



Suggested Formula	Estradiol 0.2 mg, Estriol 0.8 mg Oral Capsules (Powder Blend, 100 x Size #1 Capsules)	FIN	F 005 501
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SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Estradiol 1% Stock Powder Blend †	2.000	g				
Estriol (Micronized), USP	0.080	g				
Medisca CapsuBlend™-H	TBD					
Sodium Chloride, USP	As needed					
† Estradiol 1% Stock Powder Blend						
Estradiol (Micronized), USP	TBD					
Medisca CapsuBlend™-H	q.s. to 10.00	g				

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light sensitive (protect from light whenever possible): *Estradiol*

Hygroscopic (protect from moisture whenever possible): *Estradiol, CapsuBlend™-H*

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
Estradiol 1% Stock Powder Blend † §	2.000	g			
Estriol (Micronized), USP	0.080	g			
Medisca CapsuBlend [™] -H §	TBD				
Sodium Chloride, USP	As needed				
† Estradiol 1% Stock Powder Blend					
Estradiol (Micronized), USP §	TBD		---	---	
Medisca CapsuBlend [™] -H §	q.s. to 10.00	g	---	---	

* 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. Ingredient quantification:

A. Determine the potency of Estradiol based on the certificate of analysis:

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

2. Ingredient quantification:

A. Determine the quantity of Estradiol required to make an Estradiol 1% Stock Powder Blend, batch size (10 g).

Quantity of Estradiol required for the Stock Powder Blend	0.100 g
DIVIDED BY	
Potency of Estradiol in decimal (Step 1Ai)	_____
EQUALS	
i. Quantity of Estradiol needed for the stock powder blend	_____ g



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3.	<p>† <u>Estradiol 1% Stock Powder Blend preparation:</u></p> <p>A. By geometric addition, combine and mix the following ingredients together to form a homogeneous powder blend:</p> <ul style="list-style-type: none"> -Estradiol (Micronized) (amount determined in Step 2Ai) -Medisca CapsuBlend™-H (q.s. to 10.00 g)
4.	<p><u>Calculate the quantity of CapsuBlend™-H required for 100 x Size #1 Capsules:</u></p> <p>A. Determine the average capsule fill weight by filling and weighing five TARED capsules with the CapsuBlend™-H. Divide the total weight by 5 to obtain <u>average</u> weight. _____ g (A)</p> <p>B. Quantity of CapsuBlend™-H required per capsule = (A) – 0.0208 g* _____ g (B) *quantity of Estradiol 1% Stock Powder Blend + Estriol per capsule</p> <p>C. Total quantity of CapsuBlend™-H required for the batch = (B) x 100 capsules _____ g (C)</p> <p>D. Quantity of CapsuBlend™-H to weigh with processing error = (C) x 1.05 ~ 1.09 _____ g (D)</p>
5.	<p><u>Powder preparation:</u></p> <p>A. By geometric addition, combine and triturate the following ingredients together to form a homogeneous powder blend:</p> <ul style="list-style-type: none"> -Estradiol 1% Stock Powder Blend (2.000 g <i>plus</i> processing error adjustments) -Estriol (Micronized) -CapsuBlend™-H (D) <p>B. Pass the above powder mixture through a 40 or 50 mesh sieve.</p> <p>C. Place the sieved powder mixture in a plastic bag and shake for approximately 3 minutes to ensure homogeneity.</p>
6.	<p><u>Product transfer:</u></p> <p>Fill each of 100 Size #1 Capsules with the powder blend (Step 5C). 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>
7.	<p><u>Validation technique:</u></p> <p>The final weight of each capsule (not including capsule shell) should fall between 90 and 110% of the theoretically calculated weight (A), in accordance to USP 795 guidelines.</p>



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8.	<u>Product transfer:</u> Transfer the final product into the specified dispensing container (see “Packaging Requirements”).
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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	Keep at room temperature (20°C – 23°C).
	2	Keep out of reach of children.	7	Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.
	3	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.	8	Keep in a dry place.
	4	Cap tightly after use.	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 API to the dispensing container as deemed necessary.			
Patient Instructions	Contact your pharmacist in the event of adverse reactions.			

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

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.	Divigel. In: Canadian Pharmacists Association. <i>Compendium of Pharmacists and Specialties, 2013</i> : 899.
3.	Sodium Chloride. In: Rowe RC. <i>Handbook of Pharmaceutical Excipients, 6th Edition</i> . American Pharmaceutical Association; 2009: 637.
4.	Estradiol. In: Sweetman SC, ed. <i>Martindale: The Complete Drug Reference, 36th Edition</i> . London, England: The Pharmaceutical Press; 2009: 2097.



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5.	Estriol. In: Sweetman SC, ed. <i>Martindale: The Complete Drug Reference, 36th Edition</i> . London, England: The Pharmaceutical Press; 2009: 2101.
6.	Estradiol (Monograph). In: O'Neil MJ. <i>The Merck Index 14th Edition</i> . Whitehouse Station, NJ: Merck & Co, Inc.; 2006: Monograph #3703.
7.	Estriol (Monograph). In: O'Neil MJ. <i>The Merck Index 14th Edition</i> . Whitehouse Station, NJ: Merck & Co, Inc.; 2006: Monograph #3707.
8.	Estradiol. In: Trissel LA. <i>Trissel's Stability of Compounded Formulations, 4th Edition</i> . American Pharmaceutical Association; 2009: 222.
9.	Estradiol (Monograph). <i>United States Pharmacopeia XXXVI / National Formulary 31</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2013: 3470.
10.	Estriol (Monograph). <i>United States Pharmacopeia XXXVI / National Formulary 31</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2013: 3486.
11.	Estradiol. Thomson Micromedex. <i>USP DI – Drug Information for the Health Care Professional, 26th Edition</i> . Taunton, MA: US Pharmacopeial Convention, Inc; 2006: 1382.
12.	USP <795>. <i>United States Pharmacopeia XXXVI / National Formulary 31</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2013: 355.

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