of any individual impurity is found; and the sum of all impurities is not more than 1.0%.

Assay—

Mobile phase, *Standard preparation*, and *Chromatographic system*—Proceed as directed in the *Assay* under *Astemizole*.

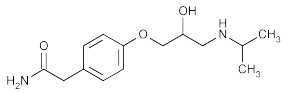
Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed quantity of the powder, equivalent to about 50 mg of astemizole, to a 50-mL volumetric flask. Add 25 mL of *Mobile phase*, mix for 30 minutes, dilute with *Mobile phase* to volume, and centrifuge. Use the supernatant as the *Assay preparation*.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of astemizole ($C_{28}H_{31}FN_4O$) in the portion of T ablets taken by the formula:

$$50C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Astemizole RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Atenolol



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

Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]-;
2-[*p*-[2-Hydroxy-3-(isopropylamino)propoxy]-phenyl]acetamide [29122-68-7].

DEFINITION

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

IDENTIFICATION

- **A. Infrared Absorption** ⟨**197K**⟩
- **B. Ultraviolet Absorption** ⟨**197U**⟩

Sample solution: 20 µg/mL in methanol

ASSAY

- **Procedure**

Mobile phase: 1.1 g of sodium 1-heptanesulfonate and 0.71 g of anhydrous dibasic sodium phosphate in 700 mL of water. Add 2 mL of dibutylamine, and adjust with 0.8 M phosphoric acid to a pH of 3.0. Add 300 mL of methanol, mix, and pass through a filter having a 0.5- µm or finer porosity. Degas this solution before use.

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

Sample solution: 0.01 mg/mL of Atenolol in *Mobile phase*. Sonicate for 5 min for complete dissolution.

Chromatographic system

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

Mode: LC
Detector: UV 226 nm
Column: 3.9-mm × 30-cm; packing L1
Flow rate: 0.6 mL/min
Injection size: 10 µL

System suitability

Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 5000 theoretical plates
Tailing factor: NMT 2.0
Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response from the *Sample solution*
r_S = peak response 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

Inorganic Impurities

- **Residue on Ignition** ⟨**281**⟩**:** NMT 0.2%
- **Chloride and Sulfate,** *Chloride* ⟨**221**⟩

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

Acceptance criteria: Shows no more turbidity with 1 mL of silver nitrate TS than 1.4 mL of 0.020 N hydrochloric acid in 100 mL of 0.15 N nitric acid (0.1%)

Organic Impurities

- **Procedure**

Mobile phase: Prepare as directed in the *Assay*.
Sample solution 1: 0.1 mg/mL of Atenolol in *Mobile phase*
Sample solution 2: 0.5 µg/mL of Atenolol, from *Sample solution 1* in *Mobile phase*
Chromatographic system: Proceed as directed in the *Assay*, except use the injection size listed below.
Injection size: 50 µL

Analysis

Samples: *Sample solution 1* and *Sample solution 2*

[Note—Chromatograph *Sample solution 1* for a period of time that is 6 times the retention time of the atenolol peak.]

Calculate the percentage of each impurity in *Sample solution 1*:

$$\text{Result} = 0.5(r_U/r_A)$$

r_U = peak response of any individual impurity in *Sample solution 1*
r_A = peak response of Atenolol in *Sample solution 2*

Acceptance criteria

Individual impurities: NMT 0.25%
Total impurities: NMT 0.5%

SPECIFIC TESTS

- **Melting Range or Temperature,** *Class I* ⟨**741**⟩**:** 152°–156.5°
- **Loss on Drying** ⟨**731**⟩**:** Dry a sample at 105 ° to constant weight: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

• **USP REFERENCE STANDARDS** ⟨11⟩
USP Atenolol RS

Atenolol Injection

» Atenolol Injection is a sterile solution of Atenolol in Water for Injection. It contains a suitable buffering agent. It contains not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of atenolol ($C_{14}H_{22}N_2O_3$).

