Amlodipine and Atorvastatin Tablets

**Type of Posting**
Notice of Intent to Revise

**Posting Date**
26–Oct–2018

**Targeted Official Date**
To Be Determined, Revision Bulletin

**Expert Committee**
Chemical Medicines Monographs 2

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Chemical Medicines Monographs 2 Expert Committee intends to revise the Amlodipine and Atorvastatin Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add Dissolution Test 2 to the monograph.

- **Dissolution Test 2** was validated using an Agilent Zorbax Eclipse XDB-C18 brand of L1 column. The typical retention times for amlodipine and atorvastatin are about 0.46 and 3.9 min, respectively.

**Labeling** information has been incorporated to support the inclusion of **Dissolution Test 2**. The revision also necessitates a change in the table numbering in the tests for **Organic Impurities Related to Amlodipine** and **Organic Impurities Related to Atorvastatin**.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.¹

Should you have any questions, please contact Edith Chang, Ph.D., Senior Scientific Liaison (301-816-8392 or yec@usp.org).

¹This text is not the official version of a USP–NF monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the USP–NF for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product’s final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the Pharmacopeial Forum must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the USP–NF.
Add the following:

▲ Amlodipine and Atorvastatin Tablets

**DEFINITION**
Amlodipine and Atorvastatin Tablets contain an amount of amlodipine besylate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of amlodipine \((\text{C}_{20}\text{H}_{25}\text{ClN}_{2}\text{O}_{3})\) and an amount of atorvastatin calcium equivalent to NLT 95.0% and NMT 105.0% of the labeled amount of atorvastatin \((\text{C}_{33}\text{H}_{36}\text{FN}_{2}\text{O}_{5})\). It may contain suitable antioxidants.

**IDENTIFICATION**
- **A.** The UV spectrum of the major peaks of the Sample solution exhibits maxima and minima at the same wavelengths as that of the Standard solution, as obtained in the Assay.
- **B.** The retention times of the major peaks of the Sample solution correspond to those of the Standard solution, as obtained in the Assay.

**ASSAY**

**Change to read:**

- **PROCEDURE**
  - **Solution A:** Dissolve 1.54 g of ammonium acetate in 1000 mL of water and add 2 mL of triethylamine. Adjust with acetic acid to a pH of 5.0.
  - **Mobile phase:** Acetonitrile, methanol, and Solution A (38:15:47)
  - **Buffer:** Transfer 7 mL of triethylamine to a 1000-mL volumetric flask containing 900 mL of water and mix. Adjust with dilute phosphoric acid (1 in 100) to a pH of 3.0 and dilute with water to volume.
  - **Diluent:** Acetonitrile, methanol, and Buffer (3:7:10)
  - **Standard stock solution 1:** 0.35 mg/mL of USP Amlodipine Besylate RS in methanol
  - **Standard stock solution 2:** 0.44 mg/mL of USP Atorvastatin Calcium RS in methanol
  - **Standard solution:** Prepare solutions of USP Amlodipine Besylate RS and USP Atorvastatin Calcium RS in Mobile phase at concentrations given in Table 1 from Standard stock solution 1 and Standard stock solution 2.

<table>
<thead>
<tr>
<th>Strength of Tablet, Amlodipine/Atorvastatin (mg/mg)</th>
<th>Concentration of Amlodipine Besylate (mg/mL)</th>
<th>Concentration of Atorvastatin Calcium (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5/10, 5/20, 10/40</td>
<td>0.028</td>
<td>0.088</td>
</tr>
<tr>
<td>2.5/20, 5/40, 10/80</td>
<td>0.014</td>
<td>0.088</td>
</tr>
<tr>
<td>5/10, 10/20</td>
<td>0.028</td>
<td>0.044</td>
</tr>
<tr>
<td>2.5/40, 5/80</td>
<td>0.014</td>
<td>0.176</td>
</tr>
<tr>
<td>10/10</td>
<td>0.028</td>
<td>0.022</td>
</tr>
</tbody>
</table>

**Sample solution:** Transfer NLT 10 Tablets to a suitable volumetric flask. Add about 20% of the final volume of the volumetric flask size in Diluent and sonicate to disperse the Tablets. Add about 40% of the final volume of the volumetric flask size in Diluent, sonicate for 20 min, and dilute with Diluent to volume. Centrifuge and transfer a suitable quantity of the supernatant to an appropriate suitable volumetric flask. Dilute with Mobile phase to volume to obtain the nominal concentrations of amlodipine and atorvastatin similar to that of the Standard solution.

