In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 2 Expert Committee intends to revise the Guanfacine Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to revise the Guanfacine Tablets monograph by adding “deaerated, if necessary” to the Medium of the current Dissolution test.

Additional editorial changes were made to update the monograph to current USP style.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.¹

Should you have any questions, please contact Yanyin Yang, Senior Scientist III (301-692-3623 or yanyin.yang@usp.org).

¹ This text is not the official version of a USP–NF monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the USP–NF for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product’s final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the Pharmacopeial Forum must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the USP–NF.
**Guanfacine Tablets**

**DEFINITION**
Guanfacine Tablets contain an amount of Guanfacine Hydrochloride (C₉H₈Cl₂N₃O · HCl) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of guanfacine (C₉H₈Cl₂N₃O).

**IDENTIFICATION**
- **A.** The retention time of the major peak of the Sample solution corresponds to that of the Standard solution as obtained in the Assay.
- **B.** Thin-Layer Chromatographic Identification Test (201)
  - **Standard solution**: 2 mg/mL of USP Guanfacine Hydrochloride RS in methanol
  - **Sample solution**: 2 mg/mL in methanol
  - **Developing solvent system**: Ethyl acetate, glacial acetic acid, and water (5:2:2)
  - **Acceptance criteria**: Meet the requirements

**ASSAY**
- **Procedure**
  - **Solution A**: pH 2.5 diethylamine phosphate prepared as follows. Add 10.3 mL of diethylamine to 70 mL of water. Adjust with phosphoric acid to a pH of 2.5 and dilute with water to 100 mL.
  - **Mobile phase**: Dissolve 600 mg of monobasic potassium phosphate and 3 mL of Solution A in 480 mL of water, and mix. Adjust with 0.2 N sodium hydroxide to a pH of 4.0. While swirling, add 520 mL of acetonitrile.
  - **Standard stock solution A**: 0.018 mg/mL of 2,6-dichlorophenylacetic acid in Mobile phase
  - **Standard stock solution B**: 0.23 mg/mL of USP Guanfacine Hydrochloride RS in Mobile phase
  - **Internal standard solution**: 0.5 mg/mL of butylparaben in Mobile phase
  - **Standard solution**: 0.046 mg/mL of USP Guanfacine Hydrochloride RS, 3.6 μg/mL of 2,6-dichlorophenylacetic acid and 0.1 mg/mL of butylparaben in Mobile phase prepared as follows. Transfer 5.0 mL each of Standard stock solution A, Standard stock solution B and Internal standard solution to a 25-mL volumetric flask and dilute with Mobile phase to volume.
  - **Sample stock solution**: Nominally 0.1 mg/mL of guanfacine in Mobile phase prepared as follows. Finely powder NLT 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to 10 mg of guanfacine, to a 100-mL volumetric flask. Add 50 mL of Mobile phase and heat on a steam bath for 5 min. Cool to room temperature and dilute with Mobile phase to volume.
  - **Sample solution**: Nominally 0.04 mg/mL of guanfacine, 3.6 μg/mL of 2,6-dichlorophenylacetic acid, and 0.1 mg/mL of butylparaben from Sample stock solution in Mobile phase prepared as follows. Transfer 10.0 mL of Sample stock solution to a 25-mL volumetric flask, add 5.0 mL of Internal standard solution and dilute with Mobile phase to volume.

**Chromatographic system**
(See Chromatography (621), System Suitability.)
- **Mode**: LC
- **Detector**: UV 220 nm
- **Column**: 3.9-mm × 30-cm; packing L1
- **Flow rate**: 1 mL/min
Injection volume: 20 µL

System suitability

Sample: Standard solution

[Note—The relative retention times for guanfacine, 2,6-dichlorophenylacetic acid, and butylparaben are 0.4, 0.6, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between guanfacine and 2,6-dichlorophenylacetic acid and NLT 1.5 between 2,6-dichlorophenylacetic acid and butylparaben

Relative standard deviation: NMT 2.0%

Analysis

Samples: Sample solution and Standard solution

Calculate the percentage of guanfacine (C₁₃H₁₄Cl₂N₃O) in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{R_U}{R_S} \right) \times \left( \frac{C_S}{C_U} \right) \times \left( \frac{M_{r1}}{M_{r2}} \right) \times 100
\]

\( R_U \) = peak response ratio of guanfacine to butylparaben from the Sample solution

\( R_S \) = peak response ratio of guanfacine to butylparaben from the Standard solution

\( C_S \) = concentration of USP Guanfacine Hydrochloride RS in the Standard solution (mg/mL)

\( C_U \) = nominal concentration of guanfacine in the Sample solution (mg/mL)

\( M_{r1} \) = molecular weight of guanfacine, 246.09

\( M_{r2} \) = molecular weight of guanfacine hydrochloride, 282.55

Acceptance criteria: 90.0%—110.0%

PERFORMANCE TESTS

Change to read:

• Dissolution (711)

  Medium: water; 500 mL, deaerated, if necessary (TBD)

  Apparatus 2: 50 rpm

  Time: 45 min

Analysis: Determine the amount of guanfacine (C₁₃H₁₄Cl₂N₃O) dissolved using the procedure in the Assay, and making any necessary modifications.

Tolerances: NLT 75% (Q) of the labeled amount of guanfacine (C₁₃H₁₄Cl₂N₃O) is dissolved.

• Uniformity of Dosage Units (905): Meet the requirements

ADDITIONAL REQUIREMENTS

• Packaging and Storage: Preserve in tight, light-resistant containers.

• USP Reference Standards (11)

  USP Guanfacine Hydrochloride RS