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 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 ($C_{18}H_{22}ClNO \cdot HCl$).

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 A_{268}/A_{272} of the maximum at 268 ± 2 nm and the minimum at 272 ± 2 nm is between 1.75 and 1.95.▲*USP40*

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*.▲*USP40*

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*.▲*USP40*

ASSAY

Change to read:

• **PROCEDURE**
Solution A: 2.2 mg/mL of anhydrous monobasic sodium phosphate in water. Adjust with ▲▲*USP40* phosphoric acid to a pH of 3.0.
Mobile phase: Filtered and degassed mixture of *Solution A* and acetonitrile (45:55)
Standard solution: 0.2 mg/mL of USP Phenoxybenzamine Hydrochloride RS in acetonitrile. [NOTE—Sonicate if necessary.]
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**
Assay: UV 268 nm
Identification A: Diode array, UV 240–340 nm▲*USP40*
Column: 4.6-mm × 150-cm; packing L7
▲▲*USP40*
Flow rate: 1 mL/min
Injection volume: 10 µL
System suitability
Samples: *Standard solution* and *System suitability solution*
▲
[NOTE—The relative retention times for the phenoxybenzamine peak and the known degradant, tertiary amine phenoxybenzamine, peak are about 1.0 and 0.3, respectively.]▲*USP40*
Suitability requirements
Resolution: NLT 4 between phenoxybenzamine and the unknown peak eluting after the phenoxybenzamine peak (at about 9.4 min), *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 ($C_{18}H_{22}ClNO \cdot HCl$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = 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_U = 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
▲▲*USP40*

©2017 The United States Pharmacopeial Convention *All Rights Reserved.*

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 ($C_{18}H_{22}ClNO \cdot HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Phenoxybenzamine Hydrochloride RS from the *Standard solution* (mg/mL)
L = label claim (mg/Capsule)
V = volume of *Medium*, 500 mL

Tolerances: NLT 75% (Q) of the labeled amount of phenoxybenzamine hydrochloride ($C_{18}H_{22}ClNO \cdot HCl$) is dissolved.

Change to read:

• **Uniformity of Dosage Units** ⟨905⟩:▲*USP40* Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**
Solution A, Mobile phase, ●(RB 1-Aug-2017) **System suitability solution, Sample solution, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay*.
Analysis
Sample: ●(RB 1-Aug-2017) *Sample solution*
Calculate the percentage of each ●degradation product●(RB 1-Aug-2017) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response of ●each degradation product●(RB 1-Aug-2017) from the *Sample solution*
r_T = sum of all the peak responses from the *Sample solution*
F = relative response factor ●(see *Table 1*)●(RB 1-Aug-2017)

Acceptance criteria: ●See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria (NMT %)
Phenoxybenzamine tertiary amine[a]	0.3	1.1	0.5
Phenoxybenzamine	1.0	—	—
Any unspecified degradation product	—	1.0	0.2
Total degradation products[b]	—	—	1.5

[a] 2-[Benzyl(1-phenoxypropan-2-yl)amino]ethan-1-ol.
[b] Includes specified and unspecified degradation products.

● (RB 1-Aug-2017)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.
• **USP Reference Standards** ⟨11⟩
USP Phenoxybenzamine Hydrochloride RS

©2017 The United States Pharmacopeial Convention *All Rights Reserved.*