In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 1 Expert Committee has revised the Tacrolimus Capsules monograph. The purpose of the revision is to add Dissolution Test 6 to accommodate FDA-approved drug products with different tolerances than the existing dissolution tests.

- **Dissolution Test 6** was validated using the Xterra RP-18 brand of L1 column. The typical retention time for tacrolimus 19-epimer is about 6.5 min and about 8.4 min for tacrolimus.

The Tacrolimus Capsules Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Praveen Pabba, Scientific Liaison (301-816-8540 or pkp@usp.org).
Tacrolimus Capsules

**DEFINITION**
Tacrolimus Capsules contain NLT 93.0% and NMT 105.0% of the labeled amount of tacrolimus (C_{44}H_{69}NO_{12}).

**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.
- **B.** The UV absorption spectrum of the major peak of the Sample solution and that of the Standard solution exhibit maxima and minima at the same wavelengths, as obtained in the Assay.

**ASSAY**

**PROCEDURE**
Allow the Standard solution and Sample solution to stand for 3 h at ambient temperature before use. Protect solutions containing tacrolimus from light.

**Solution A:** 6 mM phosphoric acid
**Solution B:** 50 g/L of polyoxyethylene (23) lauryl ether. [NOTE—Polyoxyethylene (23) lauryl ether is also called Brij-35.]
**Solution C:** Acetonitrile and tert-butyl methyl ether, and 6 mM phosphoric acid (46: 18: 36: 0.1)

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

**Mode:** LC
**Detector:** UV 205 nm. When this procedure is used for Identification test B, use a diode array detector set at 200–400 nm.
**Column:** 4.0-mm × 5.5-cm; 3-μm packing L1
**Column temperature:** 60°
**Flow rate:** 1 mL/min
**Injection volume:** 5 μL

**Suitability requirements**
- **Tailing factor:** NMT 1.5 for the sum of the tacrolimus 19-epimer and tacrolimus peaks
- **Relative standard deviation:** NMT 3.0% for the sum of the tacrolimus and tacrolimus 19-epimer peaks

**Analysis**
- **Samples:** Standard solution and Sample solution
- Calculate the percentage of the labeled amount of tacrolimus (C_{44}H_{69}NO_{12}) in the portion of Capsules taken:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_U}{C_S} \right) \times 100
\]

- **r_U** = sum of the peak responses of tacrolimus and tacrolimus 19-epimer from the Sample solution
- **r_S** = sum of the peak responses of tacrolimus and tacrolimus 19-epimer from the Standard solution
- **C_U** = concentration of USP Tacrolimus RS in the Standard solution (mg/mL)
- **C_S** = nominal concentration of the Sample solution (mg/mL)

**Acceptance criteria:** 93.0%–105.0%

**PERFORMANCE TESTS**

**Change to read:**

- **Dissolution (711)**
  **Test 1**
  **Medium:** Hydroxypropylcellulose in water (1:2 × 10^4), adjusted with 6% phosphoric acid to a pH of 4.5; 900 mL
  **Apparatus 2:** 50 rpm with sinker (see Dissolution (711), Figure 2a)
  **Time:** 90 min
  **Mobile phase:** Acetonitrile, methanol, and water, and 6% phosphoric acid (46: 18: 36: 0.1)
  **Standard solution:** (L/360) mg/mL in acetonitrile, where L is the Capsule label claim in mg
  **Standard solution:** To 20.0 mL of the Standard stock solution add 50.0 mL of Medium, and mix to obtain solutions with known concentrations as indicated in Table 1. Allow the solution to stand for NLT 6 h at 25° before use.
  **Sample solution:** Pass 10 mL of the solution under test through a G4 glass filter. To 5.0 mL of the filtrate add 2.0 mL of acetonitrile, and mix. Allow the solution to stand for NLT 1 h at 25° before use.

<table>
<thead>
<tr>
<th>Capsule Strength (mg)</th>
<th>Final Concentration (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

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

**Mode:** LC
**Detector:** UV 210 nm
**Column:** 4.6-mm × 15-cm; 5-μm packing L7
**Column temperature:** 50°
**Flow rate:** Adjust the flow rate so that the retention time of tacrolimus is approximately 14 min.
**Injection volume:** See Table 2.

