Fluorouracil Injection

» Fluorouracil Injection is a sterile solution of Fluorouracil in Water for Injection, prepared with the aid of Sodium Hydroxide. It contains, in each mL, not less than 45 mg and not more than 55 mg of fluorouracil (C₄H₃FN₂O₂).

NOTE—If a precipitate is formed as a result of exposure to low temperatures, redissolve it by heating to 60 °C with vigorous shaking, and allow to cool to body temperature prior to use.

Packaging and storage—Preserve in single-dose containers, preferably of Type I glass, and store at controlled room temperature. Avoid freezing and exposure to light.

Labeling—Label it to indicate the expiration date, which is not more than 24 months after date of manufacture.

USP Reference standards (11)—
USP Fluorouracil RS
USP Endotoxin RS

Identification—
A: The retention time of the major peak in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation as obtained in the Assay.

B: Carefully acidify a portion of Injection, equivalent to about 100 mg of fluorouracil, with glacial acetic acid. Stir and slightly chill the solution to precipitate the fluorouracil, collect the precipitate, wash with 1 mL of water, and then dry in vacuum over phosphorus pentoxide at 80 °C for 4 hours; the residue so obtained responds to Identification test A under Fluorouracil.

C: It responds to Identification test C under Fluorouracil.

Bacterial endotoxins (85)—It contains not more than 0.33 USP Endotoxin Unit per mg of fluorouracil.

pH (791): between 8.6 and 9.4.

Other requirements—It meets the requirements under Injections (1).

Assay—
Mobile phase, Standard preparation, and Chromatographic system—Proceed as directed in the Assay under Fluorouracil.

Assay preparation—Transfer a suitable volume of the Injection, equivalent to 50 mg of fluorouracil, to a 100-mL volumetric flask, dilute with water to volume, and mix. Quantitatively dilute a volume of this solution with water to obtain a concentration of 10 µg per mL.

Procedure—Separately inject equal volumes (about 10 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the peak responses for the major peaks. Calculate the quantity, in mg, of fluorouracil (C₄H₃FN₂O₂) in the portion of Solution taken by the formula:

\[ 2C(t_0 / t_r) \]

in which C is the concentration, in µg per mL, of USP Fluorouracil RS in the Standard preparation; V is the volume, in mL, of the Injection taken for the Assay preparation; and t₀ and tᵣ are the fluorouracil peak responses obtained from the Assay preparation and the Standard preparation, respectively.

Fluorouracil Topical Solution

» Fluorouracil Topical Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of C₄H₃FN₂O₂.

Packaging and storage—Preserve in tight containers, and store at controlled room temperature.

USP Reference standards (11)—
USP Fluorouracil RS

Identification—It responds to the Identification test under Fluorouracil.

Microbial enumeration tests (61) and Tests for specified microorganisms (62)—It meets the requirements of the tests for absence of Staphylococcus aureus and Pseudomonas aeruginosa.

Assay—
Mobile phase, Standard preparation, and Chromatographic system—Proceed as directed in the Assay under Fluorouracil.

Assay preparation—Transfer an accurately weighed portion of Solution, equivalent to about 20 mg of fluorouracil, to a 100-mL volumetric flask, dilute with water to volume, and mix. Quantitatively dilute a volume of this solution with water to obtain a concentration of 10 µg per mL.

Procedure—Separately inject equal volumes (about 10 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the peak responses for the major peaks. Calculate the quantity, in mg, of fluorouracil (C₄H₃FN₂O₂) in the portion of Solution taken by the formula:

**Fluoxetine Hydrochloride**

**C₁₇H₁₈F₃NO · HCl** 345.79
Benzepanopropanamine, N-methyl-γ-[4-(trifluoromethyl)phenoxy]-α-pyrrolidine hydrochloride, (±).
(±)-N-Methyl-3-phenyl-3-{[(α,α,α-trifluoro-p-tolyl)oxy]propylamine, hydrochloride [59333-67-4].

» Fluoxetine Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of C₁₇H₁₈F₃NO · HCl, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards (11)—
USP Fluoxetine Hydrochloride RS
USP Fluoxetine Related Compound A RS
N-Methyl-3-phenyl-3-{[(α,α,α-trifluoro-m-tolyl)oxy]propylamine hydrochloride.
C₁₇H₁₈F₃NO · HCl 345.79
USP Fluoxetine Related Compound B RS
N-Methyl-3-phenylpropylamine.
C₉H₁₈N 149.24

Identification—
A: Infrared Absorption (197K).
B: A solution meets the requirements of the tests for Chloride (191).
Water, Method I (921): not more than 0.5%.

