



MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

1/4/2021; Page 1

Suggested Formula	Estradiol 0.25 mg/0.5 g, Estriol 1 mg/0.5 g, Progesterone 25 mg/0.5g Topical Gel (Suspension, 30 g)	FIN	F 009 036
-------------------	-----------------------------------------------------------------------------------------------------	-----	-----------

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Estradiol 2.5% Stock Solution †	0.60	mL				
Estriol (Micronized), USP	0.060	g				
Progesterone (Micronized), USP	1.500	g				
Pentylene Glycol	0.75	mL				
Medisca VersaPro™ Anhydrous Base	27.08	g				
† Estradiol 2.5% Stock Solution						
Estradiol (Micronized), USP	TBD					
Propylene Glycol, USP	3.0	mL				
Propylene Glycol, USP	q.s. to 4.0	mL				



Suggested Formula	Estradiol 0.25 mg/0.5 g, Estriol 1 mg/0.5 g, Progesterone 25 mg/0.5g Topical Gel (Suspension, 30 g)	FIN	F 009 036
-------------------	-----------------------------------------------------------------------------------------------------	-----	-----------

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Hygroscopic (protect from moisture whenever possible): Estradiol, Pentylene Glycol, Propylene Glycol

Light Sensitive (protect from light whenever possible): Estradiol, Estriol, Progesterone, Propylene Glycol

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 **12 to 15%** 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. At this time, **General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings** is informational and not compendially applicable unless otherwise specified by regulators and enforcement bodies. For information on the scope, intended applicability, and implementation context for USP General Chapter <800>, see: <https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare>.

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 (GFI) 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.



Suggested Formula	Estradiol 0.25 mg/0.5 g, Estriol 1 mg/0.5 g, Progesterone 25 mg/0.5g Topical Gel (Suspension, 30 g)	FIN	F 009 036
-------------------	-----------------------------------------------------------------------------------------------------	-----	-----------

SUGGESTED PREPARATION (for 30 g)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): _____	Processing Error	Qty. to measure
Estradiol 2.5% Stock Solution † §	0.60	mL			
Estriol (Micronized), USP §	0.060	g			
Progesterone (Micronized), USP §	1.500	g			
Pentylene Glycol §	0.75	mL			
Medisca VersaPro™ Anhydrous Base	27.08	g			
† Estradiol 2.5% Stock Solution					
Estradiol (Micronized), USP §	TBD		---	---	
Propylene Glycol, USP §	3.0	mL	---	---	
Propylene Glycol, USP §	q.s. to 4.0	mL	---	---	

§ Weigh / measure just prior to use.

* Takes into account increased batch size conversions and density conversions, if required.



Suggested Formula	Estradiol 0.25 mg/0.5 g, Estriol 1 mg/0.5 g, Progesterone 25 mg/0.5g Topical Gel (Suspension, 30 g)	FIN	F 009 036
-------------------	-----------------------------------------------------------------------------------------------------	-----	-----------

Preparatory Instruction

1. **Ingredient quantification:**

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

MINUS	100%
Water Content (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of water free Estradiol, in decimal	_____
MULTIPLIED 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 2.5% Stock Solution, batch size (4.0 mL):

Quantity of Estradiol required for the stock solution	0.100 g
DIVIDED BY	
Potency of Estradiol, in decimal (Step 1Ai)	_____
EQUALS	
i. Quantity of Estradiol needed for the stock solution	_____ g



