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Fenofibrate Tablets

DEFINITION

Fenofibrate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$).

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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

ASSAY

Change to read:

• **Procedure**

Acidified water: Adjust the pH of water with phosphoric acid to 2.5 ± 0.1.

Mobile phase: Acetonitrile and *Acidified water* (70:30)

System suitability stock solution: 0.1 mg/mL each of USP Fenofibrate Related Compound A RS and USP Fenofibrate Related Compound B RS in acetonitrile

System suitability solution: 0.5 µg/mL each of USP Fenofibrate Related Compound A RS and USP Fenofibrate Related Compound B RS in *Mobile phase* from the *System suitability stock solution*

Standard solution: 0.05 mg/mL of USP Fenofibrate RS in *Mobile phase*

Sample stock solution: Prepare a solution containing a nominal concentration of approximately 2–4 mg/mL of fenofibrate by disintegrating a suitable number of Tablets with sonication in *Acidified water*, using 30% of the final volume of the flask. Add acetonitrile to approximately 90% of flask volume, and sonicate with periodic swirling. Dilute with acetonitrile to volume.

Sample solution: Nominally 0.05 mg/mL of fenofibrate in *Mobile phase*, from the *Sample stock solution*. Filter a portion of this solution, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 286 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-May-2019)

Column: 4.0-mm × 25-cm or 4.6-mm × 25-cm; 5-µm or 4-µm packing L1

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 2 times the retention time of the fenofibrate peak▲ (USP 1-May-2019)

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between fenofibrate related compound A and fenofibrate related compound B peaks, *System suitability solution*

Relative standard deviation: NMT 2.0% for the fenofibrate peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.025 M sodium dodecyl sulfate in water; 1000 mL

Apparatus 2: 50 rpm

Time: 30 min

Acidified water: Adjust the pH of water with phosphoric acid to 2.5 ± 0.1.

Mobile phase: Acetonitrile and *Acidified water* (70:30)

Standard stock solution: 2.5 mg/mL of USP Fenofibrate RS in acetonitrile

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of about (0.001 × *L*) mg/mL, where *L* is the label claim, in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 286 nm

Column: 2-mm × 3-cm; 3-µm packing L1

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NLT 0.9 and NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 1000 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) is dissolved.

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

Medium: 0.05 M sodium dodecyl sulfate in water; 1000 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: 136 mg/L of monobasic potassium phosphate in water. Adjust with diluted phosphoric acid to a pH of 2.9 ± 0.05.

Mobile phase: Methanol and *Buffer* (80:20)

Standard solution: (0.001 × *L*) mg/mL of USP Fenofibrate RS in *Mobile phase*, where *L* is the label claim, in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 286 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 10 µL

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 fenofibrate ($C_{20}H_{21}ClO_4$) dissolved:

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

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

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

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 1000 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

For Tablet strengths other than 40 and 120 mg of fenofibrate

Medium: 0.05 M sodium lauryl sulfate in water; 1000 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: 0.012 mg/mL of USP Fenofibrate RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few milliliters of the filtrate and appropriately diluting with *Medium* to a concentration similar to that of the *Standard solution*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 292 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 1000 mL

D = dilution factor for the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) is dissolved.

For Tablets labeled to contain 40 and 120 mg of fenofibrate

Medium: 0.75% sodium lauryl sulfate in water; 900 mL

Apparatus 2: 75 rpm

Time: 45 min

Buffer: 2.72 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 2.9 ± 0.05.

Mobile phase: Methanol and *Buffer* (85:15)

Standard stock solution: 2.22 mg/mL of USP Fenofibrate RS prepared as follows. Transfer a suitable amount of USP Fenofibrate RS into a suitable volumetric flask. Add 50% of the flask volume of acetonitrile, sonicate to dissolve, and dilute with *Medium* to volume.

Standard solution: (L/900) mg/mL of USP Fenofibrate RS in *Medium* from *Standard stock solution*, where L is the label claim, in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 2 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of fenofibrate

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 fenofibrate ($C_{20}H_{21}ClO_4$) dissolved:

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

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

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

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

Acidified water, Mobile phase, System suitability solution, Sample stock solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

▲**Sensitivity solution:** 0.25 µg/mL of USP Fenofibrate RS in *Mobile phase*▲ (USP 1-May-2019)

Standard solution: 0.5 µg/mL of USP Fenofibrate RS in *Mobile phase*

Sample solution: Nominally 0.5 mg/mL of fenofibrate in *Mobile phase*, from the *Sample stock solution*. Filter a portion of this solution, discarding the first few milliliters of filtrate.

System suitability

Samples: *System suitability solution,* ▲*Sensitivity solution,*▲ (USP 1-May-2019) and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between fenofibrate related compound A and fenofibrate related compound B, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-May-2019)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each ▲degradation product▲ (USP 1-May-2019) in the portion of Tablets taken:

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

r_U = peak response of each ▲degradation product▲ (USP 1-May-2019) from the *Sample solution*

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

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Fenofibrate related compound A	0.34	1.3	0.2
Fenofibrate related compound B	0.36	1.0	0.50
(3*RS*)-3-[4-(4-Chlorobenzoyl)phenoxy]butan-2-one[a]	0.50	—	—
Methyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-propanoate[a]	0.65	—	—
Ethyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-propanoate[a]	0.80	—	—
(4-Chlorophenyl)[4-(1-methylethoxy)phenyl]methanone[a]	0.85	—	—
Fenofibrate	1.00	—	—
Fenofibrate related compound C[a,b]	1.35	—	—
Any unspecified ▲degradation product▲ (USP 1-May-2019)	—	1.0	0.2
Total ▲degradation products▲ (USP 1-May-2019) (includes fenofibrate related compounds A and B, and unspecified ▲degradation products)▲ (USP 1-May-2019)	—	—	1.0

[a] Disregard this impurity. It is a process impurity and is controlled in the drug substance monograph.

[b] 1-Methylethyl 2-[[2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoyl]oxy]-2-methylpropanoate.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, and store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Fenofibrate RS

USP Fenofibrate Related Compound A RS

(4-Chlorophenyl)(4-hydroxyphenyl)methanone.

$C_{13}H_9ClO_2$ 232.66

USP Fenofibrate Related Compound B RS

2-[4-(4-Chlorobenzoyl)phenoxy]-2-methylpropanoic acid, or fenofibric acid.

$C_{17}H_{15}ClO_4$ 318.75

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
FENOFIBRATE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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