Formulation Record

Name: Tri-estrogen Capsules
Strength: 1.25 mg/cap
Dosage Form: Capsule
Route of Administration: Oral

Date of Last Review or Revision: 01/28/07
Person Completing Last Review or Revision: Robert Shrewsbury

Formula:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity</th>
<th>Physical Description</th>
<th>Solubility</th>
<th>Therapeutic Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estriol</td>
<td>80%</td>
<td>white to cream powder</td>
<td>insoluble in water, soluble in alcohol and vegetable oils</td>
<td>endogenous estrogen</td>
</tr>
<tr>
<td>Estrone</td>
<td>10%</td>
<td>white to cream powder</td>
<td>insoluble in water, 4 mg/ml in alcohol</td>
<td>endogenous estrogen</td>
</tr>
<tr>
<td>Estradiol</td>
<td>10%</td>
<td>white to cream powder</td>
<td>insoluble in water, 35.7 mg/ml in alcohol</td>
<td>endogenous estrogen</td>
</tr>
<tr>
<td>Lactose, hydrous</td>
<td>qs</td>
<td>white powder</td>
<td>1 g/5 ml water, slightly soluble in alcohol</td>
<td>bulk diluent</td>
</tr>
</tbody>
</table>

Additional Information:
- A #2 capsule will hold between 300 – 360 mg of hydrous lactose.
- Colored capsules may be used for aesthetic appeal or to differentiate dosages.

Example Calculations:
- The low dose of tri-estrogen requires that a triturate be made. Make a triturate using hydrous lactose such that 150 mg contains 1.25 mg of tri-estrogen (i.e., 148.75 mg of hydrous lactose and 1.25 mg of tri-estrogen). An additional 200 mg of hydrous lactose will be used to bulk fill the #2 capsule to 350 mg.
- Calculate the formula for 2 extra capsules to account for losses during compounding.

Equipment Required:
- prescription balance
- mortar and pestle

Method of Preparation:
1. Accurately weigh the stock triturate and the hydrous lactose used for bulk filling.
2. Triturate the powders using geometric dilution.
3. Hand punch the required number of capsules.
4. Verify the weight variation.
5. Verify the content analysis.

Description of Finished Product:
White powder mixture.
Quality Control Procedures:

Weight Variation:
Determine the following information for 4 randomly selected capsules. Use an empty #2 capsule on the right pan as a tare. Each capsule should be within 5% of the average. Note: this information can be collected as the capsules are made.

<table>
<thead>
<tr>
<th>Number</th>
<th>Weight of Contents in Capsule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

Average “Weight of Contents in Capsule”

Percent Difference in Average and Weight of #1
Percent Difference in Average and Weight of #2
Percent Difference in Average and Weight of #3
Percent Difference in Average and Weight of #4

Content Uniformity:
Record the following information for 4 randomly selected capsules. Dissolve the contents of a capsule in 10 ml distilled water. Read the absorbance at 274 nm with a spectrophotometer using methacrylate cuvettes. Use the standard curve and blank solution provided in the lab to determine the weight of drug in the capsule contents.

<table>
<thead>
<tr>
<th>Number</th>
<th>Absorbance @ 274 nm</th>
<th>Concentration of Estrogens (mg/10 ml)</th>
<th>Weight of Estrogens in Capsule Contents (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4</td>
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</tr>
</tbody>
</table>

Packaging Container:
Package in plastic prescription vials

Storage Requirements:
Store at room temperature

Beyond-Use Date Assignment:
USP Guidelines:
Nonaqueous liquids and solid formulations:
If the source of the ingredient(s) is a manufactured drug product, the beyond-use date is not later than 25% of the time remaining until the original product’s expiration date, or 6 months, whichever is earlier. If the source of the ingredient(s) is a USP or NF substance, the beyond-use date is not later than 6 months. Assign 6 months.

Label Information:
Possible drug-food interaction with grapefruit juice.

Source of Recipe:
Pharmaceutics Laboratory web site: http://pharmlabs.unc.edu

Literature Information: