internal standard for the *Assay preparation* and the *Standard preparation,* respectively.

Phenylephrine Bitartrate

$C_9H_{13}NO_2 \cdot C_4H_6O_6$ 317.3

R-2-(Methylamino)-1-(3-hydroxyphenyl)ethanol-, (2*R*,3*R*)-2,3-dihydroxybutanedioate (1:1) (salt).

(–)-1-(3-Hydroxyphenyl)-2-methylaminoethanol, hydrogen tartrate.

(–)-3 Hydroxy-α-[(methylamino)methyl]benzenemethanol, hydrogen tartrate.

1-*m*-Hydroxy-α-[(methylamino)methyl]benzyl alcohol, hydrogen tartrate [17162-39-9].

» Phenylephrine Bitartrate contains not less than 99.0 percent and not more than 100.5 percent of $C_9H_{13}NO_2 \cdot C_4H_6O_6$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers. Store at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Norphenylephrine Hydrochloride RS
USP Phenylephrine Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: The alkaline filtrate from the test for *Specific rotation* responds positively to the test for *Tartrate* ⟨191⟩.

Specific rotation ⟨781S⟩**:** between –53° and –57° for the prepared sample.

Test solution—Prepare a sample solution of about 240 mg per mL in water. Make the solution slightly alkaline by adding concentrated ammonium hydroxide dropwise. Rub the wall of the vessel with a glass rod so that the base precipitates out. Filter the base under suction, wash with a little water and acetone, and dry at 105° for 2 hours. Prepare and measure a 50 mg per mL solution of base precipitate in 1 M hydrochloric acid.

pH ⟨791⟩**:** between 3.0 and 4.0 in 10% w/v aqueous solution.

Loss on drying ⟨731⟩**—**Dry at 105° to a constant weight: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Chromatographic purity—

Buffer solution—Dissolve 3.25 g of 1-octanesulfonic acid sodium salt monohydrate in 1 L of water. Adjust slowly with 3 M phosphoric acid to a pH of 2.8.

Solution A—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (9:1).

Solution B—Prepare a filtered and degassed mixture of acetonitrile and *Buffer solution* (9:1).

Diluent—Prepare a mixture of *Solution A* and *Solution B* (8:2).

System suitability solution—Dissolve accurately weighed quantities of USP Phenylephrine Hydrochloride RS and USP Norphenylephrine Hydrochloride RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, to obtain a solution having known concentrations of about 1.0 mg per mL and 0.9 μg per mL, respectively.

Blank solution—Prepare a solution containing 0.8 mg per mL L(+)-tartaric acid in *Diluent*.

Test solution—Transfer 78 mg of Phenylephrine Bitartrate, accurately weighed, to a 50-mL volumetric flask. Dissolve in and dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 215-nm detector and a 4-mm × 5.5-cm column that contains packing L1. The column and injection port temperatures are maintained at 45 ± 2°. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	93	7	equilibration
0–10	93→70	7→30	linear gradient
10–10.1	70→93	30→7	linear gradient
10.1–18	93	7	equilibration

Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between norphenylephrine and (–)-phenylephrine is not less than 1.5; the tailing factor of (–)-phenylephrine is less than 1.8; and the relative standard deviation for replicate injections is not more than 5%.

Procedure—Separately inject equal volumes (about 4 μL) of the *Blank solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure all of the peak responses. Calculate the percentage of each impurity in the portion of Phenylephrine Bitartrate taken by the formula:

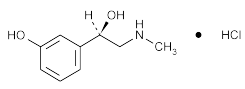
$$100(r_i / r_s)$$

in which r_i is the peak response for each impurity, and r_s is the sum of the responses of all the peaks. [NOTE—Examine the chromatogram of the *Blank solution* for peaks and disregard any corresponding peaks observed in the chromatogram of the *Test solution.*] The limits of impurities are specified in the accompanying table.

Compound	Approximate Relative Retention Time	Limit (%)
Phenylephrine	1.0	—
Norphenylephrine	0.9	0.2
Phenylephrone	1.2	0.1
Benzylphenylephrine	2.9	0.2
Benzylphenylephrone	3.1	0.1
Individual unknown impurity	—	0.1
Total impurity	—	0.5

Assay—Transfer about 280 mg of Phenylephrine Bitartrate, accurately weighed, to a 100-mL beaker, and dissolve by stirring in 60 mL of glacial acetic acid. Titrate with 0.1 N perchloric acid, determining the endpoint potentiometrically. Perform a blank determination (see *Titrimetry* ⟨541⟩), and make the necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 31.73 mg of $C_9H_{13}NO_2 \cdot C_4H_6O_6$.

Phenylephrine Hydrochloride



$C_9H_{13}NO_2 \cdot HCl$ 203.67

Benzenemethanol, 3-hydroxy-α-[(methylamino)methyl]-, hydrochloride (*R*)-.

(–)-*m*-Hydroxy-α-[(methylamino)methyl]benzyl alcohol hydrochloride [61-76-7].

» Phenylephrine Hydrochloride contains not less than 97.5 percent and not more than 102.5 percent of $C_9H_{13}NO_2 \cdot HCl$, calculated on the dried basis.