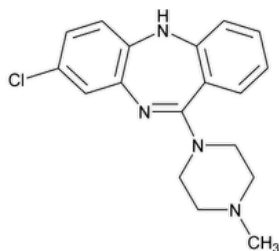


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Clozapine



$C_{18}H_{19}ClN_4$ 326.83

5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(4-methyl-1-piperazinyl)-;

8-Chloro-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e][1,4]diazepine CAS RN®: 5786-21-0.

DEFINITION

Clozapine contains NLT 98.0% and NMT 102.0% of clozapine ($C_{18}H_{19}ClN_4$), calculated on the dried basis.

IDENTIFICATION

- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197K or 197A
- **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

PROCEDURE

Mobile phase: [Methanol](#) and [water](#) (80:20). To each liter add 0.75 mL of [triethylamine](#).

Diluent: [Methanol](#) and [water](#) (80:20)

System suitability stock solution: Transfer 10 mg of [USP Clozapine RS](#) to a suitable container, add 5 mL of [0.1 N hydrochloric acid VS](#) 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: 0.1 mg/mL of [USP Clozapine RS](#) in *Diluent*

System suitability solution: *System suitability stock solution* and *Standard solution* (50:50)

Sample solution: 0.1 mg/mL of Clozapine in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 257 nm

Column: 4.6-mm × 25-cm; 5-μm packing [L7](#)

Flow rate: 1 mL/min

Injection volume: 10 μL

Run time: NLT 3 times the retention time of clozapine

System suitability

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

Suitability requirements

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

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

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. [NOTE—The pH of this solution must not be below 2.4.]

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

Time (min)	Solution A (%)	Solution B (%)
0	100	0
4	100	0
24	0	100
29	0	100
40	100	0

Diluent: [Methanol](#) and [water](#) (80:20)

System suitability solution: Dissolve 4 mg of [USP Clozapine Resolution Mixture RS](#) in 4 mL of methanol, add 1 mL of water, and dilute with *Diluent* to 10 mL.

Standard solution: 0.75 µg/mL of [USP Clozapine RS](#) in *Diluent*

Sample solution: 750 µg/mL of Clozapine prepared as follows. Transfer a suitable quantity of Clozapine to a suitable volumetric flask. Dissolve in 80% of the flask volume of [methanol](#), sonicate for about 3 min, and dilute with [water](#) to volume.

Chromatographic system

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

Mode: LC

Detector: UV 257 nm

Column: 4.6-mm × 15-cm; 5-µm packing [L1](#)

Flow rate: 1.2 mL/min

Injection volume: 20 µL

System suitability

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

[NOTE— See [Table 2](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 2.5 between demethyl clozapine and clozapine, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each related compound and any unknown impurity in the portion of Clozapine taken:  **Documents** Document Sharing Hub