Suggested Formula	Estradiol 0.25 mg/0.5 g, Estriol 1 mg/0.5 g, Progesterone 25 mg/0.5g Topical Gel (Suspension, 30 g)	FIN	F 009 036
3.	<p>† <u>Estradiol 2.5% Stock Solution preparation:</u></p> <p>A. Incrementally add the Estradiol (Micronized) (amount determined on Step 2Ai) to the Propylene Glycol (3.0 mL). <u>Specifications:</u> Continuously mix until all solid particles have completely dissolved. <u>End result:</u> Homogeneous liquid-like solution.</p> <p>B. Add additional Propylene Glycol to the mixture (Step 3A) to fill to the required batch size (4.0 mL). <u>Specifications:</u> Continuously mix. <u>End result:</u> Homogeneous liquid-like solution.</p>		
4.	<p><u>Powder-liquid preparation:</u></p> <p>A. By geometrical addition, combine and mix the following ingredients together to form a homogeneous powder blend: -Estriol (Micronized) -Progesterone (Micronized) -Testosterone (Micronized)</p> <p>B. Combine and mix the following ingredients together to form a homogeneous liquid-like solution: -Pentylene Glycol -Estradiol 1% Stock Solution (0.60 mL <i>plus</i> processing error adjustments)</p> <p>C. Levigate the homogeneous powder blend (Step 4A) with the homogeneous liquid-like solution (Step 4A). <u>End result:</u> Homogeneous liquid-like dispersion.</p>		
5.	<p><u>Medium Integration:</u></p> <p>A. Incrementally add the homogeneous liquid-like dispersion (Step 4C) to the VersaPro™ Anhydrous Base. <u>Specifications:</u> Continuously mix, using high-shear mixing techniques. <u>End result:</u> Homogeneous gel-like dispersion.</p>		
6.	<p><u>Product transfer</u></p> <p>Transfer the final product into the specified dispensing container (see “Packaging Requirements”).</p>		



Suggested Formula	Estradiol 0.25 mg/0.5 g, Estriol 1 mg/0.5 g, Progesterone 25 mg/0.5g Topical Gel (Suspension, 30 g)	FIN	F 009 036
-------------------	-----------------------------------------------------------------------------------------------------	-----	-----------

SUGGESTED PRESENTATION

Estimated Beyond-Use Date	6 months, as per USP 795*.	Packaging Requirements	- Tightly closed, light-resistant, ointment tube/jar. - To be administered with a metered-dose measuring device.	
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	6	Cap tightly after use.
	2	Keep out of reach of children.	7	Keep at controlled room temperature (20°C – 25°C).
	3	Keep in a dry place.	8	Protect from light.
	4	May impair mental and/or physical ability. Use care when operating a car or machinery.	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	For external use only.	10	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.			

* 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.	Suspensions. In: Allen, LV, Jr. <i>The Art, Science, and Technology of Pharmaceutical Compounding Fifth Edition</i> . American Pharmacists Association; 2016: 279.
2.	Divigel. In: Canadian Pharmacists Association. <i>Compendium of Pharmacists and Specialties, 2017</i> : 1081.
3.	Crinone. In: Canadian Pharmacists Association. <i>Compendium of Pharmacists and Specialties, 2017</i> : 918.
4.	Propylene Glycol. In: Sheskey, P.J., ed. <i>Handbook of Pharmaceutical Excipients, 8th Edition</i> . Pharmaceutical Press and American Pharmacists Association; 2017: 795.
5.	Estradiol. In: Brayfield, A., ed. <i>Martindale: The Complete Drug Reference, 38th Edition</i> . London, England: The Pharmaceutical Press; 2014: 2271.
6.	Estriol. In: Brayfield, A., ed. <i>Martindale: The Complete Drug Reference, 38th Edition</i> . London, England: The Pharmaceutical Press; 2014: 2274.



