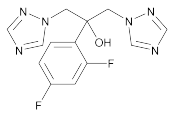
Calculate the quantity, in mg, of $C_9H_{11}FN_2O_5$ in the portion of Floxuridine for Injection taken by the formula:

$$5C(A_U / A_S)$$

in which C is the concentration, in µg per mL, of USP Floxuridine RS in the Standard solution; and A_U and A_S are the absorbances of the solution from Floxuridine for Injection and the Standard solution, respectively.

Fluconazole



$C_{13}H_{12}F_2N_6O$ 306.27

1*H*-1,2,4-Triazole-1-ethanol, 1-(2,4-difluorophenyl)-1-(1*H*-1,2,4-triazol-1-ylmethyl)-;
2,4-Difluoro-1′,1′-bis(1*H*-1,2,4-triazol-1-ylmethyl)benzyl alcohol [86386-73-4].

DEFINITION

Fluconazole contains NLT 98.0% and NMT 102.0% of $C_{13}H_{12}F_2N_6O$, calculated on the dried basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨197K⟩
- **B. Ultraviolet Absorption** ⟨197U⟩

Sample solution: 200 µg/mL
Medium: Alcohol

ASSAY

- **Procedure**

Sample solution: Dissolve 200 mg of Fluconazole in 100 mL of glacial acetic acid.
Analysis: Titrate with 0.1 N perchloric acid VS, using a suitable anhydrous electrode system. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 15.31 mg of fluconazole ($C_{13}H_{12}F_2N_6O$).
Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

[Note—On the basis of information regarding the manufacturing process, perform either: (a) *Organic Impurities, Procedure 1* or (b) *Organic Impurities, Procedure 2* and *Organic Impurities, Procedure 3*.]

- **Organic Impurities, Procedure 1**

Mobile phase: Acetonitrile and water (20:80)
Standard solution: 10 µg/mL each of USP Fluconazole RS, USP Fluconazole Related Compound A RS, USP Fluconazole Related Compound B RS, and USP Fluconazole Related Compound C RS, dissolved in acetonitrile, and then diluted in *Mobile phase*
Sample solution: 3 mg/mL of Fluconazole in *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 260 nm
Column: 4.6-mm × 15-cm; 3.5-µm packing L1
Column temperature: 40°
Flow rate: 0.5 mL/min
Injection size: 20 µL
System suitability
Sample: *Standard solution*
[Note—The retention times for fluconazole related compound A, fluconazole related compound B, fluconazole related compound C, and fluconazole are about 4.9, 8.0, 8.5, and 9.9 min, respectively.]
Suitability requirements
Resolution: NLT 1.5 between fluconazole related compound B and fluconazole related compound C
Relative standard deviation: NMT 5.0% for each peak
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of fluconazole related compound A, fluconazole related compound B, and fluconazole related compound C in the portion of Fluconazole taken:

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

r_U = peak response of fluconazole related compound A, fluconazole related compound B, or fluconazole related compound C from the *Sample solution*
r_S = average peak response of fluconazole related compound A, fluconazole related compound B, and fluconazole related compound C for replicate injections of the *Standard solution*
C_S = concentration of USP Fluconazole Related Compound A RS, USP Fluconazole Related Compound B RS, and USP Fluconazole Related Compound C RS in the *Standard solution* (mg/mL)
C_U = concentration of Fluconazole in the *Sample solution* (mg/mL)

Calculate the percentage of any other impurities in the portion of Fluconazole taken:

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

r_U = peak response of any other impurity from the *Sample solution*
r_S = average peak response of fluconazole for replicate injections of the *Standard solution*
C_S = concentration of USP Fluconazole RS in the *Standard solution* (mg/mL)
C_U = concentration of Fluconazole in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fluconazole related compound A	0.5	0.2
Fluconazole related compound B	0.81	0.1
Fluconazole related compound C	0.86	0.2
Fluconazole	1.0	—
Specified impurity	0.6	1.0
Any other individual impurity	—	0.1
Total unknown impurities	—	0.3
Total impurities	—	1.5

- **Organic Impurities, Procedure 2**

Solution A: 0.01 M anhydrous sodium acetate solution. Adjust with 1 N acetic acid to a pH of 5.0, filter, and degas.
Solution B: Acetonitrile
Solution C: Methanol
Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)	Solution C (%)
0	80	5	15
10	80	5	15
20	30	55	15
23	30	55	15
25	80	5	15
30	80	5	15

