amount, and use this solution as the sample solution. Separately, weigh accurately about 0.01 g of Estriol Reference Standard, previously dried at 105°C for 3 hours, dissolve in methanol to make exactly 100 mL, then pipet 5 mL of this solution, and add water to make exactly 100 mL. Pipet 2 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 100 μL each of the sample solution and the standard solution according to the operating conditions as directed in the Assay under Estriol, and determine the peak areas of estriol, A_T and A_S, from these solutions.

The dissolution rate of Estriol Tablets in 30 minutes is not less than 80%.

$$\text{Dissolution rate (\%) with respect to the labeled amount of estriol } (C_{18}H_{24}O_3) = W_S \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{1}{C} \times \frac{9}{10}$$

W_S: Amount (mg) of Estriol Reference Standard.
C: Labeled amount (mg) of estriol ($C_{18}H_{24}O_3$) in 1 tablet.

Assay Weigh accurately and powder not less than 20 Estriol Tablets. Weigh accurately a portion of the powder, equivalent to about 1 mg of estriol ($C_{18}H_{24}O_3$), add exactly 5 mL of water, disperse the fine particles with ultrasonic wave, shake with 25 mL of methanol for 10 minutes, centrifuge, and take the supernatant liquid. Add 25 mL of methanol, repeat the above procedure twice, combine the supernatant liquid, add exactly 5 mL of the internal standard solution, then add methanol to make 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.025 g of Estriol Reference Standard, previously dried at 105°C for 3 hours, and dissolve in methanol to make exactly 100 mL. Pipet 4 mL of this solution, add exactly 5 mL of the internal standard solution, then add methanol to make 100 mL, and use this solution as the standard solution. Proceed with 20 μL each of the sample solution and the standard solution as directed in the Assay under Estriol.

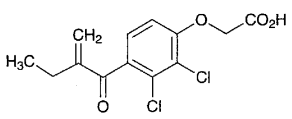
$$\text{Amount (mg) of estriol } (C_{18}H_{24}O_3) = \text{amount (mg) of Estriol Reference Standard} \times \frac{Q_T}{Q_S} \times \frac{1}{25}$$

Internal standard solution—A solution of methyl benzoate for estriol limit test in methanol (1 in 5000).

Containers and storage Containers—Tight containers.

Etacrynic Acid

エタクリン酸



$C_{13}H_{12}Cl_2O_4$: 303.14
[2,3-Dichloro-4-(2-ethylacryloyl)phenoxy]acetic acid
[*58-54-8*]

Etacrynic Acid, when dried, contains not less than 98.0% of $C_{13}H_{12}Cl_2O_4$.

Description Etacrynic Acid occurs as a white, crystalline powder. It is odorless, and has a slightly bitter taste.

It is very soluble in methanol, freely soluble in ethanol (95), in acetic acid (100) and in diethyl ether, and very slightly soluble in water.

Identification **(1)** Dissolve 0.2 g of Etacrynic Acid in 10 mL of acetic acid (100), and to 5 mL of this solution add 0.1 mL of bromine TS: the color of the test solution disappears. To the remaining 5 mL of the solution add 0.1 mL of potassium permanganate TS: the color of the test solution changes to light orange immediately.

(2) To 0.01 g of Etacrynic Acid add 1 mL of sodium hydroxide TS, and heat in a water bath for 3 minutes. After cooling, add 1 mL of disodium chlomotropate TS, and heat in a water bath for 10 minutes: a deep purple color develops.

(3) Determine the absorption spectrum of a solution of Etacrynic Acid in methanol (1 in 20,000) 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.

(4) Perform the test with Etacrynic Acid as directed under the Flame Coloration Test (2): a green color appears.

Melting point 121 - 125°C

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Etacrynic Acid in 10 mL of methanol: the solution is clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Etacrynic Acid according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of Etacrynic Acid according to Method 3, and perform the test using Apparatus B. Add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 50), then add 1.5 mL of hydrogen peroxide (30), and fire to burn (not more than 2 ppm).

(4) Related substances—Dissolve 0.20 g of Etacrynic Acid in 10 mL of ethanol (95), and use this solution as the sample solution. Pipet 3 mL of the sample solution, add ethanol (95) to make exactly 200 mL, and use this solution as the standard solution. 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 with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of chloroform, ethyl acetate and acetic acid (100) (6:5:2) to a distance of about 15 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): 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 0.25% (1 g, in vacuum, 60°C, 2 hours).

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

Assay Weigh accurately about 0.1 g of Etacrynic Acid, previously dried, place in an iodine bottle, dissolve in 20 mL of acetic acid (100), and add exactly 20 mL of 0.05 mol/L bromine VS. To this solution add 3 mL of hydrochloric

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.

Etacrynic Acid Tablets

エタクリン酸錠

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

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

Identification **(1)** Weigh a quantity of powdered Etacrynic Acid Tablets, equivalent to 0.3 g of Etacrynic 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 Etacrynic Acid.

(2) Prepare a solution of the residue obtained in (1), equivalent to a solution of Etacrynic 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 Etacrynic 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 etacrynic 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 Etacrynic Acid Tablets in 45 minutes is not less than 70%.

Dissolution rate (%) with respect to the labeled amount of etacrynic 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 etacrynic acid for assay.
C: Labeled amount (mg) of etacrynic acid ($C_{13}H_{12}Cl_2O_4$) in 1 tablet.

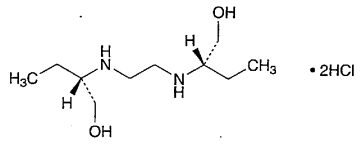
Assay Weigh accurately and powder not less than 20 Etacrynic Acid Tablets. Weigh accurately a portion of the powder, equivalent to about 0.1 g of etacrynic acid ($C_{13}H_{12}Cl_2O_4$), add 25 mL of 0.1 mol/L hydrochloric acid TS, and extract with three 30-mL portions of dichloromethane. Filter the dichloromethane 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 Etacrynic 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



$C_{10}H_{24}N_2O_2.2HCl$: 277.23
N,*N*′-Ethylenebis[(2*S*)-2-aminobutanol] dihydrochloride
[*1070-11-7*]

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

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