

Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution and the standard solution on a plate of silica gel for thinlayer chromatography. Develop the plate with a mixture of ethyl acetate, hexane, 1-butanol and ammonia solution (28) (140:40:20:1) to a distance of about 10 cm, and air-dry the plate. Spray hydrogen hexachloroplatinate (IV)-potassium iodide TS evenly 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.

Water Not more than 4.0% (0.5 g, direct titration).

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

Assay Weigh accurately about 0.5 g of Ifenprodil Tartrate, dissolve in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

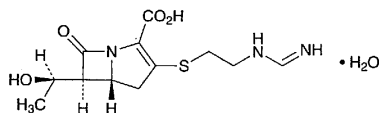
Each mL of 0.1 mol/L perchloric acid VS
= 40.05 mg of $(\text{C}_{21}\text{H}_{27}\text{NO}_2)_2 \cdot \text{C}_4\text{H}_6\text{O}_6$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Imipenem

イミペネム



$\text{C}_{12}\text{H}_{17}\text{N}_3\text{O}_4\text{S} \cdot \text{H}_2\text{O}$: 317.36
(5*R*,6*S*)-3-[2-(Formimidoylamino)ethylsulfanyl]-6-[(1*R*)-1-hydroxyethyl]-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid monohydrate [74431-23-5]

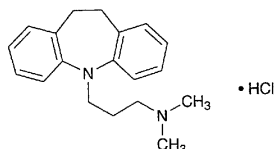
Imipenem conforms to the requirements of Imipenem in the Requirements for Antibiotic Products of Japan.

Description Imipenem occurs as a white to light yellow crystalline powder.

It is sparingly soluble in water, slightly soluble in methanol, and practically insoluble in ethanol (95) and in diethyl ether.

Imipramine Hydrochloride

塩酸イミプラミン



$\text{C}_{19}\text{H}_{24}\text{N}_2 \cdot \text{HCl}$: 316.87

N-[3-(10,11-Dihydro-5*H*-dibenz[*b,f*]azepin-5-yl)propyl]-*N,N*-dimethylamine monohydrochloride [113-52-0]

Imipramine Hydrochloride, when dried, contains not less than 98.5% of $\text{C}_{19}\text{H}_{24}\text{N}_2 \cdot \text{HCl}$.

Description Imipramine Hydrochloride occurs as a white to pale yellowish white, crystalline powder. It is odorless.

It is freely soluble in water and in ethanol (95), and practically insoluble in diethyl ether.

The pH of the aqueous solution (1 in 10) is between 4.2 and 5.2.

It is gradually colored by light.

Identification (1) Dissolve 5 mg of Imipramine Hydrochloride in 2 mL of nitric acid: a deep blue color develops.

(2) Dissolve 5 mg of Imipramine Hydrochloride in 250 mL of 0.01 mol/L hydrochloric acid TS. Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Imipramine Hydrochloride Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Dissolve 0.05 g of Imipramine Hydrochloride in 5 mL of water, add 1 mL of ammonia TS, allow to stand for 5 minutes, filter, and acidify the filtrate with dilute nitric acid: it responds to the Qualitative Tests (2) for chloride.

Melting point 170–174°C (with decomposition).

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Imipramine Hydrochloride in 10 mL of water: the solution is clear, and has no more color than the following control solution.

Control solution: Take exactly 1.0 mL of Cobaltous Chloride Colorimetric Stock Solution, 2.4 mL of Ferric Chloride Colorimetric Solution, 0.4 mL of Cupric Sulfate Colorimetric Stock Solution and 6.2 mL of diluted hydrochloric acid (1 in 40), and mix them. Pipet 0.5 mL of this solution, and add exactly 9.5 mL of water.

(2) Iminodibenzyl—Dissolve 0.050 g of Imipramine Hydrochloride in 10 mL of a mixture of hydrochloric acid and ethanol (95) (1:1) in a 25-mL brown volumetric flask. Cool the flask in ice water, add 5 mL of an ethanol (95) solution of furfural (1 in 250) and 5 mL of hydrochloric acid, and allow to stand at 25°C for 3 hours. Add a mixture of hydrochloric acid and ethanol (95) (1:1) to make 25 mL, and determine the absorbance of this solution at 565 nm as directed under the Ultraviolet-visible Spectrophotometry: it is not more than 0.16.

(3) Related substances—Dissolve 0.20 g of Imipramine Hydrochloride in 10 mL of ethanol (95), and use this solution as the sample solution. Pipet 1 mL of this solution, and add ethanol (95) to make exactly 50 mL. Pipet 5 mL of this solution, add ethanol (95) to make exactly 50 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 silica gel for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate, acetic acid (100), hydrochloric acid and water

(11:7:1:1) to a distance of about 12 cm, and air-dry the plate. Spray evenly potassium dichromate-sulfuric acid TS 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, 105°C, 2 hours).

