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Suggested Formula	Carbidopa 25 mg, Levodopa 100 mg Slow Release Oral Capsules (Powder Blend, 100 x Size #0 Capsules)	FIN	F 004 228

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Carbidopa, USP	2.500	g				
Levodopa, USP	10.000	g				
Hypromellose (4000 CPS) Methocel E4M, USP	TBD					
Cellulose (microcrystalline), NF	TBD					
Sodium Chloride, USP	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):* *Carbidopa, Levodopa*

Oxygen Sensitive *(protect from oxygen whenever possible):* *Levodopa*

Moisture Sensitive *(protect from humidity whenever possible):* *Levodopa*

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: Protective apparel, such as a lab coat, disposable gloves, eyewear and face-masks should always be worn.
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 #0 Capsules)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Carbidopa, USP §	2.500	g			
Levodopa, USP §	10.000	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 #0 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. Combine and triturate the following ingredients together: -Carbidopa -Levodopa -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 #0 opaque capsules with the powder blend (Step 2A). 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)** + 0.125 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		Tight, light-resistant capsule shells and vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	6		Keep in a dry place.
	2	Keep out of reach of children.	7		Keep at room temperature (20°C – 23°C).
	3	May impair mental and/or physical ability. Use care when operating a car or machinery.	8		Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
	4	Protect from light.	9		Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use.
	5	Cap tightly after use.			
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.			

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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, triturate the ingredient powder 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. Levodopa	0.100 **g**	_____ **g**	_____ %
b. Hypromellose (4000 CPS) Methocel	_____ **g (D)** (0.4 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)] – 0.025* _____ g **(H)**
   *quantity of Carbidopa per capsule

   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) x 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) x 1.05-1.09 _____ g **(L)**