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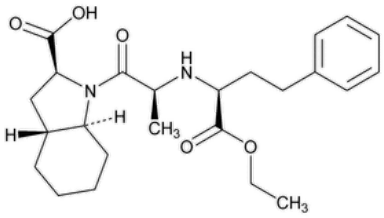
Trandolapril



$C_{24}H_{34}N_2O_5$ 430.54

1*H*-Indole-2-carboxylic acid, octahydro *N*-[(2*S*)-1-ethoxy-1-oxo-4-phenylbutan-2-yl]-1-alanyl (2*S*,3a*R*,7a*S*);

(2*S*,3a*R*,7a*S*)-1-[(*S*)-*N*-[(*S*)-1-Carboxy-3-phenylpropyl]alanyl]hexahydro-2-indolinecarboxylic acid, 1-ethyl ester CAS RN®: 87679-37-6.

DEFINITION

Trandolapril contains NLT 98.0% and NMT 102.0% of trandolapril ($C_{24}H_{34}N_2O_5$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020) or ⟨197M⟩

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

ASSAY

Change to read:

• **Procedure**

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (35:65)

Standard stock solution: 0.1 mg/mL of USP Trandolapril RS in *Mobile phase*

Standard solution: 0.002 mg/mL ▲of USP Trandolapril RS▲ (USP 1-May-2019) in *Mobile phase* from *Standard stock solution*

Sample stock solution: ▲0.1▲ (USP 1-May-2019) mg/mL of Trandolapril in *Mobile phase*

Sample solution: 0.002 mg/mL of Trandolapril in *Mobile phase* from *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 100 µL

Run time: NLT 5.5 times the retention time of trandolapril

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT ▲0.73%▲ (USP 1-May-2019)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of trandolapril ($C_{24}H_{34}N_2O_5$) in the portion of Trandolapril taken:

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

r_U = peak response ▲of trandolapril▲ (USP 1-May-2019) from the *Sample solution*

r_S = peak response ▲of trandolapril▲ (USP 1-May-2019) from the *Standard solution*

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

C_U = concentration of Trandolapril in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

Change to read:

• ▲▲ (USP 1-May-2019) **Residue on Ignition** ⟨281⟩

Sample: 2.0 g

Acceptance criteria: NMT 0.1%

Change to read:

• ▲**Organic Impurities**▲ (USP 1-May-2019)

Buffer: 6.8 g/L of monobasic potassium phosphate. Adjust with phosphoric acid to a pH of 2.5 ± 0.1.

Solution A: Acetonitrile and *Buffer* (25:75), filtered and degassed

Solution B: Acetonitrile and *Buffer* (50:50), filtered and degassed

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
20	95	5
35	5	95
45	5	95
46	95	5
60	95	5

System suitability solution: 0.05 mg/mL each of USP Trandolapril Related Compound C RS and USP Trandolapril Related Compound D RS in *Solution A*

Standard solution: 0.0025 mg/mL of USP Trandolapril RS in *Solution A*

Sample solution: 2.5 mg/mL of Trandolapril in *Solution A*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm;

▲3.5-µm▲ (USP 1-May-2019) packing L1

Column temperature: 40°

Flow rate: 1.3 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 4 between trandolapril related compound C and trandolapril related compound D, *System suitability solution*

Tailing factor: ▲NMT▲ (USP 1-May-2019) 1.5, *Standard solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each ▲specified or any unspecified▲ (USP 1-May-2019) impurity in the portion of Trandolapril taken:

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

r_U = peak response of each ▲specified or unspecified▲ (USP 1-May-2019) impurity from the *Sample solution*

r_S = peak response of trandolapril from the *Standard solution*

C_S = concentration of ▲USP Trandolapril RS in▲ (USP 1-May-2019) the *Standard solution* (mg/mL)

C_U = concentration of ▲Trandolapril in▲ (USP 1-May-2019) the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. [NOTE—Do not include trandolapril related compound D in the total impurities.]

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Trandolapril related compound C▲▲ (USP 1-May-2019)	2.1	0.45	0.2
Trandolapril related compound D▲▲ (USP 1-May-2019)	2.5	1.0	0.5
▲ Any unspecified impurity▲ (USP 1-May-2019)	—	1.0	0.1
Total impurities	—	—	0.5

▲ ▲ (USP 1-May-2019)

SPECIFIC TESTS

- **OPTICAL ROTATION,** ⟨781S⟩ *Procedures, Specific Rotation*

  Sample: 0.02 g/mL in dehydrated alcohol

  Acceptance criteria: −16.5° to −18.5° at 20°

- **WATER DETERMINATION,** ⟨921⟩ *Method I, Method Ic*

  Sample: 2 g

  Acceptance criteria: NMT 0.2%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at room temperature.
- **USP REFERENCE STANDARDS** ⟨11⟩

  USP Trandolapril RS

USP Trandolapril Related Compound C RS

(2*S*,3a*R*,7a*S*)-1-[*N*-[(*S*)-1-Carboxy-3-cyclohexylpropyl]-L-alanyl]hexahydro-2-indolinecarboxylic acid 1-ethyl ester.

$C_{24}H_{40}N_2O_5$ 436.58

USP Trandolapril Related Compound D RS

(S)-Ethyl 2-[(3*S*,5a*S*,9a*R*,10a*S*)-3-methyl-1,4-dioxodecahydropyrazino[1,2-*a*]indol-2(1*H*)-yl)]-4-phenylbutanoate.

$C_{24}H_{32}N_2O_4$ 412.52

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

Topic/Question	Contact	Expert Committee
TRANDOLAPRIL	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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