MEDISCA® NETWORK INC.
SERVICES DE SOUTIEN TECHNIQUE
DÉPARTEMENT DE FORMULATION CHIMIQUE
SANS FRAIS: 866-333-7811
TÉLÉPHONE: 514-905-5096
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Suggested Formula	Dantrolene Sodium 20 mg/Vial for Intravenous Injection (Powder Blend For Reconstitution, 50 x 60 mL Vials)	FIN	F 001 175v3

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Dantrolene Sodium, USP	TBD					
Mannitol, USP	150.0	g				
Sterile Water for Injection, USP	3,000.00	mL				
Sodium Hydroxide 10% Solution	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):* *Dantrolene Sodium*

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SPECIAL PREPARATORY CONSIDERATIONS (CONTINUED)

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 **1 to 3%** 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 3000 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Dantrolene Sodium, USP §	TBD				
Mannitol, USP §	150.0	g			
Sterile Water For Injection, USP §	3,000.00	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.

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2. **Ingredient quantification:**

A. Determine the potency of Dantrolene Sodium based on the certificate of analysis:

	100%
MINUS	
Water Content (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of water free Dantrolene Sodium, in decimal	_____
MULTIPLIED BY	
Assay on anhydrous basis result (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
i. Potency of Dantrolene Sodium, in decimal	_____

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3. **Ingredient quantification:**

A. Determine the quantity (in g) of Dantrolene Sodium to make a Dantrolene Sodium 20mg/vial for Intravenous Injection, batch size (50 vials)

Quantity of Dantrolene Sodium required for 50 vials	1.000 g
DIVIDED BY	
Potency of Dantrolene Sodium, in decimal (Step 2Ai)	_____
EQUALS	
i. Quantity of Dantrolene Sodium needed for 50 vials	_____ **g**
MULTIPLIED BY	
Processing error adjustments (10 to 12%)	1.01 to 1.03
EQUALS	
ii. Quantity Dantrolene Sodium needed *plus* processing error adjustments	_____ **g**

4. **Powder-liquid preparation:**

A. Sequentially add the following ingredients to the Sterile Water For Injection:

-Dantrolene Sodium (amount determined in Step 3Aii)
-Mannitol

Specifications: Continuously mix until all solid particles have completely dissolved.

End result: Homogeneous liquid-like solution.

Note: Add the next ingredient, once the previous one has been completely added and dissolved.

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5. **pH testing:**

A. Draw an appropriate amount of the mixture (Step 4A).

B. Test the pH of the sample. It should lie between 9.0 and 10.0.

C. If the pH < 9.0, carefully add in a dropwise manner 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 9.0 to 10.0 is obtained.

IMPORTANT: Do not allow the pH to rise above 10.0.

6. **Filtering and transferring:**

Aseptically filter the solution through a 0.22-µm sterile filter into the recommended dispensing container (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.

7. **Filter integrity test:**

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

8. **Lyophilization:**

A. Freeze-dry the sterile liquid, and seal the vials, following the instructions indicated by the Lyophilizer manufacturer.

B. Remove the samples from the machine and store appropriately.

9. **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 specification.

10. **Sterility and Endotoxin testing:**

Validate the Test sample 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, light-resistant injection vials suitable for lyophilization.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.		5	Keep at controlled room temperature, (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).
	2	Keep out of reach of children.		6	Protect from light.
	3	May impair mental and or physical ability. Use care when operating a car or machinery.		7	Discard containers after use.
	4	Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use.		8	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
Pharmacist Instructions	Add any auxiliary labels specific to the API to the dispensing container as deemed necessary. **Reconstitution Procedure:** **Allow vial to warm to room temperature before reconstitution.** **Prior to use, reconstitute using appropriate aseptic technique, each vial with Sterile Water for Injection, USP to reconstitute the powder blend. (BUD: 24 hours, once reconstituted and kept refrigerated.)** **Note: Following reconstitution, use vial only once and discard any remaining solution.** **IMPORTANT: Using proper aseptic techniques, one must dilute the reconstituted Dantrolene Sodium to the appropriate concentrations with the appropriate sterile diluent prior to intravenous injection. Also it must be administered accordingly as determined by the prescribing physician.** NOTE: Once diluted it must be used immediately and any unused portion must be discarded.				
Patient Instructions	Contact your pharmacist in the event of adverse reactions.				

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REFERENCES

1.	USP <797> Pharmaceutical Compounding – Sterile Preparations. US Pharmacopeial Convention, Inc. *United States Pharmacopeia XXVIII / National Formulary 23.* Rockville, MD. 2004: 2461.
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3.	Isotonic Solution Misc (Monograph). In: O'Neil MJ. *The Merck Index 13th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2001: 32.
4.	Dantrolene (Monograph). In: O'Neil MJ. *The Merck Index 13th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2001: 494.
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