Suggested Formula		FIN	F 009 036
7.	Progesterone. In: Brayfield, A., ed. <i>Martindale: The Complete Drug Reference, 38th Edition</i> . London, England: The Pharmaceutical Press; 2014: 2300.		
8.	Estradiol (Monograph). In: O'Neil MJ. <i>The Merck Index 15th Edition</i> . Whitehouse Station, NJ: Merck & Co, Inc.; 2013: Monograph #3758.		
9.	Estriol (Monograph). In: O'Neil MJ. <i>The Merck Index 15th Edition</i> . Whitehouse Station, NJ: Merck & Co, Inc.; 2013: Monograph #3762.		
10.	Progesterone (Monograph). In: O'Neil MJ. <i>The Merck Index 15th Edition</i> . Whitehouse Station, NJ: Merck & Co, Inc.; 2013: Monograph #7889.		
11.	Estradiol. In: Trissel LA. <i>Trissel's Stability of Compounded Formulations, 5th Edition</i> . American Pharmaceutical Association; 2012: 195.		
12.	Progesterone. In: Trissel LA. <i>Trissel's Stability of Compounded Formulations, 5th Edition</i> . American Pharmaceutical Association; 2012: 409.		
13.	Estradiol (Monograph). <i>United States Pharmacopeia XLIII / National Formulary 38</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2020: 1724.		
14.	Estriol (Monograph). <i>United States Pharmacopeia XLIII / National Formulary 38</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2020: 1741.		
15.	Progesterone (Monograph). <i>United States Pharmacopeia XLIII / National Formulary 38</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2020: 3704.		
16.	Estradiol. Thomson Micromedex. <i>USP DI – Drug Information for the Health Care Professional, 26th Edition</i> . Taunton, MA: US Pharmacopeial Convention, Inc; 2006: 1382.		
17.	Progesterone. Thomson Micromedex. <i>USP DI – Drug Information for the Health Care Professional, 26th Edition</i> . Taunton, MA: US Pharmacopeial Convention, Inc; 2006: 2526.		
18.	USP <795>. <i>United States Pharmacopeia XLIII / National Formulary 38</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2020: 7025.		

DISCLAIMER: THIS DOCUMENT IS COPYRIGHT© 2020 MEDISCA PHARMACEUTIQUE INC. MEDISCA NETWORK INC., HEREBY REFERRED TO AS 'THE NETWORK', HAS PROVIDED THE FORMULA AND INSTRUCTIONS ABOVE AS A MODEL FOR EDUCATIONAL PURPOSES ONLY ON THE BASIS OF THE RECOGNIZED COMPENDIA AND TEXTS REFERENCED AT THE END OF THIS DOCUMENT. THE NETWORK TAKES NO RESPONSIBILITY FOR THE VALIDITY, SCHEDULING OR ACCURACY OF THIS INFORMATION OR FOR ITS SAFETY OR EFFECTIVENESS, NOR FOR ANY USE THEREOF, WHICH IS AT THE SOLE RISK OF THE LICENSED PHARMACIST OR OTHER APPROPRIATELY STATE LICENSED PROFESSIONAL. ADJUSTMENTS MAY BE NEEDED TO MEET SPECIFIC PATIENT NEEDS AND IN ACCORDANCE WITH A LICENSED PRESCRIBER'S PRESCRIPTION. THE PHARMACIST OR OTHER APPROPRIATELY STATE LICENSED PROFESSIONAL MUST EMPLOY APPROPRIATE TESTS TO DETERMINE THE STABILITY OF THIS SUGGESTED FORMULA. THE NETWORK CANNOT BE HELD LIABLE TO ANY PERSON OR ENTITY CONCERNING CLAIMS, LOSS, OR DAMAGE CAUSED BY, OR ALLEGED TO BE CAUSED BY, DIRECTLY OR INDIRECTLY, THE USE OR MISUSE OF THE INFORMATION CONTAINED IN THIS SUGGESTED FORMULA. IN ALL CASES IT IS THE RESPONSIBILITY OF THE LICENSED PHARMACIST OR OTHER APPROPRIATELY STATE LICENSED PROFESSIONAL TO KNOW THE LAW, TO COMPOUND ANY FINISHED PRODUCT AND TO DISPENSE THESE PRODUCTS IN ACCORDANCE WITH FEDERAL AND STATE LAW. MEDISCA NETWORK INC. MAKES NO WARRANTIES WITH RESPECT TO INFRINGEMENT OR NON-INFRINGEMENT BY THE FORMULA OF ANY PATENT OR OTHER INTELLECTUAL PROPERTY OF ANY OTHER PARTY, AND IT IS THE RESPONSIBILITY OF THE PHARMACIST OR OTHER APPROPRIATELY STATE LICENSED PROFESSIONAL TO INVESTIGATE AND DETERMINE ANY SUCH ISSUE.