Diluent: Methanol and *Solution A* (16:84)
Standard solution: 0.01 mg/mL of USP Fluconazole RS in *Diluent*
System suitability solution: 0.02 mg/mL of USP Fluconazole RS and 6 µg/mL of USP Desacetyl Diltiazem Hydrochloride RS in *Diluent*
Sample solution: 2 mg/mL of Fluconazole in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 261 nm
Column: 4.0-mm × 10-cm; packing L1
Flow rate: 1 mL/min
Injection size: 20 µL
System suitability
Samples: *Standard solution* and *System suitability solution*
[NOTE—The relative retention times for fluconazole and desacetyl diltiazem are 1.0 and 1.2, respectively, *System suitability solution*.]
Suitability requirements
Resolution: NLT 10.0 between fluconazole and desacetyl diltiazem hydrochloride, *System suitability solution*
Column efficiency: NLT 30,000 theoretical plates for the fluconazole peak, *System suitability solution*
Tailing factor: NMT 1.4 for the fluconazole peak, *System suitability solution*
Relative standard deviation: NMT 5.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Fluconazole taken:

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

r_U = peak response of each impurity from the *Sample solution*
r_S = peak response of fluconazole from the *Standard solution*
C_S = concentration of USP Fluconazole RS in the *Standard solution* (mg/mL)
C_U = concentration of Fluconazole in the *Sample solution* (mg/mL)
F = relative response factor (see *Table 3*)
Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Specified impurity	0.17–0.37	0.72	0.1
Specified impurity	0.48–0.60	0.85	0.1
Specified impurity	0.67–0.79	1.21	0.1
Specified impurity	1.14–1.18	0.96	0.1
Specified impurity	1.20–1.32	0.97	0.1
Any unspecified impurity	—	1.0	0.1
Total impurities	—	—	0.5

- **ORGANIC IMPURITIES, PROCEDURE 3**
Standard solution A: 1 mg/mL of USP Fluconazole RS in methanol (2.0%)
Standard solution B: 0.1 mg/mL of USP Fluconazole RS from *Standard solution A* in methanol (0.2%)
Standard solution C: 0.05 mg/mL of USP Fluconazole RS from *Standard solution A* in methanol (0.1%)
Sample solution: 50 mg/mL of Fluconazole in methanol
Chromatographic system
(See *Chromatography* ⟨621⟩, *Thin-Layer Chromatography*.)
Mode: TLC
Adsorbent: 0.25-mm layer of chromatographic silica gel mixture
Application volume: 10 µL
Developing solvent system: Chloroform, methanol, and ammonium hydroxide (80:20:1)
Spray reagent A: 1.7 mg/mL of silver nitrate in water
Spray reagent B (potassium iodoplatinate solution): 375 mg of chloroplatinic acid in 5 mL of 1 N hydrochloric acid. Dissolve 5 g of potassium iodide in 50 mL of water, and store in a light-resistant container. Prepare a mixture of water, potassium iodide solution, and chloroplatinic acid solution (20:9:1).
Analysis
Samples: *Standard solution A*, *Standard solution B*, *Standard solution C*, and *Sample solution*
Spray the dry plate with *Spray reagent A*, and expose the plate to 365-nm UV light for 10–20 min. Dry the plate for 20 min between 80° and 90°, then spray the plate with *Spray reagent B*. Allow the plate to dry. Examine the plate and compare the intensities of any secondary spots observed in the *Sample solution* with those of the principal spots in the *Standard solutions*.
Acceptance criteria: No spot from the *Sample solution* with an R_F value between 0.10–0.25 and 0.27–0.41 is larger or more intense than that from *Standard solution B* (0.2%).
- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
Sample: 0.5 g
- **IRON ⟨241⟩**
Sample solution: Transfer 0.5 g of the sample into a test tube. Dissolve in 5 mL of alcohol, and add 5 mL of distilled water.
Acceptance criteria: NMT 20 ppm

SPECIFIC TESTS
- **LOSS ON DRYING ⟨731⟩:** Dry a sample at 105° for 3 h: it loses NMT 0.5% of its weight.
- **CLARITY AND COLOR OF SOLUTION**
Sample solution: Dissolve a sample in methanol to obtain a 5-in-100 solution (w/v).
Acceptance criteria: The solution is clear and colorless.

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight containers, and store below 30°.
- **LABELING:** If a procedure for *Organic Impurities* other than *Procedure 1* is used, then the labeling states with which *Organic Impurities* procedure(s) the article complies.
- **USP REFERENCE STANDARDS ⟨11⟩**
USP Desacetyl Diltiazem Hydrochloride RS
$C_{20}H_{24}N_2O_3S \cdot HCl$ 408.95
USP Fluconazole RS
USP Fluconazole Related Compound A RS
2-[2-Fluoro-4-(1*H*-1,2,4-triazol-1-yl)phenyl]-1,3-bis(1*H*-1,2,4-triazol-1-yl)-propan-2-ol.
USP Fluconazole Related Compound B RS
2-(4-Fluorophenyl)-1,3-bis(1*H*-1,2,4-triazol-1-yl)-propan-2-ol.
USP Fluconazole Related Compound C RS
1,1′-(1,3-Phenylene)di(1*H*-1,2,4-triazole).

Fluconazole Injection

DEFINITION
Fluconazole Injection is a sterile solution of Fluconazole in a suitable vehicle. It contains NLT 90.0% and NMT 110.0% of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$).

IDENTIFICATION
- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.