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 the 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: 0.9–1.5
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 is dissolved.

•**Test 3:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.
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 *Spectrophotometry and Light-Scattering* ⟨851⟩.)
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:

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

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/Tablet)
D = dilution factor
V = volume of *Medium*, 1000 mL

Tolerances: NLT 75% (*Q*) of the labeled amount of fenofibrate is dissolved.● (RB 1-Aug-2013)

• **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*.
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 the 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 for 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● (RB 1-Dec-2013)
(3*RS*)-3-[4-(4-Chlorobenzoyl) phenoxy]butan-2-one	0.50	—	—[a]
Methyl 2-[4-(4-chlorobenzoyl) phenoxy]-2-methyl-propanoate	0.65	—	—[a]
Ethyl 2-[4-(4-chlorobenzoyl) phenoxy]-2-methyl-propanoate	0.80	—	—[a]
(4-Chlorophenyl)[4-(1-methylethoxy) phenyl]methanone	0.85	—	—[a]
Fenofibrate	1.00	—	—
Fenofibrate related compound C[b]	1.35	—	—[a]

[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.

Table 1 *(Continued)*

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Any unspecified impurity	—	1.0	0.2
Total impurities (includes fenofibrate related compounds A and B, and unspecified impurities)	—	—	●1.0● (RB 1-Dec-2013)

[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