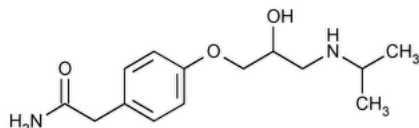


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Atenolol

Change to read:



$C_{14}H_{22}N_2O_3$ 266.34

Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]-;

2-{[▲]4[▲] (USP 1-May-2022) -[2-Hydroxy-3-(isopropylamino)propoxy]-phenyl}acetamide CAS RN[®]: 29122-68-7; UNII: 50VV3VW0T1.

DEFINITION

Atenolol contains NLT 98.0% and NMT 102.0% of atenolol ($C_{14}H_{22}N_2O_3$), calculated on the dried basis.

IDENTIFICATION

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

Change to read:

• **B.** [▲]The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay. [▲] (USP 1-May-2022)

ASSAY

Change to read:

PROCEDURE

[▲]**Buffer:** 3.4 g/L of [potassium phosphate, monobasic](#), 1.25 g/L of [octanesulfonic acid sodium salt](#), and 0.5 g/L of [tetrabutylammonium hydrogen sulfate](#)

0.8 M phosphoric acid solution: Dilute 5.2 mL of [phosphoric acid](#) in 100 mL of [water](#).

Mobile phase: [Methanol](#), [tetrahydrofuran](#), and *Buffer* (18:2:80). Adjust with 0.8 M phosphoric acid solution to a pH of 3.0.

Standard solution: 0.01 mg/mL of [USP Atenolol RS](#) in *Mobile phase*. Sonication may be necessary for complete dissolution.

Sample solution: 0.01 mg/mL of Atenolol in *Mobile phase*. Sonication may be necessary for complete dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

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

Flow rate: 1 mL/min

Injection volume: 10 μL

Run time: NLT 2 times the retention time of atenolol

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73% [▲] (USP 1-May-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of atenolol ($C_{14}H_{22}N_2O_3$) in the portion of Atenolol taken:

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

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

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

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

C_u = concentration of Atenolol in the *Sample solution* (mg/mL)

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

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.2%

Change to read:

- [CHLORIDE AND SULFATE \(221\)](#), *Chloride*

▲ **Standard solution:** 1.4 mL of [0.020 N hydrochloric acid](#) in 100 mL of 0.15 N nitric acid ▲ (USP 1-May-2022)

Sample solution: 1.0 g in 100 mL of 0.15 N nitric acid

Acceptance criteria: ▲ The *Sample solution* shows no more turbidity with 1 mL of silver nitrate TS than the *Standard solution* ▲ (USP 1-May-2022) (0.1%).

Change to read:

- **ORGANIC IMPURITIES**

▲ **Buffer and Mobile phase:** Prepare as directed in the Assay.

Impurity stock solutions 1–3: 0.1 mg/mL each of [USP Atenolol Related Compound A RS](#), [USP Atenolol Related Compound B RS](#), and [USP Atenolol Related Compound F RS](#) prepared as follows. Separately transfer an appropriate quantity of [USP Atenolol Related Compound A RS](#), [USP Atenolol Related Compound B RS](#), and [USP Atenolol Related Compound F RS](#) to individual suitable volumetric flasks. Add [methanol](#) to 10% of the final volume and sonicate to dissolve. Dilute with *Mobile phase* to volume.

Impurity stock solution 4: 0.1 mg/mL of [USP Atenolol Related Compound E RS](#) prepared as follows. Transfer an appropriate quantity of [USP Atenolol Related Compound E RS](#) to a suitable volumetric flask. Add [acetonitrile](#) to 50% of the final volume and sonicate to dissolve. Dilute with [water](#) to volume.

Sensitivity solution: 0.5 µg/mL of [USP Atenolol RS](#) in *Mobile phase*

Standard solution: 0.01 mg/mL of [USP Atenolol RS](#) and 0.005 mg/mL each of [USP Atenolol Related Compound A RS](#), [USP Atenolol Related Compound B RS](#), [USP Atenolol Related Compound E RS](#), and [USP Atenolol Related Compound F RS](#) from the corresponding *Impurity stock solution* in *Mobile phase*

Sample solution: 2 mg/mL of Atenolol in *Mobile phase* prepared as follows. Transfer a suitable amount of Atenolol to a suitable volumetric flask. Add *Mobile phase* to 50% of the final volume and sonicate to dissolve. Dilute with *Mobile phase* to volume.

Chromatographic system: Proceed as directed in the Assay, except for the *Run time*.

Run time: NLT 5 times the retention time of atenolol

System suitability

Samples: *Sensitivity solution* and *Standard solution*

[NOTE—See [Table 1](#) for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between atenolol related compound B and atenolol related compound A, *Standard solution*

Relative standard deviation: NMT 2.0% for atenolol and NMT 5.0% each for atenolol related compounds A, B, E, and F, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of atenolol related compounds A, B, E, and F in the portion of Atenolol taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times 100$$

r_u = peak response of atenolol related compound A, B, E, or F from the *Sample solution*

r_s = peak response of atenolol related compound A, B, E, or F from the *Standard solution*

C_s = concentration of the corresponding Reference Standard in the *Standard solution* (mg/mL)

C_u = concentration of Atenolol in the *Sample solution* (mg/mL)

Calculate the percentage of atenolol related compound G and any unspecified impurity in the portion of Atenolol taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times (1/F) \times 100$$

r_u = peak response of atenolol related compound G or any unspecified impurity from the *Sample solution*

r_s = peak response of atenolol from the *Standard solution*

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

C_u = concentration of Atenolol in the *Sample solution* (mg/mL)