<table>
<thead>
<tr>
<th>Capsule Strength (mg)</th>
<th>Injection Volume (μL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>800</td>
</tr>
<tr>
<td>1</td>
<td>400</td>
</tr>
<tr>
<td>5</td>
<td>80</td>
</tr>
</tbody>
</table>

[NOTE—For products with strengths other than those listed in Table 2, adjust the Injection volume to deliver an equivalent amount of tacrolimus into the column.]

**System suitability**
- **Sample:** Standard solution

**Suitability requirements**
- **Resolution:** NLT 1.5 between tacrolimus 19-epimer and tacrolimus
- **Tailing factor:** NMT 1.5
- **Relative standard deviation:** NMT 1.5%

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

Calculate the percentage of the labeled amount of tacrolimus (C_{44}H_{69}NO_{12}) dissolved:

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

\[ r_U = \text{peak response of tacrolimus from the Sample solution} \]
\[ r_S = \text{peak response of tacrolimus from the Standard solution} \]
\[ C_S = \text{concentration of USP Tacrolimus RS in the Standard solution (mg/mL)} \]
\[ D = \text{dilution factor of the Sample solution} \]
\[ V = \text{volume of Medium, 900 mL} \]
\[ L = \text{label claim (mg/Capsule)} \]

Tolerances: NLT 80% (Q) of the labeled amount of tacrolimus (C_{44}H_{69}NO_{12}) is dissolved.

**Test 2:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 2.
[Note—Allow the Standard solution to stand for 3 h at ambient temperature before use. Protect solutions containing tacrolimus from light.]

**Buffer:** Dissolve 6 g of sodium dodecyl sulfate and 8.28 g of monobasic sodium phosphate in 6000 mL of water. Adjust with 2 N sodium hydroxide to a pH of 7.0.

**Medium:** Buffer, 900 mL

**Apparatus 2:** 50 rpm, with sinkers

**Time:** 60 min

**Standard stock solution:** 0.2 mg/mL of USP Tacrolimus RS in alcohol and Medium (3:7). [Note—Dissolve USP Tacrolimus RS in alcohol using 30% of the final volume. Sonicate until dissolved, and dilute with Medium to volume.]

**Standard solution:** Dilute the Standard stock solution with Medium to obtain a final concentration of 5 μg/mL.

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

**Solution A:** 6 mM phosphoric acid

**Mobile phase:** Acetonitrile, tert-butyl methyl ether, and Solution A (335:50:600)

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

**Mode:** LC

**Detector:** UV 210 nm

**Column:** 4.6-mm × 10-cm; 5-μm packing L1

**Column temperature:** 60°C

**Flow rate:** 1.3 mL/min

**Injection volume:** 100 μL

**System suitability**

**Sample:** Standard solution
[Note—The relative retention times for tacrolimus 19-epimer, tacrolimus open ring, and tacrolimus are 0.67, 0.79, and 1.0, respectively.]

**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 tacrolimus (C_{44}H_{69}NO_{12}) dissolved:

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

\[ r_U = \text{sum of the peak responses of tacrolimus and tacrolimus 19-epimer from the Sample solution} \]
\[ r_S = \text{sum of the peak responses of tacrolimus and tacrolimus 19-epimer from the Standard solution} \]
\[ C_S = \text{concentration of the Standard solution (mg/mL)} \]
\[ L = \text{label claim (mg/Capsule)} \]
\[ V = \text{volume of Medium, 900 mL} \]

Tolerances: NLT 75% (Q) of the labeled amount of tacrolimus (C_{44}H_{69}NO_{12}) is dissolved.

**Test 4:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 4.

**Medium:** Hydroxypropylcellulose in water (1 in 20,000), adjusted with phosphoric acid to a pH of 4.5. See Table 3 for the volume.
Official August 1, 2018

Revision Bulletin

Table 3

<table>
<thead>
<tr>
<th>Capsule Strength (mg)</th>
<th>Volume of Medium (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>500</td>
</tr>
<tr>
<td>1</td>
<td>900</td>
</tr>
<tr>
<td>5</td>
<td>900</td>
</tr>
</tbody>
</table>

Apparatus 2: 50 rpm, with sinkers
Time: 120 min
Diluent: 1 mg/mL of hydroxypropylcellulose in water. Sonicate as needed to dissolve.
Buffer: To a solution of 1 g/L of sodium 1-hexanesulfonate in water add 0.1 mL/L of trifluoroacetic acid.
Mobile phase: Acetonitrile, methanol, and Buffer (550:50:400)
Standard stock solution: Dissolve USP Tacrolimus RS in acetonitrile. See Table 4 for the concentrations (L is the Capsule label claim in mg).

