

The concentration of Aminophylline Injection is expressed as the quantity of aminophylline ($C_{16}H_{24}N_{10}O_4 \cdot 2H_2O$: 456.46).

Method of preparation Prepare as directed under Injections, with Aminophylline. It may be prepared with Theophylline and its equivalent Ethylenediamine, instead of Aminophylline.

It may contain not more than 0.060 g of Ethylenediamine as a stabilizer for each g of Aminophylline.

Description Aminophylline Injection is a clear and colorless liquid. It has a slightly bitter taste.

It gradually changes in color by light.

pH: 8.0 - 10.0

Identification To a volume of Aminophylline Injection, equivalent to 0.75 g of Aminophylline according to the labeled amount, add water to make 30 mL. Proceed with this solution as directed in the Identification under Aminophylline.

Assay (1) Theophylline—To an accurately measured volume of Aminophylline Injection, equivalent to about 0.2 g of theophylline ($C_7H_8N_4O_2$) (about 0.25 g of Aminophylline), add 15 mL of water, 8 mL of ammonia TS and 20 mL of silver nitrate TS, and warm on a water bath for 15 minutes. Cool to between 5°C and 10°C for 20 minutes, filter the precipitate through a glass filter (G4), and wash with three 10-mL portions of water. Dissolve the precipitate in 5 mL of nitric acid, and wash the filter with three 10-mL portions of water. Combine the nitric acid solution and washings, and titrate with 0.1 mol/L ammonium thiocyanate VS (indicator: 2 mL of ammonium iron (III) sulfate TS).

Each mL of 0.1 mol/L ammonium thiocyanate VS
= 18.017 mg of $C_7H_8N_4O_2$

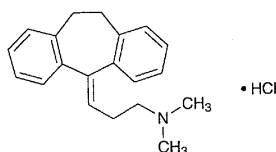
(2) Ethylenediamine—To an accurately measured volume of Aminophylline Injection, equivalent to about 0.03 g of ethylenediamine ($C_2H_8N_2$) (about 0.2 g of Aminophylline), add water to make 30 mL, and titrate with 0.1 mol/L hydrochloric acid VS (indicator: 2 to 3 drops of bromophenol blue TS).

Each mL of 0.1 mol/L hydrochloric acid VS
= 3.0049 mg of $C_2H_8N_2$

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

Amitriptyline Hydrochloride

塩酸アミトリプチリン



$C_{20}H_{23}N \cdot HCl$: 313.86

N-[3-(10,11-Dihydro-5*H*-dibenzo[*a,d*]cyclohepten-5-

ylidene)propyl]-*N,N*-dimethylamine monohydrochloride [549-18-8]

Amitriptyline Hydrochloride, when dried, contains not less than 99.0% of $C_{20}H_{23}N \cdot HCl$.

Description Amitriptyline Hydrochloride occurs as colorless crystals or a white to pale yellow crystalline powder. It has a bitter taste and a numbing effect.

It is freely soluble in water, in ethanol (95) and in acetic acid (100), soluble in acetic anhydride, and practically insoluble in diethyl ether.

The pH of a solution of Amitriptyline Hydrochloride (1 in 20) is between 4.0 and 5.0.

Identification (1) Dissolve 5 mg of Amitriptyline Hydrochloride in 3 mL of sulfuric acid: a red color develops. Add 5 drops of potassium dichromate TS to this solution: it turns dark brown.

(2) Acidify 1 mL of a solution of Amitriptyline Hydrochloride (1 in 500) with 0.5 mL of dilute nitric acid, and add 1 drop of silver nitrate TS: a white, opalescent precipitate is produced.

(3) Determine the absorption spectrum of a solution of Amitriptyline Hydrochloride (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Amitriptyline Hydrochloride Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

Melting point 195 - 198°C

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Amitriptyline Hydrochloride in 20 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 2.0 g of Amitriptyline Hydrochloride according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

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 0.5 g of Amitriptyline Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), 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
= 31.387 mg of $C_{20}H_{23}N \cdot HCl$

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

Amitriptyline Hydrochloride Tablets

塩酸アミトリプチリン錠

Amitriptyline Hydrochloride Tablets contain not

less than 90% and not more than 110% of the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N.HCl$: 313.86).

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

Identification (1) Weigh a quantity of powdered Amitriptyline Hydrochloride Tablets, equivalent to 0.1 g of Amitriptyline Hydrochloride according to the labeled amount. Add 10 mL of chloroform, shake thoroughly, and filter. Evaporate the filtrate on a water bath to about 2 mL, add diethyl ether until turbidity is produced, and allow to stand. Filter the crystals formed through a glass filter (G4), and proceed as directed in the Identification (1) and (2) under Amitriptyline Hydrochloride.

