MEDISCA® NETWORK INC.
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Suggested Formula	Betamethasone Acetate 3 mg/mL, Betamethasone 3 mg/mL Intramuscular Injection (Suspension, 1000 mL)	FIN	F 005 353v3

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Betamethasone Acetate (Micronized), USP	TBD					
Betamethasone Sodium Phosphate, USP	TBD					
Sodium Phosphate, Dibasic, Anhydrous, USP	7.10	g				
Sodium Phosphate, Monobasic, Anhydrous, USP	3.40	g				
Edetate Disodium, USP	0.10	g				
Benzalkonium Chloride, NF	0.20	g				
Sodium Chloride, USP	2.71	g				
Sterile Water for Injection, USP	900.0	mL				
Sterile Water for Injection, USP	q.s. to 1000.0	mL				
Hydrochloric Acid 10% Solution	As required					
Sodium Hydroxide 10% Solution	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):*	*Benzalkonium Chloride*
Hygroscopic *(protect from moisture whenever possible):*	*Edetate Disodium, Benzalkonium Chloride Betamethasone Sodium Phosphate, Sodium Phosphate, Dibasic, Anhydrous*
Air Sensitive *(protect from air whenever possible):*	*Benzalkonium Chloride*
Metal Reactive *(protect from metals whenever possible):*	*Benzalkonium Chloride*

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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 1000 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Betamethasone Acetate (Micronized), USP §	TBD				
Betamethasone Sodium Phosphate, USP §	TBD				
Sodium Phosphate, Dibasic, Anhydrous, USP §	7.10	g			
Sodium Phosphate, Monobasic, Anhydrous, USP §	3.40	g			
Edetate Disodium, USP §	0.10	g			
Benzalkonium Chloride, NF §	0.20	g			
Sodium Chloride, USP §	2.71	g			
Sterile Water for Injection, USP §	900.0	mL			
Sterile Water for Injection, USP §	q.s. to 1000.0	mL			
Hydrochloric Acid 10% Solution §	As required				
Sodium Hydroxide 10% Solution §	As required				

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

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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. **Ingredient quantification:**

   A. Determine the potency of Betamethasone Acetate (Micronized) based on the certificate of analysis:

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

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3. **Ingredient quantification:**

A. Determine the quantity (in g) of Betamethasone Acetate (Micronized) to make a 1000 mL batch of Betamethasone Acetate 3 mg/mL Intramuscular Injection:

Quantity of Betamethasone Acetate (Micronized) required for 1000 mL	3.000 g
DIVIDED BY	
Potency of Betamethasone Acetate (Step 2Ai)	_____
EQUALS	
i. Quantity of Betamethasone Acetate needed for 1000 mL	_____ **g**
MULTIPLIED BY	
Processing error adjustments (1 to 3%):	1.01 to 1.03
EQUALS	
ii. Quantity of Betamethasone Acetate needed *plus* processing error adjustments	_____ **g**

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4. **Ingredient quantification:**

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

	100%
MINUS	
Water Content (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of water free Betamethasone Sodium Phosphate, in decimal	_____
MULTIPLIED BY	
Assay on anhydrous basis result (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Potency of Betamethasone Sodium Phosphate on dried basis, in decimal	_____
DIVIDED BY (Salt to Base conversion)	1.316
EQUALS	
i. Potency of Betamethasone Sodium Phosphate (base equivalent), in decimal	_____

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5. **Ingredient quantification:**

A. Determine the quantity (in g) of Betamethasone Sodium Phosphate to make a 1000 mL batch of Betamethasone 3 mg/mL Intramuscular Injection:

Quantity of **Betamethasone (Base)** for 1000 mL	3.000 g
DIVIDED BY	
Potency of Betamethasone Sodium Phosphate (Base equivalent), in decimal (Step 4Ai)	_____
EQUALS	
i. Quantity of Betamethasone Sodium Phosphate needed for 1000 mL	_____ **g**
MULTIPLIED BY	
Processing error adjustments (1 to 3%):	1.01 to 1.03
EQUALS	
ii. Quantity of Betamethasone Sodium Phosphate needed *plus* processing error adjustments	_____ **g**

6. **Powder preparation:**

A. Combine and mix the following ingredients together to form a homogeneous powder blend:

-Betamethasone Acetate (Micronized) (amount determined from Step 3Aii)
-Betamethasone Sodium Phosphate (amount determined from Step 5Aii)
-Sodium Phosphate, Dibasic, Anhydrous
-Sodium Phosphate, Monobasic, Anhydrous
-Edetate Disodium
-Benzalkonium Chloride
-Sodium Chloride

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7. **Powder to liquid integration:**

A. Incrementally add the homogeneous powder blend (Step 6A) to the Sterile Water for Injection (900.0 mL plus processing error adjustments).

Specifications: Continuously mix.

