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Fenofibrate Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-fenofibrate-caps-notice-20210430.

DEFINITION

Fenofibrate Capsules 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*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

- **Procedure**

Use *Sample stock solution 2* for Capsules labeled to meet the requirements of *Dissolution Test 2*. For all other products, use *Sample stock solution 1*.

Solution A: 136 mg/L of ▲potassium phosphate, monobasic▲ (RB 1-May-2021) in water. Adjust with dilute phosphoric acid (1 in 10) to a pH of 2.9 ± 0.05.

Mobile phase: Methanol and *Solution A* (4:1)

Standard solution: 67 µg/mL of USP Fenofibrate RS in *Mobile phase*

Sample stock solution 1: Accurately weigh the contents of NLT 20 Capsules. Mix the contents, and transfer a weighed portion of the powder, equivalent to about 67 mg of fenofibrate, to a 100-mL volumetric flask. Add 80 mL of *Mobile phase*, sonicate for 10 min, stir for 15 min, and dilute with *Mobile phase* to volume.

Sample stock solution 2 (for Capsules labeled to meet the requirements of *Dissolution Test 2*)**:** Weigh the contents of NLT 20 Capsules. Mix the contents, melt in an oven at 80° for NLT 30 min, and homogenize. Allow the sample to solidify. Transfer a weighed portion of the sample, equivalent to about 67 mg of fenofibrate, to a 100-mL volumetric flask, dissolve in 30 mL of methanol with the aid of a mechanical shaker for NLT 4 h, and dilute with *Mobile phase* to volume.

Sample solution: Nominally 67 µg/mL of fenofibrate from the designated *Sample stock solution*, in *Mobile phase*. Pass a portion of this solution through a polyvinylidene difluoride (PVDF) filter of 0.45-µm pore size, discarding the first 5 mL.

Chromatographic system

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

Mode: LC

Detector: UV 285 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

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

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of the fenofibrate peak

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 ($C_{20}H_{21}ClO_4$) in the portion of Capsules 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 the *Standard solution* (µg/mL)

C_U = nominal concentration of the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Test 1

Medium: 0.05 M ▲sodium dodecyl sulfate▲ (RB 1-May-2021) in water; 1000 mL, deaerated

Apparatus 2: 75 rpm

Time: 40 min

Solution A and **Mobile phase:** Prepare as directed in the *Assay*.

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

Sample solution: Pass a portion of the solution under test through a suitable PVDF filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

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

Flow rate: 1 mL/min

Injection volume: 10 µL for Capsules labeled to contain 67 mg; 5 µL for Capsules labeled to contain 134 or 200 mg

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 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/Capsule)

Tolerances: NLT 70% (*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: Phosphate buffer pH 6.8 ± 0.1 containing 0.1% pancreatin and 2% polysorbate 80; 900 mL, deaerated by vacuum

Apparatus 2: 75 rpm with sinkers (see *Dissolution* ⟨711⟩, *Figure 2a*)

Time: 2 h

Standard solution: (*L*/1000) mg/mL of USP Fenofibrate RS in *Medium*, where *L* is the label claim in mg/Capsule. A volume of methanol, not exceeding 10%, can be used in the first dilution to solubilize fenofibrate.

Sample solution: Pass 20 mL of the solution under test through a suitable PVDF filter of 0.45-µm pore size, discarding the first 2 mL.

Blank: *Medium*

Instrumental conditions

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

Mode: Spectrophotometry

Detector: UV 288 nm

Path length: 0.1-cm flow cell

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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*, 900 mL

L = label claim (mg/Capsule)

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 the product meets USP *Dissolution Test 3*.

Medium: 0.72% ▲sodium dodecyl sulfate▲ (RB 1-May-2021) in water; 1000 mL, deaerated

Apparatus 2: 75 rpm, with sinkers with three prongs

Time: 30 min

Standard solution: (L/10) mg/mL of USP Fenofibrate RS in methanol, where L is the label claim in mg/Capsule. Transfer 10.0 mL of this solution to a 1000-mL volumetric flask, and dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable PVDF filter of 0.45-µm pore size. Dilute with *Medium*, if necessary.

