Phenoxybenzamine Hydrochloride Capsules

Type of Posting: Revision Bulletin
Posting Date: 28–Jul–2017
Official Date: 01–Aug–2017
Expert Committee: Chemical Medicines Monographs 2
Reason for Revision: Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the Chemical Medicines Monographs 2 Expert Committee has revised the Phenoxybenzamine Hydrochloride Capsules monograph. The purpose of this revision is to widen the acceptance criteria for any unspecified degradation products from NMT 0.1% to NMT 0.2% and total degradation products from NMT 0.5% to NMT 1.5% to be consistent with the FDA-approved drug products.

Minor editorial changes have been made to update the monograph to the current USP style.

The Phenoxybenzamine Hydrochloride Capsules Revision Bulletin supersedes the currently official Phenoxybenzamine Hydrochloride Capsules monograph. The Revision Bulletin will be incorporated in the First Supplement to USP 41–NF 36.

Should you have any questions, please contact Sujatha Ramakrishna, Ph.D., MBA. Principal Scientific Liaison (301–816–8349 or sxr@usp.org).
Phenoxybenzamine Hydrochloride Capsules

DEFINITION
Phenoxybenzamine Hydrochloride Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of phenoxybenzamine hydrochloride (C₁₈H₂₂ClNO·HCl).

IDENTIFICATION

Delete the following:

**A. ULTRAVIOLET ABSORPTION**
Analytical wavelengths: 268 and 272 nm
Sample solution: 0.15 mg/mL of phenoxybenzamine hydrochloride in acidic alcohol (1 in 1000 solution of hydrochloric acid in alcohol)
Acceptance criteria: The ratio A₂₆₈/A₂₇₂ of the maximum at 268 ± 2 nm and the minimum at 272 ± 2 nm is between 1.75 and 1.95.

Add the following:

**A.** The UV absorption spectra of the phenoxybenzamine peak of the Sample solution exhibit maxima and minima at the same wavelengths as those of the corresponding peak from the Standard solution, as obtained in the Assay.

Add the following:

**B.** The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

ASSAY

Change to read:

**PROCEDURE**
Sample solution: 0.15 mg/mL of phenoxybenzamine hydrochloride in acidic alcohol (1 in 1000 solution of hydrochloric acid in alcohol)
Sample solution: Nominally 0.2 mg/mL of USP Phenoxybenzamine Hydrochloride RS in acetonitrile.

System suitability solution: 10 mL of the Standard solution and 0.5 mL of 0.1 N sodium hydroxide taken in a vial. [NOTE—Basic solutions of phenoxybenzamine hydrochloride will produce the known degradant, tertiary amine phenoxybenzamine—the second major peak that elutes before the phenoxybenzamine peak and has a relative retention time of about 0.3 and an unknown related substance. Severe degradation of the drug substance will be observed if the solution is allowed to stand for more than 1 h.]

Sample solution: Nominally 0.2 mg/mL of phenoxybenzamine hydrochloride in acetonitrile prepared as follows. Remove, as completely as possible, the contents of NLT 20 Capsules. Transfer a portion of the mixed powder, equivalent to about 10 mg of phenoxybenzamine hydrochloride, to a 50-mL volumetric flask. Add about 40 mL of acetonitrile, and sonicate for 15 min with occasional swirling. Cool, and dilute with acetonitrile to volume to obtain the concentration, based on the label claim. Allow the sample to stand undisturbed for 30 min such that the undissolved material settles to the bottom. Transfer the top clear solution into HPLC vials, and use as the Sample solution.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 268 nm
Identification A: Diode array, UV 240–340 nm
Column: 4.6-mm × 150-cm; packing L7
Flow rate: 1 mL/min
Injection volume: 10 μL

System suitability
Samples: Standard solution and System suitability solution

Relative standard deviation: NMT 2%, Standard solution

Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of phenoxybenzamine hydrochloride (C₁₈H₂₂ClNO·HCl) in the portion of Capsules taken:

Result = \( \frac{r_o}{r_s} \times \frac{C_s}{C_o} \times 100 \)

\( r_o \) = peak response from the Sample solution
\( r_s \) = peak response from the Standard solution
\( C_s \) = concentration of USP Phenoxybenzamine Hydrochloride RS in the Standard solution (mg/mL)
\( C_o \) = nominal concentration of phenoxybenzamine hydrochloride in the Sample solution (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

**DISSOLUTION (711)**
Medium: 0.1 N hydrochloric acid; 500 mL
Apparatus 1: 100 rpm
Time: 45 min
Buffer: 2.2 g/L of monobasic sodium phosphate in water. Adjust with phosphoric acid to a pH of 3.00 ± 0.05.
Mobile phase: Buffer and acetonitrile (9:11)
Standard solution: 0.02 mg/mL of USP Phenoxybenzamine Hydrochloride RS in Medium
Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 268 nm
Column: 4.6-mm × 150-cm; packing L7
Phenoxybenzamine

Flow rate: 1 mL/min
Injection volume: 10 µL
System suitability
Sample: Standard solution
Suitability requirements
Relative standard deviation: NMT 2%
Calculate the percentage of the labeled amount of phenoxybenzamine hydrochloride (C\textsubscript{18}H\textsubscript{22}ClNO·HCl) dissolved:

\[ \text{Result} = \left( \frac{r_0}{r_T} \right) \times \left( \frac{C_S}{L} \right) \times V \times 100 \]

\[ r_0 = \text{peak response from the Sample solution} \]
\[ r_T = \text{sum of all the peak responses from the Sample solution} \]
\[ C_S = \text{concentration of USP Phenoxybenzamine Hydrochloride RS from the Standard solution (mg/mL)} \]
\[ L = \text{label claim (mg/Capsule)} \]
\[ V = \text{volume of Medium, 500 mL} \]

Tolerances: NLT 75% (Q) of the labeled amount of phenoxybenzamine hydrochloride (C\textsubscript{18}H\textsubscript{22}ClNO·HCl) is dissolved.

**Change to read:**

- **UNIFORMITY OF DOSAGE UNITS (905):** Meet the requirements

**IMPURITIES**

**Change to read:**

- **ORGANIC IMPURITIES**
  Solution A, Mobile phase, System suitability solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Analysis Sample: Sample solution
Calculate the percentage of each degradation product in the portion of Capsules taken:

\[ \text{Result} = \left( \frac{r_0}{r_T} \right) \times \left( \frac{1}{F} \right) \times 100 \]

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards (11)**
  USP Phenoxybenzamine Hydrochloride RS