Formulation Record

Name: Theophylline - Guaifenesin Syrup
Strength: 10 mg/ml - 6.0 mg/ml
Dosage Form: Solution
Route of Administration: Oral

Date of Last Review or Revision: 09/07/00
Person Completing Last Review or Revision: RPS

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>Theophylline USP</td>
<td>4.73 g</td>
<td>white powder</td>
<td>1 g/120 ml water; soluble in hot water</td>
<td>bronchodilator</td>
</tr>
<tr>
<td>Guaifenesin USP</td>
<td>2.84 g</td>
<td>white powder</td>
<td>1 g/20 ml water; more in hot water; soluble in glycerin</td>
<td>expectorant</td>
</tr>
<tr>
<td>Glycerin USP</td>
<td>95.0 ml</td>
<td>clear, very viscous liquid</td>
<td>miscible with water</td>
<td>sweetener, solvent</td>
</tr>
<tr>
<td>10% NaOH solution</td>
<td>24.0 ml</td>
<td>clear liquid</td>
<td>soluble in water</td>
<td>pH adjuster</td>
</tr>
<tr>
<td>Water</td>
<td>75.0 ml</td>
<td>clear liquid</td>
<td>N/A</td>
<td>solvent</td>
</tr>
<tr>
<td>Sodium Citrate Anhydrous USP</td>
<td>0.473 gm</td>
<td>white powder</td>
<td>soluble in 1.3 parts water</td>
<td>buffer component</td>
</tr>
<tr>
<td>Citric Acid Hydrous USP</td>
<td>3.8 gm</td>
<td>white powder</td>
<td>59.2% w/w in water at 20°C; 84.0% at 100°C</td>
<td>buffer component</td>
</tr>
<tr>
<td>Sodium Saccharin USP</td>
<td>0.165 gm</td>
<td>white powder</td>
<td>1 g/1.5 ml water</td>
<td>sweetening agent</td>
</tr>
<tr>
<td>Lemon Oil</td>
<td>2-3 drops</td>
<td>clear, slightly yellow, slightly viscous liquid</td>
<td>miscible with glycerin</td>
<td>aromatic flavoring agent</td>
</tr>
<tr>
<td>Lime Oil</td>
<td>1 drop</td>
<td>clear, slightly green, slightly viscous liquid</td>
<td>miscible with glycerin</td>
<td>aromatic flavoring agent</td>
</tr>
<tr>
<td>Sorbitol Solution 70% USP</td>
<td>qs 473 ml</td>
<td>clear, viscous liquid, consistency of syrup</td>
<td>miscible with water</td>
<td>solvent, sweetener, reduce saccharin aftertaste</td>
</tr>
</tbody>
</table>

Example Calculations:
Least Weighable Quantity (LWQ) on Class A Prescription Balance is 120 mg. In quantities less than 344 ml, sodium saccharin will need to be added as a lactose trituration. In quantities less than 120 ml, sodium citrate anhydrous will need to be added as a lactose trituration.

NaOH solutions should be freshly prepared. Generally suitable for 1 week after preparation.

Equipment Required:
- Class A prescription balance meeting USP specifications
- adapta-cap bottle - glycerin (viscous liquid)
- low temperature hot plate - aid in powder dissolution
- 50 ml and 100 ml graduated cylinder - sodium hydroxide solution and water

Method of Preparation:
1. Using the prescription balance, weigh the powders. Mark each weigh boat with the drug name.
2. Put the guaifenesin in a 600 ml beaker.
3. Add the glycerin to the beaker, and stir the guaifenesin to disperse it in the glycerin.
4. Heat at low heat (not exceeding 80°C) for 10 minutes, then add theophylline with stirring.
5. Add water and continue heating until powders dissolve.
6. Turn the hot plate off and remove the beaker from the hot plate.
7. Add sodium saccharin, sodium citrate, and citric acid. Stir until dissolved.
8. Add a portion of the sorbitol (150 ml), mix and add sodium hydroxide solution. Mix.
9. Transfer the mixture into a calibrated prescription bottle.
10. Add the lemon oil and the lime oil directly to the prescription bottle.
11. Rinse the beaker with portions of sorbitol, adding each portion to the product in the prescription bottle.
12. Bring the solution to final volume.

Description of Finished Product:
Clear solution with "lemon - lime" type aroma

Quality Control Procedures:
Product should be free of any visible particles.
Product should be well mixed.

Packaging Container:
16 oz. plastic prescription bottle with tight closure

Storage Requirements:
Store in refrigerator. See beyond-use assignment for explanation

Beyond-Use Date Assignment:
USP Guidelines:
Aqueous solutions:
When prepared from ingredients in solid form, the beyond-use date should be not later than 14 days when stored at cold temperature.

Glycerin has some preservation properties. It will preserve "free water" equal to its volume.

Saturated sorbitol solutions are self-preserving (Thompson: A Practical Guide to Contemporary Pharmacy Practice, p. 21.4). Solutions that are diluted will require refrigeration or preservatives.

Sorbitol 70% is resistant to some organisms, but is not self-preserving. Preservatives are required (Handbook of Pharmaceutical Excipients, 1998).

Label Information:
Store in refrigerator.

Source of Recipe:
RPS/PCL staff
supporting web page: http://www.unc.edu/courses/phar051l/, then select Pharmaceutical Solutions 1: Simple, Saturated, Syrups

Literature Information:

Handbook of Pharmaceutical Excipients, 1998