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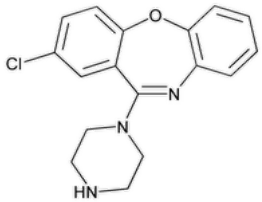
Amoxapine



$C_{17}H_{16}ClN_3O$ 313.78

Dibenz[*b*,*f*][1,4]oxazepine, 2-chloro-11-(1-piperazinyl)-;

2-Chloro-11-(1-piperazinyl)dibenz[*b*,*f*][1,4]oxazepine CAS RN®: 14028-44-5; UNII: R63VQ857OT.

DEFINITION

Amoxapine contains NLT 98.0% and NMT 102.0% of amoxapine ($C_{17}H_{16}ClN_3O$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **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**

Buffer: 3.9 g/L of ammonium acetate in water adjusted with acetic acid or diluted ammonia solution to a pH of 7.3

Mobile phase: Acetonitrile and *Buffer* (30:70)

Diluent: Acetonitrile and *Buffer* (70:30)

System suitability solution: 0.1 mg/mL each of USP Amoxapine RS and USP Amoxapine Related Compound G RS in *Diluent*

Standard solution: 0.1 mg/mL of USP Amoxapine RS in *Diluent*

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

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 7.5-cm; 2.5-µm or 2.7-µm packing L1

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

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

[Note—The relative retention times for amoxapine and amoxapine related compound G are 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 1.5 between amoxapine and amoxapine related compound G, *System suitability solution*

Tailing factor: 0.8–1.8, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amoxapine ($C_{17}H_{16}ClN_3O$) in the portion of Amoxapine taken:

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

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

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

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

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Solution A: 3.9 g/L of ammonium acetate in water adjusted with acetic acid or diluted ammonia solution to a pH of 7.3

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
5	70	30
7.5	60	40
15	60	40
20	20	80
25	20	80
30	70	30
35	70	30

Diluent: *Solution A* and *Solution B* (30:70)

System suitability solution: 1 mg/mL of USP Amoxapine RS and 1.5 µg/mL of USP Amoxapine Related Compound G RS in *Diluent*

Standard solution: 1 µg/mL of USP Amoxapine RS, and 1.5 µg/mL each of USP Amoxapine Related Compound G RS and USP Amoxapine Related Compound D RS in *Diluent*

Sample solution: 1000 µg/mL of Amoxapine in *Diluent*

Chromatographic system: Proceed as directed in the *Assay*.

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Peak-to-valley ratio: NLT 3 between amoxapine and amoxapine related compound G, *System suitability solution*

Relative standard deviation: NMT 5.0% each for amoxapine, amoxapine related compound G, and amoxapine related compound D, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of amoxapine related compound G and amoxapine related compound D in the portion of Amoxapine taken:

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

r_U = peak response of amoxapine related compound G or amoxapine related compound D from the *Sample solution*

r_S = peak response of amoxapine related compound G or amoxapine related compound D from the *Standard solution*

C_S = concentration of USP Amoxapine Related Compound G RS or USP Amoxapine Related Compound D RS in the *Standard solution* (µg/mL)

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

Calculate the percentage of any other impurity in the portion of Amoxapine taken:

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

r_U = peak response of any other impurity from the *Sample solution*

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

C_S = concentration of USP Amoxapine RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: See *Table 2*. Disregard peaks that are less than 0.02% of the amoxapine peak.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Chlorophenoxyaniline urea analog[a]	0.57	0.10
Amoxapine	1.0	—
Amoxapine related compound G	1.4	0.15
Amoxapine related compound D	1.7	0.15
Chlorophenoxyaniline[b]	2.9	0.10
Chlorophenoxyaniline carbamate[c]	3.8	0.10
N-Carbamoyl amoxapine[d]	4.3	0.10
Amoxapine dimer[e]	5.0	0.10
Any individual unspecified impurity	—	0.10
Total impurities	—	0.50

[a] *N*-[2-(4-Chlorophenoxy)phenyl]piperazine-1-carboxamide.

[b] 2-(4-Chlorophenoxy)aniline.

[c] Ethyl [2-(4-Chlorophenoxy)phenyl]carbamate.

[d] 4-(2-Chlorodibenzo[*b*,*f*][1,4]oxazepin-11-yl)-*N*-[2-(4-chlorophenoxy)phenyl]piperazine-1-carboxamide.

[e] 1,4-Bis(2-chlorodibenzo[*b*,*f*][1,4]oxazepine-11-yl)piperazine.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards** ⟨11⟩

USP Amoxapine RS

USP Amoxapine Related Compound D RS

2-Chlorodibenzo[*b*,*f*]-[1,4]-oxazepin-11-one.

$C_{13}H_8ClNO_2$ 245.66

USP Amoxapine Related Compound G RS

3-Chloro-11-(piperazin-1-yl)dibenzo[*b*,*f*][1,4]oxazepine.

$C_{17}H_{16}ClN_3O$ 313.78

Topic/Question	Contact	Expert Committee
AMOXAPINE	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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