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 ($C_4H_3FN_2O_2$).
NOTE—If a precipitate is formed as a result of exposure to low temperatures, redissolve it by heating to 60° 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° 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. Dilute quantitatively a known volume of this solution with water to obtain a solution having 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 $C_4H_3FN_2O_2$ in the volume of Injection taken by the formula:

$$5(C / V)(r_U / r_S)$$

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 r_U and r_S 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 $C_4H_3FN_2O_2$.

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 Cream.*

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.*

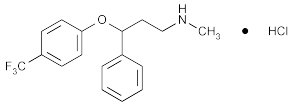
Assay preparation—Transfer an accurately weighed portion of Solution, equivalent to about 20 mg of fluorouracil, to a 100-mL volumetric flask, dilute with water to volume, and mix. Quantitatively dilute a volume of this solution with water to obtain a concentration of 10 µg per mL.

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 ($C_4H_3FN_2O_2$) in the portion of Solution taken by the formula:

$$2C(r_U / r_S)$$

in which C is the concentration, in µg per mL, of USP Fluorouracil RS in the *Standard preparation;* and r_U and r_S are the fluorouracil responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Fluoxetine Hydrochloride



$C_{17}H_{18}F_3NO \cdot HCl$ 345.79
Benzenepropanamine, *N*-methyl-γ-[4-(trifluoromethyl)phenoxy]-, 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 per cent of $C_{17}H_{18}F_3NO \cdot HCl$, 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.
$C_{17}H_{18}F_3NO \cdot HCl$ 345.79
USP Fluoxetine Related Compound B RS
N-Methyl-3-phenylpropylamine.
$C_{10}H_{15}N$ 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 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 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 *System suitability solution*, 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 for not less than twice the elution time for fluoxetine, and measure the peak responses. Calculate the percentage of fluoxetine related compound A in the portion of Fluoxetine Hydrochloride taken by the formula:

$$100 r_A / (r_A + r_U)$$

in which r_A is the peak response of fluoxetine related compound A obtained from *Test solution 2;* and r_U is the peak response of fluoxetine obtained from *Test solution 2*.

Calculate the percentage of each of the other impurities in the portion of Fluoxetine Hydrochloride taken by the formula:

$$100 r_i / (r_s + 5 r_U)$$

in which r_i is the peak response for each impurity obtained from *Test solution 1;* r_s is the sum of the responses of all the peaks, excluding fluoxetine, obtained from *Test solution 1;* and r_U is as defined above: not more than 0.15% of fluoxetine related compound A is found; not more than 0.25% of α-[2-(methylamino)ethyl]benzenemethanol is found; not more than 0.25% of fluoxetine related compound B is found; and not more than 0.1% of any other individual impurity is found. The sum of all impurities found is not more than 0.5%.

Assay—

Triethylamine buffer—Transfer about 10 mL of triethylamine, accurately measured, to a suitable container, add about 980 mL of water, and adjust with phosphoric acid to a pH of 6.0.

Mobile phase—Prepare a filtered and degassed mixture of *Triethylamine buffer*, stabilizer-free tetrahydrofuran, and methanol (6:3:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Fluoxetine Hydrochloride RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.11 mg per mL.

Assay preparation—Transfer about 11 mg of Fluoxetine Hydrochloride, accurately weighed, to a 100-mL volumetric flask, dissolve in and 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 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 $C_{17}H_{18}F_3NO \cdot HCl$ in the portion of Fluoxetine Hydrochloride taken by the formula:

$$100 C (r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Fluoxetine Hydrochloride RS in the *Standard preparation;* and r_U 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 ($C_{17}H_{18}F_3NO$).

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 $C_{17}H_{18}F_3NO$ dissolved by employing the following method.

Diethylamine phosphate suspension—Transfer 250 mL of acetonitrile 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.