MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
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technicalservices@medisca.net

Suggested Formula	Mannitol 25% Intravenous Injection (Solution, 100 mL)	FIN	F 004 962v2

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Mannitol, USP	25.000	g				
Sterile Water for Injection, USP	80.0	mL				
Sterile Water for Injection, USP	q.s. to 100.0	mL				
Sodium Hydroxide 10% Solution	As required					

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SPECIAL PREPARATORY CONSIDERATIONS

Suggested Preparatory Guidelines

☐ Non-Sterile Preparation ■ Sterile Preparation

Processing Error / Testing Considerations: To account for processing error, pH testing, sterility and endotoxin testing considerations during preparation, it is suggested to measure an additional **5 to 9%** of the required quantities of ingredients.

Special Instruction: This formula may contain one or more Active Pharmaceutical Ingredients (APIs) that may be classified as hazardous, please refer & verify the current NIOSH list of Antineoplastic and Other Hazardous Drugs in Healthcare Settings. At this time, **General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings** is informational and not compendially applicable unless otherwise specified by regulators and enforcement bodies. For information on the scope, intended applicability, and implementation context for USP General Chapter <800>, see: https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare.

This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 797* and *USP 800* when handling hazardous drugs. Only trained and qualified personnel must prepare this formula.

All heat stable, reusable materials and equipment must be sterilized and depyrogenated by dry heat sterilization at 250°C for 2 hours prior to use.

Compounder needs to verify as per USP, if every batch of final product compounded using this procedure must be sterility and endotoxin tested before being dispensed.

All required personal protective equipment (sterile and hazardous if applicable), such as but not limited to, gowns, aprons, sleeves, gloves both inner and outer if applicable, shoe covers, hairnet, head cap, beard cover, eyewear, appropriate face mask, respirator and face shield, etc., where applicable must be worn at all times. In addition, proper personnel cleansing must be done before entering the buffer or clean area.

If applicable, follow all required procedures for hazardous drug handling including but not limited to procurement, transport, storage, preparation, dispensing, administration, clean up (spills) & disposal.

Filter integrity must be validated by performing a filter stress test. If the test demonstrates that the filter might be defective, the solution must be discarded and remade.

If you are a registered 503B facility, please refer to all relevant guidance documents including but not limited to the Code of Federal Regulations (CFR), Guidance for Industry (GFIs) and Compliance Policy Guides (CPGs).

This procedure requires the use of very small quantities of ingredients. All calculations and preparation techniques must be verified before dispensing the final product.

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SUGGESTED PREPARATION (for 100 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Mannitol, USP §	25.000	g			
Sterile Water for Injection, USP §	80.0	mL			
Sterile Water for Injection, USP §	q.s. to 100.0	mL			
Sodium Hydroxide 10% Solution §	As required				

* Takes into account increased batch size conversions and density conversions, if required.
§ Weigh / measure just prior to use.

	Preparatory Instruction **IMPORTANT: All preparatory procedures must be performed using proper Aseptic Technique**
1.	**Equipment sterilization:** Following the manufacturer's specifications, sterilize and depyrogenate all heat stable, reusable materials and equipment, then return to ambient temperature.
2.	**Preparatory step:** A. Prepare a hot water bath. Specifications: Temperature: 75 to 85°C.
3.	**Powder to Medium preparation:** A. Using the hot water bath, incrementally add the Mannitol to the Sterile Water for Injection (80.0 mL *plus* processing error adjustments). Specifications: Maintain the temperature at 75 to 85°C and continuously mix until all the particles have been completely dissolved. End result: Homogeneous liquid-like solution.

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4. **pH testing:**

A. Draw an appropriate amount of the mixture (Step 3A).

B. Test the pH of the sample. It should lie between 5.7 and 6.1.

C. If the pH < 5.7, carefully add, in a dropwise fashion, the Sodium Hydroxide 10% Solution to the mixture:

1. Draw and transfer 1 or 2 drops of the Sodium Hydroxide 10% Solution to the mixture.
2. Stir for at least 5 minutes to evenly disperse the Sodium Hydroxide 10% Solution.
3. Re-test the pH.
4. Continue to add the Sodium Hydroxide 10% Solution until the pH of 5.7 and 6.1 is obtained.

IMPORTANT: Do not allow the pH to rise above 6.1 and mix until a clear solution forms.

5. **Filling to volume:**

A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (100.0 mL *plus* processing error adjustments).

Specifications: Continuously mix.

End result: Homogeneous liquid-like solution.

B. Transfer the final product (Step 5A) into the recommended dispensing containers (see Packaging requirements). Transfer the remainder into a separate dispensing container. This is to be used as the Test sample for sterility and endotoxin testing.

6. **Terminal Sterilization:**

In relation to the chemical composition of the formulation, final packaging, etc., select and validate an end-stage sterilization method and follow the manufacturer's specifications.

7. **Sterility and Endotoxin testing:**

Validate the Test samples for sterility and endotoxins, in accordance to current USP 797 regulatory guidelines.

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SUGGESTED PRESENTATION

Estimated Beyond-Use Date		24 hours controlled room temperature, 3 days refrigerated, or 45 days frozen, as per USP 797. BUD based on successful endotoxin test result.	Packaging Requirements		Sterile, tightly closed, unit-dose injection vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.		6	Discard container after use.
	2	**Do not use vials if crystals or any other particulate matter is present.**		7	Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use.
	3	Keep at controlled room temperature, (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).		8	Do not use if product changes color.
	4	**Preservative free solution, single use only. Discard any unused portion.**		9	**Hypertonic solution, inject slowly.**
	5	Keep out of reach of children.			
Pharmacist Instructions		Add any auxiliary labels specific to the active ingredients to the dispensing container as deemed necessary. **Warning: If crystals are present- Warm or autoclave for 15 minutes at 120°C, shake vigorously, and allow to cool to body temperature before administering. Discard unused portion. Use only if solution is clear.** **To be administered by intravenous infusion only under the close supervision of the prescribing physician.**			
Patient Instructions		Contact your pharmacist in the event of adverse reactions.			

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REFERENCES

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