

MARQIBO® (vinCRISStine sulfate LIPOSOME injection)

# Pharmacy Instructions for Preparation

## Important Information for Preparation<sup>1</sup>

The instructions for the constitution of MARQIBO are provided in each kit. There is a 26-step constitution procedure that must be followed. This takes approximately 60 to 90 minutes and includes water bath setup and warming, drug mixing and warming, and 30 minutes for drug cooldown to room temperature. The preparer should have dedicated uninterrupted time to prepare MARQIBO due to the extensive monitoring of temperature and time required for the preparation. Also note:

- Procedures for handling and disposal of anticancer drugs should be followed
- Aseptic technique must be strictly observed since no preservative or bacteriostatic agent is present in MARQIBO
- The preparation steps of MARQIBO that involve mixing the Sodium Phosphate Injection, Sphingomyelin/Cholesterol Liposome Injection, and VinCRISStine Sulfate Injection must be done in a biological safety cabinet or by established pharmacy safety procedures for the preparation of sterile injectable formulations and hazardous drugs
  - Preparation steps that involve placement of the vial in the water bath must be done outside of the sterile area
- MARQIBO Kits should be stored in a controlled refrigerator (2°C to 8°C; 36°F to 46°F)
- Do not use with in-line filters
- Do not use with bacteriostatic agents such as benzyl alcohol<sup>2</sup>
- Do not mix with other drugs

**Indication:** For the treatment of adult patients with Philadelphia chromosome–negative (Ph–) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following 2 or more anti-leukemia therapies. This indication is based on overall response rate. Clinical benefit such as improvement in overall survival has not been verified.

### IMPORTANT SAFETY INFORMATION

#### WARNING

- **For Intravenous Use Only—Fatal if Given by Other Routes**
- **Death has occurred with intrathecal administration**
- **MARQIBO has different dosage recommendations than vincristine sulfate injection. Verify drug name and dose prior to preparation and administration to avoid overdose**

Please see enclosed full Prescribing Information, including **BOXED WARNINGS** for MARQIBO. Please see full Important Safety Information on back cover.

**After reading these instructions, please call 1-888-292-9617 if you have questions about the preparation of MARQIBO.**

**Marqibo**<sup>®</sup>  
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for intravenous infusion

# Items Required by Pharmacy to Prepare MARQIBO



## MARQIBO Kit<sup>1</sup>

- 1 set of constitution instructions
- 1 vial containing VinCRiStine Sulfate Injection, USP (1 mg/mL, 5 mL)—active ingredient
- 1 vial containing Sphingomyelin/Cholesterol Liposome Injection (103 mg/mL, 1 mL)
- 1 vial of Buffer, which contains Sodium Phosphate Injection (14.2 mg/mL, 25 mL)
- 1 flotation ring
- 1 MARQIBO Overlabel for Sodium Phosphate Injection vial
- 1 infusion bag label

## Additional Required Items<sup>1</sup>

- 1 water bath for constitution\*
- 1 calibrated MARQIBO thermometer (0°C to 100°C)\*
- 1 calibrated MARQIBO timer\*
- Sterile venting needle or other suitable device equipped with a sterile 0.2-micron filter
- 1-mL or 3-mL sterile syringe with needle
- 5-mL sterile syringe with needle

MARQIBO Kits should be stored in a controlled refrigerator (2°C to 8°C; 36°F to 46°F) until the time of constitution. **Do not freeze.**<sup>1</sup>

\*The manufacturer will provide the water bath, calibrated thermometer, and calibrated timer to the medical facility at the initial order of MARQIBO and will replace these materials every 2 years.<sup>1</sup>

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## Please Follow These Steps<sup>1</sup>

### STEP 1



Fill the water bath with water to a level of at least 8 cm (3.2 inches) measured from the bottom and maintain this minimum water level throughout the procedure. The water bath must remain outside of the sterile area.

### STEP 2



Place the calibrated thermometer in the water bath to monitor water temperature and leave it in the water bath until the procedure has been completed.

### STEP 3



Preheat water bath to 63°C to 67°C. Maintain this water temperature until completion of the procedure. Use the calibrated thermometer to confirm acceptable temperature throughout the process.