**Chromatographic system**
(See Chromatography (621), System Suitability.)

- **Mode:** LC
- **Detector:** UV 237 nm. For Identification A, use a diode array detector in the range of 200–400 nm.
- **Column:** 4.6-mm × 15-cm; 5-µm packing L1
- **Column temperature:** 35°C
- **Flow rate:** 1 mL/min
- **Injection volume:** 20 µL
- **Run time:** NLT 3.5 times the retention time of amlodipine

**System suitability**
- **Sample:** Standard solution
- **Suitability requirements**
  - **Tailing factor:** NMT 2.0 for both peaks
  - **Relative standard deviation:** NMT 2.0% for both peaks

**Analysis**
- **Samples:** Standard solution and Sample solution

Calculate the percentage of the labeled amount of amlodipine \((\text{C}_{20}\text{H}_{25}\text{ClN}_{2}\text{O}_{3})\) in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_i}{r_0} \right) \times \left( \frac{S}{C_0} \right) \times \left( \frac{M_{12}}{M_{11}} \right) \times 100
\]

- **Acceptance criteria**
  - **Amlodipine:** 90.0%–110.0%
  - **Atorvastatin:** 94.5%–105.0%
PERFORMANCE TESTS

Change to read:

• **DISSOLUTION (711)**
  Test 1a (TBD)
  Solution A, Mobile phase, Standard stock solution 1, Standard stock solution 2, Chromatographic system, and System suitability: Proceed as directed in the Assay.
  Medium: 0.1% polysorbate 80 in pH 6.8 phosphate buffer; 900 mL
  Apparatus 2: 75 rpm
  Time: 20 min
  Standard solution: \((L_1/900)\) mg/mL of amlodipine and \((L_2/900)\) mg/mL of atorvastatin in Medium from Standard stock solution 1 and Standard stock solution 2, where \(L_1\) is the label claim of amlodipine in mg/Tablet and \(L_2\) is the label claim of atorvastatin in mg/Tablet
  Sample solution: Centrifuge the solution under test and use the supernatant.

Analysis
  Samples: Standard solution and Sample solution
  Calculate the percentage of the labeled amount of amlodipine \((C_{20}H_{23}CIN_{3}O_{5})\) dissolved:
  \[
  \text{Result} = \left(\frac{r_1}{r_2}\right) \times C_s \times V \times \left(M_1/M_2\right) \times (1/L) \times 100
  \]
  \(r_0\) = peak response of amlodipine from the Sample solution
  \(r_1\) = peak response of amlodipine from the Standard solution
  \(C_s\) = concentration of USP Amlodipine Besylate RS in the Standard solution \((\text{mg/mL})\)
  \(V\) = volume of Medium, 900 mL
  \(M_1\) = molecular weight of amlodipine, 408.88
  \(M_2\) = molecular weight of amlodipine besylate, 567.05
  \(L\) = label claim of amlodipine (mg/Tablet)

Calculate the percentage of the labeled amount of atorvastatin \((C_{12}H_{15}FN_{2}O_5)\) dissolved:
  \[
  \text{Result} = \left(\frac{r_1}{r_2}\right) \times C_s \times V \times \left[M \times (M_1/M_2)\right] \times (1/L) \times 100
  \]
  \(r_0\) = peak response of atorvastatin from the Sample solution
  \(r_1\) = peak response of atorvastatin from the Standard solution
  \(C_s\) = concentration of USP Atorvastatin Calcium RS in the Standard solution \((\text{mg/mL})\)
  \(V\) = volume of Medium, 900 mL
  \(M\) = number of moles of atorvastatin per mole of atorvastatin calcium, 2
  \(M_1\) = molecular weight of atorvastatin, 558.64
  \(M_2\) = molecular weight of atorvastatin calcium, 1155.34
  \(L\) = label claim of atorvastatin (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of amlodipine \((C_{20}H_{23}CIN_{3}O_{5})\) and atorvastatin \((C_{12}H_{15}FN_{2}O_5)\) are dissolved.

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

Medium: 0.05 M phosphate buffer prepared as follows: Dissolve 4.0 g of potassium phosphate, monobasic and 5 g of sodium hydroxide in 6 L of water. Adjust with 1 N sodium hydroxide or phosphoric acid to a pH of 6.8; 900 mL.

