DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE

Bromhexine Hydrochloride, Chlorpheniramine Maleate & Phenylephrine Hydrochloride Syrup

Analytical Profile No.: Brom Chlor Phen 077/078/AP 087

Bromhexine Hydrochloride, Chlorpheniramine Maleate & Phenylephrine Hydrochloride Syrup contains not less than 90% and not more than 110% of the stated amount of Chlorpheniramine Maleate, Bromhexine Hydrochloride & Phenylephrine Hydrochloride.

Usual Strength: Each 5ml contains

Bromhexine HCl 4mg

Phenylephrine HCl 5mg

Chlorpheniramine Maleate 2mg

1. Identification:

In the assay, the principle peaks in the chromatogram obtained with the sample solution should correspond to the peaks in the chromatogram obtained with the reference standard solution.

Tests:

2. pH: As per manufacturer's specification

3. Wt/ml: As per manufacturer's specification

4. Assay: *Determine by liquid chromatography*

4.1 Test Solution: Shake well the contents of the bottle and pipette out 5 ml of syrup into a 25 ml volumetric flask. Add about 15 ml of methanol and sonicate for about 10 mins to dissolve, cool to room temperature and make up the volume to 25 ml with the same solvent. Filter the resulting solution and dilute 5 ml of the filtrate to 25 ml with the mobile phase. Filter the resulting solution through 0.2 µm membrane filter.

4.2 Reference Solution:

4.2.1 Chlorpheniramine Maleate stock solution: Weigh accurately about 25 mg of Chlorpheniramine Maleate RS in 50 ml volumetric flask. Add about 30 ml of methanol, sonicate for about 10 minutes to dissolve and make up the volume with same solvent.

4.2.2 Bromhexine Hydrochloride stock solution: Weigh accurately about 25 mg of Bromhexine Hydrochloride RS in 50 ml volumetric flask. Add about 30 ml of methanol, sonicate for about 10 minutes to dissolve and make up the volume with same solvent.

4.2.3 Phenylephrine Hydrochloride stock solution: Weigh accurately about 25 mg of Phenylephrine Hydrochloride RS in 50 ml volumetric flask. Add about 30 ml of methanol, sonicate for about 10 minutes to dissolve and make up the volume with same solvent.

4.2.4 Combined reference solution: Take 2 ml Chlorpheniramine Maleate stock solution, 5 ml Bromhexine Hydrochloride stock solution and 5 ml Phenylephrine Hydrochloride stock solution in 50 ml volumetric flask and make up the volume with mobile phase.

4.3 Chromatographic system:

- **Column:** Nitrile, 15 cm x 4.6 mm, 5µm particle size
- **Flow rate:** 1.0 ml/min
- **Wavelength:** 278 nm
- **Injection volume:** 20 µl
- **Detector:** UV/PDA
- **Column temperature:** ambient
- **Mobile Phase:** A mixture of 40 volumes of buffer, 50 volumes of methanol and 10 volumes of Acetonitrile
- **Buffer:** Dissolve 6.8 g of potassium dihydrogen phosphate in 1000 ml of water. Adjust the pH to 5.8 with 20 % sodium hydroxide solution.

4.4 Procedure: Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0, the relative standard deviation for replicate injections is not more than 2.0% and resolution between peaks of Phenylephrine Hydrochloride & Chlorpheniramine Maleate and peaks of Chlorpheniramine Maleate & Bromhexine Hydrochloride are not less than 2. Measure the peak responses. Calculate the content of Chlorpheniramine Maleate, Bromhexine Hydrochloride & Phenylephrine Hydrochloride in the syrup.

5. Other tests: As per pharmacopoeial requirement.