Instrumental conditions

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

Mode: Spectrophotometry

Detector: UV 290 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*

V = volume of *Medium*, 1000 mL

L = label claim (mg/Capsule)

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

Test 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: 0.05 M ▲sodium dodecyl sulfate▲ (RB 1-May-2021) in water; 1000 mL

Apparatus 2: 75 rpm, with helix sinkers or hose clamp sinkers

Times: 30 min for products labeled to contain 67, 134, and 200 mg; 40 min for products labeled to contain 43 and 130 mg

Standard stock solution: 0.5 mg/mL of USP Fenofibrate RS in *Medium* prepared as follows. Dissolve a suitable quantity of USP Fenofibrate RS, taken in a suitable volumetric flask, in about 6% of the total volume of methanol, and dilute with *Medium* to volume.

Standard solution: Prepare solutions of USP Fenofibrate RS in *Medium* as per *Table 1* from *Standard stock solution*.

Table 1

Capsule Strength (mg)	Concentration (mg/mL)
67	0.065
130 and 134	0.13
200	0.2
43	0.045

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 3 mL of the filtrate.

Instrumental conditions

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

Mode: Spectrophotometry

Detector: UV 291 nm

Path length: 0.1-cm flow cell

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

L = label claim (mg/Capsule)

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

Test 5: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 5*.

Medium: 0.025 M ▲sodium dodecyl sulfate▲ (RB 1-May-2021) in water; 1000 mL, deaerated

Apparatus 2: 75 rpm, with suitable sinkers

Time: 20 min

Standard stock solution: 0.5 mg/mL of USP Fenofibrate RS in methanol. Sonicate if necessary.

Standard solution: 12.5 µg/mL of USP Fenofibrate RS prepared by diluting quantitatively from *Standard stock solution* with *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size and discard the first few milliliters. Dilute quantitatively with *Medium* to the nominal concentration as per *Table 2*.

Table 2

Capsule Strength (mg)	Concentration (µg/mL)
30	12.0
90	13.5

Instrumental conditions

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

Mode: Spectrophotometry

Detector: UV 290 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Capsule)

D = dilution factor for the *Sample solution*

V = volume of *Medium*, 1000 mL

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

Test 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Dissolution Test 6 is suitable for products labeled to contain 200 mg of fenofibrate.

Medium, Solution A, Mobile phase, and **System suitability:** Proceed as directed in *Test 1*.

Apparatus 2: 75 rpm, with suitable sinkers

Time: 60 min

Standard solution: 0.2 mg/mL of USP Fenofibrate RS prepared as follows. Transfer a suitable amount of USP Fenofibrate RS into a suitable volumetric flask. Add methanol to 2% of the total volume of the flask and sonicate to dissolve. Dilute with *Medium* to volume.

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

Chromatographic system: Proceed as directed in *Test 1* except for *Run time*.

Run time: NLT 2 times the retention time of the fenofibrate

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 USP Fenofibrate RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 1000 mL

L = label claim (mg/Capsule)

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

▲**Test 7:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 7*.

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

Apparatus 2: 75 rpm

Time: 60 min

Buffer: 136 mg/L of potassium phosphate, monobasic in water. Adjust with dilute phosphoric acid (1:10, v/v) to a pH of 2.9 ± 0.05.

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

Standard solution: (L/1000) mg/mL of USP Fenofibrate RS in *Mobile phase*, where L is the label claim in mg/Capsule. Sonicate if necessary.

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

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

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

Flow rate: 1 mL/min

Injection volume: 10 µL for Capsules labeled to contain 67 mg; 5 µL for Capsules labeled to contain 134 or 200 mg

Run time: NLT 1.5 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 USP Fenofibrate RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 1000 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) is dissolved.▲ (RB 1-May-2021)

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

Procedure for content uniformity

Solution A, Mobile phase, Standard solution, Chromatographic system, System suitability, and **Analysis:** Proceed as directed in the *Assay*, except to prepare the *Sample stock solution* and *Sample solution* as follows.

