

15-DAY PHYSICAL AND CHEMICAL STABILITY of HepaSphere™ Microspheres Loaded with Doxorubicin HCl (Adriablastin®/Adriamycin® Pfizer)

PROTOCOL

Each 50 mg vial of lyophilized doxorubicin HCl was reconstituted with preservative-free 0.9% sodium chloride. HepaSphere Microspheres were hydrated using 10 mL of reconstituted doxorubicin HCl for a duration of 10 minutes. The contents of the HepaSphere Microspheres vial were then withdrawn into the syringe containing the remaining doxorubicin HCl solution to obtain the target dose of 50 mg or 75 mg of doxorubicin HCl per HepaSphere Microspheres vial.

RESULTS

The table shows the bench test results for physical and chemical stability of HepaSphere Microspheres that have been loaded with doxorubicin HCl, when not mixed with a contrast agent and when stored at 2-8°C. The user is responsible for aseptic preparation and any resulting microbiological contamination.

HepaSphere Microspheres	Physical and Chemical Stability
Loaded with Doxorubicin HCl (50 mg or 75 mg per vial)	15 days
30-60 µm and 50-100 µm HepaSphere Microspheres were tested. When hydrated with nonionic contrast media or normal saline (NaCl 0.9%), HepaSphere Microspheres expand to approximately 4x their dry state diameter.	When not mixed with a contrast agent and stored at 2-8°C. Physical and chemical stability testing was limited to a 15-day period and may not be indicative of instability beyond 15 days.

Data on file at Biosphere Medical, S.A.

IMPORTANT INFORMATION

Indications for 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.

The above indication may not be available in your territory.

Precautions:

- HepaSphere Microspheres must only be used by physicians trained in vascular embolisation 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.

Instruction for use:

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

Potential Complications:

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:

- Post-embolization syndrome (such as nausea, vomiting, pain, fever)
- Fatigue and loss of appetite
- Hypertension
- Liver disorders or failure (including liver enzyme anomalies and ascites)
- 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)
- Vessel or lesion rupture and hemorrhage
- Vasospasm
- Recanalisation
- Allergic reaction to medications (e.g. analgesics)
- Allergic reaction to non-ionic contrast media or embolic material
- 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
- Pleural effusion
- Ischemia at an undesired location, including ischemic stroke, ischemic infarction (including myocardial infarction), and tissue necrosis
- Capillary bed occlusion and tissue damage (cholecystitis, cholangitis, pancreatitis)



- Paralysis resulting from untargeted embolization or ischemic injury from adjacent tissue oedema
- Blindness, hearing loss, and loss of smell
- Foreign body reactions necessitating medical intervention Infection necessitating medical intervention (including liver abscess)
- Death

Please refer to the HepaSphere Microspheres Instructions For Use for indications, contraindications, precautions, warnings, potential complications, and detailed use instructions.

Follow the doxorubicin HCl Instructions For Use concerning drug stability after solubilisation, and the storage standards for your country and your facility for compounded products.

Merit Medical is a global company. Not all sizes are available in every country. HepaSphere Microspheres are not available for sale in the United States.

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Before using refer to Instructions for Use for indications, contraindications, warnings, precautions, and directions for use.



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