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Add the following:

▲Fenofibric Acid Delayed-Release Capsules

DEFINITION

Fenofibric Acid Delayed-Release Capsules contain an amount of Choline Fenofibrate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K

Sample: Grind the contents of one Capsule, excluding the gelatin shell, to a fine powder. Use an appropriate amount of sample.

Acceptance criteria: The IR absorption spectrum of the *Sample* exhibits maxima at about 1700–1200 and 950–650 cm^{-1} wavenumbers, typical for choline fenofibrate.

• **B.** 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**

Protect all solutions containing fenofibric acid from light.

Solution A: Water adjusted with phosphoric acid to a pH of 2.5

Mobile phase: Acetonitrile and *Solution A* (55:45)

Diluent: Methanol and water (50:50)

Standard solution: Equivalent to 0.25 mg/mL of fenofibric acid from USP Choline Fenofibrate RS in *Diluent*

Sample stock solution: Nominally equivalent to 1 mg/mL of fenofibric acid from Capsules prepared as follows. Empty, weigh, and mix the contents of Capsules (NLT 20) and transfer a suitable amount of the mixture to a suitable volumetric flask. Add 50% of the flask volume of methanol and sonicate for about 15 min. Add an additional 40% of the flask volume of water and stir for about 30 min. Cool to room temperature and dilute with water to volume. Centrifuge a portion and use the clear supernatant.

Sample solution: Nominally equivalent to 0.25 mg/mL of fenofibric acid in *Diluent* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 286 nm

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

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.3 times the retention time of the fenofibric acid

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.7

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of fenofibric acid from the *Sample solution*

r_S = peak response of fenofibric acid from the *Standard solution*

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

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

M_{r1} = molecular weight of fenofibric acid, 318.75

M_{r2} = molecular weight of choline fenofibrate, 421.91

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Protect all solutions containing fenofibric acid from light.

Acid stage medium: 0.05 M monobasic sodium phosphate, pH 3.5 prepared as follows. Dissolve 6.9 g of monobasic sodium phosphate in 1 L of water. Adjust with 0.05 M phosphoric acid to a pH of 3.5; 510 mL.

Buffer concentrate: 0.05 M sodium phosphate, pH 11.5 prepared as follows. Dissolve 6.9 g of monobasic sodium phosphate and 2.4 g of sodium hydroxide in 1 L of water.

Buffer stage medium: 0.05 M sodium phosphate buffer, pH 6.8 (add 400 mL of *Buffer concentrate* over a period of time not exceeding 5 min, to the vessel containing the *Acid stage medium*); 900 mL

Apparatus 2: 50 rpm

Times

Acid stage: 2 h

Buffer stage: 2.5, 3.5, and 6 h

Acidified water: 0.3% perchloric acid in water

Mobile phase: Acetonitrile and *Acidified water* (65:35)

Standard stock solution: 0.9 mg/mL of USP Fenofibric Acid RS prepared as follows. Weigh a known amount of USP Fenofibric Acid RS into a suitable volumetric flask. Dissolve in 10% of the total volume of acetonitrile, mix, and sonicate for about 30 min. Dilute with *Buffer stage medium* to volume.

Standard solutions: Prepare *Standard solutions* in *Buffer stage medium* as described in *Table 1*, from the *Standard stock solution*.

Table 1

Standard Solutions for 135-mg Capsules	Concentration (mg/mL)
I	0.01
II	0.05
III	0.13
IV	0.15
V	0.2

Standard Solutions for 45-mg Capsules	Concentration (mg/mL)
I	0.005
II	0.01
III	0.03
IV	0.045

Standard Solutions for 45-mg Capsules	Concentration (mg/mL)
V	0.06

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 286 nm

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

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

Run time: NLT 1.5 times the retention time of fenofibric acid

System suitability

Samples: *Standard solution I*, *Standard solution II*, *Standard solution III*, *Standard solution IV*, and *Standard solution V*

Suitability requirements

Correlation coefficient: NLT 0.9990 for fenofibric acid of the standard curve from the linear regression in the *Analysis*

Tailing factor: NMT 2.0, *Standard solution V*

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

Analysis

Samples: *Standard solution I*, *Standard solution II*, *Standard solution III*, *Standard solution IV*, *Standard solution V*, and *Sample solution*

Acid stage: At the 2-h time point, remove a 10-mL aliquot from each vessel. Dilute the aliquot with *Buffer concentrate* at a 5:4 ratio.

