Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Aug-2023
Document Type: USP Monographs
DocId: GUID-0EA19159-B65C-4BFE-8700-822FDE2A54D4_3_en-US
DOI: https://doi.org/10.31003/USPNF_M18650_03_01
DOI Ref: ae2z0

Clonidine Hydrochloride Tablets

DEFINITION
Clonidine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$).

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*.

Change to read:

• **B. Thin-Layer Chromatography**

Standard solution: 10 mg/mL of USP Clonidine Hydrochloride RS in methanol

Sample solution: ▲Nominally 10 mg/mL of clonidine hydrochloride prepared as follows.▲ (USP 1-Aug-2023) Transfer ▲▲ (USP 1-Aug-2023) 1 mg of clonidine hydrochloride, from a quantity of finely powdered Tablets, to a separator containing 30 mL of water and 5 mL of 1 N sodium hydroxide. Swirl gently to dissolve the sample specimen, and extract with 20 mL of chloroform. Allow the layers to separate, and filter the chloroform extract. Evaporate the filtrate to dryness, and dissolve the residue in 0.1 mL of methanol.

Chromatographic system
(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

▲Mode: TLC▲ (USP 1-Aug-2023)

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 2 µL

Developing solvent system: Methanol and ammonium hydroxide (200:3)

Analysis

Samples: *Standard solution* and *Sample solution*

▲▲ (USP 1-Aug-2023) Position the plate in a chromatographic chamber, and develop in *Developing solvent system* until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Examine the plate under short-wavelength UV light.

Acceptance criteria: The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*.

ASSAY

Change to read:

• **Procedure**

Solution A: 2.2 ▲g/L▲ (USP 1-Aug-2023) of ▲octanesulfonic acid sodium salt▲ (USP 1-Aug-2023) in water

Mobile phase: Methanol, *Solution A*, and phosphoric acid (500:500:1). Adjust with 1 N sodium hydroxide to a pH of 3.0.

▲▲ (USP 1-Aug-2023)

Standard stock solution: 100 µg/mL of USP Clonidine Hydrochloride RS in *Mobile phase*.▲Sonicate to dissolve if necessary.▲ (USP 1-Aug-2023)

Standard solution: 1 µg/mL of ▲USP Clonidine Hydrochloride RS▲ (USP 1-Aug-2023) from the *Standard stock solution* in *Mobile phase*

▲▲ (USP 1-Aug-2023)

Sample solution: ▲Nominally 1 µg/mL of clonidine hydrochloride in *Mobile phase* prepared as follows.▲ (USP 1-Aug-2023) Weigh and finely powder Tablets (NLT 20). Transfer ▲a suitable portion▲ (USP 1-Aug-2023) equivalent to 0.1 mg of clonidine hydrochloride ▲▲ (USP 1-Aug-2023) to a 100-mL volumetric flask. Add about 60 mL of *Mobile phase*, shake by mechanical means for 15–30 min, and dilute with *Mobile phase* to volume.▲▲ (USP 1-Aug-2023) Centrifuge a portion of this solution to obtain a clear solution.

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; packing L7, deactivated for basic compounds

Flow rate: 1.5 mL/min

Injection volume: 50 µL

▲**Run time:** NLT 3 times the retention time of clonidine▲ (USP 1-Aug-2023)

System suitability

Sample: *Standard solution*▲▲ (USP 1-Aug-2023)

Suitability requirements

Tailing factor: NMT 1.5

▲▲ (USP 1-Aug-2023)

Relative standard deviation: NMT ▲1.0%▲ (USP 1-Aug-2023)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$) in the portion of ▲Tablets▲ (USP 1-Aug-2023) taken:

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

r_U = peak response ▲of clonidine▲ (USP 1-Aug-2023) from the *Sample solution*

r_S = peak response ▲of clonidine▲ (USP 1-Aug-2023) from the *Standard solution*

C_S = concentration of ▲USP Clonidine Hydrochloride RS in▲ (USP 1-Aug-2023) the *Standard solution* (µg/mL)

C_U = nominal concentration of clonidine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: 0.01 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm

Time: 30 min

▲**Solution A, Mobile phase, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay*.▲ (USP 1-Aug-2023)

Standard solution: Prepare as directed in the *Assay*, except use *Medium* instead of *Mobile phase*.

▲**Sample solution:** A portion of the solution under test▲ (USP 1-Aug-2023)

Analysis

▲**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$) dissolved:

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

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)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)▲ (USP 1-Aug-2023)

Tolerances: NLT 75% (Q) of the labeled amount of clonidine hydrochloride ($C_9H_9Cl_2N_3 \cdot HCl$) is dissolved.

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

Add the following:

▲IMPURITIES

• **Organic Impurities**

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

System suitability solution: 10 µg/mL each of USP Clonidine Hydrochloride RS and USP Clonidine Related Compound C RS in *Mobile phase*. Sonicate to dissolve if necessary.

Standard solution: 0.2 µg/mL of USP Clonidine Hydrochloride RS in *Mobile phase*. Sonicate to dissolve if necessary.

Sensitivity solution: 0.04 µg/mL of USP Clonidine Hydrochloride RS from the *Standard solution* in *Mobile phase*

Sample solution: Nominally 40 µg/mL of clonidine hydrochloride in *Mobile phase* prepared as follows. Transfer an appropriate quantity of clonidine hydrochloride from the powdered Tablets (NLT 20) to a suitable volumetric flask. Add *Mobile phase* to 80% of the total volume and sonicate for 15 min. Dilute with *Mobile phase* to volume. Centrifuge a portion of this solution and pass the supernatant through a suitable nylon membrane filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 50 µL

Run time: NLT 8 times the retention time of clonidine

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between clonidine and clonidine related compound C, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any specified and unspecified degradation product in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of any specified or unspecified degradation product 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)

C_U = nominal concentration of clonidine hydrochloride in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.1%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Ethylenediamine tosylate[a]	0.23	0.98	0.10
Clonidine	1.0	—	—
Clonidine related compound C	1.20	1.6	0.20
Any unspecified degradation			

[a] Ethane-1,2-diamine 4-methylbenzenesulfonate.	—	1.0	0.50
Total degradation products	—	—	1.0▲ (USP 1-Aug-2023)

ADDITIONAL REQUIREMENTS

Change to read:

• **PACKAGING AND STORAGE:** Preserve in well-closed containers. ▲Store at controlled room temperature.▲ (USP 1-Aug-2023)

Change to read:

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Clonidine Hydrochloride RS

▲ USP Clonidine Related Compound C RS

Methyl *N*'-(2,6-dichlorophenyl)carbamimidothioate.

$C_8H_8Cl_2N_2S$ 235.13▲ (USP 1-Aug-2023)

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 47(5)

Current DocID: GUID-0EA19159-B65C-4BFE-8700-822FDE2A54D4_3_en-US

DOI: https://doi.org/10.31003/USPNF_M18650_03_01

DOI ref: ae2z0