

acid, stopper tightly at once, shake, and allow to stand in a dark place for 60 minutes. Add carefully 50 mL of water and 15 mL of potassium iodide TS, stopper tightly at once, shake well, and titrate the liberated iodine with 0.1 mol/L sodium thiosulfate VS (indicator: 1 mL of starch TS). Perform a blank determination.

Each mL of 0.05 mol/L bromine VS
= 15.157 mg of $C_{13}H_{12}Cl_2O_4$

Containers and storage Containers—Well-closed containers.

Etacrylic Acid Tablets

エタクリン酸錠

Etacrylic Acid Tablets contain not less than 90% and not more than 110% of the labeled amount of etacrylic acid ($C_{13}H_{12}Cl_2O_4$: 303.14).

Method of preparation Prepare as directed under Tablets, with Etacrylic Acid.

Identification (1) Weigh a quantity of powdered Etacrylic Acid Tablets, equivalent to 0.3 g of Etacrylic Acid according to the labeled amount, add 25 mL of 0.1 mol/L hydrochloric acid TS, and extract with 50 mL of Dichloromethane. Filter the dichloromethane extract, and evaporate the filtrate on a water bath to dryness. Proceed with the residue as directed in the Identification (1), (2) and (4) under Etacrylic Acid.

(2) Prepare a solution of the residue obtained in (1), equivalent to a solution of Etacrylic Acid in methanol (1 in 20,000), and determine the absorption spectrum as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 268 nm and 272 nm.

Dissolution test Perform the test with 1 tablet of Etacrylic Acid Tablets at 50 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of water as the test solution. Take 20 mL or more of the dissolved solution 45 minutes after starting the test, and filter through a membrane filter with pore size of not more than 0.8 μm . Discard the first 10 mL of the filtrate, and use the subsequent as the sample solution. Separately, weigh accurately about 0.055 g of etacrylic acid for assay, previously dried at 60°C for 2 hours, dissolve in 10 mL of methanol, and add water to make exactly 100 mL. Pipet 5 mL of this solution, add water 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 277 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Etacrylic Acid Tablets in 45 minutes is not less than 70%.

Dissolution rate (%) with respect to
the labeled amount of etacrylic acid ($C_{13}H_{12}Cl_2O_4$)

$$= W_s \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{1}{C} \times 900$$

W_s : Amount (mg) of etacrylic acid for assay.

C : Labeled amount (mg) of etacrylic acid ($C_{13}H_{12}Cl_2O_4$) in 1 tablet.

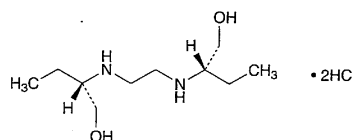
Assay Weigh accurately and powder not less than 20 Etacrylic Acid Tablets. Weigh accurately a portion of the powder, equivalent to about 0.1 g of etacrylic acid ($C_{13}H_{12}Cl_2O_4$), add 25 mL of 0.1 mol/L hydrochloric acid TS, and extract with three 30-mL portions of dichloromethane. Filter the dichloromethane extracts through a pledget of absorbent cotton into an iodine bottle. Wash the pledget of absorbent cotton with a small amount of dichloromethane, and combine the washing with the extracts. Evaporate this solution on a water bath to dryness in a current of air, to the residue add 20 mL of acetic acid (100), and proceed as directed in the Assay under Etacrylic Acid.

Each mL of 0.05 mol/L bromine VS
= 15.157 mg of $C_{13}H_{12}Cl_2O_4$

Containers and storage Containers—Well-closed containers.

Ethambutol Hydrochloride

塩酸エタンブトール



$C_{10}H_{24}N_2O_2 \cdot 2HCl$: 277.23

N,N'-Ethylenebis[(2*S*)-2-aminobutanol] dihydrochloride
[1070-11-7]

Ethambutol Hydrochloride, when dried, contains not less than 98.5% of $C_{10}H_{24}N_2O_2 \cdot 2HCl$.

Description Ethambutol Hydrochloride occurs as white crystals or crystalline powder. It is odorless, and has a bitter taste.

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

The pH of a solution of Ethambutol Hydrochloride (1 in 20) is between 3.4 and 4.0.

Identification (1) To 10 mL of a solution of Ethambutol Hydrochloride (1 in 100) add 0.5 mL of copper (II) sulfate TS and 2 mL of sodium hydroxide TS: a deep blue color is produced.

(2) Dissolve 0.1 g of Ethambutol Hydrochloride in 40 mL of water, add 20 mL of 2,4,6-trinitrophenol TS, and allow to stand for 1 hour. Collect the precipitate, wash with 50 mL of water, and dry at 105°C for 2 hours: the precipitate melts between 193°C and 197°C.

(3) A solution of Ethambutol Hydrochloride (1 in 30) responds to the Qualitative Tests for chloride.

Optical rotation $[\alpha]_D^{20}$: +5.5 – +6.1° (after drying, 5 g, water, 50 mL, 200 mm).

