Fenofibrate Tablets

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Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2015-2020 Council of Experts, the *Chemical Medicines Monographs 2 Expert Committee* has revised the Fenofibrate Tablets monograph. The purpose of this revision is to include the dissolution conditions and tolerances for two newly approved tablet strengths in the *Dissolution Test 3*.

The liquid chromatographic procedure is validated using an Inertsil ODS 3V brand of L1 column. The typical retention time for fenofibrate is about 3.1 min.

Minor editorial changes have been made to update the monograph to the current *USP* style.

The Fenofibrate Tablets Revision Bulletin supersedes the currently official Fenofibrate Tablets monograph. The Revision Bulletin will be incorporated in the *Second supplement* to *USP 40–NF 35.*

Should you have any questions, please contact Sujatha Ramakrishna, Ph.D., MBA. Senior Scientific Liaison (301–816–8349 or sxr@usp.org).

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*.

ASSAY

• **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 approximately 2–4 mg/mL of fenofibrate by disintegrating the appropriate 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: 0.05 mg/mL of fenofibrate in *Mobile phase*, based on the label claim from the *Sample stock solution*. Filter a portion of this solution, discarding the first few mL of the filtrate.

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 286 nm
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

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%, *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 from the *Sample solution*
r_S = peak response 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

Change to read:

• **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 mL 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:

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

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)
L = label claim (mg/Tablet)
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 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)
Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few mL of the filtrate.
Standard solution: (0.001 × *L*) mg/mL of USP Fenofibrate RS in *Mobile phase*, where *L* is the label claim, in mg/Tablet
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:

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

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)
L = label claim (mg/Tablet)
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 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

•**For tablet strengths other than 40 mg and 120 mg of fenofibrate**• (RB 1-Dec-2016)
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 mL 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: Spectrophotometry
Detector: UV 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
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 mg 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 from *Standard stock solution* in *Medium*, 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 mL 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:

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

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)
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$) is dissolved.• (RB 1-Dec-2016)

• **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES

• **ORGANIC IMPURITIES**
Acidified water, Mobile phase, System suitability solution, Sample stock solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
Standard solution: 0.5 µg/mL of USP Fenofibrate RS in *Mobile phase*
Sample solution: 0.5 mg/mL of fenofibrate in *Mobile phase*, based on the label claim from the *Sample stock solution*. Filter a portion of this solution, discarding the first few mL of filtrate.
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 5.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity 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 impurity 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	0.50	—	—[a]
Methyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoate	0.65	—	—[a]
Ethyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoate	0.80	—	—[a]
(4-Chlorophenyl)[4-(1-methylethoxy)phenyl]methanone	0.85	—	—[a]
Fenofibrate	1.00	—	—
Fenofibrate related compound C[b]	1.35	—	—[a]
Any unspecified impurity	—	1.0	0.2
Total impurities (includes fenofibrate related compounds A and B, and unspecified impurities)	—	—	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