Fluphenazine Hydrochloride Tablets

Type of Posting	Revision Bulletin
Posting Date	20–Jul–2020
Official Date	21–Jul–2020
Expert Committee	Chemical Medicines Monographs 4
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 4 Expert Committee has revised the Fluphenazine Hydrochloride Tablets monograph. The purpose for the revision is to add a new *Dissolution Test 2* to accommodate FDA-approved drug products with different dissolution conditions and tolerances than the existing dissolution tests.

- *Dissolution Test 2* was validated using a Zorbax SB C8 brand of L7 column. The typical retention time for Fluphenazine is about 2.3 min.

Labeling information has been incorporated to support the inclusion of *Dissolution Test 2*.

The Fluphenazine Hydrochloride Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Ren-Hwa Yeh, Senior Scientific Liaison (301-998-6818 or rhy@usp.org).

Revision Bulletin
Official: July 21, 2020

Fluphenazine Hydrochloride Tablets

DEFINITION

Fluphenazine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of fluphenazine hydrochloride ($C_{22}H_{26}F_3N_3OS \cdot 2HCl$).

[Note—Throughout the following procedures, protect samples, the Reference Standard, and solutions containing them by conducting the procedures without delay, under subdued light, or using low-actinic glassware.]

IDENTIFICATION

• **A. Thin-Layer Chromatography**

Diluent: Methanol and water (80:20)

Standard solution: 20 mg/mL of USP Fluphenazine Hydrochloride RS in *Diluent* prepared as follows. Transfer 10 mg of USP Fluphenazine Hydrochloride RS to a separator. Add 5 mL of water and 20 mL of dilute hydrochloric acid (1 in 120) to the separator, shake for 10 min, and add 20 mL of chloroform-saturated sodium carbonate solution (1 in 10). Extract the resulting mixture with five 20-mL portions of chloroform, shaking gently to avoid emulsion formation, and pass the extract through a chloroform-washed cotton filter into a 150-mL beaker. Evaporate the extract on a steam bath to dryness, and dissolve the residue in 0.5 mL of *Diluent*.

Sample solution: Nominally 20 mg/mL of fluphenazine hydrochloride from Tablets in *Diluent* prepared as follows. Transfer a portion of finely powdered Tablets, equivalent to 10 mg of fluphenazine hydrochloride, to a separator. Add 5 mL of water and 20 mL of dilute hydrochloric acid (1 in 120) to the separator, shake for 10 min, and add 20 mL of chloroform-saturated sodium carbonate solution (1 in 10). Extract the resulting mixture with five 20-mL portions of chloroform, shaking gently to avoid emulsion formation, and pass the extract through a chloroform-washed cotton filter into a 150-mL beaker. Evaporate the extract on a steam bath to dryness, and dissolve the residue in 0.5 mL of *Diluent*.

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Acetone, cyclohexane, and diethylamine (40:15:1)

Spray reagent: Sulfuric acid in methanol (2 in 5)

Analysis

Samples: *Standard solution* and *Sample solution*

Allow the spots to dry, and develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Locate the spots on the plate by lightly spraying it with *Spray reagent*.

Acceptance criteria: The R_F value and color of the principal spot of the *Sample solution* correspond to those of the *Standard solution*.

ASSAY

• **Procedure**

Buffer: 0.05 M monobasic potassium phosphate adjusted with phosphoric acid to a pH of 2.5

Diluent: Acetonitrile, methanol, and *Buffer* (30:30:40)

Mobile phase: 0.2% triethylamine in *Diluent*

Standard solution: 0.06 mg/mL of USP Fluphenazine Hydrochloride RS in *Diluent*

Sample stock solution: Transfer 6 Tablets to a suitable volumetric flask, add *Diluent*, shake for 1 h, and sonicate for 10 min or until a fine suspension is obtained.

Sample solution: Nominally 0.06 mg/mL of fluphenazine hydrochloride from *Sample stock solution* in *Diluent*. Filter, and use the filtrate after discarding the first 5 mL of the filtrate.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 12.5-cm; packing L7

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluphenazine hydrochloride ($C_{22}H_{26}F_3N_3OS \cdot 2HCl$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Fluphenazine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of fluphenazine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- **Dissolution ⟨711⟩**

▲Test 1▲ (RB 21-Jul-2020)

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 45 min

Buffer: 0.05 M monobasic potassium phosphate adjusted with phosphoric acid to a pH of 2.5

Diluent: Acetonitrile, methanol, and *Buffer* (30:30:40)

Mobile phase: 0.3% triethylamine in *Diluent*

Sample solution: Dilute a portion of the solution under test with an equal volume of *Mobile phase*.

Standard solution: USP Fluphenazine Hydrochloride RS at a concentration and composition similar to that of the *Sample solution*

Chromatographic system and **System suitability:** Proceed as directed in the *Assay*, except use a flow rate of 2 mL/min and an injection volume of 100 µL.

Analysis

Samples: *Sample solution* and *Standard solution*

Determine the amount of fluphenazine hydrochloride ($C_{22}H_{26}F_3N_3OS \cdot 2HCl$) dissolved.

Tolerances: NLT 75% (*Q*) of the labeled amount of fluphenazine hydrochloride ($C_{22}H_{26}F_3N_3OS \cdot 2HCl$) is dissolved.

▲**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.1 N hydrochloric acid; 500 mL

Apparatus 1: 100 rpm

Time: 30 min

Diluted phosphoric acid solution: Transfer 10 mL of phosphoric acid to a 100-mL volumetric flask containing about 50 mL of water. Cool and dilute with water to volume.

Buffer: 6.8 g/L of monobasic potassium phosphate in water, adjusted with *Diluted phosphoric acid solution* to a pH of 2.5

Solution A: Acetonitrile, methanol, and *Buffer* (30:30:40)

Mobile phase: To each liter of *Solution A*, add 3.0 mL of triethylamine.

Diluent: *Medium* and *Mobile phase* (50:50)

Standard stock solution: 0.1 mg/mL of USP Fluphenazine Hydrochloride RS in *Diluent*. Sonicate to dissolve if needed.

Standard solution: (*L*/1000) mg/mL of USP Fluphenazine Hydrochloride RS from the *Standard stock solution* in *Diluent*, where *L* is the label claim in mg/Tablet

Sample stock solution: Pass a portion of the solution under test through an appropriate filter, and discard the first 2 mL of filtrate.

Sample solution: Transfer an equal volume of the *Sample stock solution* and the *Mobile phase* to a suitable container, and mix well.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 5-cm; 3.5-µm packing L7

Column temperature: 40°

Flow rate: 2 mL/min

Injection volume: 100 µL

Run time: NLT 2 times the retention time of fluphenazine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluphenazine hydrochloride ($C_{22}H_{26}F_3N_3OS \cdot 2HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times D \times V \times (1/L) \times 100$$

r_U = peak response of fluphenazine from the *Sample solution*

r_S = peak response of fluphenazine from the *Standard solution*

C_S = concentration of USP Fluphenazine Hydrochloride RS in the *Standard solution* (mg/mL)

D = dilution factor for the *Sample solution*, 2

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of fluphenazine hydrochloride ($C_{22}H_{26}F_3N_3OS \cdot 2HCl$) is dissolved. ▲ (RB 21-Jul-2020)

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.

Add the following:

▲● **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used. ▲ (RB 21-Jul-2020)

- **USP Reference Standards ⟨11⟩**
  USP Fluphenazine Hydrochloride RS

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