Buffer stage: At the specified sampling times for the *Buffer stage*, remove a 10-mL aliquot from each vessel and filter.

Using linear regression analysis, generate a standard curve for the fenofibric acid peak responses versus concentrations of *Standard solution I*, *Standard solution II*, *Standard solution III*, *Standard solution IV*, and *Standard solution V*. Determine the concentration (C_i), in mg/mL, of the fenofibric acid in the *Sample solution* using the standard curve.

Calculate the percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$) dissolved in the acid stage:

$$\text{Result}_1 = C_1 \times V \times D \times (1/L) \times 100$$

C_1 = concentration of fenofibric acid in the *Acid stage* (mg/mL)

V = volume of *Acid stage medium*, 510 mL

D = dilution factor

L = label claim (mg/Capsule)

Calculate the percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$) dissolved in the buffer stage at each time point (i):

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S] \times (1/L) \times 100$$

$$\text{Result}_4 = \{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S] \times (1/L) \times 100$$

C_i = concentration of fenofibric acid in the *Sample solution* (from the Standard curve) at the specified time point (i) (mg/mL)

V = volume of *Buffer stage medium*, 900 mL

V_S = volume of the *Sample solution* withdrawn at each time point in the *Buffer stage* (mL)

L = label claim (mg/Capsule)

Tolerances: See *Table 2*.

Table 2

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 10
2	2.5	NMT 30
3	3.5	49–69
4	6	NLT 80

The percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$), dissolved at the times specified in *Table 2*, conform to *Dissolution ⟨711⟩, Acceptance Table 2*.

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

Acid stage medium: 0.05 M sodium phosphate prepared as follows. Dissolve 7.8 g of sodium phosphate monobasic dihydrate and 11.68 g of sodium chloride in 1 L of water. Adjust with diluted phosphoric acid to a pH of 3.5; 500 mL.

Buffer concentrate: Dissolve 19.0 g of tribasic sodium phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 11.5.

Buffer stage medium: 0.05 M sodium phosphate buffer, pH 6.8 prepared as follows. Add 400 mL of *Buffer concentrate* to the vessel containing 500 mL of the *Acid stage medium*. The pH of the final solution is about 6.8 (if necessary adjust with phosphoric acid or 0.1 N sodium hydroxide VS solution to the required pH); 900 mL.

Apparatus 2: 50 rpm, with suitable sinkers

Times

Acid stage: 2 h

Buffer stage: 2.5, 3.5, and 8 h

Buffer: Dissolve 1.4 g of potassium phosphate monobasic in 1 L of water.

Mobile phase: Acetonitrile and *Buffer* (50:50). Adjust with phosphoric acid to a pH of 3.0.

Diluent: 0.05 M sodium phosphate prepared as follows. Dissolve 7.8 g of sodium phosphate monobasic dihydrate and 11.68 g of sodium chloride in 1 L of water. Adjust with diluted phosphoric acid to a pH of 3.0.

Standard solution

For capsule strength of 45 mg: Equivalent to 0.1 × (*L*/900) mg/mL of fenofibric acid from USP Choline Fenofibrate RS prepared as follows. Transfer a suitable amount of USP Choline Fenofibrate RS into a suitable volumetric flask. Add 5% of the flask volume of methanol and sonicate to dissolve and then dilute with *Buffer stage medium*. Further dilute a suitable amount of this solution in a suitable volumetric flask with *Diluent* to volume.

For capsule strength of 135 mg: Equivalent to 0.1 × (*L*/900) mg/mL of fenofibric acid from USP Choline Fenofibrate RS prepared as follows. Transfer a suitable amount of USP Choline Fenofibrate RS into a suitable volumetric flask. Add 5% of the flask volume of methanol and sonicate to dissolve and then dilute with *Buffer stage medium*. Transfer a suitable amount of this solution to a suitable volumetric flask, add 5% of the flask volume of *Buffer stage medium*, and dilute with *Diluent* to volume.

