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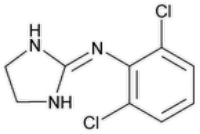
Clonidine Hydrochloride



· HCl

$C_9H_9Cl_2N_3 \cdot HCl$ 266.55

Benzenamine, 2,6-dichloro-*N*-2-imidazolidinylidene-, monohydrochloride;

2-[(2,6-Dichlorophenyl)imino]imidazolidine monohydrochloride CAS RN®: 4205-91-8; UNII: W76I6XXF06.

DEFINITION

Change to read:

Clonidine Hydrochloride contains NLT ▲98.0%▲ (USP 1-May-2020) and NMT ▲102.0%▲ (USP 1-May-2020) of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197A or 197K▲ (CN 1-May-2020)

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2020)

• **C.** Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*: Meets the requirements

ASSAY

Change to read:

• **Procedure**

Solution A: 1.0 mL/L of triethylamine in water

Mobile phase: Acetonitrile and *Solution A* (32:68). Adjust with phosphoric acid to a pH of 6.9.

▲▲ (USP 1-May-2020)

Standard solution: 0.05 mg/mL of USP Clonidine Hydrochloride RS in *Mobile phase*▲▲ (USP 1-May-2020)

Sample solution: 0.05 mg/mL of Clonidine Hydrochloride in *Mobile phase*▲▲ (USP 1-May-2020)

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: 2 mL/min

Injection volume: 50 µL

▲**Run time:** NLT 3 times the retention time of clonidine▲ (USP 1-May-2020)

System suitability

Sample: ▲▲ (USP 1-May-2020) *Standard solution*

Suitability requirements

▲▲ (USP 1-May-2020)

Tailing factor: NMT 2.0

Relative standard deviation: NMT ▲0.73%▲ (USP 1-May-2020)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$) in the portion of Clonidine Hydrochloride taken:

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

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

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

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

C_U = concentration of Clonidine Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: ▲98.0%–102.0%▲ (USP 1-May-2020) on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities**

Solution A and **Mobile phase:** Prepare as directed in the *Assay*.

Standard stock solution: 0.06 mg/mL each of USP Clonidine Hydrochloride RS, USP Clonidine Related Compound A RS, and 2,6-dichloroaniline in acetonitrile ▲▲ (USP 1-May-2020)

Standard solution: 0.6 µg/mL each of USP Clonidine Hydrochloride RS, ▲USP Clonidine Related Compound A RS, and 2,6-dichloroaniline▲ (USP 1-May-2020) in *Mobile phase* from the *Standard stock solution*

▲**Sensitivity solution:** 0.06 µg/mL each of USP Clonidine Hydrochloride RS, USP Clonidine Related Compound A RS, and 2,6-dichloroaniline in *Mobile phase* from the *Standard solution*

Sample stock solution: 1.5 mg/mL of Clonidine Hydrochloride in *Mobile phase* prepared as follows. Transfer 150 mg of Clonidine Hydrochloride to a 100-mL volumetric flask. Add *Mobile phase* to about 60% of the volume of the flask, sonicate for 5 min, and then dilute with *Mobile phase* to volume.▲ (USP 1-May-2020)

Sample solution: 150 µg/mL of Clonidine Hydrochloride in *Mobile phase* ▲from the *Sample stock solution*▲ (USP 1-May-2020)

Chromatographic system: ▲Proceed as directed in the *Assay*, except for the *Run time*.▲ (USP 1-May-2020)

Run time: ▲NLT 6▲ (USP 1-May-2020) times the retention time of clonidine

System suitability

Samples: *Standard solution*▲and *Sensitivity solution*

[Note—See *Table 1* for the relative retention times.]▲ (USP 1-May-2020)

Suitability requirements

Resolution: NLT 2.0 between clonidine related compound A and 2,6-dichloroaniline, *Standard solution*

▲▲ (USP 1-May-2020)

Relative standard deviation: NMT 5% for ▲clonidine, clonidine related compound A, and 2,6-dichloroaniline,▲ (USP 1-May-2020) *Standard solution*

▲**Signal-to-noise ratio:** NLT 10 for clonidine, clonidine related compound A, and 2,6-dichloroaniline, *Sensitivity solution*▲ (USP 1-May-2020)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clonidine related compound A and 2,6-dichloroaniline in the portion of Clonidine Hydrochloride taken:

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

r_U = peak response of clonidine related compound A or 2,6-dichloroaniline from the *Sample solution*

r_S = peak response of clonidine related compound A or 2,6-dichloroaniline from the *Standard solution*

C_S = concentration of USP Clonidine Related Compound A RS or 2,6-dichloroaniline in the *Standard solution* ▲(µg/mL)▲ (USP 1-May-2020)

C_U = concentration of Clonidine Hydrochloride in the *Sample solution* ▲(µg/mL)▲ (USP 1-May-2020)

Calculate the percentage of any ▲▲ (USP 1-May-2020) unspecified impurity in the portion of Clonidine Hydrochloride taken:

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

r_U = peak response of any ▲▲ (USP 1-May-2020) unspecified impurity from the *Sample solution*

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

C_S = concentration of USP Clonidine Hydrochloride RS in the *Standard solution* ▲(µg/mL)▲ (USP 1-May-2020)

C_U = concentration of Clonidine Hydrochloride in the *Sample solution* ▲(µg/mL)▲ (USP 1-May-2020)

Acceptance criteria: See *Table 1*. ▲The reporting threshold is▲ (USP 1-May-2020) 0.04%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Clonidine ▲▲ (USP 1-May-2020)	1.0	—
Clonidine related compound A ▲▲ (USP 1-May-2020)	2.5	0.1
2,6-Dichloroaniline	3.3	0.1
Any ▲▲ (USP 1-May-2020) unspecified impurity	—	0.1
Total impurities	—	0.2

▲ ▲ (USP 1-May-2020)

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 50 mg/mL

Acceptance criteria: 3.5–5.5

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° to constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Clonidine Hydrochloride RS

USP Clonidine Related Compound A RS

1-Acetyl-2-(2,6-dichlorophenylimino)-imidazolidine).

$C_{11}H_{11}Cl_2N_3O$ 272.13

Topic/Question	Contact	Expert Committee
CLONIDINE HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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