

Status: Currently Official on 14-Feb-2025
 Official Date: Official as of 01-May-2021
 Document Type: USP Monographs
 DocId: GUID-E4E0BAD5-FDD5-4B55-97FD-325E01D7143F_3_en-US
 DOI: https://doi.org/10.31003/USPNF_M19050_03_01
 DOI Ref: tl3wd

© 2025 USPC
 Do not distribute

Clozapine Tablets

DEFINITION

Clozapine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of clozapine ($C_{18}H_{19}ClN_4$).

IDENTIFICATION

Change to read:

- **A.** ▲The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay. ▲ (USP 1-May-2021)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

• PROCEDURE

Mobile phase: [Methanol](#) ▲ (USP 1-May-2021) and [water](#) ▲ (80:20). To each liter add 0.75 mL of [triethylamine](#). ▲ (USP 1-May-2021)

System suitability stock solution: Transfer 10 mg of clozapine to a suitable container, add 5 mL of ▲[0.1 N hydrochloric acid VS](#), ▲ (USP 1-May-2021) and heat for 2 h at 90°. Transfer this solution to a 100-mL volumetric flask, add 15 mL of [water](#), and dilute with [methanol](#) to volume.

Standard solution: 0.125 mg/mL of [USP Clozapine RS](#) prepared as follows. Transfer ▲a suitable portion of [USP Clozapine RS](#) to an appropriate volumetric flask. ▲ (USP 1-May-2021) Dissolve in 80% of the flask volume of [methanol](#). ▲Dilute with [water](#) to volume. ▲ (USP 1-May-2021)

System suitability solution: *System suitability stock solution* and *Standard solution* ▲(50:50) ▲ (USP 1-May-2021)

Sample solution: ▲Nominally 0.125 mg/mL of clozapine from Tablets prepared as follows. Finely powder NLT 20 Tablets and transfer a portion of powder equivalent to 125 mg of clozapine to a 1-L volumetric flask. Dissolve in 640 mL of [methanol](#), sonicate for 10 min, and dilute with [water](#) to volume. Pass the resulting solution through an appropriate filter and use the filtrate. ▲ (USP 1-May-2021)

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 257 nm. ▲For *Identification A*, use a diode array detector in the range of 210–400 nm. ▲ (USP 1-May-2021)

Column: 4.0-mm × 25-cm; ▲10-μm ▲ (USP 1-May-2021) packing [L7](#)

Flow rate: 1 mL/min

Injection ▲volume: ▲ (USP 1-May-2021) 10 μL

▲**Run time:** NLT 3 times the retention time of clozapine ▲ (USP 1-May-2021)

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between the clozapine peak and any other peak, *System suitability solution*

Column efficiency: NLT 1500 theoretical plates, *Standard solution*

Relative standard deviation: NMT ▲1.0% ▲ (USP 1-May-2021) for replicate injections, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clozapine ($C_{18}H_{19}ClN_4$) in the portion of Tablets taken:

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

r_U = peak response ▲ of clozapine ▲ (USP 1-May-2021) from the *Sample solution*

r_S = peak response ▲ of clozapine ▲ (USP 1-May-2021) from the *Standard solution*

C_S = concentration of [USP Clozapine RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of clozapine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#)

Medium: pH 4.0 acetate buffer ▲ (USP 1-May-2021) (Dissolve 2 g of [sodium hydroxide](#) in 450 mL of [water](#). Adjust with [glacial acetic acid](#) to a pH of 4.0. Dilute ▲ with [water](#) ▲ (USP 1-May-2021) to 1 L.); 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Standard solution: ▲ (L/900) mg/mL of [USP Clozapine RS](#) in *Medium*, where L is the label claim, in mg/Tablet. Dilute with *Medium*, if necessary. ▲ (USP 1-May-2021)

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary.

Instrumental conditions

Mode: UV

Analytical wavelength: 290 nm

Analysis

Samples: *Standard solution* and *Sample solution*

▲ Calculate the percentage of the labeled amount of clozapine ($C_{18}H_{19}ClN_4$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = absorbance of clozapine from the *Sample solution*

A_S = absorbance of clozapine from the *Standard solution*

C_S = concentration of [USP Clozapine RS](#) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

D = dilution factor, if needed

L = label claim (mg/Tablet) ▲ (USP 1-May-2021)

Tolerances: NLT 85% (Q) of the labeled amount of clozapine ($C_{18}H_{19}ClN_4$) is dissolved.

• [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

▲ **Buffer:** 2.0 g/L of [monobasic potassium phosphate](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 2.4–2.5.

Solution A: [Acetonitrile](#), [methanol](#), and *Buffer* (10:10:80)

Solution B: [Acetonitrile](#), [methanol](#), and *Buffer* (40:40:20)

Mobile phase: See [Table 1](#).

Table 1