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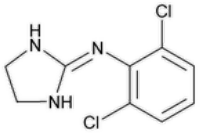
Clonidine



$C_9H_9Cl_2N_3$ 230.09

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

2-[(2,6-Dichlorophenyl)imino]imidazolidine CAS RN®: 4205-90-7; UNII: MN3L5RMN02.

DEFINITION

Clonidine contains NLT 99.0% and NMT 101.0% of clonidine ($C_9H_9Cl_2N_3$), calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**
- **B. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

Medium: 0.01 N hydrochloric acid

Sample solution: 0.3 mg/mL of Clonidine in *Medium*

Acceptance criteria: Absorptivities are about 2.1 and 1.8 for the maxima at 271 nm and 279 nm, respectively, calculated on the dried basis.

ASSAY

- **Procedure**

Sample solution: 190 mg of Clonidine in 100 mL of glacial acetic acid

Analysis: Titrate with 0.1 N perchloric acid VS, using a silver–silver chloride glass combination electrode with liquid junction. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 23.01 mg of clonidine ($C_9H_9Cl_2N_3$).

Acceptance criteria: 99.0%–101.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩**

Analysis: Ignite at 500 ± 25° to constant weight.

Acceptance criteria: NMT 0.1%

- **Organic Impurities**

1 M phosphoric acid: 115 g/L of phosphoric acid in water

Buffer: 4 g/L of monobasic potassium phosphate in water. Adjust with *1 M phosphoric acid* to a pH of 4.0.

Solution A: Acetonitrile and *Buffer* (75:25)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Buffer (%)	Solution A (%)
0	90	10
15	30	70
15.1	90	10

Time (min)	Buffer (%)	Solution A (%)
20	90	10

Acetylclonidine solution: 0.05 mg/mL of USP Clonidine Related Compound A RS, prepared as follows. Initially dissolve USP Clonidine Related Compound A RS in acetonitrile (1 mg/mL), and dilute with *Buffer* to volume.

System suitability solution: 0.86 mg/mL of USP Clonidine RS and 0.86 µg/mL of clonidine related compound A from *Acetylclonidine solution* in *Buffer*

Standard solution: 8.6 µg/mL of USP Clonidine RS in *Buffer*

Sample solution: 0.86 mg/mL of Clonidine in *Buffer*

Blank: *Buffer*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 3.0-mm × 15-cm; 5-µm packing L56

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 5 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 5 between clonidine and acetylclonidine, *System suitability solution*

Tailing factor: NMT 2.5 for clonidine, *System suitability solution*

Relative standard deviation: NMT 5%, *Standard solution*

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Calculate the percentage of each impurity in the portion of Clonidine taken:

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

r_U = peak response for each impurity from the *Sample solution*

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

C_S = concentration of the *Standard solution* (µg/mL)

C_U = concentration of the *Sample solution* (µg/mL)

Acceptance criteria

Individual impurity: NMT 0.1%

Total impurities: NMT 0.2%

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩**

Analysis: Dry a sample at 60° under vacuum to constant weight.

Acceptance criteria: NMT 0.5%

- **Appearance of Solution**

Color of solution

Standard solution: 4.8 µg/mL of potassium chromate in water

Sample solution: 100 mg/mL in methanol

Acceptance criteria: The color of 10 mL of *Sample solution* is not more intense than that of 10 mL of *Standard solution* when compared in matched color-comparison tubes (see *Visual Comparison ⟨630⟩*).

Turbidity

Sample solution: Prepare as directed in *Color of solution*.

Acceptance criteria: 10 mL of *Sample solution* has no more turbidity than 10 mL of methanol when compared in matched color-comparison tubes (see *Visual Comparison ⟨630⟩*).

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Clonidine RS

USP Clonidine Related Compound A RS

1-Acetyl-2-(2,6-▲dichlorophenylimino)imidazolidine.▲ (ERR 1-Mar-2021)

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

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 49(2)

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