Apparatus 2: 75 rpm
  Time: 30 min
  Buffer: Dissolve 4.0 g of sodium phosphate, monobasic in 1200 mL of water and add 6 mL of triethylamine. Adjust with phosphoric acid to a pH of 2.5.
  Mobile phase: Acetonitrile and Buffer (40:60)
  Diluent: Acetonitrile and water (50:50)
  Standard stock solution 1: 155 µg/mL of USP Amlodipine Besylate RS in Diluent
  Standard stock solution 2: 460 µg/mL of USP Atorvastatin Calcium RS in Diluent

**Standard solution:** Prepare solutions of USP Amlodipine Besylate RS and USP Atorvastatin Calcium RS at concentrations given in Table 2 from Standard stock solution 1 and Standard stock solution 2.

### Table 2

<table>
<thead>
<tr>
<th>Strength of Tablet, Amlodipine/Atorvastatin (mg/mg)</th>
<th>Volume of Standard Stock Solution 1 to Be Added (mL)</th>
<th>Volume of Standard Stock Solution 2 to Be Added (mL)</th>
<th>Volume of Diluent to Be Added (mL)</th>
<th>Final Volume with Medium (mL)</th>
<th>Final Concentration of USP Amlodipine Besylate RS/USP Atorvastatin Calcium RS (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/10</td>
<td>10</td>
<td>5</td>
<td>45</td>
<td>200</td>
<td>7.75/11.5</td>
</tr>
<tr>
<td>5/20</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>200</td>
<td>7.75/23</td>
</tr>
<tr>
<td>5/40</td>
<td>10</td>
<td>20</td>
<td>30</td>
<td>200</td>
<td>7.75/46</td>
</tr>
<tr>
<td>5/80</td>
<td>10</td>
<td>40</td>
<td>10</td>
<td>200</td>
<td>7.75/92</td>
</tr>
<tr>
<td>10/10</td>
<td>20</td>
<td>5</td>
<td>35</td>
<td>200</td>
<td>15.5/11.5</td>
</tr>
<tr>
<td>10/20</td>
<td>20</td>
<td>10</td>
<td>30</td>
<td>200</td>
<td>15.5/23</td>
</tr>
<tr>
<td>10/40</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>200</td>
<td>15.5/46</td>
</tr>
<tr>
<td>10/80</td>
<td>20</td>
<td>40</td>
<td>–</td>
<td>200</td>
<td>15.5/92</td>
</tr>
</tbody>
</table>

Sample solution: Pass a portion of the solution under test through a suitable filter. Discard the first few milliliters of filtrate.

**Chromatographic system**
(See Chromatography (621), System Suitability.)

Mode: LC
  Detector: UV 240 nm
  Column: 4.6-mm × 5-cm; 1.8-µm packing L1
  Column temperature: 50°C
  Flow rate: 2 mL/min
  Injection volume: 20 µL
  Run time: NLT 1.8 times the retention time of atorvastatin

**System suitability**
Sample: Standard solution

[NOTE—The relative retention times for amlodipine and atorvastatin are 0.12 and 1.0, respectively.]

**Suitability requirements**
Tailing factor: NMT 1.5 for amlodipine
  Relative standard deviation: NMT 2.0% for amlodipine and atorvastatin

Analysis
Samples: Standard solution and Sample solution
  Calculate the percentage of the labeled amount of amlodipine \((C_{20}H_{23}CIN_{3}O_{5})\) dissolved:

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Notice of Intent to Revise
Official: To Be Determined

Result = \( \frac{r_o}{r_i} \times C_1 \times V \times \frac{(M_{rel}/M_1)}{(1/L)} \times 100 \)

- peak response of amlodipine from the Sample solution
- peak response of amlodipine from the Standard solution
- concentration of USP Amlodipine Besylate RS in the Standard solution (mg/mL)
- volume of Medium, 900 mL
- molecular weight of amlodipine, 408.88
- molecular weight of amlodipine besylate, 567.05
- label claim of amlodipine (mg/Tablet)

Calculate the percentage of the labeled amount of atorvastatin dissolved:

Result = \( \frac{r_o}{r_i} \times C_1 \times V \times \frac{(M \times (M_{rel}/M_0))}{(1/L)} \times 100 \)

- peak response of atorvastatin from the Sample solution
- peak response of atorvastatin from the Standard solution
- concentration of USP Atorvastatin Calcium RS in the Standard solution (mg/mL)
- volume of Medium, 900 mL
- number of moles of atorvastatin per mole of atorvastatin calcium, 2
- molecular weight of atorvastatin, 558.64
- molecular weight of atorvastatin calcium, 1155.34
- label claim of atorvastatin (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of amlodipine \((C_{amlodipine}H_{21}FN_{2}O_{8})\) and atorvastatin \((C_{atorvastatin}H_{22}ClN_{2}O_{9})\) are dissolved.▲(TB0)

**Uniformity of Dosage Units (905)**: Meet the requirements

**Impurities**

**Organic Impurities Related to Amlodipine**

**Buffer 1**: Add 7 mL of triethylamine in 1000 mL of water. Adjust with phosphoric acid to a pH of 3.0. Add 1.8 g of tetrabutylammonium hydrogen sulfate and mix well.