Table 4

<table>
<thead>
<tr>
<th>Capsule Strength (mg)</th>
<th>Concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>L/25</td>
</tr>
<tr>
<td>1</td>
<td>L/45</td>
</tr>
<tr>
<td>5</td>
<td>L/45</td>
</tr>
</tbody>
</table>

Standard solution: Dilute the Standard stock solution with Diluent. See Table 5 for the concentrations (L is the Capsule label claim in mg).

Table 5

<table>
<thead>
<tr>
<th>Capsule Strength (mg)</th>
<th>Concentration (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>L/500</td>
</tr>
<tr>
<td>1</td>
<td>L/900</td>
</tr>
<tr>
<td>5</td>
<td>L/900</td>
</tr>
</tbody>
</table>

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 210 nm
Column: 4.6-mm × 15-cm; 5-μm packing L1
Column temperature: 60°
Flow rate: 1 mL/min
Injection volume: 100 μL
System suitability
Sample: Standard solution
Suitability requirements
Tailing factor: NMT 2.0
Relative standard deviation: NMT 3.0%
Analysis
Samples: Standard solution and Sample solution
Calculate the percentage of the labeled amount of tacrolimus (C44H69NO12) dissolved:

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

\[r_u\] = sum of the peak responses of tacrolimus, tacrolimus open-ring, and tacrolimus 19-epimer from the Sample solution
\[r_s\] = sum of the peak responses of tacrolimus, tacrolimus open-ring, and tacrolimus 19-epimer from the Standard solution
\[C_s\] = concentration of USP Tacrolimus RS in the Standard solution (mg/mL)

Tolerances: NLT 75% (Q) of the labeled amount of tacrolimus (C44H69NO12) is dissolved.

Test 5: If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 5.
Medium: 0.05 g/L hydroxypropylcellulose in water. Adjust with phosphoric acid to a pH of 4.5; 900 mL
Apparatus 2: 50 rpm, with sinkers
Time: 90 min
Solution A: 0.1 mL/L of trifluoroacetic acid in water
Mobile phase: Acetonitrile and Solution A (50:50)
Standard stock solution: 0.22 mg/mL of USP Tacrolimus RS in acetonitrile
Standard solution: (L/900) mg/mL of USP Tacrolimus RS from the Standard stock solution in Medium, where L is the label claim in mg/Capsule
Sample solution: Centrifuge a portion of the solution under test. Use the supernatant.

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Buffer: 3.6 g/L of monobasic potassium phosphate in water. Adjust with dilute phosphoric acid to a pH of 2.5.

Mobile phase: Acetonitrile and buffer (1:1)

Standard stock solution: 0.11 mg/mL of USP Tacrolimus RS in acetonitrile

Standard solution: Dilute the standard stock solution with medium to obtain a final concentration of (L) mg/mL, where L is the label claim in mg/Capsule.

Sample solution: Centrifuge a portion of the solution under test. Use the supernatant.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 210 nm
Column: 4.6-mm × 10-cm; 5-μm packing L1
Column temperature: 60° C
Flow rate: 1.3 mL/min
Injection volume: 100 μL

System suitability
Sample: Standard solution
[Note—The relative retention times for tacrolimus 19-epimer, tacrolimus open ring, and tacrolimus are 0.77, 0.89, and 1.0, respectively.]

