Levallophan Tartrate

Spray evenly Dragendorff’s TS for spraying on the plate: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 80°C, 4 hours).

**Residue on ignition** Not more than 0.10% (1 g).

**Assay** Weigh accurately about 0.5 g of Levallophan Tartrate, previously dried, dissolve in 30 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS = 43.35 mg of C\textsubscript{19}H\textsubscript{25}NO\textsubscript{4}C\textsubscript{8}H\textsubscript{4}O\textsubscript{6}

**Containers and storage** Containers—Well-closed containers.

### Levallophan Tartrate Injections

Levallophan Tartrate Injection is an aqueous solution for injection. It contains not less than 93% and not more than 107% of the labeled amount of levallophan tartrate (C\textsubscript{19}H\textsubscript{25}NO\textsubscript{4}C\textsubscript{8}H\textsubscript{4}O\textsubscript{6}: 433.49).

**Method of preparation** Prepare as directed under Injections, with Levallophan Tartrate.

**Description** Levallophan Tartrate Injection is a clear, colorless liquid.

**pH** 3.0 - 4.5

**Identification** Take an exact volume of Levallophan Tartrate Injection, equivalent to 3 mg of Levallophan Tartrate according to the labeled amount, add 5 mL of water and 2 drops of dilute hydrochloric acid, and wash with five 15-mL portions of diethyl ether by a vigorous shaking. Take the water layer, evaporate the diethyl ether remained by warming on a water bath, and after cooling, add 0.01 mol/L hydrochloric acid TS to make 50 mL. Determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 277 nm and 281 nm.

**Assay** Take exactly a volume of Levallophan Tartrate Injection, equivalent to about 2 mg of levallophan tartrate (C\textsubscript{19}H\textsubscript{25}NO\textsubscript{4}C\textsubscript{8}H\textsubscript{4}O\textsubscript{6}), add exactly 10 mL of the internal standard solution, and use this solution as the sample solution. Separately, weigh accurately about 0.1 g of levallophan tartrate for assay, previously dried at 80°C for 4 hours on phosphorus (V) oxide under reduced pressure, and dissolve in water to make exactly 100 mL. Pipet 2 mL of this solution, add exactly 10 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following operating conditions, and calculate the ratios, Q\textsubscript{T} and Q\textsubscript{s}, of the peak area of levallophan to that of the internal standard:
Amount (mg) of C<sub>9</sub>H<sub>15</sub>N<sub>2</sub>O<sub>4</sub>C<sub>6</sub>H<sub>4</sub>NO<sub>6</sub> = amount (mg) of levallorphan tartrate for assay
\[ \times \frac{Q_1}{Q_2} \times \frac{1}{50} \]

Internal standard solution—Dissolve 0.04 g of isobutyl para-hydroxybenzoate in 10 mL of ethanol (95), add water to make 100 mL, and to 10 mL of this solution add water to make 100 mL.

Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 280 nm).
Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).
Column temperature: A constant temperature of about 40°C.
Mobile phase: Dissolve 1.0 g of sodium lauryl sulfate in 500 mL of diluted phosphoric acid (1 in 1000), and adjust the pH to 3.0 with sodium hydroxide TS. To 300 mL of this solution add 200 mL of acetonitrile.
Flow rate: Adjust the flow rate so that the retention time of levallorphan is about 12 minutes.

System suitability—
System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the internal standard and levallorphan are eluted in this order with the resolution between these peaks being not less than 5.
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of levallorphan to that of the internal standard is not more than 1.0%.

Containers and storage  Containers—Hermetic containers.

Levodopa

Levodopa occurs as white or slightly grayish white crystals or crystalline powder. It is odorless.
It is freely soluble in formic acid, slightly soluble in water, and practically insoluble in ethanol (95) and in diethyl ether.
It dissolves in dilute hydrochloric acid.
The pH of a saturated solution of Levodopa is between 5.0 and 6.5.
Melting point: about 275°C (with decomposition).

Identification
(1) To 5 mL of a solution of Levodopa (1 in 1000) add 1 mL of ninhydrin TS, and heat for 3 minutes in a water bath: a purple color develops.
(2) To 2 mL of a solution of Levodopa (1 in 5000) add 10 mL of 4-aminoantipyrine TS, and shake: a red color develops.
(3) Dissolve 3 mg of Levodopa in 0.001 mol/L hydrochloric acid TS to make 100 mL. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

Absorbance  \( E_{1%}^{10} \) (280 nm): 136 - 146 (after drying, 0.03 g, 0.001 mol/L hydrochloric acid TS, 1000 mL).

Optical rotation  \( [\alpha]_{D}^{20} \): -11.5 - -13.0° (after drying, 2.5 g, 1 mol/L hydrochloric acid TS, 50 mL, 100 nm).

Purity
(1) Clarity and color of solution—Dissolve 1.0 g of Levodopa in 20 mL of 1 mol/L hydrochloric acid TS; the solution is clear and colorless.
(2) Chloride—Dissolve 0.5 g of Levodopa in 6 mL of dilute nitric acid, and add water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.3 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.021%).
(3) Sulfate—Dissolve 0.40 g of Levodopa in 1 mL of dilute hydrochloric acid and 30 mL of water, and add water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.25 mL of 0.005 mol/L sulfuric acid VS (not more than 0.030%).
(4) Heavy metals—Proceed with 1.0 g of Levodopa according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).
(5) Arsenic—Dissolve 1.0 g of Levodopa in 5 mL of dilute hydrochloric acid, and perform the test with this solution as the test solution using Apparatus B (not more than 2 ppm).
(6) Other amino acids—Dissolve 0.10 g of Levodopa in 10 mL of sodium sulfite TS, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add sodium sulfite TS to make exactly 25 mL. Pipet 1 mL of this solution, add sodium sulfite TS to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate of cellulose for thin-layer chromatography. Develop the plate with a mixture of 1-butanol, water, and acetic acid (100) and methanol (10:5:5:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly a solution of ninhydrin in acetone (1 in 50) on the plate and heat at 90°C for 10 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying  Not more than 0.30% (1 g, 105°C, 3 hours).

Residue on ignition  Not more than 0.10% (1 g).

Assay  Weigh accurately about 0.3 g of Levodopa, previously dried, dissolve in 3 mL of formic acid, add 80 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple