Purity (1) Chloride—Dissolve 0.6 g of Flurbiprofen in 40 mL of acetone, and add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.25 mL of 0.01 mol/L hydrochloric acid VS add 40 mL of acetone, 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.015%).

(2) Heavy metals—Dissolve 2.0 g of Flurbiprofen in 30 mL of acetone, and add 2 mL of dilute acetic acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 2.0 mL of Standard Lead Solution add 30 mL of acetone, 2 mL of dilute acetic acid and water to make 50 mL (not more than 10 ppm).

(3) Related substances—Dissolve 0.020 g of Flurbiprofen in 10 mL of a mixture of water and acetonitrile (11:9), and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add a mixture of water and acetonitrile (11:9) to make exactly 200 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of both solutions by the automatic integration method: each area of the peaks other than the peak of flurbiprofen from the sample solution is not larger than the peak area of flurbiprofen from the standard solution, and the total area of these peaks is not larger than twice the peak area of flurbiprofen from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 to 10 μm in particle diameter).

Column temperature: A constant temperature of about 30°C.

Mobile phase: A mixture of water, acetonitrile and acetic acid (100) (12:7:1).

Flow rate: Adjust the flow rate so that the retention time of flurbiprofen is about 20 minutes.

Selection of column: Dissolve 0.2 g of flurbiprofen and 1 mg of 2-(4-biphenylyl)propionic acid in 100 mL of a mixture of water and acetonitrile (11:9). Proceed with 20 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of 2-(4-biphenylyl)propionic acid and flurbiprofen in this order with the resolution of these peaks being not less than 2.0.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of flurbiprofen obtained from 20 μL of the standard solution is between 5 mm and 15 mm.

Time span of measurement: About twice as long as the retention time of flurbiprofen.

Loss on drying Not more than 0.10% (1 g, in vacuum at a pressure not exceeding 0.67 kPa, silica gel, 4 hours).

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

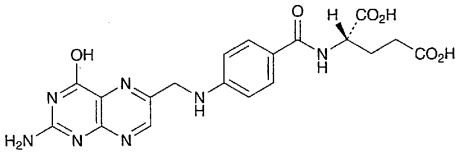
Assay Weigh accurately about 0.6 g of Flurbiprofen, previously dried, dissolve in 50 mL of ethanol (95), and titrate with 0.1 mol/L sodium hydroxide VS (indicator: 3 drops of phenolphthalein TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L sodium hydroxide VS
= 24.426 mg of $C_{15}H_{13}FO_2$

Containers and storage Containers—Well-closed containers.

Folic Acid

葉酸



$C_{19}H_{19}N_7O_6$: 441.40

N-{4-[(2-Amino-4-hydroxypteridin-6-ylmethyl)amino]-benzoyl}-L-glutamic acid [*59-30-3*]

Folic Acid contains not less than 98.0% and not more than 102.0% of $C_{19}H_{19}N_7O_6$, calculated on the anhydrous basis.

Description Folic Acid occurs as a yellow to orange-yellow, crystalline powder. It is odorless.

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

It dissolves in hydrochloric acid, in sulfuric acid, in dilute sodium hydroxide TS and in a solution of sodium carbonate decahydrate (1 in 100), and these solutions are yellow in color.

It is slowly affected by light.

Identification (1) Dissolve 1.5 mg of Folic Acid in dilute sodium hydroxide 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 or the spectrum of a solution of Folic Acid Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) To 10 mL of the solution obtained in (1) add 1 drop of potassium permanganate TS, and mix well until the color changes to blue, and immediately observe under ultraviolet light (main wavelength: 365 nm): a blue fluorescence is produced.

Purity (1) Clarity and color of solution—Dissolve 0.10 g of Folic Acid in 10 mL of dilute sodium hydroxide TS : the solution is clear and yellow in color.

(2) Free amines—Pipet 30 mL of the sample solution obtained in the Assay, add 20 mL of dilute hydrochloric acid and water to make exactly 100 mL, and use this solution as the sample solution. Weigh accurately about 0.05 g of *p*-Aminobenzoylglutamic Acid Reference Standard, previously dried in a desiccator (in vacuum, silica gel) for 4 hours, dissolve in diluted ethanol (95) (2 in 5) to make exactly 100 mL. Pipet 3 mL of this solution, add water to make exactly 1000 mL, and use this solution as the standard solution. Pipet 4 mL each of the sample solution and the standard solution, proceed as directed in the Assay, and perform the test as directed under the Ultraviolet-visible Spectrophoto-

metry. Determine the absorbances, A_T and A_S, of subsequent solutions of the sample solution and the standard solution at 550 nm: the content of free amines is not more than 1.0%.

$$\text{Content (\%) of free amines} = \frac{A_T}{A_S} \times \frac{W'}{W}$$

W : Weighed amount (mg) of Folic Acid, calculated on the anhydrous basis.
W': Weighed amount (mg) of *p*-Aminobenzoylglutamic Acid Reference Standard.

