**Fenofibrate Tablets**

**DEFINITION**
Fenofibrate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of fenofibrate (C20H21ClO4).

**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 (C20H21ClO4) dissolved in the portion of Tablets taken:

\[ \text{Result} = \left( \frac{r_0}{r_s} \right) \times \left( \frac{C_s}{C_d} \right) \times 100 \]

- \( r_0 \) = peak response from the Sample solution
- \( r_s \) = peak response from the Standard solution
- \( C_s \) = concentration of the Standard solution (mg/mL)
- \( C_d \) = 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 (C20H21ClO4) dissolved:

\[ \text{Result} = \left( \frac{r_0}{r_s} \right) \times \left( \frac{C_s}{C_d} \right) \times V \times 100 \]

- \( r_0 \) = peak response from the Sample solution
- \( r_s \) = peak response from the Standard solution
- \( C_s \) = concentration of the Standard solution (mg/mL)
- \( C_d \) = nominal concentration of fenofibrate in the Sample solution (mg/mL)
- \( L \) = label claim (mg/Tablet)
- \( V \) = volume of Medium, 1000 mL

**Tolerances**: NLT 80% (Q) of the labeled amount of fenofibrate (C20H21ClO4) 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.)
2 Fenofibrate

Mode: LC
Detector: UV 286 nm
Column: 4.6-mm x 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 (C20H21ClO4) dissolved:

Result = \( \frac{r_U}{r_S} \times \frac{C_S}{L} \times V \times 100 \)

- \( r_U \) = 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 (C20H21ClO4) dissolved:

Result = \( \frac{A_U}{A_S} \times \frac{C_S}{L} \times D \times V \times 100 \)

- \( A_U \) = 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.

**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 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:

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

- \( r_U \) = peak response for each impurity from the Sample solution
- \( r_S \) = peak response for each impurity from the Standard solution
- \( C_S \) = concentration of USP Fenofibrate RS in the Sample 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

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fenofibrate related compound A</td>
<td>0.34</td>
<td>1.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Fenofibrate related compound B</td>
<td>0.36</td>
<td>1.0</td>
<td><img src="https://example.com" alt="0.50" /> (2013-Dec)</td>
</tr>
<tr>
<td>(3R)-3-[4-(4-Chlorobenzoyl) phenoxy]-2-methylpropanoate</td>
<td>0.50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Methyl 2-[4-(4-chlorobenzoyl) phenox]-2-methylpropanoate</td>
<td>0.65</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ethyl 2-[4-(4-chlorobenzoyl) phenox]-2-methylpropanoate</td>
<td>0.80</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(4-Chlorophenyl)4-(1-methylethoxy) phenylmethane</td>
<td>0.85</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fenofibrate related compound C&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.35</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

<sup>a</sup> Disregard this impurity. It is a process impurity and is controlled in the drug substance monograph.
<sup>b</sup> 1-Methylethyl 2-[(2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropoxy)]oxy]-2-methylpropanoate.
Table 1 (Continued)

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any unspecified impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Total impurities (includes fenofibrate related compounds A and B, and unspecified impurities)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

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

- 1-Methylethyl 2-[2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropionyloxy]-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. 
  \[\text{C}_{17}\text{H}_{15}\text{ClO}_4\] 318.75
- USP Fenofibrate Related Compound B RS 2-[4-(4-Chlorobenzoyl)phenoxy]-2-methylpropanoic acid, or fenofibric acid.
  \[\text{C}_{17}\text{H}_{15}\text{ClO}_4\] 318.75