Guanfacine Tablets

Type of Posting	Notice of Intent to Revise
Posting Date	28-Apr-2023
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 2

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 to add *Dissolution Test 2*. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

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 II (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*.

Notice of Intent to Revise
Official: To Be Determined

Guanfacine Tablets

DEFINITION

Guanfacine Tablets contain an amount of Guanfacine Hydrochloride ($C_9H_9Cl_2N_3O \cdot HCl$) equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of guanfacine ($C_9H_9Cl_2N_3O$).

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 and 0.1 mg/mL of butylparaben 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 ($C_9H_9Cl_2N_3O$) in the portion of Tablets taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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⟩

▲Test 1▲ (TBD)

Medium: water; 500 mL

Apparatus 2: 50 rpm

Time: 45 min

Analysis: Determine the amount of guanfacine ($C_9H_9Cl_2N_3O$) dissolved using the procedure in the *Assay*, and making any necessary modifications.

Tolerances: NLT 75% (Q) of the labeled amount of guanfacine ($C_9H_9Cl_2N_3O$) is dissolved.

▲Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Solution A: Add 10.3 mL of diethylamine to 70 mL of water. Adjust with phosphoric acid to a pH of 2.5. Dilute to 100 mL with water.

Mobile phase: Dissolve 662.5 mg of potassium phosphate, monobasic and 3 mL of *Solution A* in 530 mL of water. Adjust with 0.2 N sodium hydroxide solution to a pH of 4.0. Add 470 mL of acetonitrile

and mix.

Standard solution: (*L*/500) mg/mL of guanfacine from USP Guanfacine Hydrochloride RS in *Medium*, where *L* is the label claim in mg/Tablet. Sonicate to dissolve.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of the filtrate.

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of guanfacine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of guanfacine ($C_9H_9Cl_2N_3O$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

r_U = peak response of guanfacine from the *Sample solution*

r_S = peak response of guanfacine from the *Standard solution*

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

V = volume of *Medium*, 500 mL

M_{r1} = molecular weight of guanfacine, 246.09

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

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of guanfacine ($C_9H_9Cl_2N_3O$) is dissolved. ▲ (TBD)

- **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

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

Add the following:

▲- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used. ▲ (TBD)

- **USP Reference Standards** ⟨11⟩

USP Guanfacine Hydrochloride RS

Page Information:

Not Applicable

Current DocID: