MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
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Suggested Formula	Diltiazem Hydrochloride 180 mg Slow Release Oral Capsules (Powder Blend, 100 x Size #1 Capsules)	FIN	F 008 142

IMPORTANT: This formula is for a **slow release** capsule. Please note that the rate of drug release may not be identical to the release rates of commercial formulations labeled as sustained-release, sustained action, prolonged-action, controlled-release, extended-release, timed-release, targeted release, long-acting, modified-release, etc. As such, this preparation should be prescribed and monitored under the close supervision of the prescribing physician.

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Diltiazem Hydrochloride, USP	18.000	g				
Hypromellose (4000 CPS) Methocel E4M, USP	TBD					
Cellulose (microcrystalline), NF	TBD					
Sodium Chloride, USP	As required					

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SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):* *Diltiazem Hydrochloride*

Hygroscopic *(protect from moisture whenever possible):* *Hypromellose (4000 CPS) Methocel E4M, Cellulose (microcrystalline)*

Suggested Preparatory Guidelines

■ Non-Sterile Preparation ☐ Sterile Preparation

Processing Error / Testing Considerations: To account for processing error 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, 2016. **General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings** was formally published February 1, 2016 in the First Supplement to USP 39-NF 34 and has a delayed **official implementation date of December 31st, 2019**.

This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 795* and *USP 800*, when handling hazardous drugs. Only trained and qualified personnel must prepare this formula.

All required personal protective equipment (hazardous if applicable), such as but not limited to, lab coat, protective sleeves, gloves both inner and outer if applicable, dedicated shoe covers, hairnet, beard cover, eyewear, appropriate face mask, respirator and face shield, etc., where applicable must be worn at all times.

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.

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 Size #1 Capsules)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Diltiazem Hydrochloride, USP §	18.000	g			
Hypromellose (4000 CPS) Methocel E4M, USP §	TBD				
Cellulose (microcrystalline), NF §	TBD				
Sodium Chloride, USP	As required				

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

	Preparatory Instruction
1.	**Excipient requirements for 100 x size #1 capsules** A. Calculate the amount of Cellulose (microcrystalline) and Hypromellose (4000 CPS) Methocel E4M required for the batch. Refer to attached appendix for details.
2.	**Powder preparation:** A. Triturate the Diltiazem Hydrochloride to form a fine, homogeneous powder. B. By geometric addition, combine and mix the following ingredients together to form a homogeneous powder blend: -Fine, homogeneous powder (Step 2A) -Cellulose (microcrystalline) (Quantity determined in appendix **(J)**) -Hypromellose (4000 CPS) Methocel E4M (Quantity determined in appendix **(L)**) End result: Homogeneous powder blend.
3.	**Product transfer:** Fill each of 100 Size #1 capsules with the mixture (Step 2B). Close each capsule tightly. Clean each capsule by placing the capsules in a container filled with Sodium chloride, and then gently rolling the container. Pour the container contents into a 10-mesh sieve, and allow the Sodium chloride to pass through. Finally, roll the capsules on a cloth-covered surface.
4.	**Validation technique (average capsule weight):** The final weight of each capsule (not including capsule shell) should fall between 90 and 110% of the theoretically calculated weight, in accordance to USP 795 guidelines. The theoretically calculated weight can be determined by adding the amount in appendix **(D)** + **(H)** + 0.180 g together.

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5.	**Product transfer:** Transfer the final product into the specified dispensing container (see "Packaging Requirements").

SUGGESTED PRESENTATION

Estimated Beyond-Use Date		6 months, as per USP*.	Packaging Requirements		Tightly closed, light-resistant capsule shells and vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	6		Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use.
	2	Keep out of reach of children.	7		Cap tightly after use.
	3	Protect from light.	8		Keep at room temperature (20°C – 23°C).
	4	May impair mental and/or physical ability. Use care when operating a car or machinery.	9		Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
	5	Keep in a dry place.	10		
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.			

*** The BUD is not later than the time remaining until the earliest expiration date of any API or 6 months, whichever is earlier.**

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REFERENCES

1. Capsules. In: Allen, LV, Jr. *The Art, Science, and Technology of Pharmaceutical Compounding Fifth Edition.* American Pharmacists Association; 2016: 189.
2. Cellulose (microcrystalline). In: Rowe RC. *Handbook of Pharmaceutical Excipients, 7th Edition*. American Pharmaceutical Association; 2012: 140.
3. Hypromellose. In: Rowe RC. *Handbook of Pharmaceutical Excipients, 7th Edition*. American Pharmaceutical Association; 2012: 373.
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9. USP <795>. *United States Pharmacopeia XLI / National Formulary 36.* Rockville, MD. US Pharmacopeial Convention, Inc. 2018: 6546.

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Appendix	Calculating the quantity of excipient required for the batch		

Procedure

1. **Capsule filling:**

   a. For each ingredient powder below, determine the average capsule fill weight by filling and weighing five TARED CAPSULES. Do not forget to divide the total weight by 5 to obtain an average capsule fill weight. Also, crush and triturate the ingredient first if required in formulation.

   Plug each amount into Step 2, column B.

2. **Volume Percent Occupied:**

Ingredients	**Column A** Quantity Required per capsule	**Column B** Average capsule fill weight	**Column C** A/B x 100 equals percent filled
a. Diltiazem Hydrochloride	0.180 **g**	_____ **g**	_____ %
b. Hypromellose (4000 CPS) Methocel	_____ **g (D)** (0.40 x column B)	_____ **g**	40%
c. Cellulose (microcrystalline)		_____ **g**	
d. Total (add column C together)			_____ % **(E)**

3. **Calculate the quantity of Cellulose and Hypromellose required for the batch:**

   a. Percent of Cellulose (microcrystalline) required = 100% – E _____ % **(F)**

   b. Average capsule fill weight of Cellulose (microcrystalline) (from column B, Step 2c): _____ g **(G)**

   c. Quantity of Cellulose (microcrystalline) required per capsule = [(F) ÷ 100 × (G)] _____ g **(H)**

   d. Total Quantity of Cellulose (microcrystalline) required for the batch = 100 capsules × (H) _____ g **(I)**

   e. Total quantity of Cellulose (microcrystalline) *plus* processing error = (I) × 1.05-1.09 _____ g **(J)**

   f. Total quantity of Hypromellose (4000 CPS) Methocel required for the batch = 100 capsules × (D)_____ g **(K)**

   g. Total quantity of Hypromellose (4000 CPS) Methocel *plus* processing error = (K) × 1.05-1.09 _____ g **(L)**