Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Aug-2016
Document Type: USP Monographs
DocId: GUID-999DE782-2271-4FCC-A976-A38D3D7CBC96_1_en-US
DOI: https://doi.org/10.31003/USPNF_M6001_01_01
DOI Ref: om5ga

Perindopril Erbumine Tablets

DEFINITION
Perindopril Erbumine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of perindopril erbumine ($C_{19}H_{32}N_2O_5 \cdot C_4H_{11}N$).

IDENTIFICATION
• **A.** The UV absorption spectra of the major peak of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the corresponding peak of the *Standard solution*, as obtained in the *Assay*.
• **B.** 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**

Solution A: Dissolve 0.92 g of sodium 1-heptanesulfonate in 1 L of water and add 1 mL of triethylamine. Adjust with a solution of perchloric acid and water (1:1) to a pH of 2.0.

Mobile phase: Acetonitrile and *Solution A* (38:62)

Diluent: Acetonitrile and *Solution A* (40:60)

Standard solution: 0.08 mg/mL of USP Perindopril Erbumine RS in *Diluent* prepared as follows. Dissolve a suitable quantity of USP Perindopril Erbumine RS in 80% of the total volume of *Diluent*, sonicate for 5 min, and dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size and discard the first 3 mL of filtrate.

Sample solution: Nominally equivalent to 0.08 mg/mL of perindopril erbumine in *Diluent* prepared as follows. Weigh and transfer the number of Tablets into a suitable volumetric flask, as indicated in *Table 1*.

Table 1

Tablet Strength (mg)	Number of Tablets (NLT)	Volumetric Flask (mL)
2	20	500
4	10	500
8	10	1000

Add *Diluent* to about 70% of the flask volume, shake mechanically for about 60 min at 180 rpm, and sonicate for 20 min. Dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size and discard the first 3 mL of filtrate.

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

Mode: LC

Detector: UV 210 nm

Column: 4-mm × 25-cm; 4-µm packing L7

Temperatures

Column: 60°

Sample cooler: 5°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2.5 times the retention time of perindopril

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 perindopril erbumine ($C_{19}H_{32}N_2O_5 \cdot C_4H_{11}N$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = nominal concentration of perindopril erbumine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Solution A: Proceed as directed in the *Assay*.

Mobile phase: Acetonitrile and *Solution A* (350:650)

Standard stock solution: 0.55 mg/mL of USP Perindopril Erbumine RS in acetonitrile

Standard solution: Prepare solutions of USP Perindopril Erbumine RS in *Medium* from the *Standard stock solution*, with final concentrations from *Table 2*.

Table 2

Tablet Strength (mg)	Concentration (mg/mL)
2	0.0022
4	0.0044
8	0.0088

Sample solution: Pass a portion of the solution under test through a suitable filter and discard the first 1 mL of filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Column temperature: 50°

Flow rate: 1.2 mL/min

Injection volume: 100 µL

Run time: NLT 1.6 times the retention time of perindopril

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of perindopril erbumine ($C_{19}H_{32}N_2O_5 \cdot C_4H_{11}N$) dissolved.

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

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*, 900 mL

Tolerances: NLT 85% (Q) of the labeled amount of perindopril erbumine ($C_{19}H_{32}N_2O_5 \cdot C_4H_{11}N$) is dissolved.

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

IMPURITIES

- **Organic Impurities**

Solution A: Proceed as directed in the *Assay*.

Solution B: Acetonitrile

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	80	20
5	80	20
27	68	32
45	50	50
60	20	80
70	20	80
71	80	20
80	80	20

Diluent: *Solution B* and *Solution A* (20:80)

System suitability stock solution A: 0.03 mg/mL of USP Imidazole RS in *Diluent*

System suitability stock solution B: 0.12 mg/mL each of USP Perindopril Related Compound C RS and USP Perindopril Related Compound D RS in *Diluent*. Initially add 80% of the total volume of *Diluent*, sonicate for 5 min, and dilute with *Diluent* to volume.

System suitability solution: Accurately weigh about 1.5 mg each of USP Perindopril Related Compound B RS and USP Perindopril Related Compound F RS into a 50-mL volumetric flask. Add 30 mL of *Diluent* and sonicate for 5 min. Transfer 5.0 mL each of *System suitability stock solution A*, *System suitability stock solution B*, and *Standard stock solution*. Dilute with *Diluent* to volume.

