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

Identification (1) Take a quantity of powdered Folic Acid Tablets, equivalent to 1.5 mg of Folic Acid according to the labeled amount, add 100 mL of dilute sodium hydroxide TS, shake, and filter. Discard the first 10 mL of the filtrate, use the subsequent filtrate as the sample solution, and proceed as directed in the Identification (2) under Folic Acid.

(2) Determine the absorption spectrum of the filtrate 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 filtrate, 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.

Assay Weigh accurately and powder not less than 20 Folic Acid Tablets. Weigh accurately a portion of the powder, equivalent to about 0.05 g of folic acid ($C_{19}H_{19}N_7O_6$). Add 50 mL of dilute sodium hydroxide TS, shake frequently, then filter into a 100-mL volumetric flask, and wash with dilute sodium hydroxide TS. To the combined filtrate and washings 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. Take 30 mL each of the sample solution and the standard solution, exactly measured, and proceed as directed in the Assay under Folic Acid.

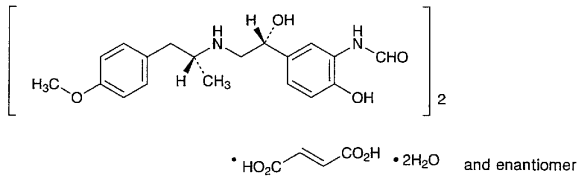
Amount (mg) of folic acid ($C_{19}H_{19}N_7O_6$)
= amount (mg) of Folic Acid Reference Standard, calculated on the anhydrous basis
$\times \frac{A_T - A_C}{A_S}$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Formoterol Fumarate

フマル酸ホルモテロール



$(C_{19}H_{24}N_2O_4)_2.C_4H_4O_4.2H_2O$: 840.91

N-(2-Hydroxy-5-{(1*RS*)-1-hydroxy-2-[(1*RS*)-2-(4-methoxyphenyl)-1-methylethylamino]ethyl}phenyl)formamide hemifumarate monohydrate [*43229-80-7*, anhydride]

Formoterol Fumarate contains not less than 98.5% of $[(C_{19}H_{24}N_2O_4)_2.C_4H_4O_4$ (mol. wt.: 804.88)], calculated on the anhydrous basis.

Description Formoterol Fumarate occurs as a white to yellowish white, crystalline powder.

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

A solution of Formoterol Fumarate in methanol (1 in 100) shows no optical rotation.

Melting point: about 138°C (with decomposition).

Identification (1) Dissolve 0.5 g of Formoterol Fumarate in 20 mL of 0.5 mol/L sulfuric acid TS, and extract with three 25-mL portions of diethyl ether. Wash the combined diethyl ether extracts with 10 mL of 0.5 mol/L sulfuric acid TS, and evaporate the ether layer under reduced pressure, and dry the residue at 105°C for 3 hours: the residue melts at about 290°C (with decomposition, in a sealed tube).

(2) Determine the absorption spectrum of a solution of Formoterol Fumarate in methanol (1 in 40,000) 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.

(3) Determine the infrared absorption spectrum of Formoterol Fumarate as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

Purity (1) Heavy metals—Proceed with 1.0 g of Formoterol Fumarate according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(2) Related Substances—Dissolve 0.20 g of Formoterol Fumarate in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol 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 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 chloroform, 1,4-dioxane, ethanol (99.5) and ammonia solution (28) (20:20:10:3) to a distance of about 12 cm, and air-dry the plate. Allow the plate to stand for 5 minutes in iodine vapor: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Water 4.0 - 5.0% (0.5 g, direct titration).

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

Assay Weigh accurately about 0.7 g of Formoterol Fumarate, 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
= 40.24 mg of $(C_{19}H_{24}N_2O_4)_2.C_4H_4O_4$

Containers and storage Containers—Tight containers.