### STEP 4



Visually inspect each vial in the MARQIBO Kit for particulate matter and discoloration prior to preparation, whenever solution and container permit. Do not use if a precipitate or foreign matter is present.

NOTE: SpHINGomyelin/cholesterol liposomes are a white to off-white homogenous suspension, essentially free of visible foreign matter and aggregates.

### STEP 5



Remove all the caps on the vials and swab the vials with sterile alcohol pads.

### STEP 6



Vent the Sodium Phosphate Injection vial with a sterile venting needle equipped with a sterile 0.2-micron filter or other suitable venting device in the biological safety cabinet. Always position venting needle point well above liquid level before adding SpHINGomyelin/Cholesterol Liposome Injection and VinCRISTine Sulfate Injection.

### STEP 7



Withdraw 1 mL of SpHINGomyelin/Cholesterol Liposome Injection.

### STEP 8



Inject 1 mL of SpHINGomyelin/Cholesterol Liposome Injection into the Sodium Phosphate Injection vial.

### STEP 9



Withdraw 5 mL of VinCRISTine Sulfate Injection.

### STEP 10



Inject 5 mL of VinCRISTine Sulfate Injection into the Sodium Phosphate Injection vial.

#### STEP 11



Remove the venting needle and gently invert Sodium Phosphate Injection vial 5 times to mix.

**DO NOT SHAKE.**

#### STEP 12



Fit flotation ring around neck of the Sodium Phosphate Injection constitution vial.

#### STEP 13



Confirm that the water bath temperature is at 63°C to 67°C using the calibrated thermometer. Remove the Sodium Phosphate Injection vial containing VinCRISTine Sulfate Injection, Sphingomyelin/Cholesterol Liposome Injection, and Sodium Phosphate Injection from the biological safety cabinet and place into the water bath at 63°C to 67°C for 10 minutes using the calibrated timer.

#### STEP 14



**IMMEDIATELY** after placing the Sodium Phosphate Injection vial into the water bath, record the constitution start time and water temperature on the MARQIBO Overlabel.

#### STEP 15



At the end of the 10 minutes, confirm that the water temperature is 63°C to 67°C using the calibrated thermometer. Using tongs to prevent burns, remove the vial from the water bath and remove flotation ring.

#### STEP 16



Record the final constitution time and the water temperature on the MARQIBO Overlabel.

#### STEP 17



Dry the exterior of the Sodium Phosphate Injection vial with a clean paper towel, affix MARQIBO Overlabel, and gently invert 5 times to mix.

**DO NOT SHAKE.**

#### STEP 18



Permit the constituted vial contents to equilibrate for at least 30 minutes to controlled room temperature (15°C to 30°C, 59°F to 86°F).

#### STEP 19



MARQIBO contains 5 mg/31 mL (0.16 mg/mL) vincristine sulfate.

**ONCE PREPARED, STORE AT CONTROLLED ROOM TEMPERATURE (15°C to 30°C, 59°F to 86°F) FOR NO MORE THAN 12 HOURS.**

#### STEP 20



Swab the top of the vial now containing MARQIBO with a sterile alcohol pad and return the vial back into the biological safety cabinet.

#### STEP 21



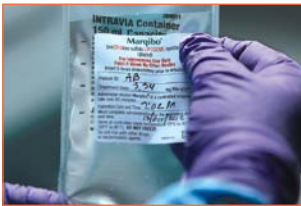
Calculate the patient's MARQIBO dose based on the patient's actual body surface area and remove the volume corresponding to the patient's MARQIBO dose from an infusion bag containing 100 mL of 5% Dextrose Injection or 0.9% Sodium Chloride Injection.

#### STEP 22



Inject the dose of MARQIBO into the infusion bag to result in a final volume of 100 mL.

#### STEP 23



Complete the information required on the infusion bag label and apply to the infusion bag.

#### STEP 24



Finish administration of the diluted product within 12 hours of the initiation of MARQIBO preparation.

#### STEP 25



Empty, clean, and dry the water bath after each use.