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

Assay Weigh accurately about 0.3 g of Imipramine Hydrochloride, previously dried, and dissolve in 20 mL of water. Add 5 mL of sodium hydroxide TS, and extract with three 20-mL portions of chloroform. Filter each extract through a pledget of absorbent cotton on which a small quantity of anhydrous sodium sulfate is placed. Combine the chloroform extracts, and titrate with 0.1 mol/L perchloric acid VS until the yellow solution changes to red-purple (indicator: 10 drops of metanil yellow TS). Perform a blank determination.

$$\begin{aligned} \text{Each mL of 0.1 mol/L perchloric acid VS} \\ = 31.687 \text{ mg of } C_{19}H_{24}N_2.HCl \end{aligned}$$

Containers and storage Containers—Tight containers.
Storage—Light-resistant.

Imipramine Hydrochloride Tablets

塩酸イミプラミン錠

Imipramine Hydrochloride Tablets contain not less than 93% and not more than 107% of the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2.HCl$: 316.87).

Method of preparation Prepare as directed under Tablets, with Imipramine Hydrochloride.

Identification (1) Weigh a quantity of powdered Imipramine Hydrochloride Tablets, equivalent to 0.25 g of Imipramine Hydrochloride according to the labeled amount, add 25 mL of chloroform, shake thoroughly, and filter. Evaporate the filtrate on a water bath, and proceed with the residue as directed in the Identification (1) under Imipramine Hydrochloride.

(2) Dissolve an amount of the residue obtained in (1), equivalent to 5 mg of Imipramine Hydrochloride, in 250 mL of 0.01 mol/L hydrochloric acid TS, and determine the absorption spectrum as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 249 nm and 253 nm, and a shoulder between 270 nm and 280 nm.

(3) Dry the residue obtained in (1) at 105°C for 2 hours: the residue melts between 170°C and 174°C (with decomposition).

Dissolution test Perform the test with 1 tablet of Imipramine Hydrochloride Tablet at 75 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of diluted pH 6.8 phosphate buffer solution (1 in 2) as the test solution. Take 20 mL or more of the dissolved solution after 60 minutes from the start of the dissolution test, and filter through a membrane filter with pore size of not more than 0.8 μ m. Discard the first 10 mL of the filtrate, pipet the subsequent V mL, add diluted pH 6.8 phosphate

buffer solution (1 in 2) to make exactly V' mL so that each mL of the filtrate contains about 10 μ g of imipramine hydrochloride ($C_{19}H_{24}N_2.HCl$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 0.025 g of Imipramine Hydrochloride Reference Standard, previously dried at 105°C for 2 hours, dissolve in diluted pH 6.8 phosphate buffer solution (1 in 2) to make exactly 100 mL. Pipet 4 mL of this solution, add diluted pH 6.8 phosphate buffer solution (1 in 2) to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at 250 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Imipramine Hydrochloride Tablets in 60 minutes should be not less than 75%.

Dissolution rate (%) with respect to the labeled amount of imipramine hydrochloride ($C_{19}H_{24}N_2.HCl$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{1}{C} \times 36$$

W_S : Amount (mg) of Imipramine Hydrochloride Reference Standard.

C : Labeled amount (mg) of imipramine hydrochloride ($C_{19}H_{24}N_2.HCl$) in 1 tablet.

Assay Take 20 Imipramine Hydrochloride Tablets, add exactly 200 mL of 0.01 mol/L hydrochloric acid TS, and shake well until the tablets are completely disintegrated. After centrifuging the solution, pipet a volume of the supernatant liquid, equivalent to about 0.025 g of imipramine hydrochloride ($C_{19}H_{24}N_2.HCl$) according to the labeled amount, add 0.01 mol/L hydrochloric acid TS to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.025 g of Imipramine Hydrochloride for Assay, previously dried at 105°C for 2 hours, dissolve in 0.01 mol/L hydrochloric acid TS to make exactly 100 mL, and use this solution as the standard solution. Pipet 3 mL each of these solutions into separators which contain 15 mL of potassium hydrogen phthalate buffer solution, pH 5.6, 8 mL of bromocresol green-sodium hydroxide TS and 30 mL of chloroform, and shake. Filter the chloroform layer through a pledget of absorbent cotton into a 100-mL volumetric flask. Repeat the extraction with two 30-mL portions of chloroform, combine the chloroform layers in the 100-mL volumetric flask, and add chloroform to make exactly 100 mL. Perform the test with these solutions as directed under the Ultraviolet-visible Spectrophotometry, using a solution obtained by proceeding with 3 mL of 0.01 mol/L hydrochloric acid TS in the same manner as the blank. Determine the absorbances, A_T and A_S , of these solutions at 416 nm.

$$\begin{aligned} \text{Amount (mg) of imipramine hydrochloride } (C_{19}H_{24}N_2.HCl) \\ = \text{amount (mg) of Imipramine Hydrochloride for Assay} \\ \times \frac{A_T}{A_S} \end{aligned}$$

Containers and storage Containers—Tight containers.