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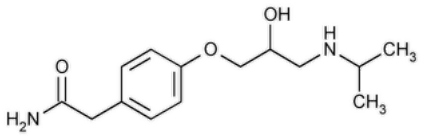
Atenolol

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: 50VV3VW0TI.

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)

F = relative response factor for atenolol related compound G or any unspecified impurity (see *Table 1*)

Acceptance criteria: See *Table 1*. The reporting threshold is 0.025%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Atenolol related compound B	0.31	—	0.15
Atenolol related compound A	0.41	—	0.15
Atenolol	1.0	—	—
Atenolol related compound E	1.72	—	0.15
Atenolol related compound F[a]	2.04 and 2.17	—	0.15
Atenolol related compound G[b]	3.58	0.84	0.15
Any unspecified impurity	—	1.00	0.10
Total impurities	—	—	0.50▲ (USP 1-May-2022)

[a] For quantification purposes, integrate the doublet peaks of atenolol related compound F.

[b] 2-{4-[2-Hydroxy-3-(isopropylamino)propoxy]phenyl}acetic acid.

SPECIFIC TESTS

Delete the following:

▲• **Melting Range or Temperature,** *Class I*⟨741⟩**:** 152°–156.5°▲ (USP 1-May-2022)

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° to constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in well-closed containers. Store at ▲controlled▲ (USP 1-May-2022) room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Atenolol RS

▲ USP Atenolol Related Compound A RS

2-(4-Hydroxyphenyl)acetamide.

$C_8H_9NO_2$ 151.17

USP Atenolol Related Compound B RS

2-[4-(2,3-Dihydroxypropoxy)phenyl]acetamide.

$C_{11}H_{15}NO_4$ 225.24

USP Atenolol Related Compound E RS

2,2'-{[(2-Hydroxypropane-1,3-diyl)bis(oxy)]bis(4,1-phenylene)}diacetamide.

$C_{19}H_{22}N_2O_5$ 358.39

USP Atenolol Related Compound F RS

2,2'-[{[(Isopropylazanediyl)bis(2-hydroxypropane-3,1-diyl)]bis(oxy)}bis(4,1-phenylene)]diacetamide.

$C_{25}H_{35}N_3O_6$ 473.57▲ (USP 1-May-2022)

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

Topic/Question	Contact	Expert Committee
ATENOLOL	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(6)
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