(2) Determine the absorption spectrum of a solution of the crystals obtained in (1) (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 238 nm and 240 nm, and a minimum between 228 nm and 230 nm.

Dissolution test Perform the test with 1 tablet of Amitriptyline Hydrochloride Tablets at 50 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of diluted phosphate buffer solution, pH 6.8, (1 in 2) as the test solution. Take 20 mL or more of the dissolved solution 60 minutes after starting the 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 of the filtrate, add diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly V' mL so that each mL contains about 11 μ g of amitriptyline hydrochloride ($C_{20}H_{23}N.HCl$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 0.055 g of Amitriptyline Hydrochloride Reference Standard, previously dried at 105°C for 2 hours, and dissolve in diluted phosphate buffer solution, pH 6.8, (1 in 2) to make exactly 250 mL. Pipet 5 mL of this solution, add diluted phosphate buffer solution, pH 6.8, (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 239 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Amitriptyline Hydrochloride Tablets in 60 minutes should be not less than 70%.

Dissolution rate (%) with respect to the labeled amount of amitriptyline hydrochloride ($C_{20}H_{23}N.HCl$)

$$= W_s \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{1}{C} \times 18$$

W_s : Amount (mg) of Amitriptyline Hydrochloride Reference Standard.

C : Labeled amount (mg) of amitriptyline hydrochloride ($C_{20}H_{23}N.HCl$) in 1 tablet.

Assay Weigh accurately and powder not less than 20 Amitriptyline Hydrochloride Tablets. Weigh accurately a portion of the powder, equivalent to about 0.02 g of amitriptyline hydrochloride ($C_{20}H_{23}N.HCl$), and add 75 mL of diluted methanol (1 in 2). After shaking for 30 minutes, add diluted methanol (1 in 2) to make exactly 100 mL, and filter. Discard the first 20-mL portion of the filtrate, measure exactly the subsequent 5-mL portion, add methanol to make exactly 100 mL, and use this solution as the sample solution.

Separately, weigh accurately about 0.02 g of Amitriptyline Hydrochloride Reference Standard, previously dried at 105°C for 2 hours, and dissolve in diluted methanol (1 in 2) to make exactly 100 mL. Measure exactly 5 mL of this solution, add methanol 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 239 nm as directed under the Ultraviolet-visible Spectrophotometry, respectively.

$$\begin{aligned} & \text{Amount (mg) of amitriptyline hydrochloride} \\ & (C_{20}H_{23}N.HCl) \\ & = \text{amount (mg) of Amitriptyline Hydrochloride} \\ & \text{Reference Standard} \\ & \times \frac{A_T}{A_S} \end{aligned}$$

Containers and storage Containers—Tight containers.

Ammonia Water

アンモニア水

Ammonia Water contains not less than 9.5 w/v% and not more than 10.5 w/v% of ammonia (NH_3 : 17.03).

Description Ammonia Water occurs as a clear, colorless liquid, having a very pungent, characteristic odor.

It is alkaline.

Specific gravity d_{20}^{20} : 0.95 – 0.96

Identification (1) Hold a glass rod moistened with hydrochloric acid near the surface of Ammonia Water: dense white fumes are produced.

(2) Hold moistened red litmus paper near the surface of Ammonia Water: it turns blue.

Purity (1) Residue on evaporation—Evaporate 10.0 mL of Ammonia Water to dryness, and dry the residue at 105°C for 1 hour: the mass of the residue is not more than 2.0 mg.

(2) Heavy metals—Evaporate 5.0 mL of Ammonia Water to dryness on a water bath, add 1 mL of dilute hydrochloric acid to the residue, and evaporate to dryness. Dissolve the residue in 2 mL of dilute acetic acid, add water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 2.5 mL of Standard Lead Solution, 2 mL of dilute acetic acid and water to make 50 mL (not more than 5 ppm).

(3) Potassium permanganate-reducing substances—To 10.0 mL of Ammonia Water add 40 mL of dilute sulfuric acid while cooling, and add 0.10 mL of 0.02 mol/L potassium permanganate VS: the red color of the potassium permanganate does not disappear within 10 minutes.

Assay Measure exactly 5 mL of Ammonia Water, add 25 mL of water, and titrate with 0.5 mol/L sulfuric acid VS (indicator: 2 drops of methyl red TS).

$$\begin{aligned} & \text{Each mL of 0.5 mol/L sulfuric acid VS} \\ & = 17.031 \text{ mg of } NH_3 \end{aligned}$$

Containers and storage Containers—Tight containers. Storage—Not exceeding 30°C.