Sample stock solution: Place 1 Capsule in a suitable volumetric flask, add *Solution A* to 10%–20% of the final volume, and stir for 20 min to disintegrate the Capsule. Fill the flask to about 80% with methanol, sonicate for 10 min, and stir for 15 min. Dilute with methanol to volume to obtain a solution having a known concentration of about 0.4–0.7 mg/mL of fenofibrate, based on the label claim.

Sample solution: Nominally 60–70 µg/mL of fenofibrate, from the *Sample stock solution*, in *Mobile phase*. Pass a portion of this solution through a PVDF filter of 0.45-µm pore size, discarding the first 5 mL.

IMPURITIES

Change to read:

• **Organic Impurities**

Use *Sample solution 2* for Capsules labeled to meet the requirements of *Dissolution Test 2*. For all other products, use *Sample solution 1*.

Solution A: 136 mg/L of ▲potassium phosphate, monobasic.▲ (RB 1-May-2021) Adjust with dilute phosphoric acid (1 in 10) to a pH of 2.9 ± 0.05.

Mobile phase: Methanol and *Solution A* (4:1)

System suitability solution: 0.67 mg/mL of USP Fenofibrate RS and 3.35 µg/mL of USP Fenofibrate Related Compound B RS in *Mobile phase*

Standard solution: 3.35 µg/mL of USP Fenofibrate RS and 3.35 µg/mL of USP Fenofibrate Related Compound B RS in *Mobile phase*

Sensitivity solution: 0.67 µg/mL of USP Fenofibrate RS and 0.67 µg/mL of USP Fenofibrate Related Compound B RS in *Mobile phase*, from the *Standard solution*

Sample solution 1: Nominally 0.67 mg/mL of fenofibrate prepared as follows. Accurately weigh the contents of NLT 20 Capsules. Mix the contents, and transfer a weighed portion of the powder, equivalent to about 67 mg of fenofibrate, to a 100-mL volumetric flask. Add 80 mL of *Mobile phase*, sonicate for 10 min, stir for 15 min, and dilute with *Mobile phase* to volume. Pass a portion of this solution through a PVDF filter of 0.45-µm pore size, discarding the first 5 mL.

Sample solution 2 (for Capsules labeled to meet the requirements of *Dissolution Test 2*)**:** Nominally 0.67 mg/mL of fenofibrate prepared as follows. Weigh the contents of NLT 20 Capsules. Mix the contents, melt in an oven at 80° for NLT 30 min, and homogenize. Allow the sample to solidify. Transfer a weighed portion of the sample, equivalent to about 67 mg of fenofibrate, to a 100-mL volumetric flask, dissolve in 30 mL of methanol with the aid of a mechanical shaker for NLT 4 h, and dilute with *Mobile phase* to volume. Pass through a PVDF filter of 0.45-µm pore size, discarding the first 1–2 mL.

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

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

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of the fenofibrate peak

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between fenofibrate and fenofibrate related compound B, *System suitability solution*

Tailing factor: NMT 2.0 for fenofibrate related compound B, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Signal-to-noise ratio: NLT 10 for the fenofibrate peak, *Sensitivity solution*

Analysis

Samples: *Standard solution* and designated *Sample solution*

Calculate the percentage of fenofibrate related compound B in the portion of Capsules taken:

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

r_U = peak response of fenofibrate related compound B from the *Sample solution*

r_S = peak response of fenofibrate related compound B from the *Standard solution*

C_S = concentration of fenofibrate related compound B in the *Standard solution* (mg/mL)

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

Calculate the percentage of any unspecified impurity in the portion of Capsules taken:

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

r_U = peak response of each unspecified impurity from the *Sample solution*

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

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

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

Acceptance criteria

Individual impurities: NMT 0.5% for fenofibrate related compound B; NMT 0.2% for any other unspecified impurity

Total impurities: NMT 2.0%

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 test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Fenofibrate RS

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 CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2

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