphere 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 (10ml) 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 HepaSphere 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 HepaSphere Microspheres to reconstitute and expand fully.
- Use a 30ml 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.

Note: HepaSphere Microspheres reconstituted as described above can be used in the presence of chemotherapeutic agents such as cisplatin, epirubicin, doxorubicin HCl, fluorouracil, irinotecan and mitomycin after hydration. However for drug delivery, HepaSphere Microspheres are only indicated for use with doxorubicin HCl (see below Option 2) or irinotecan (see below Option 3).

- If microspheres were reconstituted using 100% NaCl 0.9%, non-ionic contrast medium must be added to the syringe containing the HepaSphere Microspheres for visualization under fluoroscopy. If non-ionic contrast medium was used to reconstitute the microspheres, additional non-ionic contrast medium may be added.

OPTION 2: PREPARATION FOR EMBOLIZATION LOADED WITH DOXORUBICIN HCl

WARNING: Liposomal formulations of doxorubicin HCl are not suitable for loading into HepaSphere Microspheres.

As a general guideline the loading of lyophilized doxorubicin HCl solubilized in NaCl 0.9% solution into HepaSphere Microspheres will take one hour. The HepaSphere Microspheres should not be used before they are fully hydrated and expanded. Loading kinetics of pre-solubilized doxorubicin HCl may vary, depending on the concentration and pH of the solution.

- Choose the appropriate dose of doxorubicin HCl to load into the HepaSphere Microspheres.

Note: A maximum dose of doxorubicin HCl 75mg can be loaded into each vial of 25 mg HepaSphere Microspheres. Solubilize the desired dose of lyophilized doxorubicin HCl in 20ml of NaCl 0.9% solution for injection.

NEVER USE PURE WATER

Note: Maximum recommended concentration of doxorubicin HCl is 5mg/ml. Concentrations of doxorubicin HCl above 5mg/ml substantially increase the solution viscosity and make it difficult to handle with HepaSphere Microspheres.

- Aspirate the 20ml of doxorubicin HCl solution into two separate 30ml syringes. Each 30ml syringe should contain 10ml of doxorubicin HCl solution.
- Connect one of the 30ml syringes containing 10ml of the doxorubicin HCl solution to a needle of 20 gauge diameter or larger.
- To ensure proper reconstitution of the HepaSphere Microspheres, grasp the HepaSphere Microspheres 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 of one of the 30ml syringes containing 10ml of doxorubicin HCl solution through the stopper of the vial. Continue rolling the vial in your fingertips and inject the full 10ml of doxorubicin HCl solution into the vial.
- Place the HepaSphere Microspheres vial vertically. Carefully remove the syringe with the needle attached, and allow the vial to stand for 10 minutes in order to completely hydrate the spheres.
- During the 10 minutes hydration period, shake the HepaSphere Microspheres vial several times back and forth so that the liquid contacts the grey stopper. Repeat this process every 2-3 minutes to ensure a homogenous reconstitution of the HepaSphere Microspheres.

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 media into the vial. If aspiration of air from the vial is performed prior to reconstitution, exercise caution not to remove the spheres from the vial.

- After the 10 minutes hydration period, attach a 20 gauge or larger needle to the second 30ml syringe containing

the remaining 10ml of doxorubicin HCl solution and insert into the HepaSphere Microspheres vial. Aspirate the contents of the HepaSphere Microspheres vial into the 30ml syringe containing the remaining 10 ml of doxorubicin HCl solution. 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.

- Prior to removing the needle from the HepaSphere Microspheres vial, while holding the syringe vertically, gently pull the plunger of the syringe down, removing any solution that may be in the hub of the needle.
- Replace the needle with a syringe cap and invert the syringe back and forth to disperse the contents within the syringe.
- Wait a minimum of 60 minutes to allow the HepaSphere Microspheres to expand fully and load the doxorubicin HCl. During the 60 minutes, the syringe should be inverted every 10 – 15 minutes in order to optimize the drug distribution into the spheres.
- After 60 minutes, let the syringe stand for the spheres to settle down and purge all supernatant and discard it following facility approved standards.
- Add a minimum of 20ml of non-ionic contrast medium to the 30ml syringe containing the doxorubicin HCl loaded HepaSphere Microspheres, however larger volume of solution can provide better control during embolization. Gently invert the syringe 2 or 3 times and wait 5 min until solution homogeneity is reached.
- Before any injection, check the spheres are in suspension, if not, invert the syringe back and forth to disperse contents within the syringe.

OPTION 3: PREPARATION FOR EMBOLIZATION LOADED WITH IRINOTECAN

HepaSphere Microspheres loaded with irinotecan are only applicable to the 30-60µ and 50-100µ sizes.