**Solution A**: Methanol and Buffer 1 (40:60)

**Solution B**: Acetonitrile, methanol, and Buffer 1 (40:40:20)

**Mobile phase**: See Table 3▲(TB0)

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode**: LC

**Detector**: UV 270 nm for amlodipine related compound A; 360 nm for all other impurities

**Column**: 2.1-mm x 15-cm; 1.8-µm packing L1

**Column temperature**: 40°

**Flow rate**: 0.3 mL/min

**Injection volume**: 5 µL

**System suitability**

**Sample**: Standard solution 2

**Suitability requirements**

- Tailing factor: NMT 2.0
- Relative standard deviation: NMT 5.0%

**Analysis**

**Samples**: Standard solution 1, Standard solution 2, and Sample solution

Calculate the percentage of amlodipine related compound A in the portion of Tablets taken:

Result = \( \frac{r_o}{r_i} \times C_1 \times C_{Amlodipine} \times (M_{rel}/M_0) \times 100 \)

- peak response of amlodipine related compound A from the Sample solution
- peak response of amlodipine related compound A from Standard solution 1
- concentration of USP Amlodipine Related Compound A RS in Standard solution 1 (mg/mL)
- nominal concentration of amlodipine in the Sample solution (mg/mL)
- molecular weight of amlodipine related compound A free base, 406.86
- molecular weight of amlodipine related compound A fumarate, 522.94

Calculate the percentage of atorvastatin–amlodipine adduct or any unspecified degradation product in the portion of Tablets taken:

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>16</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>18</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>24</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>30</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>31</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>35</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>36</td>
<td>90</td>
<td>10</td>
</tr>
</tbody>
</table>
4 Amlodipine

Result = \( (r_u/r_s) \times (C_i/C_o) \times (M_1/M_2) \times (1/F) \times 100 \)

- \( r_u \): peak response of each degradation product from the Sample solution
- \( r_s \): peak response of amlodipine from Standard solution
- \( C_i \): concentration of USP Amlodipine Besylate RS in Standard solution (mg/mL)
- \( C_o \): nominal concentration of amlodipine in the Sample solution (mg/mL)
- \( M_1 \): molecular weight of amlodipine, 408.88
- \( M_2 \): molecular weight of amlodipine besylate, 567.05
- \( F \): relative response factor (see Table 4 (TBD))

Acceptance criteria: See Table 4 (TBD). Disregard peaks at the relative retention times of 2.18, 2.47 (atorvastatin), and 2.79 min.

<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>Amlodipine related compound A</td>
<td>0.59</td>
<td>—</td>
<td>0.50</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>1.00</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Atorvastatin-amlodipine adduct</td>
<td>3.49</td>
<td>0.47</td>
<td>0.50</td>
</tr>
<tr>
<td>Any unspecified degradation product</td>
<td>—</td>
<td>1.0</td>
<td>0.20</td>
</tr>
<tr>
<td>Total degradation products for amlodipine</td>
<td>—</td>
<td>—</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Change to read:

- **Organic Impurities Related to Atorvastatin**
  - **Buffer 1**: Dissolve 6.8 g of potassium dihydrogen phosphate in 1000 mL of water and adjust with dilute phosphoric acid (1 in 10) to a pH of 3.4.
  - **Buffer 2**: Dissolve 6.8 g of potassium dihydrogen phosphate in 1000 mL of water and adjust with triethylamine to a pH of 7.0.
  - **Solution A**: Tetrahydrofuran, acetonitrile, and Buffer 1 (5:25:70)
  - **Solution B**: Tetrahydrofuran, acetonitrile, and Buffer 2 (5:70:25)
  - **Mobile phase**: See Table 5 (TBD)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>30</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>70</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>75</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>80</td>
<td>25</td>
<td>75</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>85</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>90</td>
<td>85</td>
<td>15</td>
</tr>
</tbody>
</table>

Diluent: Acetonitrile and water (50:50)

**System suitability solution**: Heat a suitable amount of USP Atorvastatin Calcium RS at 60°C for 1 h for degradation; 0.55 mg/mL of degraded USP Atorvastatin Calcium RS, 3 µg/mL each of USP Atorvastatin Related Compound A RS, USP Atorvastatin Related Compound B RS, USP Atorvastatin Related Compound C RS, and USP Atorvastatin Related Compound H RS in Diluent. Sonication may be necessary for complete dissolution.

