



Suggested Formula	Tramadol Hydrochloride 50 mg Slow Release Oral Capsules (Powder Blend, 100 x Size #1 Capsules)	FIN	F 003 787v2
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SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Tramadol Hydrochloride, EP	5.000	g				
Hypromellose (4000 CPS) Methocel E4M, USP	TBD					
Cellulose (microcrystalline), NF	TBD					
Sodium Chloride, USP	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Hygroscopic (protect from moisture whenever possible):

*Hypromellose (4000 CPS) Methocel E4M
Cellulose (microcrystalline)*

Light sensitive (protect from light whenever possible):

Tramadol Hydrochloride

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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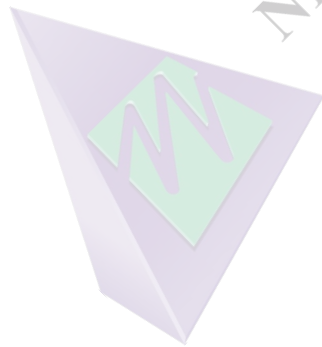
SUGGESTED PREPARATION (for 100 Size #1 Capsules)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Tramadol Hydrochloride, EP §	5.000	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.



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Preparatory Instruction

1.	<p><u>Excipient requirements for 100 x size #1 capsules</u></p> <p>A. Calculate the amount of Cellulose (microcrystalline) and Hypromellose (4000 CPS) Methocel E4M required for the batch. Refer to attached appendix for details.</p>
2.	<p><u>Powder preparation:</u></p> <p>A. Combine and triturate the following ingredients together to form a fine, homogeneous powder blend:</p> <ul style="list-style-type: none">-Tramadol Hydrochloride-Cellulose (microcrystalline) (Quantity determined in appendix (J))-Hypromellose (4000 CPS) Methocel E4M (Quantity determined in appendix (L)) <p><u>End result:</u> Homogeneous powder blend.</p>
3.	<p><u>Product transfer:</u></p> <p>Fill each of 100 Size #1 capsules with the mixture (Step 2A). Close each capsule tightly.</p> <p>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.</p>
4.	<p><u>Validation technique (average capsule weight):</u></p> <p>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) + 0.050 g together.</p>
5.	<p><u>Product transfer:</u></p> <p>Transfer the final product into the specified dispensing container (see “Packaging Requirements”).</p>



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SUGGESTED PRESENTATION

Estimated Beyond-Use Date	6 months	Packaging Requirements	Tight, light-resistant vial.	
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	Cap tightly after use.
	3	Keep at room temperature (20°C – 23°C).	8	Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.
	4	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.	9	May impair mental and/or physical ability. Use care when operating a car or machinery.
	5	Protect from light.		
Pharmacist Instructions	Add any auxiliary labels specific to the active ingredient to the dispensing container as deemed necessary.			
Patient Instructions	Contact your pharmacist in the event of adverse reactions.			

REFERENCES

1.	Capsules. In: Allen, LV, Jr. <i>The Art, Science and Technology of Pharmaceutical Compounding Third Edition</i> . American Pharmaceutical Association; 2008: 127.
2.	Cellulose, microcrystalline. In: Rowe RC. <i>Handbook of Pharmaceutical Excipients, 5th Edition</i> . American Pharmaceutical Association; 2006: 132.
3.	Hypromellose. In: Rowe RC. <i>Handbook of Pharmaceutical Excipients, 5th Edition</i> . American Pharmaceutical Association; 2006: 346.
4.	Tramadol Hydrochloride. In: Sweetman SC, ed. <i>Martindale: The Complete Drug Reference, 34th Edition</i> . London, England: The Pharmaceutical Press; 2005: 94.
5.	Tramadol (Monograph). In: O'Neil MJ. <i>The Merck Index 14th Edition</i> . Whitehouse Station, NJ: Merck & Co, Inc.; 2006: Monograph #9566.
6.	Tramadol. Thomson Micromedex. <i>USP DI – Drug Information for the Health Care Professional, 26th Edition</i> . Taunton, MA: US Pharmacopeial Convention, Inc; 2006: 2871.
7.	USP <795>. <i>United States Pharmacopeia XXXI / National Formulary 26</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2009: 314.

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Appendix	Calculating the quantity of excipient required for the batch		
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Procedure			
1.	<u>Capsule filling:</u>		
	a.	For <u>each</u> 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 <u>average</u> capsule fill weight. Also, triturate the ingredient powder first if required in formulation.	
		Plug each amount into Step 2, column B.	
2.	<u>Volume Percent Occupied:</u>		
	<u>Ingredients</u>	Column A Quantity Required per capsule	Column B Average capsule fill weight
		Column C A/B x 100 equals percent filled	
	a. Tramadol Hydrochloride	0.050 g	_____ g
	b. Hypromellose (4000 CPS) Methocel	_____ g (D) (0.4 x column B)	_____ g
	c. Cellulose (microcrystalline)		_____ g
	d. Total (add column C together)		_____ % (E)
3.	<u>Calculate the quantity of Cellulose and Hypromellose required for the batch:</u>		
	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) <i>plus</i> 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 <i>plus</i> processing error = (K) x 1.05-1.09 _____ g (L)	

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