Heavy metals, Method II (231): 0.003%.

Related compounds—
Mobile phase—Proceed as directed in the Assay.

Test solution 1—Transfer about 56 mg of Fluoxetine Hydrochloride, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with Mobile phase to volume, and mix.

Test solution 2—Transfer 2 mL of Test solution 1, accurately measured, to a 10-mL volumetric flask, dilute with Mobile phase to volume, and mix.

System suitability solution—Dissolve about 22 mg of USP Fluoxetine Hydrochloride RS in 10 mL of 0.1 N sulfuric acid, and heat to 85° for 3 hours. Cool, transfer 0.4 mL of this solution to a 25-mL volumetric flask, and add about 28 mg of USP Fluoxetine Hydrochloride RS, 1 mg of USP Fluoxetine Related Compound A RS, and 1 mg of USP Fluoxetine Related Compound B RS. Dilute with Mobile phase to volume, and mix.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 227-nm detector and a 4.6-mm × 25-cm column that contains 5-μm base-deactivated packing L7. The flow rate is about 1 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the relative retention times are about 0.24 for α-[2-(methylamino)ethyl]benzenemethanol (if present), 0.27 for fluoxetine related compound B, 0.94 for fluoxetine related compound A, 1.0 for fluoxetine, and 2.17 for 4-trifluoromethylphenol; and the ratio of the height of the fluoxetine related compound A peak to the depth of the valley between the fluoxetine and fluoxetine related compound A peaks (measured from the fluoxetine related compound A peak height) is not more than 1.1.

Procedure—Separately inject equal volumes (about 10 μL) of Test solution 1 and Test solution 2 into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of fluoxetine related compound A, 1.0 for fluoxetine, and 2.17 for 4-trifluoromethylphenol.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 215-nm detector and a 4.6-mm × 25-cm column that contains 5-μm base-deactivated packing L7. The flow rate is about 1 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the tailing factor is not more than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 μL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of C_{17}H_{18}F_{3}NO·HCl in the portion of Fluoxetine Hydrochloride taken by the formula:

\[
100C(r_t / r_S)
\]

in which \(C\) is the concentration, in mg per mL, of USP Fluoxetine Hydrochloride RS in the Standard preparation; and \(r_t\) and \(r_S\) are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

Fluoxetine Capsules

» Fluoxetine Capsules contain an amount of Fluoxetine Hydrochloride equivalent to not less than 90.0 percent and not more than 110.0 percent of the labeled amount of fluoxetine (C_{17}H_{18}F_{3}NO).

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards (11)—USP Fluoxetine Hydrochloride RS

Identification—
A: Infrared Absorption (197K)—
Test specimen—Transfer a quantity of Capsule contents, equivalent to about 10 mg of fluoxetine, to a suitable container, dissolve in 10 mL of methanol, and filter. Rinse the container and filter with 5 mL of methanol, and evaporate with the aid of a current of air and mild heat to dryness.

Dissolution (711)—
Medium: water; 900 mL.
Apparatus 2: 50 rpm.
Time: 30 minutes.
Determine the amount of C_{17}H_{18}F_{3}NO dissolved by employing the following method.

Diethylamine phosphate suspension—Transfer 250 mL of acetone to a suitable container, add 1.0 mL of diethylamine, mix, and adjust with phosphoric acid to a pH of 3.5. (Note—Diethylamine phosphate will precipitate; therefore, keep well-mixed.)

Mobile phase—Prepare a filtered and degassed mixture of water, acetonitrile, and diethylamine (600:400:4), and adjust with phosphoric acid to a pH of 3.5. Make adjustments if necessary (see System Suitability under Chromatography (621)).

Standard solution—Prepare a solution of USP Fluoxetine Hydrochloride RS having a concentration similar to that of the Test solution, and filter. Transfer 5.0 mL of this solution to a suitable container, add 2.0 mL of Diethylamine phosphate suspension, and mix.

Test solution—Filter 20 mL of the solution under test. Transfer 5.0 mL of this solution to a suitable container, add 2.0 mL of Diethylamine phosphate suspension, and mix.