MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
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Suggested Formula	Edetate Calcium Disodium 250 mg/mL Intravenous Injection (Solution, 100 mL)	FIN	F 002 331v2

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Edetate Calcium Disodium, USP	TBD					
Benzyl Alcohol (Parenteral Application), NF	2.0	mL				
Sterile Water for Injection, USP	70.0	mL				
Sterile Water for Injection, USP	q.s. to 100.0	mL				
Sodium Hydroxide 10% Solution	As required					
Hydrochloric Acid 10% Solution	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):* *Benzyl Alcohol*

Hygroscopic *(protect from moisture whenever possible):* *Edetate Calcium Disodium*

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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 **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
Edetate Calcium Disodium, USP §	TBD				
Benzyl Alcohol (Parenteral Application), NF §	2.0	mL			
Sterile Water for Injection, USP §	70.0	mL			
Sterile Water for Injection, USP §	q.s. to 100.0	mL			
Sodium Hydroxide 10% Solution §	As required				
Hydrochloric Acid 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 Edetate Calcium Disodium based on the certificate of analysis:

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

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3. **Ingredient quantification:**

A. Determine the quantity (in g) of Edetate Calcium Disodium to make an Edetate Calcium Disodium 250 mg/mL Injection, batch size (100 mL):

Quantity of Edetate Calcium Disodium required for a 100 mL Injection	25.000 g
DIVIDED BY	
Potency of Edetate Calcium Disodium, in decimal (Step 2Ai)	_____
EQUALS	
i. Quantity of Edetate Calcium Disodium needed for a 100 mL Injection	_____ **g**
MULTIPLIED BY	
Processing error adjustments (5 to 9%)	1.05 to 1.09
EQUALS	
ii. Quantity of Edetate Calcium Disodium needed *plus* processing error adjustments	_____ **g**

4. **Medium preparation:**

A. Combine and mix the following ingredients together:

-Benzyl Alcohol (Parenteral Application)
-Sterile Water for Injection (70.0 mL plus processing error adjustments)

Specifications: Mix until homogeneous.

End result: Homogeneous liquid-like solution.

5. **Powder to medium integration:**

A. Incrementally add the Edetate Calcium Disodium (amount determine from Step 3Aii) to the homogeneous liquid-like solution (Step 4A).

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

End result: Homogeneous liquid-like solution.

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6. **pH testing:**

A. Draw an appropriate amount of the mixture (Step 5A).

B. Test the pH of the sample. It should lie between 6.5 and 8.0.

C. If the pH < 6.5, 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 6.5 to 8.0 is obtained.

IMPORTANT: Do not allow the pH to rise above 8.0.

D. If the pH > 8.0, carefully add in a dropwise manner the Hydrochloric Acid 10% Solution to the mixture:

1. Draw and transfer 1 or 2 drops of the Hydrochloric Acid 10% Solution to the mixture.
2. Stir for at least 5 minutes to evenly disperse the Hydrochloric Acid 10% Solution.
3. Re-test the pH.
4. Continue to add the Hydrochloric Acid 10% Solution until the pH of 6.5 to 8.0 is obtained.

IMPORTANT: Do not allow the pH to fall below 6.5.

7. **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.

8. **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.

9. **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.

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10.	**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.
11.	**Sterility and Endotoxin testing:** Validate the Test sample for sterility and endotoxins, in accordance to current USP 797 regulatory guidelines.

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, light-resistant injection vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.		6	Protect from light.
	2	Keep out of reach of children.		7	Equilibrate to room temperature before use.
	3	**Hypertonic solution, inject slowly.**		8	Discard container after use.
	4	Keep at controlled room temperature (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).		9	Discard in the presence of particulate matter.
	5	Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.		10	Do not use if discolored.
Pharmacist Instructions		Add any auxiliary labels specific to the API to the dispensing container as deemed necessary. **IMPORTANT: Using proper aseptic techniques, one must dilute the Edetate Calcium Disodium to the appropriate concentration with the appropriate sterile diluent prior to intravenous injection. Also it must be administered accordingly as determined by the prescribing physician.**			
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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8.	Chapter 18: Tonicity, Osmoticity, Osmolality and Osmolarity. In: AR Gennaro, Remington: *The science and practice of pharmacy*, 20th pp. 246~262.
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