

Formulation Record

Name: Triple Estrogen, Progesterone, and Testosterone Sublingual Drops

Strength: triple estrogen 2.5 mg/ml; progesterone 100 mg/ml; testosterone 1 mg/ml

Dosage Form: Buccal

Route of Administration: Sublingual

Date of Last Review or Revision: 10/01/03

Person Completing Last Review or Revision: Robert Shrewsbury

| Ingredient | Quantity | Physical Description | Solubility | Therapeutic Activity |
|---------------------------------|------------|--|---|-------------------------------|
| Estriol USP | 20.0 mg | white, crystalline powder | practically insoluble in water; soluble in alcohol and vegetable oils | naturally occurring estrogen |
| Estradiol USP | 2.5 mg | white to creamy-white crystalline powder | practically insoluble in water; 35.7 mg/ml in alcohol | naturally occurring estrogen |
| Estrone USP | 2.5 mg | white to creamy-white crystalline powder | practically insoluble in water; 4 mg/ml alcohol; soluble in vegetable oils | naturally occurring estrogen |
| Progesterone USP | 1.0 g | white to creamy-white crystalline powder | practically insoluble in water, soluble in alcohol; sparingly soluble in vegetable oils | naturally occurring progestin |
| Testosterone USP | 10.0 mg | white or slightly creamy white crystalline powder | practically insoluble in water; 1 g/5 ml of ethanol; soluble in vegetable oils | naturally occurring androgen |
| Silica Gel, micronized | 200.0 mg | white, fine, amorphous powder | practically insoluble in water and alcohol | suspending agent |
| Saccharin, Insoluble NF | 120.0 mg | white crystals or crystalline powder | 1 g/290 ml water; 1 g/ 50 ml glycerin; 1 g/31 ml of alcohol | sweetening agent |
| Flavor, Tangerine Oil, natural | 3% | clear, straw-colored non-viscous oil | not miscible with almond or grapeseed oil | flavoring agent |
| Flavor, Marshmallow, Artificial | 1% | clear, colorless non-viscous oil | not miscible with almond or grapeseed oil | flavoring agent |
| Almond Oil, Sweet | qs 10.0 ml | clear, colorless to straw-colored oil with nutty taste | not miscible with water; slightly soluble in alcohol | vehicle |

Additional Information:

Grapeseed Oil can be substituted for Almond Oil, Sweet

| Steroid Powder Blend (FR 34) | | Vehicle Stock Solution (FR 59) | |
|------------------------------|----------|--------------------------------|-----------|
| estriol USP | 0.0200 g | silica gel, micronized | 0.20 g |
| estradiol USP | 0.0025 g | saccharin, insoluble NF | 0.12 g |
| estrone USP | 0.0025 g | tangerine oil, natural | 0.3 ml |
| progesterone USP | 1.0000 g | marshmallow, artificial | 0.1 ml |
| testosterone USP | 0.0100 g | vehicle | qs 8.0 ml |

Example Calculations:

Equipment Required:

- Class A prescription balance
- mortar and pestle
- 10 ml graduated cylinder

Method of Preparation:

1. Calibrate the final container with alcohol to 10 ml. Turn on mouth to drain dry.
2. Using the prescription balance, weigh estriol, estradiol, estrone, progesterone, testosterone, silica gel, and saccharin. Blend together using geometric dilution in a mortar.
3. Add a small portion of the vehicle to wet the powders and make a paste.
4. Transfer paste to final container, and add the flavors.
5. Bring final container to volume with vehicle with repeated rinsing of the mortar.

Alternative Method of Preparation:

1. Prepare a steroid powder blend of estriol, estradiol, estrone, progesterone, and testosterone (see FR 34).
2. Prepare a vehicle stock solution of silica gel, saccharin, flavorings, and vehicle (see FR 59).
3. Calibrate the final container with alcohol to 10 ml. Turn on mouth to drain dry.
4. Using the prescription balance, weigh the appropriate amount of steroid powder blend.
5. Place an appropriate volume of the **vehicle stock solution** to the final container. Add the **powder blend** in portions with shaking after each addition.
6. Bring final container to volume with **vehicle**.

Description of Finished Product:

Almond Oil vehicle: creamy white colored suspension, light “nutty” odor.
Grapeseed Oil vehicle: light lime colored suspension, light “grape” odor.

Quality Control Procedures:

Easily resuspended when shaken
Very fine suspended powder particles: no visible clumps
Product weight

Packaging Container:

Tight, light-resistant container

Storage Requirements:

Store in a cool place (46°F to 59°F)
USP 23 directs that “cool place” can alternatively be “store in refrigerator”

Beyond-Use Date Assignment:

USP Guidelines: Nonaqueous solutions: Active ingredient is not from a manufactured product, but is a USP/NF substance: 6 months beyond use date.

Label Information:

Shake Well

Source of Recipe:

Allen's Compounded Formulations: the complete U.S. Pharmacist collection. Loyd V. Allen, Jr., editor, APhA Publications, Washington, D.C., copyright 2003, pp. 212-213.

Literature Information:

International Journal Pharmaceutical Compounding 3:395 1999
The Merck Index, 12th edition, 1996; solubility information for ingredients
Remington: The Science and Practice of Pharmacy, 19th edition, 1995; solubility information for ingredients