Status: Currently Official on 13-Feb-2025
Official Date: Official as of 01-May-2022
Document Type: USP Monographs
DocId: GUID-CADBAAB6-2C0C-496C-B9CC-93C2C29F654B_3_en-US
DOI: https://doi.org/10.31003/USPNF_M6335_03_01
DOI Ref: s10jk



# Atenolol Tablets

**DEFINITION**
Atenolol Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of atenolol ($C_{14}H_{22}N_2O_3$).

**IDENTIFICATION**

***Change to read:***

• **A.** ▲The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

***Change to read:***

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

**ASSAY**

***Change to read:***

• **Procedure**

▲**0.8 M phosphoric acid solution:** Dilute 5.2 mL of phosphoric acid in 100 mL of water.

**Buffer:** 1.1 g of sodium 1-heptanesulfonate; 0.71 g of sodium phosphate, dibasic, anhydrous; and 2 mL of dibutylamine in 700 mL of water. Adjust with *0.8 M phosphoric acid solution* to a pH of 3.0.▲ (USP 1-May-2022)

**Mobile phase:** ▲Methanol and *Buffer* (30:70)▲ (USP 1-May-2022)

**Standard solution:** 0.01 mg/mL of USP Atenolol RS in *Mobile phase*

▲▲ (USP 1-May-2022)

**Sample solution:** ▲Nominally 0.01 mg/mL of atenolol in *Mobile phase* prepared as follows. Transfer 10 Tablets to a 1000-mL volumetric flask. Add 500 mL of *Mobile phase* and sonicate for 15 min to disintegrate the Tablets. Dilute with *Mobile phase* to volume. Centrifuge a portion of the solution.▲ (USP 1-May-2022) Dilute a volume of the supernatant with *Mobile phase* to obtain a solution nominally containing 0.01 mg/mL of atenolol.

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

**Mode:** LC

**Detector:** UV 226 nm. ▲For *Identification A*, use a diode array detector in the range of 190–400 nm.▲ (USP 1-May-2022)

**Column:** 3.9-mm × 30-cm; ▲4-µm▲ (USP 1-May-2022) packing L1

**Flow rate:** 0.6 mL/min

**Injection volume:** 10 µL

**System suitability**

**Sample:** *Standard solution*

**Suitability requirements**

▲▲ (USP 1-May-2022)

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of ▲the labeled amount of▲ (USP 1-May-2022) atenolol ($C_{14}H_{22}N_2O_3$) in ▲the portion of Tablets▲ (USP 1-May-2022) 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)

$C_U$ = nominal concentration of atenolol in the *Sample solution* (mg/mL)

**Acceptance criteria:** 90.0%–110.0%

**PERFORMANCE TESTS**

***Change to read:***

• **Dissolution** ⟨711⟩

**Medium:** 0.1 N acetate buffer, pH 4.6 [prepared by mixing 44.9 parts (v/v) of 0.1 N sodium acetate with 55.1 parts (v/v) of 0.1 N acetic acid solution, and adjust with either diluted sodium hydroxide or diluted acetic acid to a pH of 4.6]; 900 mL

**Apparatus 2:** 50 rpm

**Time:** 30 min

▲▲ (USP 1-May-2022)

**Mobile phase, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay*. ▲▲ (USP 1-May-2022)

**Standard solution:** 0.01 mg/mL of USP Atenolol RS in *Mobile phase*

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Quantitatively dilute a measured volume of the filtrate with *Mobile phase* to obtain a solution estimated to contain about 0.01 mg/mL of atenolol.

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of ▲the labeled amount of▲ (USP 1-May-2022) atenolol ($C_{14}H_{22}N_2O_3$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times D \times (100/L)$$

$r_U$ = 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)

$V$ = volume of *Medium*, 900 mL

$D$ = dilution factor of the *Sample solution*

$L$ = label claim (mg/Tablet)

**Tolerances:** NLT 80% ($Q$) of the labeled amount of atenolol ($C_{14}H_{22}N_2O_3$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩**:** Meet the requirements

***Add the following:***

**▲IMPURITIES**

• **Organic Impurities**

**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.

**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:** 0.001 mg/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:** Nominally 2 mg/mL of atenolol in *Mobile phase* prepared as follows. Transfer an appropriate quantity of atenolol from powdered Tablets (NLT 20) to a suitable volumetric flask. Add *Mobile phase* to 50% of the final volume and sonicate for 15 min to dissolve. Dilute with *Mobile phase* to volume. Pass through a suitable filter of 0.45-µm pore size and discard the first 5 mL of filtrate.

**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 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 Tablets 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)

$C_U$ = nominal 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 Tablets 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)

$C_U$ = nominal 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 0.05%.

**Table 1**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Atenolol related compound B | 0.31 | — | 0.20 |
| Atenolol related compound A | 0.41 | — | 0.20 |
| Atenolol | 1.00 | — | — |
| Atenolol related compound E | 1.72 | — | 0.20 |
| Atenolol related compound F[a] | 2.04 and 2.17 | — | 0.20 |
| Atenolol related compound G[b] | 3.58 | 0.84 | 0.25 |
| Any unspecified impurity | — | 1.00 | 0.2 |
| Total impurities | — | — | 0.60▲ (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.

**ADDITIONAL REQUIREMENTS**

***Change to read:***

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

***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 TABLETS | Documentary Standards Support | SM22020 Small Molecules 2 |

**Chromatographic Database Information:** Chromatographic Database

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

**Current DocID: GUID-CADBAAB6-2C0C-496C-B9CC-93C2C29F654B_3_en-US**

**DOI: https://doi.org/10.31003/USPNF_M6335_03_01**

**DOI ref: s10jk**