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, in a cool place or at controlled room temperature, protected from light. Avoid freezing.

USP Reference standards ⟨11⟩**—**
USP Atenolol RS
USP Endotoxin RS

Identification—

A: The retention time of the main peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* obtained as directed in the *Assay*.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 10 µg of atenolol per mL.

Medium: methanol.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 33.3 USP Endotoxin Units per mg of atenolol.

Sterility ⟨71⟩**—**It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*.

pH ⟨791⟩: between 5.5 and 6.5.

Particulate matter ⟨788⟩: meets the requirements for small-volume injections.

Assay—

Citric acid buffer—Transfer 2.5 g of citric acid to a 500-mL volumetric flask, add 400 mL of water, and swirl to dissolve. Adjust the solution with 2 N sodium hydroxide to a pH of 6.0, dilute with water to volume, and mix.

Mobile phase—Dissolve 930 mg of sodium octyl sulfate in 740 mL of water, add 8 mL of 3.6 N sulfuric acid, mix, and pass through a 1-µm or finer porosity filter. To the filtrate add 250 mL of acetonitrile, mix, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Transfer about 50 mg of USP Atenolol RS to a 100-mL volumetric flask, add 80 mL of *Citric acid buffer*, and sonicate for about 30 seconds to achieve dissolution. Dilute with *Citric acid buffer* to volume, and mix. Transfer 4.0 mL of this solution to a 10-mL volumetric flask, dilute with *Citric acid buffer* to volume, and mix. This solution contains about 0.2 mg of USP Atenolol RS per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to 2 mg of atenolol, to a 10-mL volumetric flask, dilute with *Citric acid buffer* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 275-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.7 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of $C_{14}H_{22}N_2O_3$ in each mL of the Injection taken by the formula:

$$10(C / V)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Atenolol RS in the *Standard preparation; V* is the volume, in mL, of Injection taken; and r_U and r_S are the atenolol peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Atenolol Oral Solution

DEFINITION

Atenolol Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of $C_{14}H_{22}N_2O_3$.

Prepare Atenolol Oral Solution at a 0.2% concentration, for example, as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Atenolol	200 mg
Glycerin	5 mL
Vehicle for Oral Suspension	45 mL
Vehicle for Oral Solution, Sugar Free, a sufficient quantity to make	100 mL

Calculate the quantity of each ingredient required for the total volume and atenolol strength to be prepared. Mix the *Atenolol*, previously pulverized, and *Glycerin* to form a smooth paste. Incorporate the *Vehicle for Oral Suspension* or an equal volume of *Vehicle for Oral Solution, Sugar Free.* [NOTE—The *Vehicle for Oral Suspension* may be omitted.] Incorporate sufficient *Vehicle for Oral Solution, Sugar Free* in increments to bring to volume, and mix well. [NOTE—Do not use a sucrose-containing vehicle for oral solution.] Package, and label.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Package in amber, tight containers, and store at controlled room temperature.
- **LABELING:** Label it to state that it is to be shaken well before use, and discarded after 60 days. Label it to state that it is to be kept out of reach of children. Label it to indicate the nominal atenolol concentration.
- **BEYOND-USE DATE:** NMT 60 days after the day on which it was compounded

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

- **A. INFRARED ABSORPTION** ⟨197K⟩
Sample: Mix a quantity of powdered Tablets, equivalent to 100 mg of atenolol, with 15 mL of methanol, heat the mixture to 50°, and shake for 5 min. Filter, and evaporate the filtrate on a water bath to dryness. Add 10 mL of 0.1 N hydrochloric acid to the residue, warm the solution, shake, and filter. To the filtrate add sufficient 1 N sodium hydroxide to make it alkaline, and extract the solution with 10 mL of chloroform, drying the chloroform extract over anhydrous sodium sulfate. Filter the dried chloroform solution, evaporate the filtrate on a water bath to dryness, and dry the residue at 105° for 1 h.
- **B.** The retention time of the atenolol peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay.*