MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
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Suggested Formula	Diclofenac Sodium 0.1% Preservative Free Ophthalmic Liquid (Solution, 7.5 mL)	FIN	F 006 637v2

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Diclofenac Sodium 5% Stock Powder Blend †	0.150	g				
Boric Acid, NF	0.038	g				
Edetate Disodium, USP	0.008	g				
Sodium Chloride, USP	0.019	g				
Sterile Water for Injection, USP	7.0	mL				
Sterile Water for Injection, USP	q.s. to 7.5	mL				
Hydrochloric Acid 10% Solution	As required					
Sodium Hydroxide 10% Solution	As required					
† **Diclofenac Sodium 5% Stock Powder Blend**						
Diclofenac Sodium, USP	0.100	g				
Mannitol, USP	1.90	g				

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SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

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

Hygroscopic *(protect from moisture whenever possible):* *Diclofenac Sodium, Boric Acid, Edetate Disodium*

Suggested Preparatory Guidelines

☐ Non-Sterile Preparation ■ Sterile Preparation

Processing Error / Testing Considerations: To account for processing error, pH testing and sterility testing considerations during preparation, it is suggested to measure an additional **30 to 40%** of the required quantities of ingredients.

Special Instruction: This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 797*. 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.

Every batch of final product compounded using this procedure must be sterility and endotoxin tested before being dispensed.

Protective apparel, such as a sterile gown, sterile gloves, shoe covers, head cap, eyewear and face-masks should always be worn. In addition, proper personnel cleansing must be done before entering the buffer or clean area.

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.

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 7.5 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Diclofenac Sodium 5% Stock Powder Blend † §	0.150	g			
Boric Acid, NF §	0.038	g			
Edetate Disodium, USP §	0.008	g			
Sodium Chloride, USP §	0.019	g			
Sterile Water for Injection, USP §	7.0	mL			
Sterile Water for Injection, USP §	q.s. to 7.5	mL			
Hydrochloric Acid 10% Solution §	As required				
Sodium Hydroxide 10% Solution §	As required				
† **Diclofenac Sodium 5% Stock Powder Blend**					
Diclofenac Sodium, USP §	0.100	g	---	---	
Mannitol, USP §	1.90	g	---	---	

* 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. † **Diclofenac Sodium 5% Stock Powder Blend preparation:**

   A. By geometric addition, combine and triturate the following ingredients together to form a fine, homogenous powder blend:

   -Mannitol
   -Diclofenac Sodium

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3. **Powder-liquid preparation:**

A. In the given order, sequentially add the following ingredients to the Sterile Water for Injection (7.0 mL *plus* processing error adjustments):

-Diclofenac Sodium 5% Stock Powder Blend (0.150 g *plus* processing error adjustments)
-Sodium Chloride
-Boric Acid
-Edetate Disodium

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.

4. **pH testing:**

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

B. Test the pH of the sample. It should lie between 7.0 and 7.4.

C. If the pH < 7.0, carefully add 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 7.0 to 7.4 is obtained.

IMPORTANT: Do not allow the pH to rise above 7.4.

D. If the pH > 7.4, carefully add 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 7.0 to 7.4 is obtained.

IMPORTANT: Do not allow the pH to fall below 7.0.

5. **Filling to volume:**

A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (7.5 mL *plus* processing error adjustments).

Specifications: Continuously mix.

End result: Homogeneous liquid-like solution.

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

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SUGGESTED PRESENTATION

Estimated Beyond-Use Date		14 days, refrigerated, as per USP 797. BUD based on a successful sterility test result.	Packaging Requirements		Sterile, tightly closed, light-resistant unit dose ophthalmic dropper.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	8		Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.
	2	Keep out of reach of children.	9		For ophthalmic use only.
	3	Do not use if product changes color.	10		Preservative free solution; discard after each use.
	4	Keep refrigerated. Do not freeze.	11		Keep in a dry place.
	5	Protect from light.	12		Do not allow the dropper tip to come into contact with the body or any type of surface in order to prevent contamination.
	6	Discard in the presence of particulate matter.	13		May impair mental and/or physical ability. Use care when operating a car or machinery.
	7	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.				
Patient Instructions	Contact your pharmacist in the event of adverse reactions. **IMPORTANT:** The quantity of API administered is directly dependent on the quantity of product applied.				

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REFERENCES

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