Melting point 200 – 204°C

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Ethambutol Hydrochloride in 10 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 2.0 g Ethambutol

Hydrochloride according to Method 1, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of Ethambutol Hydrochloride according to Method 1, and perform the test using Apparatus B (not more than 2 ppm).

(4) 2-Aminobutanol—Dissolve 5.0 g of Ethambutol Hydrochloride in methanol to make exactly 100 mL, and use this solution as the sample solution. Dissolve 0.05 g of 2-amino-1-butanol in methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 2 μ L 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 10 cm, air-dry the plate, and heat at 105°C for 5 minutes. Cool, spray evenly ninhydrin-L-ascorbic acid TS upon the plate, air-dry the plate, and heat at 105°C for 5 minutes: the spot from the sample solution, corresponding to that from the standard solution, has no more color than that from the standard solution.

Loss on drying Not more than 0.5% (1 g, 105°C, 3 hours).

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

Assay Weigh accurately about 0.2 g of Ethambutol Hydrochloride, previously dried, dissolve in 20 mL of water, and add 1.8 mL of copper (II) sulfate TS. To the solution add 7 mL of sodium hydroxide TS with shaking, add water to make exactly 50 mL, and centrifuge. Pipet 10 mL of the supernatant liquid, add 10 mL of ammonia-ammonium chloride buffer solution, pH 10.0 and 100 mL of water, and titrate with 0.01 mol/L disodium dihydrogen ethylenediamine tetraacetate VS until the color of the solution changes from blue-purple through light red to light yellow (indicator: 0.15 mL of Cu-PAN TS). Perform a blank determination, and make any necessary correction.

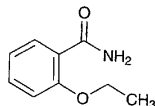
Each mL of 0.01 mol/L disodium dihydrogen ethylenediamine tetraacetate VS
= 2.7723 mg of $C_{10}H_{24}N_2O_2 \cdot 2HCl$

Containers and storage Containers—Tight containers.

Ethenzamide

Ethoxybenzamide

エテンザミド



$C_9H_{11}NO_2$: 165.19

2-Ethoxybenzamide [938-73-8]

Ethenzamide, when dried, contains not less than 98.0% of $C_9H_{11}NO_2$.

Description Ethenzamide occurs as white crystals or crys-

talline powder. It is odorless and tasteless.

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

Its saturated solution is neutral.

It begins to sublime slightly at about 105°C.

Identification (1) To 0.5 g of Ethenzamide add 5 mL of sodium hydroxide TS, and heat the mixture gently: the gas evolved turns moistened red litmus paper to blue.

(2) To 0.2 g of Ethenzamide add 10 mL of hydrobromic acid, and boil the mixture gently for 1 hour under a reflux condenser. Cool in ice water, collect the separated crystalline precipitate, wash with three 5-mL portions of ice water, and dry in a desiccator (in vacuum, silica gel) for 2 hours: the precipitate melts between 158°C and 161°C.

Melting point 131 – 134°C

Purity (1) Chloride—Dissolve 0.5 g of Ethenzamide in 30 mL of acetone, add 6 mL of dilute nitric acid, and dilute with water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.7 mL of 0.01 mol/L hydrochloric acid VS add 30 mL of acetone and 6 mL of dilute nitric acid, and dilute with water to make 50 mL (not more than 0.050%).

(2) Sulfate—Dissolve 0.5 g of Ethenzamide in 30 mL of acetone, add 1 mL of dilute hydrochloric acid, and dilute with water to 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.50 mL of 0.005 mol/L sulfuric acid VS add 30 mL of acetone and 1 mL of dilute hydrochloric acid, and dilute with water to 50 mL (not more than 0.048%).

(3) Heavy metals—Proceed with 2.0 g of Ethenzamide 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).

(4) Arsenic—To 0.40 g of Ethenzamide add 0.3 g of potassium nitrate and 0.5 g of anhydrous sodium carbonate, mix thoroughly, ignite the mixture gradually, and cool. Dissolve the residue in 10 mL of dilute sulfuric acid, and heat the solution until white fumes begin to evolve. After cooling, add water carefully to make 5 mL, use this solution as the test solution, and perform the test using Apparatus B (not more than 5 ppm).

(5) Salicylamide—Dissolve 0.20 g of Ethenzamide in 15 mL of diluted ethanol (95) (2 in 3), and add 2 to 3 drops of dilute iron (III) chloride TS: no purple color develops.

Loss on drying Not more than 1.0% (1 g, silica gel, 3 hours).

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

Assay Weigh accurately about 0.02 g each of Ethenzamide and Ethenzamide Reference Standard, previously dried, and dissolve each in 70 mL of ethanol (95) by warming, and after cooling, add ethanol (95) to make exactly 100 mL. Pipet 5 mL each of these solutions, add ethanol (95) to make exactly 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at 290 nm as directed under the Ultraviolet-visible Spectrophotometry, using ethanol (95) as the blank.