Suitability requirements
Tailing factor: NMT 2.0 for tacrolimus
Relative standard deviation: NMT 2.0% for the sum of tacrolimus 19-epimer, tacrolimus open ring, and tacrolimus

Analysis
Samples: Standard solution and sample solution
Calculate the percentage of the labeled amount of tacrolimus (C44H69NO12) dissolved:

Result = (r0/rS) × (C/L) × V × 100

r0 = sum of the peak responses of tacrolimus, tacrolimus 19-epimer, and tacrolimus open ring from the sample solution
rS = sum of the peak responses of tacrolimus, tacrolimus 19-epimer, and tacrolimus open ring from the standard solution
C = concentration of USP Tacrolimus RS in the standard solution (mg/mL)
L = label claim (mg/Capsule)
V = volume of medium, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of tacrolimus (C44H69NO12) is dissolved. ▲ (08 1-Aug-2018)

• Uniformity of dosage units (905): Meet the requirements

Impurities

• Organic impurities, procedure 1
Use organic impurities, Procedure 1 when the impurity profile includes tacrolimus diene and tacrolimus regioisomer. It is suggested that new columns be conditioned with about 500 mL of ethanol before use to meet the resolution criterion.

Mobile phase: Hexane, n-butyl chloride, and acetonitrile (7:2:1). Add n-butyl chloride to hexane, and mix well before adding acetonitrile. After adding acetonitrile, mix the mobile phase for 2 h to get a clear solution. Any deviations from the ratio of components in the mobile phase and the order of mixing will result in a two-phase solution.

System suitability solution: 0.1 mg/mL each of USP Tacrolimus RS and USP Tacrolimus Related Compound A RS in mobile phase

Sample solution: Transfer the contents of a suitable number of capsules (equivalent to about 5 mg of tacrolimus for 0.5-mg capsules or 10 mg of tacrolimus for 1-mg and 5-mg capsules) into a centrifuge tube. Add 1.5 mL of a mixture of n-butyl chloride and acetonitrile (2:1), sonicate in an ultrasonic bath for 2 min, add 3.5 mL of n-hexane, and mix. Centrifuge this solution, and collect the supernatant or pass the solution through a 0.5-μm membrane filter. Use the solution within 30 min of preparation.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode: LC
Detector: UV 225 nm
Columns: Two 4.6-mm × 25-cm columns; 5-μm packing L20
Column temperature: 28 ± 2° C
Flow rate: 1.5 mL/min. Adjust the flow rate so that the retention time of tacrolimus is approximately 15 min.
Injection volume: 20 μL
Run time: 3 times the retention time of tacrolimus

System suitability
Sample: System suitability solution
Suitability requirements
Resolution: NLT 1.1 between tacrolimus and tacrolimus related compound A
Tailing factor: NMT 1.5
Relative standard deviation: NMT 2.0%

Analysis
Sample: Sample solution
Calculate the percentage of each impurity in the portion of capsules taken:

Result = (r0/Fi) × {1/(rT + Σ(r0/Fi))} × 100

ri = peak response of each impurity from the sample solution
Fi = relative response factor for each corresponding impurity (see Table 6)

rT = peak response of tacrolimus from the sample solution

Acceptance criteria: See Table 6. Disregard peaks due to the solvent.

Table 6

<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>Tacrolimus diene*</td>
<td>0.79</td>
<td>2.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Tacrolimus regioisomer*</td>
<td>0.88</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Tacrolimus impurity 1c</td>
<td>0.96</td>
<td>1.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Tacrolimus related compound A*</td>
<td>0.96</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tacrolimus 19-epimer*</td>
<td>1.1</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tacrolimus open ring*</td>
<td>1.3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Any individual unspecified impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

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Table 6 (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>Total impurities</td>
<td>—</td>
<td>—</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Tacrolimus open ring and tacrolimus 19-epimer are isomers of tacrolimus, which are present in equilibrium with the active ingredient. They are not to be reported as degradation products and are not included in total impurities.

Tacrolimus open ring and tacrolimus 19-epimer related compound A is listed here to indicate the relative retention time of this compound. It is used in the procedure to evaluate system suitability and is not to be reported. It is not to be included in total impurities.

Organic Impurities, Procedure 2

Use Organic Impurities, Procedure 2 when the impurity profile includes tacrolimus hydroxy acid and tacrolimus 8-epimer. It is suggested to equilibrate the column overnight with a mixture of Solution C and Solution D (17:3) before performing this procedure. Allow the System suitability solution, Standard solution, and Sample solution to stand for 3 h at ambient temperature before use. Protect solutions containing tacrolimus from light.

Solution A: 6 mM phosphoric acid

Solution B: Acetonitrile and tert-butyl methyl ether (81:19). [NOTE—The ratio of acetonitrile to tert-butyl methyl ether is critical.]

