Analysis
Samples: *Standard solution* and *Sample solution*
Measure the responses for all the impurities and fluvoxamine maleate. Calculate the per centage of impurities in the portion of T ablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = individual peak area of each impurity from the *Sample solution*
r_S = peak area of fluvoxamine maleate from the *Standard solution*
C_S = concentration of USP Fluvoxamine Maleate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of fluvoxamine maleate in the *Sample solution* (mg/mL)
F = relative response factor of each impurity as given in *Impurity Table 2*

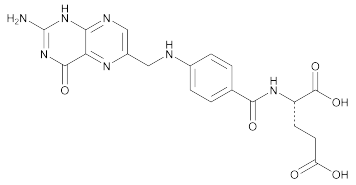
Acceptance criteria
Individual impurities: See *Impurity Table 2*.
Total impurities: NMT 1.5%

Impurity Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
(*E*)-5-methoxy-4′-difluoromethyl valerophenone-*O*-2-amino ethyloxime	0.58	1.0	0.2
(*E*)-*N*-[2[[[α-(4-methoxybutyl)-4-(trifluoro-methyl) benzylidene] amino] oxy]ethyl] aspartic acid	0.70	1.0	1.2
(*E*)-5-methoxy-4′-trifluoromethyl valerophenone-*O*-[2-N-(aminoethyl) aminoethyl] oxime	0.75	1.0	0.2
Z-isomer	0.85	0.5	0.5
Fluvoxamine	1.0	—	—
(*E*)-4′-trifluoro-methylvalero-phenone-*O*-2-amino-ethyloxime	1.86	1.0	0.2
5-Methoxy-4′-trifluoromethyl valerophenone oxime	1.99	1.0	0.2
5-Methoxy-4-trifluoromethyl valerophenone	2.17	1.0	0.2
Unknown impurities	—	1.0	0.2

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight containers. Store at room temperature.
- **LABELING:** If a test in *Procedure* under *Organic Impurities* other than *Test 1* is used, then the labeling states with which test the article complies.
- **USP REFERENCE STANDARDS** ⟨11⟩
USP Fluvoxamine Maleate RS

Folic Acid



$C_{19}H_{19}N_7O_6$ 441.40
L-Glutamic acid, *N*-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-;
N-[*p*-[[(2-Amino-4-hydroxy-6-pteridinyl)methyl]amino]benzoyl]-L-glutamic acid [59-30-3].

DEFINITION
Folic Acid contains NLT 97.0% and NMT 102.0% of folic acid ($C_{19}H_{19}N_7O_6$), calculated on the anhydrous basis.

IDENTIFICATION
- **A. ULTRAVIOLET ABSORPTION** ⟨197U⟩
Sample solution: 10 µg/mL in 0.1 N sodium hydroxide solution
Acceptance criteria: Meets the requirements. The ratio A_{256}/A_{365} is 2.80–3.00.

ASSAY
- **PROCEDURE**
[NOTE—Use low-actinic glassware throughout the following procedure.]
3 N phosphoric acid: 98 g/L of phosphoric acid in water
6 N ammonium hydroxide: Dilute 40 mL of ammonium hydroxide with water to 100 mL.
Mobile phase: Transfer 2.0 g of monobasic potassium phosphate into a 1000-mL volumetric flask, and dissolve in 650 mL of water. Add 15.0 mL of a solution of 0.5 M tetrabutylammonium hydroxide in methanol, 7.0 mL of *3 N phosphoric acid*, and 270 mL of methanol. Cool to room temperature, adjust with *3 N phosphoric acid* or *6 N ammonium hydroxide* to a pH of 5.0, and dilute with water to volume. Recheck the pH before use.
Internal standard solution: 2 mg/mL of methylparaben in *Mobile phase*. Dissolve the methylparaben first with methanol (about 4% of the final volume), and dilute with *Mobile phase* to volume.
Standard stock solution: 1 mg/mL of USP Folic Acid RS in *Mobile phase*. Dissolve the folic acid with the aid of 10% ammonium hydroxide (about 1% of the final volume), and dilute with *Mobile phase* to volume.
Standard solution: Transfer 4.0 mL of *Standard stock solution* and 4.0 mL of *Internal standard solution* to a 50-mL volumetric flask, and dilute with *Mobile phase* to volume.
Sample stock solution: Transfer 100 mg of Folic Acid to a 100-mL volumetric flask, and dissolve in 40 mL of *Mobile phase* and 1 mL of 10% ammonium hydroxide. Dilute with *Mobile phase* to volume.