Standard stock solution: 0.05 mg/mL of USP Perindopril Erbumine RS in *Diluent* prepared as follows. Dissolve a suitable quantity of USP Perindopril Erbumine RS in 80% of the total volume of *Diluent*, sonicate for 5 min, and dilute with *Diluent* to volume.

Standard solution: 0.005 mg/mL of USP Perindopril Erbumine RS in *Diluent* from the *Standard stock solution*. Pass through a suitable filter of 0.45-µm pore size and discard the first 3 mL of filtrate.

Sample solution: Nominally equivalent to 2 mg/mL of perindopril erbumine in *Diluent* prepared as follows. Transfer a quantity equivalent to about 20 mg of perindopril erbumine from powdered Tablets (NLT 20) into a test tube. Pipet 10.0 mL of *Diluent* into the test tube, sonicate for about 10 min, and vortex for about 1 min. Pass through a suitable filter of 0.45-µm pore size and discard the first 3 mL of filtrate.

Chromatographic system

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

Proceed as directed in the *Assay*, except for the *Run time*. [NOTE—The run time is determined by the gradient from Table 3.]

System suitability

Sample: *System suitability solution*

Suitability requirements

Tailing factor: NMT 1.5 for the perindopril peak

Relative standard deviation: NMT 5.0% for the perindopril peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity 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 impurity from the *Sample solution*

r_S = peak response of perindopril erbumine from the *Standard solution*

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

C_U = nominal concentration of perindopril erbumine in the *Sample solution* (mg/mL)

F = relative response factor for each individual impurity (see Table 4)

Acceptance criteria: See Table 4. Disregard peaks less than 0.1%.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Imidazole[a]	0.08	—	—
Perindopril related compound B[b]	0.42	1.21	2.0
Perindopril related compound C[c]	0.74	0.97	0.5
Perindopril related compound D[d]	0.85	0.98	0.5
Perindopril erbumine	1.0	—	—
Perindopril related compound F[e]	1.38	0.86	3.0
Any unspecified impurity	—	—	0.2
Total impurities[f]	—	—	1.5

[a] Imidazole is given for identification only and is not quantitated using this procedure.

[b] (2*S*,3a*S*,7a*S*)-1-{(*S*)-2-[(*S*)-1-Carboxybutylamino]propanoyl}octahydro-1*H*-indole-2-carboxylic acid.

[c] (*S*)-2-{(3*S*,5a*S*,9a*S*,10a*S*)-3-Methyl-1,4-dioxodecahydropyrazino[1,2-a]indol-2(1*H*)-yl}pentanoic acid.

[d] (*S*)-2-{(3*S*,5a*S*,9a*S*,10a*R*)-3-Methyl-1,4-dioxodecahydropyrazino[1,2-a]indol-2(1*H*)-yl}pentanoic acid.

[e] (*S*)-Ethyl 2-{(3*S*,5a*S*,9a*S*,10a*S*)-3-methyl-1,4-dioxodecahydropyrazino[1,2-a]indol-2(1*H*)-yl}pentanoate.

[f] Total impurities excludes perindopril related compound F and perindopril related compound B.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in air-tight containers. Protect from heat and moisture.

• **USP Reference Standards** ⟨11⟩

USP Imidazole RS

USP Perindopril Erbumine RS

USP Perindopril Related Compound B RS

(2*S*,3a*S*,7a*S*)-1-{(*S*)-2-[(*S*)-1-Carboxybutylamino]propanoyl}octahydro-1*H*-indole-2-carboxylic acid.

$C_{17}H_{28}N_2O_5$ 340.41

USP Perindopril Related Compound C RS

(*S*)-2-{(3*S*,5a*S*,9a*S*,10a*S*)-3-Methyl-1,4-dioxodecahydropyrazino[1,2-*a*]indol-2(1*H*)-yl}pentanoic acid.

$C_{17}H_{26}N_2O_4$ 322.40

USP Perindopril Related Compound D RS

(*S*)-2-{(3*S*,5a*S*,9a*S*,10a*R*)-3-Methyl-1,4-dioxodecahydropyrazino[1,2-*a*]indol-2(1*H*)-yl}pentanoic acid.

$C_{17}H_{26}N_2O_4$ 322.40

USP Perindopril Related Compound F RS

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

$C_{19}H_{30}N_2O_4$ 350.45

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

Topic/Question	Contact	Expert Committee
PERINDOPRIL ERBUMINE 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 41(1)

Current DocID: GUID-999DE782-2271-4FCC-A976-A38D3D7CBC96_1_en-US

DOI: https://doi.org/10.31003/USPNF_M6001_01_01

DOI ref: om5ga