Solution C: Solution A and Solution B (4:1)

Solution D: Solution A and Solution B (1:4)

Mobile phase: See Table 7.

<table>
<thead>
<tr>
<th>Table 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (min)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>45</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>75</td>
</tr>
<tr>
<td>76</td>
</tr>
<tr>
<td>85</td>
</tr>
</tbody>
</table>

Solution E: 50 g/L of polyoxyethylene (23) lauryl ether in Solution A. [NOTE—Polyoxyethylene (23) lauryl ether is also called Brij-35.]

Diluent: Acetonitrile and Solution E (7:3)

System suitability solution: 1.5 mg/mL of USP Tacrolimus System Suitability Mixture RS in Diliuent

Standard solution: 7.5 μg/mL of USP Tacrolimus RS in Diliuent

Acceptance criteria: See Table 8. Identify tacrolimus 8-epimer and tacrolimus 8-propyl analog using Peak identification solution 1 and Peak identification solution 2. Disregard peaks that are smaller than the tacrolimus peak in the Sensitivity solution.

Peak identification solution 1: 10 μg/mL of USP Tacrolimus 8-epimer RS in Diliuent

Peak identification solution 2: 10 μg/mL of USP Tacrolimus 8-propyl Analog RS in Diliuent

Sample solution: Equivalent to 1.5 mg/mL of tacrolimus in Diliuent. [NOTE—Shake the mixture on a mechanical shaker for 30 min, and pass through a suitable filter.]

Chromatographic system

See Chromatography (621), System Suitability.

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 3-μm packing L1

Column temperature: 60°

Flow rate: 1.5 mL/min

Injection volume: 40 μL

System suitability:

Samples: System suitability solution, Standard solution, and Sensitivity solution

Suitability requirements

Resolution: NLT 3.0 between tacrolimus and ascomycin, System suitability solution

Relative standard deviation: NMT 10.0% for the sum of the responses of tacrolimus and tacrolimus 19-epimer, Standard solution

Signal-to-noise ratio: NLT 10.0, Sensitivity solution

Analysis

Samples: Standard solution, Peak identification solution 1, Peak identification solution 2, and Sample solution

Acceptance criteria: See Table 8.
**Table 8 (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>Tacrolimus 8-epimer&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.28</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Tacrolimus 8-propyl analog&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.30</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Any individual unspecified impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>1.5</td>
</tr>
</tbody>
</table>


<sup>b</sup> Tacrolimus open ring and tacrolimus 19-epimer are isomers of tacrolimus, which are present in equilibrium with the active ingredient. They are not to be reported as degradation products and are not included in total impurities.

<sup>c</sup> (35,4R,5S,8R,12S,13S,15R,16S,18R,26aS,3S)-Allyl-5,6,11,12,13,14,15,16,17,18,19,20,22,23,24,25,26a-docosahydropyrido[2,1-c][1,4]oxazacyclodocosine-19-carboxylic acid.

**ADDITIONAL REQUIREMENTS**

- **PACKAGING AND STORAGE:** Store in tight containers. Store at controlled room temperature.

**LABELING:** If a test for *Organic Impurities* other than *Procedure 1* is used, then the labeling states with which test for *Organic Impurities* the article complies. 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 Tacrolimus RS**

USP Tacrolimus Related Compound A RS (E)-8-Ethyl-5,6,8,11,12,13,14,15,16,17,18,19,24,25,26a-hexadecahydro-5,19-dihydroxy-3-(((E)-2-((1R,3R,4S)-4-hydroxy-3-methoxycyclohexyl)1-methylvinyl)-14,16-dimethoxy-4,10,12-tetramethyl-1,7,20-tetradecahydro-3-((E)-2-((1R,3R,4S)-4-hydroxy-3-methoxycyclohexyl)1-methylvinyl)-14,16-dimethoxy-4,10,12-tetramethyl-3H-pyrido[2,1-c][1,4]oxazacyclotricosine-19-carboxylic acid.

**USP Tacrolimus 8-epimer RS**


**USP Tacrolimus 8-propyl Analog RS**


**USP Tacrolimus Related Compound A analog RS**


**USP Tacrolimus System Suitability Mixture RS**


**REFERENCES**

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