Sample solution: Transfer 4.0 mL of *Sample stock solution* and 4.0 mL of *Internal standard solution* to a 50-mL volumetric flask, and dilute with *Mobile phase* to volume.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 280 nm
Column: 4.0-mm × 25-cm; packing L1
Flow rate: 1.2 mL/min
Injection size: 10 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Resolution: NLT 3.6 between methylparaben and folic acid
Relative standard deviation: NMT 2.0% for the ratios of the folic acid peak area to the internal standard peak area
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of folic acid ($C_{19}H_{19}N_7O_6$) in the sample taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = internal standard ratio (peak response of folic acid/peak response of the internal standard) from the *Sample solution*
R_S = internal standard ratio (peak response of folic acid/peak response of the internal standard) from the *Standard solution*
C_S = concentration of USP Folic Acid RS in the *Standard stock solution* (mg/mL)
C_U = concentration of Folic Acid in the *Sample stock solution* (mg/mL)
Acceptance criteria: 97.0%–102.0% on the anhydrous basis

IMPURITIES
• **Residue on Ignition** ⟨**281**⟩**:** NMT 0.3%
• **Related Compounds**
3 N phosphoric acid, 6 N ammonium hydroxide, Internal standard solution, Standard stock solution, Standard solution, and **Chromatographic system:** Proceed as directed in the *Assay.*
Sample solution: Use the *Sample stock solution*, prepared as directed in the *Assay.*
Analysis
Sample: *Sample solution*
Allow the *Sample solution* to elute for NLT 2 times the retention time of folic acid. Record the chromatogram, and measure the areas of all the peaks.
Calculate the percentage of total secondary peaks in the portion of Folic Acid taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = sum of the areas of all the peaks except that of the folic acid peak
r_T = sum of the areas of all the peaks
Acceptance criteria: NMT 2.0%

SPECIFIC TESTS
• **Water Determination,** *Method I* ⟨**921**⟩
Analysis: Proceed as directed in the chapter, except stir the methanol solvent before and during the addition of the test specimen and during the titration.
Acceptance criteria: NMT 8.5%

ADDITIONAL REQUIREMENTS
• **Packaging and Storage:** Preserve in well-closed, light-resistant containers.
• **USP Reference Standards** ⟨**11**⟩
USP Folic Acid RS

Folic Acid Injection

» Folic Acid Injection is a sterile solution of Folic Acid in Water for Injection prepared with the aid of Sodium Hydroxide or Sodium Carbonate. It contains not less than 95.0 per cent and not more than 110.0 per cent of the labeled amount of folic acid ($C_{19}H_{19}N_7O_6$).

Packaging and storage—Preserve in single-dose or multiple-dose containers, preferably of Type I glass, protected from light.

USP Reference standards ⟨11⟩**—**
USP Folic Acid RS
USP Endotoxin RS

Identification—To a volume of the Injection equivalent to about 100 mg of folic acid add water to make about 25 mL. Adjust with hydrochloric acid to a pH of 3.0, cool to 5 °, then filter, and wash the precipitate of folic acid with cold water until the last washing shows an absence of chloride. Then wash with acetone, and dry at 80° for 1 hour: the UV absorption spectrum of a 1 in 100,000 solution of the folic acid so obtained in sodium hydroxide solution (1 in 250) exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Folic Acid RS, concomitantly measured. The ratio A_{256}/A_{365} is between 2.80 and 3.00.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 357.1 USP Endotoxin Units per mg of folic acid.

pH ⟨791⟩: between 8.0 and 11.0.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

Mobile phase, System suitability solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Folic Acid Tablets*.

Assay preparation—Dilute an accurately measured volume of Injection, quantitatively and stepwise, with an aqueous solvent containing 2 mL of ammonium hydroxide and 1 g of sodium perchlorate per 100 mL, to obtain a solution having a concentration close to that of the *Standard preparation* and between 0.20 and 0.80 mg per mL.

Procedure—Proceed as directed in the *Assay* under *Folic Acid Tablets*, and calculate the quantity, in mg, of folic acid ($C_{19}H_{19}N_7O_6$) in each mL of the Injection.

Folic Acid Tablets

DEFINITION
Folic Acid Tablets contain NLT 90.0% and NMT 115.0% of the labeled amount of folic acid ($C_{19}H_{19}N_7O_6$).

IDENTIFICATION
• **A. Ultraviolet Absorption**
Sample solution: Digest the quantity of powdered Tablets, equivalent to 100 mg of folic acid, with 100 mL of 0.1 N sodium hydroxide, and filter. Adjust with hydrochloric acid to a pH of 3.0. Cool to 5 °, filter, and wash the precipitate of folic acid with cold water until the last washing shows an absence of chloride. Then wash with acetone, and dry at 80° for 1 h. Dissolve the residue in 0.1 N sodium hydroxide to obtain a 10-µg/mL solution.
Acceptance criteria: The UV absorption spectrum of the *Sample solution* exhibits maxima and minima at the same