Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2018
Document Type: USP Monographs
DocId: GUID-44B66B7C-23EF-4B52-B4A9-6854F76A9EF7_3_en-US
DOI: https://doi.org/10.31003/USPNF_M84409_03_01
DOI Ref: 75z8o

Trandolapril Tablets

DEFINITION
Trandolapril Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of trandolapril ($C_{24}H_{34}N_2O_5$).

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 spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **Procedure**

Buffer: To 1 L of 8.9 g/L of dibasic sodium phosphate anhydrous, add 1 mL of triethylamine and adjust with phosphoric acid to a pH of 3.5. Pass through a suitable filter of 0.45-µm pore size.

Mobile phase: Acetonitrile and *Buffer* (40:60)

Diluent: Acetonitrile and water (40:60)

Standard solution: 40 µg/mL of USP Trandolapril RS in *Diluent* prepared as follows. Transfer a suitable quantity of USP Trandolapril RS to a suitable volumetric flask. Add *Diluent* up to 70% of the flask volume. Sonicate if necessary. Dilute with *Diluent* to volume.

Sample solution: Nominally 40 µg/mL of trandolapril in *Diluent* prepared as follows. Transfer a suitable quantity of trandolapril from NLT 10 Tablets to a suitable volumetric flask. Add *Diluent* up to 70% of the flask volume. Sonicate up to 30 min, if necessary, with occasional swirling. Dilute with *Diluent* to volume. Pass a portion of the solution through a membrane filter of 0.45-µm pore size.

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

Mode: LC

Detector: UV 216 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.

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

Flow rate: 1.2 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of trandolapril

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 3000 theoretical plates

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

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

r_U = peak response of trandolapril from the *Sample solution*

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

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

C_U = nominal concentration of trandolapril in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: Water, deaerated; 500 mL

Apparatus 2: 50 rpm

Time: 45 min

Mobile phase and **System suitability:** Proceed as directed in the *Assay*.

Standard stock solution: 0.2 mg/mL of USP Trandolapril RS prepared as follows. Transfer a suitable quantity of USP Trandolapril RS to a suitable volumetric flask. Add acetonitrile to about 5% of the flask volume, sonicate to dissolve, and dilute with *Medium* to volume.

Standard solution: (*L*/500) mg/mL of USP Trandolapril RS from the *Standard stock solution* in *Medium*, 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.

Chromatographic system: Proceed as directed in the *Assay*, except for the *Injection volume*.

Injection volume: 100 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of trandolapril ($C_{24}H_{34}N_2O_5$) dissolved:

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

r_U = peak response of trandolapril from the *Sample solution*

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of trandolapril ($C_{24}H_{34}N_2O_5$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Buffer: To 1 L of 7.0 g/L of sodium perchlorate monohydrate in water (0.05 M), add 2 g of octanesulfonic acid sodium salt followed by 1 mL of triethylamine. Adjust with diluted perchloric acid (1 in 10) to a pH of 2.0. Pass through a membrane filter of 0.45-µm pore size.

Solution A: Acetonitrile, tetrahydrofuran, and *Buffer* (11:1:28)

Solution B: Acetonitrile and *Buffer* (75:25)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
25	85	15
50	50	50
55	85	15
65	85	15

Diluent: Acetonitrile and *Buffer* (40:60)

Standard stock solution 1: 0.06 mg/mL each of USP Trandolapril Related Compound C RS and USP Trandolapril Related Compound D RS in acetonitrile. Sonicate to dissolve.

System suitability solution: 0.6 mg/mL of USP Trandolapril RS and 6 µg/mL each of USP Trandolapril Related Compound C RS and USP Trandolapril Related Compound D RS from *Standard stock solution 1* in *Diluent*. Add *Diluent* up to 70% of the flask volume, sonicate to

dissolve, and cool to room temperature. Dilute with *Diluent* to volume.

Standard stock solution 2: 0.3 mg/mL of USP Trandolapril RS in *Diluent* prepared as follows. Transfer a suitable quantity of USP Trandolapril RS to a suitable volumetric flask. Add *Diluent* up to 70% of the flask volume, sonicate, and cool to room temperature. Dilute with *Diluent* to volume.

Standard solution: 6 µg/mL of USP Trandolapril RS in *Diluent* from *Standard stock solution 2*.

Sample solution: Nominally 600 µg/mL of trandolapril in *Diluent* prepared as follows. Transfer a suitable quantity of trandolapril from NLT 15 Tablets to a suitable volumetric flask. Add *Diluent* up to 50% of the flask volume and sonicate for 30 min. Dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

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

Suitability requirements

Resolution: NLT 3.0 between trandolapril related compound C and trandolapril related compound D, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of each specified and unspecified degradation product from the *Sample solution*

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

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

C_U = nominal concentration of trandolapril in the *Sample solution* (µg/mL)

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

Acceptance criteria: See *Table 2*. Reporting threshold: 0.1%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Trandolaprilat[a]	0.41	1.0	2.0
Trandolapril	1.00	1.0	—
Trandolapril related compound C	1.84	—	—[b]
Trandolapril related compound D	1.96	0.78	5.0
Any unspecified degradation product	—	1.00	1.0
Total degradation products	—	—	7.0

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

[b] Process-related impurity used for resolution measurement only.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled 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 hydrochloride.

$C_{24}H_{40}N_2O_5 \cdot HCl$ 473.05

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 TABLETS	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:
Pharmacopeial Forum: Volume No. PF 42(5)

Current DocID: GUID-44B66B7C-23EF-4B52-B4A9-6854F76A9EF7_3_en-US
Previous DocID: GUID-44B66B7C-23EF-4B52-B4A9-6854F76A9EF7_1_en-US
DOI: https://doi.org/10.31003/USPNF_M84409_03_01
DOI ref: 75z8o