#### STEP 26

Deviations in temperature, time, and preparation procedures may fail to ensure proper encapsulation of vincristine sulfate into the liposomes. In the event that the preparation deviates from the instructions in the above steps, the components of the kit should be discarded and a new kit should be used to prepare the dose.

#### Important Notes:

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

- Do not use if a precipitate or foreign matter is present

Constituted MARQIBO is a white to off-white translucent suspension, essentially free of foreign matter and aggregates.

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## Indication

- MARQIBO is indicated for the treatment of adult patients with Philadelphia chromosome–negative (Ph–) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following 2 or more anti-leukemia therapies. This indication is based on overall response rate. Clinical benefit such as improvement in overall survival has not been verified

## IMPORTANT SAFETY INFORMATION

### WARNING

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## Contraindications

- MARQIBO is contraindicated in patients with demyelinating conditions, including Charcot-Marie-Tooth syndrome; in patients with hypersensitivity to vincristine sulfate or any of the other components of MARQIBO; and for intrathecal administration

## Warnings and Precautions

- MARQIBO is for intravenous use only—fatal if given by other routes. Intrathecal use is fatal. Extravasation causes tissue injury. If extravasation is suspected, discontinue infusion immediately and consider local treatment measures
- Sensory and motor neuropathy are common and cumulative. Monitor patients for peripheral motor and sensory, central and autonomic neuropathy and reduce, interrupt, or discontinue dosing. Patients with preexisting severe neuropathy should be treated with MARQIBO only after careful risk-benefit assessment
- Neutropenia, thrombocytopenia, or anemia may occur. Monitor blood counts prior to each dose. Consider dose modification or reduction as well as supportive care measures if Grade 3 or 4 myelosuppression develops
- Anticipate, monitor for, and manage tumor lysis syndrome
- A prophylactic bowel regimen should be instituted with MARQIBO to prevent constipation, bowel obstruction, and/or paralytic ileus

Please see enclosed full Prescribing Information, including **BOXED WARNINGS** for MARQIBO.

- Severe fatigue can occur requiring dose delay, reduction, or discontinuation of MARQIBO
- Fatal liver toxicity and elevated levels of aspartate aminotransferase have occurred. Monitor liver function and modify or interrupt dosing for hepatic toxicity
- MARQIBO can cause fetal harm. Advise women of potential risk to fetus

## Adverse Events

- The most commonly reported adverse reactions (incidence >30%) in clinical studies include constipation (57%), nausea (52%), pyrexia (43%), fatigue (41%), peripheral neuropathy (39%), febrile neutropenia (38%), diarrhea (37%), anemia (34%), decreased appetite (33%), and insomnia (32%)
- A total of 75.9% of patients experienced serious adverse events (SAEs) during the studies. The most commonly reported SAEs included febrile neutropenia (20.5%), pyrexia (13.3%), hypotension (7.2%), respiratory distress (6.0%), and cardiac arrest (6.0%)
- Twenty-eight percent of patients experienced adverse reactions leading to treatment discontinuation. The most common adverse reactions that caused treatment discontinuation were peripheral neuropathy (10%), leukemia-related (7%), and tumor lysis syndrome (2%)
- Deaths occurred in 23% of patients in study 1. The nonleukemia-related causes of death were brain infarct (1), intracerebral hemorrhage (2), liver failure (1), multisystem organ failure (2), pneumonia and septic shock (3), respiratory failure (4), pulmonary hemorrhage (1), and sudden cardiac death (1)

## Drug Interactions

- MARQIBO is expected to interact with drugs known to interact with non-liposomal vincristine sulfate, therefore the concomitant use of strong CYP3A inhibitors or the use of potent P-glycoprotein inhibitors or inducers should be avoided

## Use in Specific Populations

- The safety and effectiveness of MARQIBO in pediatric patients have not been established
- It is not known whether MARQIBO is excreted in human milk

**After reading these instructions, please call 1-888-292-9617 if you have questions about the preparation of MARQIBO.**

**References:** 1. MARQIBO [prescribing information]. October 2012. 2. Data on file. Talon Therapeutics, Inc.



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