**Standard solution**: 2.7 µg/mL of USP Atorvastatin Calcium RS in Diluent

**Sample solution**: Nominally 0.5 mg/mL of atorvastatin in Diluent, prepared as follows. Transfer an amount equivalent to 50 mg of atorvastatin from a portion of NLT 20 finely powdered Tablets to a 100-mL volumetric flask. Add about 10 mL of acetonitrile, shake to disperse, and sonicate for 5 min. Add about 70 mL of Diluent and sonicate for another 20 min. Dilute with Diluent to volume and centrifuge. Prepare this solution fresh.

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode**: LC

**Detector**: UV 246 nm

**Column**: 4.6-mm × 25-cm; 4-µm packing L11

**Column temperature**: 45°C

**Flow rate**: 1.2 mL/min

**Injection volume**: 20 µL

**System suitability**

- **Samples**: System suitability solution and Standard solution

**Suitability requirements**

- **Resolution**: NLT 1.0 between atorvastatin pyrrolidone analog and atorvastatin related compound A, System suitability solution

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

**Analysis**

- **Samples**: Standard solution and Sample solution

Calculate the percentage of each atorvastatin specified or unspecified degradation product in the portion of Tablets taken:

Result = \( (r_u/r_s) \times (C_i/C_o) \times [M \times (M_1/M_2)] \times (1/F) \times 100 \)

- \( r_u \): peak response of each atorvastatin degradation product from the Sample solution
- \( r_s \): peak response of atorvastatin from the Standard solution
- \( C_i \): concentration of USP Atorvastatin Calcium RS in the Standard solution (mg/mL)
- \( C_o \): nominal concentration of atorvastatin in the Sample solution (mg/mL)
- \( M \): number of moles of atorvastatin per mole of atorvastatin calcium, 2
- \( M_1 \): molecular weight of atorvastatin, 558.64
- \( M_2 \): molecular weight of atorvastatin calcium, 1155.34 (ER 1-Mar-2018)
- \( F \): relative response factor (see Table 6 (TBD))

Acceptance criteria: See Table 6 (TBD). Disregard any impurity peaks less than 0.05% and the peaks from amlodipine related impurities.
When more than one Official: To Be Determined

### ADDITIONAL REQUIREMENTS

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

### Add the following:

#### • Labeling:
When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used.▲(TBD)

#### • USP Reference Standards (11)

- **USP Amlodipine Besylate RS**
- **USP Amlodipine Related Compound A RS**
- **USP Amlodipine Related Compound B RS**
- **USP Amlodipine Related Compound C RS**
- **USP Amlodipine Related Compound H RS**
- **USP Amlodipine Besylate RS**

### Table *(6)▲(TBD)*

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
</table>
| Atorvastatin pyrrolidone analog
|                                           |                         |                          |                              |
| Atorvastatin related compound A
|                                           |                         |                          |                              |
| Atorvastatin related compound B
|                                           |                         |                          |                              |
| Atorvastatin
|                                           |                         |                          |                              |
| Atorvastatin related compound C
|                                           |                         |                          |                              |
| Atorvastatin epoxy pyrrolooxazin 6-hydroxy analog
|                                           |                         |                          |                              |
| Atorvastatin epoxy pyrrolooxazin 7-hydroxy analog
|                                           |                         |                          |                              |
| Atorvastatin related compound H
|                                           |                         |                          |                              |
| Atorvastatin epoxy tetrahydrofuran analog
|                                           |                         |                          |                              |
| Atorvastatin oxirane
|                                           |                         |                          |                              |
| Atorvastatin tert-butyl ester
|                                           |                         |                          |                              |
| Any unspecified degradation product
|                                           |                         |                          |                              |
| Total degradation products for atorvastatin
|                                           |                         |                          |                              |
| Total degradation products
|                                           |                         |                          |                              |

- ▲ Add the following:  
- B Reference
- C USP
- D Reference
- E USP
- F USP
- G USP
- H USP
- I USP

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