



Suggested Formula	Estradiol Cypionate 5 mg/mL Intramuscular Injection (Solution, 100 mL)	FIN	F 007 096v3
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SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Estradiol Cypionate, USP	0.500	g				
Benzyl Benzoate, USP	23.0	mL				
Benzyl Alcohol (Parenteral Application), NF	2.0	mL				
Corn Oil, NF	70.0	mL				
Corn Oil, NF	q.s. to 100.0	mL				

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive (protect from light whenever possible):

Estradiol Cypionate, Benzyl Benzoate, Benzyl Alcohol, Corn Oil





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SPECIAL PREPARATORY CONSIDERATIONS (CONTINUED)

Suggested Preparatory Guidelines

Non-Sterile Preparation Sterile Preparation

Processing Error / Testing Considerations: To account for processing error, sterility and endotoxin testing 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. 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 797* and *USP 800* when handling hazardous drugs. Only trained and qualified personnel must prepare this formula.

All heat stable, reusable materials and equipment must be sterilized and depyrogenated by dry heat sterilization at 250°C for 2 hours prior to use.

Compounder needs to verify as per USP, if every batch of final product compounded using this procedure must be sterility and endotoxin tested before being dispensed.

All required personal protective equipment (sterile and hazardous if applicable), such as but not limited to, gowns, aprons, sleeves, gloves both inner and outer if applicable, shoe covers, hairnet, head cap, beard cover, eyewear, appropriate face mask, respirator and face shield, etc., where applicable must be worn at all times. In addition, proper personnel cleansing must be done before entering the buffer or clean area.

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.

Filter integrity must be validated by performing a filter stress test. If the test demonstrates that the filter might be defective, the solution must be discarded and remade.

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.



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SUGGESTED PREPARATION (for 100 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): _____	Processing Error	Qty. to measure
Estradiol Cypionate, USP §	0.500	g			
Benzyl Benzoate, USP §	23.0	mL			
Benzyl Alcohol (Parenteral Application), NF §	2.0				
Corn Oil, NF §	70.0	mL			
Corn Oil, NF §	q.s.to 100.0	mL			

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

§ Weigh / measure just prior to use.

Preparatory Instruction

IMPORTANT: All preparatory procedures must be performed using proper Aseptic Technique

1.	<u>Equipment sterilization:</u> Following the manufacturer's specifications, sterilize and depyrogenate all heat stable, reusable materials and equipment, then return to ambient temperature.
2.	<u>Powder-liquid preparation:</u> A. Levigate the Estradiol Cypionate with the Benzyl Alcohol (Parenteral Application). <u>End result:</u> Homogeneous liquid-like dispersion. B. Incrementally add the homogeneous liquid-like dispersion (Step 2A) into the Benzyl Benzoate. <u>End result:</u> Homogeneous liquid-like dispersion.
3.	<u>Phase incorporation:</u> A. Incrementally add the homogeneous liquid-like dispersion (Step 2B) into the Corn Oil (70.0 mL <i>plus</i> processing error adjustments). <u>Specifications:</u> Continuously mix, until all solid particles have completely dissolved. <u>End result:</u> Homogeneous liquid-like solution.



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4.	<p><u>Filling to volume:</u></p> <p>A. Add additional Corn Oil to the mixture (Step 3A) to fill to the required batch size (100.0 mL <i>plus</i> processing error adjustments).</p> <p><u>Specifications:</u> Continuously mix.</p> <p><u>End result:</u> Homogeneous liquid-like solution.</p>
5.	<p><u>Filtering and transferring:</u></p> <p>Aseptically filter the solution through a 0.22-μm sterile Teflon filter into the recommended dispensing container (see Packaging requirements). Transfer the remainder into a separate dispensing container. This is to be used as the Test sample for sterility and endotoxin testing.</p>
6.	<p><u>Filter integrity test:</u></p> <p>Validate filter integrity by performing a filter stress test. If the test demonstrates that the filter might be defective, the solution must be discarded and remade.</p>
7.	<p><u>Terminal Sterilization:</u></p> <p>In relation to the chemical composition of the formulation, final packaging, etc., select and validate an end-stage sterilization method and follow the manufacturer's specifications.</p>
8.	<p><u>Sterility and Endotoxin testing:</u></p> <p>Validate the Test sample for sterility and endotoxins, in accordance to current USP 797 regulatory guidelines.</p>



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SUGGESTED PRESENTATION

Estimated Beyond-Use Date	24 hours controlled room temperature, 3 days refrigerated, or 45 days frozen, as per USP 797. BUD based on successful endotoxin test result.	Packaging Requirements	Sterile, tightly closed, light-resistant unit-dose injection vials.	
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	5	Protect from light.
	2	Keep out of reach of children.	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.
	3	Keep at controlled room temperature, (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).	7	For veterinary (Equine) use only.
	4	Discard container after use.	8	Storage at low temperatures may result in the separation of some solid material which redissolves readily on warming.
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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REFERENCES

1.	Parenteral Preparations. In: Allen, LV, Jr. <i>The Art, Science and Technology of Pharmaceutical Compounding Fifth Edition</i> . American Pharmaceutical Association; 2016: 399.
2.	Estradiol Cypionate. In: Sweetman SC, ed. <i>Martindale: The Complete Drug Reference, 36th Edition</i> . London, England: The Pharmaceutical Press; 2009: 2097.
3.	Estradiol (Monograph). In: O'Neil MJ. <i>The Merck Index 15th Edition</i> . Whitehouse Station, NJ: Merck & Co, Inc.; 2013: #3758.
4.	Estradiol Cypionate (Monograph). <i>United States Pharmacopeia XXXX / National Formulary 35</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2017: 4075.
5.	USP <797>. <i>United States Pharmacopeia XXXX / National Formulary 35</i> . Rockville, MD. US Pharmacopeial Convention, Inc. 2017: 683.

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