Sample solution

Acid stage: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Dilute 3 mL of the filtrate with *Diluent* to 50 mL.

Buffer stage: At the end of the acid stage, add 400 mL of *Buffer concentrate* to the vessel. Withdraw 10 mL samples at the specified times and pass through a suitable filter of 0.45-µm pore size and discard the first few milliliters. Dilute 2 mL of the filtrate with *Diluent* to 20 mL.

Chromatographic system

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

Mode: LC

Detector: UV 299 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Temperatures

Autosampler: 10°

Column: 30°

Flow rate: 1.5 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of fenofibric acid

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 concentration (C_i) of fenofibric acid ($C_{17}H_{15}ClO_4$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response of fenofibric acid from the *Sample solution*

r_S = peak response of fenofibric acid from the *Standard solution*

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

M_{r1} = molecular weight of fenofibric acid, 318.75

M_{r2} = molecular weight of choline fenofibrate, 421.91

Calculate the percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$) dissolved in the acid stage:

$$\text{Result}_1 = C_1 \times V \times D \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

C_1 = concentration of fenofibric acid in the *Acid stage* (mg/mL)

V = volume of *Acid stage medium*, 500 mL

D = dilution factor

L = label claim (mg/Capsule)

M_{r1} = molecular weight of fenofibric acid, 318.75

M_{r2} = molecular weight of choline fenofibrate, 421.91

Calculate the percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$) dissolved in the buffer stage at each time point (i):

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

$$\text{Result}_3 = \{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S] \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

$$\text{Result}_4 = \{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S] \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

C_i = concentration of fenofibric acid in the *Sample solution* at the specified time point (i) (mg/mL)

V = volume of *Buffer stage medium*, 900 mL

V_S = volume of the *Sample solution* withdrawn at each time point in the buffer stage (mL)

L = label claim (mg/Capsule)

M_{r1} = molecular weight of fenofibric acid, 318.75

M_{r2} = molecular weight of choline fenofibrate, 421.91

Tolerances: See *Table 3*.

Table 3

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 10
2	2.5	NMT 30
3	3.5	50–75
4	8	NLT 80

The percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$), dissolved at the times specified in *Table 3*, conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

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

Acid stage medium: 0.05 M sodium phosphate, monobasic, pH 3.5 prepared as follows. Dissolve 6.9 g of sodium phosphate, monobasic in 1 L of water. Adjust with 0.1% hydrochloric acid to a pH of 3.5; 500 mL.

Buffer concentrate: 0.05 M sodium phosphate, pH 11.2 prepared as follows. Dissolve 6.9 g of sodium phosphate, monobasic in 1 L of water. Adjust with a solution of 0.2 g/mL of sodium hydroxide to a pH of 11.2.

Buffer stage medium: 0.05 M sodium phosphate buffer, pH 6.8 prepared as follows. Add 400 mL of *Buffer concentrate* to the vessel containing 500 mL of the *Acid stage medium*. The pH of the final solution is about 6.8; 900 mL.

Apparatus 2: 50 rpm

Times

Acid stage: 2 h

Buffer stage: 2.5, 3.5, and 6 h

Acidified water: 0.1% v/v phosphoric acid in water

Mobile phase: Acetonitrile and *Acidified water* (55:45)

Standard stock solution: Equivalent to 0.5 mg/mL of fenofibric acid from USP Choline Fenofibrate RS prepared as follows. Weigh a known amount of USP Choline Fenofibrate RS into a suitable volumetric flask. Add 20% of the total volume of methanol and sonicate to dissolve. Dilute with *Buffer stage medium* to volume.

Standard solution

Acid stage: Equivalent to 0.18 × (*L*/1000) mg/mL of fenofibric acid in *Acid stage medium* from the *Standard stock solution*

Buffer stage: Equivalent to 1.12 × (*L*/1000) mg/mL of fenofibric acid in *Buffer stage medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter. Replace with an amount equivalent to the sample withdrawn with the *Acid stage medium* at the end of acid stage or the *Buffer concentrate* at the specified sampling times in the buffer stage.