Water Take 5 mL of pyridine for water determination and 20 mL of methanol for Karl Fischer method in a dried titration flask, and titrate with Karl Fischer TS until the solution reaches the end point. Weigh accurately about 0.2 g of Folic Acid, immediately place in the titration flask, and add a known excess volume of Karl Fischer TS. Mix well for 30 minutes, and perform the test: the water content is not more than 8.5%.

Residue on ignition Not more than 0.5% (1 g).

Assay Weigh accurately about 0.05 g each of Folic Acid and Folic Acid Reference Standard. To each add 50 mL of dilute sodium hydroxide TS, mix well to dissolve, add dilute sodium hydroxide TS to make exactly 100 mL, and use these solutions as the sample solution and the standard solution. To 30 mL each of these solutions, accurately measured, add 20 mL of dilute hydrochloric acid and water to make exactly 100 mL. To 60 mL each of these solutions add 0.5 g of zinc powder, and allow to stand with frequent shaking for 20 minutes. Filter each mixture through a dry filter paper, and discard the first 10 mL of the filtrate. Pipet 10 mL each of the subsequent filtrate, and add water to make exactly 100 mL. To 4 mL each of solutions, accurately measured, add 1 mL of water, 1 mL of dilute hydrochloric acid and 1 mL of a solution of sodium nitrite (1 in 1000), mix well, and allow to stand for 2 minutes. To each solution add 1 mL of a solution of ammonium amidosulfate (1 in 200), mix thoroughly, and allow to stand for 2 minutes. To each of these solutions, add 1 mL of a solution of *N*-(1-naphthyl)-*N'*-diethylethylenediamine oxalate (1 in 1000), shake, allow to stand for 10 minutes, and add water to make exactly 20 mL. Separately, to 30 mL of the sample solution, accurately measured, add 20 mL of dilute hydrochloric acid and water to make exactly 100 mL. Pipet 10 mL of this solution, add 18 mL of dilute hydrochloric acid and water to make exactly 100 mL. Pipet 4 mL of this solution, and prepare the blank solution in the same manner as the sample solution. Perform the test with these solutions as directed under the Ultraviolet-visible Spectrophotometry, using a solution prepared with 4 mL of water in the same manner as a blank. Determine the absorbances, A_T, A_S and A_C, of the subsequent solution of the sample solution, the standard solution and the blank solution at 550 nm.

Amount (mg) of $C_{19}H_{19}N_7O_6$
= amount (mg) of Folic Acid Reference Standard, calculated on the anyhdrous basis
$\times \frac{A_T - A_C}{A_S}$

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

Folic Acid Injection

葉酸注射液

Folic Acid Injection is an aqueous solution for injection. It contains not less than 95% and not more than 115% of the labeled amount of folic acid ($C_{19}H_{19}N_7O_6$: 441.40).

Method of preparation Dissolve Folic Acid in water with the aid of Sodium Hydroxide or Sodium Carbonate, and prepare as directed under Injections.

Description Folic Acid Injection is a yellow to orange-yellow, clear liquid.
pH: 8.0 - 11.0

Identification **(1)** To a volume of Folic Acid Injection, equivalent to 1.5 mg of Folic Acid according to the labeled amount, add dilute sodium hydroxide TS to make 100 mL. Proceed as directed in the Identification (2) under Folic Acid, using this solution as the sample solution.
(2) Determine the absorption spectrum of the sample solution obtained in (1) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 255 nm and 257 nm, between 281 nm and 285 nm and between 361 nm and 369 nm. Separately, determine the maximal absorbances of the sample solution, A_1 and A_2, between 255 nm and 257 nm and between 361 nm and 369 nm, respectively: the ratio of A_1/A_2 is between 2.80 and 3.00.
(3) Folic Acid Injection responds to the Qualitative Test (1) for sodium salt.

Assay To an exactly measured volume of Folic Acid Injection, equivalent to about 0.05 g of folic acid ($C_{19}H_{19}N_7O_6$) add dilute sodium hydroxide TS to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of Folic Acid Reference Standard, dissolve in dilute sodium hydroxide TS to make exactly 100 mL, and use this solution as the standard solution. Proceed with 30 mL each of the sample solution and the standard solution, exactly measured, as directed in the Assay under Folic Acid.

Amount (mg) of folic acid ($C_{19}H_{19}N_7O_6$)
= amount (mg) of Folic Acid Reference Standard, calculated on the anhydrous basis
$\times \frac{A_T - A_C}{A_S}$

Containers and storage Containers—Hermetic containers, and colored containers may be used.
Storage—Light-resistant.

Folic Acid Tablets

葉酸錠

Folic Acid Tablets contain not less than 90% and not more than 115% of the labeled amount of folic acid ($C_{19}H_{19}N_7O_6$: 441.40).