

15-DAY PHYSICAL AND CHEMICAL STABILITY of HepaSpheres™ 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. HepaSpheres Microspheres were hydrated using 10 mL of reconstituted doxorubicin HCl for a duration of 10 minutes. The contents of the HepaSpheres Microspheres vial were then withdrawn into the syringe containing the remaining doxorubicin HCl solution to obtain the target dose of 50 mg or 75 mg of doxorubicin HCl per HepaSpheres Microspheres vial.

RESULTS

The table shows the bench test results for physical and chemical stability of HepaSpheres 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.

HepaSpheres Microspheres	Physical and Chemical Stability
Loaded with Doxorubicin HCl (50 mg or 75 mg per vial)	15 days
<i>30-60 µm and 50-100 µm HepaSpheres Microspheres were tested. When hydrated with nonionic contrast media or normal saline (NaCl 0.9%), HepaSpheres Microspheres expand to approximately 4x their dry state diameter.</i>	<i>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.</i>

Data on file at Biosphere Medical, S.A.

IMPORTANT INFORMATION

HepaSpheres Microspheres Indications for Use:

HepaSpheres Microspheres are CE marked and indicated for use in embolisation of blood vessels with or without delivery of doxorubicin HCl for therapeutic or preoperative purposes in the following procedures:

- Embolisation of hepatocellular carcinoma
- Embolisation of metastases to the liver

The above indication may not be available in your territory.

Precautions:

- HepaSpheres 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 HepaSpheres Microspheres.
- A maximum dose of 75 mg of doxorubicin HCl can be loaded into each vial of HepaSpheres Microspheres.

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:

- Paralysis resulting from untargeted embolisation or ischemic injury from adjacent tissue oedema
- Undesirable reflux or passage of HepaSpheres 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 catheterisation (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 haemorrhage
- Death

Please refer to the HepaSpheres 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. HepaSpheres Microspheres are not available for sale in the United States.

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