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: 2 mL/min

Injection volume: 10 µL

Run time: NLT 1.6 times the retention time of fenofibric acid

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solutions* and *Sample solution*

Acid stage: Add one Capsule to each vessel containing *Acid stage medium*. At the 2-h time point, remove a 5-mL aliquot from each vessel and replace with 5 mL of fresh *Acid stage medium*.

Buffer stage: After 2 h into the acid stage, add 400 mL of the *Buffer concentrate*. At the specified sampling times for the buffer stage, remove a 10-mL aliquot from each vessel and replace with 10 mL of fresh *Buffer concentrate* and filter.

Calculate the concentration of the fenofibric acid ($C_{17}H_{15}ClO_4$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2})$$

r_U = peak response of fenofibric acid from the *Sample solution*

r_S = peak response of fenofibric acid from the *Standard solution*

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

M_{r1} = molecular weight of fenofibric acid, 318.75

M_{r2} = molecular weight of choline fenofibrate, 421.91

Calculate the percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$) dissolved in the acid stage:

$$\text{Result}_1 = C_1 \times V \times D \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

C_1 = concentration of fenofibric acid in the acid stage (mg/mL)

V = volume of *Acid stage medium*, 500 mL

D = dilution factor

L = label claim (mg/Capsule)

M_{r1} = molecular weight of fenofibric acid, 318.75

M_{r2} = molecular weight of choline fenofibrate, 421.91

Calculate the percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$) dissolved in the buffer stage at each time point (*i*):

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

$$\text{Result}_3 = (C_3 \times V) + [(C_2 + C_1) \times V_S] \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

$$\text{Result}_4 = (C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S] \times (1/L) \times (M_{r1}/M_{r2}) \times 100$$

C_i = concentration of fenofibric acid in the *Sample solution* at the specified time point (*i*) (mg/mL)

V = volume of *Buffer stage medium*, 900 mL

V_S = volume of the *Sample solution* withdrawn at each time point in the buffer stage (mL)

L = label claim (mg/Capsule)

M_{r1} = molecular weight of fenofibric acid, 318.75

M_{r2} = molecular weight of choline fenofibrate, 421.91

Tolerances: See *Table 4*.

Table 4

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 10
2	2.5	10–30
3	3.5	50–70

Time Point (*i*)	Time (h)	Amount Dissolved (%)
4	6	NLT 80

The percentage of the labeled amount of fenofibric acid ($C_{17}H_{15}ClO_4$), dissolved at the times specified in *Table 4*, conform to *Dissolution ⟨711⟩*, *Acceptance Table 2*.

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

IMPURITIES

• **Organic Impurities**

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

Standard stock solution: Equivalent to 0.25 mg/mL of fenofibric acid from USP Choline Fenofibrate RS in *Diluent*

Standard solution: Equivalent to 0.01 mg/mL of fenofibric acid from the *Standard stock solution* in *Diluent*

Sensitivity solution: Equivalent to 0.001 mg/mL of fenofibric acid from the *Standard solution* in *Diluent*

Sample solution: Nominally 1 mg/mL of fenofibric acid from Capsules prepared as follows. Empty, weigh, and mix the contents of Capsules (NLT 20) and transfer a suitable amount of the mixture to a suitable volumetric flask. Add 50% of the flask volume of methanol and sonicate for about 15 min. Add an additional 40% of the flask volume of water and stir for about 30 min. Dilute with water to volume. Centrifuge a portion of the solution and use the clear supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 286 nm

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

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 1.3 times the retention time of fenofibric acid

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any degradation product in the portion of Capsules taken:

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

r_U = peak response of any degradation product from the *Sample solution*

r_S = peak response of fenofibric acid from the *Standard solution*

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

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

Acceptance criteria: See *Table 5*. The reporting threshold is 0.1%.

Table 5

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fenofibric acid	1.0	—
Any degradation product	—	0.2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Total degradation products	—	0.8

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature. Protect from moisture.

• **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 Choline Fenofibrate RS

USP Fenofibric Acid RS

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

$C_{17}H_{15}ClO_4$ 318.75▲ (USP 1-Dec-2024)

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

Topic/Question	Contact	Expert Committee
FENOFIBRIC ACID DELAYED-RELEASE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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