End result: Homogeneous liquid-like dispersion.

8. **pH testing:**

A. Draw an appropriate amount of the mixture (Step 7A).

B. Test the pH of the sample. It should lie between 6.8 and 7.2.

C. If the pH < 6.8, 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 6.8 to 7.2 is obtained.

IMPORTANT: Do not allow the pH to rise above 7.2.

D. If the pH > 7.2, carefully add, in a dropwise fashion, 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 6.8 to 7.2 is obtained.

IMPORTANT: Do not allow the pH to fall below 6.8.

9. **Filling to volume:**

A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (1000.0 mL *plus* processing error adjustments).

Specifications: Continuously mix.

End result: Homogeneous liquid-like dispersion.

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10. **Product transfer:**

A. Transfer the final product 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.

Note: Continuously mix the final product during the transfer process in order to maintain homogeneity.

11. **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.

12. **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, tightly closed, light-resistant, heat stable multi-dose injection vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	7	**Shake well before use.**
	2	Keep out of reach of children.	8	Discard container after use.
	3	Do not use if discolored.	9	Protect from light.
	4	Keep at controlled room temperature, (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).	10	Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.
	5	Equilibrate to room temperature before use.	11	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
	6	Do not use if irreversible sedimentation or caking occurs.	12	May produce psychological and/or physical dependence.
Pharmacist Instructions	Add any auxiliary labels specific to the API to the dispensing container as deemed necessary.			
Patient Instructions	Contact your pharmacist in the event of adverse reactions.			

REFERENCES

1.	Parenteral Preparations. In: Allen, LV, Jr. *The Art, Science and Technology of Pharmaceutical Compounding Third Edition.* American Pharmaceutical Association; 2008: 313.
2.	Betaject. In: Canadian Pharmacists Association. *Compendium of Pharmacists and Specialties, 2013*: 388.
3.	Sodium Chloride. In: Rowe RC. Handbook of Pharmaceutical Excipients, 6th Edition. American Pharmaceutical Association; 2009: 637.
4.	Benzalkonium Chloride. In: Rowe RC. Handbook of Pharmaceutical Excipients, 6th Edition. American Pharmaceutical Association; 2009: 56.
5.	Disodium Edetate. In: Rowe RC. Handbook of Pharmaceutical Excipients, 6th Edition. American Pharmaceutical Association; 2009: 242.

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6.	Sodium Phosphate, Monobasic. In: Rowe RC. Handbook of Pharmaceutical Excipients, 6th Edition. American Pharmaceutical Association; 2009: 659.
7.	Sodium Phosphate Dibasic. In: Rowe RC. Handbook of Pharmaceutical Excipients, 6th Edition. American Pharmaceutical Association; 2009: 656.
8.	Betamethasone Acetate. In: Sweetman SC, ed. Martindale: The Complete Drug Reference, 36th Edition. London, England: The Pharmaceutical Press; 2009: 1518.
9.	Betamethasone Sodium Phosphate. In: Sweetman SC, ed. Martindale: The Complete Drug Reference, 36th Edition. London, England: The Pharmaceutical Press; 2009: 1518.
10.	Betamethasone (Monograph). In: O'Neil MJ. The Merck Index 14th Edition. Whitehouse Station, NJ: Merck & Co, Inc.; 2006: Monograph #1180.
11.	Betamethasone. In: Trissel LA. *Trissel's Stability of Compounded Formulations, 4th Edition.* American Pharmaceutical Association; 2009: 67.
12.	Betamethasone Acetate (Monograph). *United States Pharmacopeia XXXV / National Formulary 30.* Rockville, MD. US Pharmacopeial Convention, Inc. 2012: 2339.
13.	Betamethasone Sodium Phosphate (Monograph). *United States Pharmacopeia XXXV / National Formulary 30.* Rockville, MD. US Pharmacopeial Convention, Inc. 2012: 2343.
14.	Betamethasone. Thomson Micromedex. *USP DI – Drug Information for the Health Care Professional, 26th Edition.* Taunton, MA: US Pharmacopeial Convention, Inc; 2006: 1020.
15.	Chapter 18: Tonicity, Osmoticity, Osmolality and Osmolarity. In: D.B Troy. *Remington: The Science and Practice of Pharmacy, 21st Edition.* Baltimore, MD: Lippincott Williams & Wilkins; 2006: 250~265.
16.	Chapter 8: Buffered and Isotonic Solutions. In: Sinko, D. J. and Singh, Y. *Martin's Physical Pharmacy and Pharmaceutical Sciences, Sixth Edition.* Philadelphia, PA: Lipponcott Williams & Wilkins; 2011: 163-181.
17.	USP <797>. *United States Pharmacopeia XXXV / National Formulary 30.* Rockville, MD. US Pharmacopeial Convention, Inc. 2012: 350.