As a general guideline the loading of irinotecan into HepaSphere Microspheres will take 30 minutes. The HepaSphere Microspheres should not be used before they are fully hydrated and expanded.

- Choose the appropriate dose of irinotecan solution to load into the HepaSphere Microspheres. A maximum dose of 100 mg irinotecan can be loaded in each vial of 25 mg HepaSphere MicroSpheres. Irinotecan solution is typically available in a concentration of 20 mg/ml.
- Aspirate the irinotecan into a syringe connected to a needle of 20 gauge diameter or larger.
- To ensure proper reconstitution of the HepaSphere Microspheres, grasp the HepaSphere Microspheres 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 of the syringe containing the irinotecan solution through the stopper of the vial. Continue rolling the vial in your fingertips and inject the irinotecan solution into the vial.
- Place the HepaSphere Microspheres vial vertically. Carefully remove the syringe with the needle attached, and allow the vial to stand for 30 minutes in order to completely hydrate the spheres.
- During those 30 minutes, shake the HepaSphere Microspheres vial several times back and forth so that the liquid contacts the grey stopper. Repeat this process every 2-3 minutes to ensure a homogenous reconstitution of the HepaSphere Microspheres.

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 media into the vial. If aspiration of air from the vial is performed prior to reconstitution, exercise caution not to remove the spheres from the vial.

- After the 30 minutes hydration and loading period, attach a 20 gauge or larger needle to an appropriately sized syringe and insert it into the HepaSphere Microspheres vial. Aspirate the contents of the HepaSphere Microspheres vial into the syringe. 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.

- Prior to removing the needle from the HepaSphere Microspheres vial, while holding the syringe vertically, gently pull the plunger of the syringe down, removing any solution that may be in the hub of the needle.
- Replace the needle with a syringe cap and invert the syringe back and forth to disperse the contents within the syringe.
- Add an equal volume of non-ionic contrast medium to the syringe containing the irinotecan loaded HepaSphere Microspheres immediately before use.
- Larger volume of non-ionic contrast media can lead to irinotecan release into the supernatant.
- Gently invert the syringe 2 or 3 times and wait 5 min until solution homogeneity is reached.
- Before any injection, check that the microspheres are in suspension. If not, invert the syringe back and forth to disperse contents within the syringe.
- Do not remove the supernatant.

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 3ml for the delivery of doxorubicin/irinotecan/bland loaded HepaSphere Microspheres. Use of a 1ml injection syringe is recommended.
- Aspirate the HepaSphere Microspheres mixture into the injection syringe.
- Two methods for embolic aliquot sequestering for injection may be used:
  Option 1: Connect a 3way-stopcock to the syringe containing the doxorubicin/irinotecan/bland loaded HepaSphere Microspheres to the infusion micro catheter and use a 1ml syringe for injection through the open port of the 3 way-stopcock.
  Option 2: Serial aliquots of the doxorubicin/irinotecan/bland loaded HepaSphere Microspheres can be drawn from the syringe into a 1ml injection syringe through a 3 way-stop cock that is not attached to the infusion catheter. The 1ml syringe containing each aliquot can be attached independently to the infusion microcatheter and injected.
- Invert the syringe back and forth to maintain the homogenous suspension of the HepaSphere Microspheres mixture.
- Under continuous fluoroscopic guidance, inject the aliquot of HepaSphere Microspheres in a slow, non forceful, 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 untargeted tissues and vessels.

- When stasis in the feeding pedicle occurs while delivering the doxorubicin/irinotecan/bland loaded HepaSphere Microspheres, wait a minimum of 5 minutes then perform a selective angiogram after the full 5 minutes 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 HepaSphere Microsphere infusion is completed, remove the catheter while maintaining gentle aspiration to avoid dislodging any residual HepaSphere Microspheres that may still be in the catheter lumen. Discard the catheter after removal and do not reuse.
- Discard any open vial or unused HepaSphere 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

HepaSphere 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 HepaSphere Microspheres in 2 to 8°C conditions and use within 24 hours, IF not used immediately. Do not store HepaSphere Microspheres after contrast medium has been added.

Size of dry products (µm)	Colour code (label borders)	Quantity of microspheres (mg)	Reference
30-60	Orange	25 50	V 225 HS V 250 HS
50-100	Yellow	25 50	V 325 HS V 350 HS
100-150	Blue	25 50	V 525 HS V 550 HS
150-200	Red	25 50	V 725 HS V 750 HS

INFORMATION ON PACKAGING

Symbol	Designation
	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: Consult accompanying documents
	Non-pyrogenic
STERILE R	Sterilized using irradiation
CE	EC mark logo - Notified body identification: 0459
•/●	Size of dry microspheres / Size of hydrated microspheres

All serious or life threatening adverse events or deaths associated with use of HepaSphere Microspheres should be reported to the device manufacturer.

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