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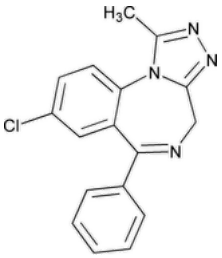
Alprazolam



$C_{17}H_{13}ClN_4$ 308.76

4*H*-[1,2,4]Triazolo[4,3-α][1,4]benzodiazepine, 8-chloro-1-methyl-6-phenyl-;

8-Chloro-1-methyl-6-phenyl-4*H*-*s*-triazolo[4,3-α][1,4] benzodiazepine CAS RN®: 28981-97-7; UNII: YU55MQ3IZY.

DEFINITION

Alprazolam contains NLT 98.0% and NMT 102.0% of $C_{17}H_{13}ClN_4$.

[CAUTION—Care should be taken to prevent inhaling particles of Alprazolam and exposing the skin to it.]

IDENTIFICATION

Change to read:

• **A.** ▲SPECTROSCOPIC IDENTIFICATION TESTS ⟨197⟩, *Infrared Spectroscopy*: **197M**▲ (CN 1-MAY-2020)

• **B.** The retention time of the major peak from the *Sample solution* corresponds to that from the *Standard solution*, as obtained in the *Assay.*

ASSAY

• **PROCEDURE**

Diluent: Acetonitrile and water (1:1)

Buffer: 1.4 g/L of monobasic potassium phosphate in water

Mobile phase: Acetonitrile and *Buffer* (1:1)

Standard solution: 25 µg/mL of USP Alprazolam RS in *Diluent*. [NOTE—The solution is stable for 48 h at room temperature when stored in closed containers.]

Sample solution: 25 µg/mL of Alprazolam in *Diluent*. Sonicate for about 1 min. [NOTE—The solution is stable for 48 h at room temperature when stored in closed containers.]

Chromatographic system

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

Mode: LC

Detector: UV 231 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of alprazolam ($C_{17}H_{13}ClN_4$) in the portion of Alprazolam taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0%

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.5%

• **Organic Impurities**

Diluent, Buffer, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 20 µg/mL each of USP Alprazolam RS, USP Alprazolam Related Compound A RS, and USP 2-Amino-5-chlorobenzophenone RS in *Diluent*

Standard solution: 0.25 µg/mL of USP Alprazolam RS in *Diluent*.[Note—When stored in closed containers, the solution is stable for 48 h at room temperature.]

Sample solution: 250 µg/mL of Alprazolam in *Diluent*. Sonicate for about 1 min. [Note—When stored in closed containers, the *Sample solution* is stable for 24 h at room temperature.]

System suitability

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

[Note—For relative retention times, see *Table 1*.]

Suitability requirements

Resolution: NLT 2.0 between alprazolam related compound A and alprazolam, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak response for alprazolam from the *Standard solution*

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Alprazolam related compound A	0.8	0.76	0.15
Alprazolam	1.0	1.0	—
2-Amino-5-chloro benzophenone	4.0	1.0	0.15
Individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩:** Dry a sample at 105° for 1 h: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Alprazolam RS

USP Alprazolam Related Compound A RS
2-(2-Acetylhydrazino)-7-chloro-5-phenyl-3*H*-1,4-benzodiazepine.
USP 2-Amino-5-chlorobenzophenone RS
2-Amino-5-chlorobenzophenone.
$C_{13}H_{10}ClNO$ 231.68

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

Topic/Question	Contact	Expert Committee
ALPRAZOLAM	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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