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Guanfacine Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-guanfacine-tabs-20240126.

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

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▲, deaerated, if necessary▲ (RB 1-Feb-2024)

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.

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

ADDITIONAL REQUIREMENTS

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

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

• **USP Reference Standards ⟨11⟩**

USP Guanfacine Hydrochloride RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
GUANFACINE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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