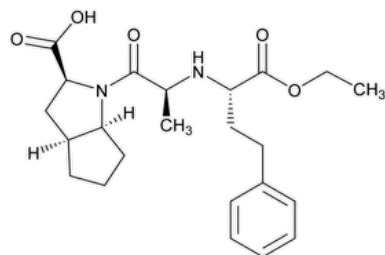


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Ramipril

Change to read:



$C_{23}H_{32}N_2O_5$ ▲416.52▲ (USP 1-Aug-2022)

Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,6aβ]]-; (2S,3aS,6aS)-1-[(S)-N-[(S)-1-Carboxy-3-phenylpropyl]alanyl]octahydrocyclopenta[b]pyrrole-2-carboxylic acid, 1-ethyl ester

▲(2S,3aS,6aS)-1-[(S)-1-Ethoxy-1-oxo-4-phenylbutan-2-yl]-L-alanyl]octahydrocyclopenta[b]pyrrole-2-carboxylic acid▲ (USP 1-Aug-2022) CAS RN®: 87333-19-5; UNII: L35JN3I7SJ.

DEFINITION

Ramipril contains NLT 98.0% and NMT 102.0% of ramipril ($C_{23}H_{32}N_2O_5$), calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K
- **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

Change to read:

• PROCEDURE

Buffer: 0.1% solution of [sodium dodecyl sulfate](#). Adjust with [phosphoric acid](#) to a pH of 2.4 ± 0.1 .

Mobile phase: [Acetonitrile](#) and *Buffer* (45:55). Adjust with phosphoric acid to a pH of 2.75 ± 0.1 .

System suitability solution: 0.2 mg/mL of [USP Ramipril RS](#) and 0.01 mg/mL of [USP Ramipril Related Compound A RS](#), in *Mobile phase*

Standard solution: 0.2 mg/mL of [USP Ramipril RS](#) in *Mobile phase*

Sample stock solution: 1 mg/mL of Ramipril prepared as follows. Dissolve 100 mg of Ramipril in 10 mL of [Acetonitrile](#) in a 100-mL volumetric flask, and dilute with *Mobile phase* to volume.

Sample solution: 0.2 mg/mL of Ramipril 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; ▲5 μm▲ (USP 1-Aug-2022) packing [L1](#)

Flow rate: 1.8 mL/min

Injection volume: 20 μL

▲**Run time:** NLT 2 times the retention time of ramipril▲ (USP 1-Aug-2022)

System suitability

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

[NOTE—The relative retention time for ramipril related compound A and ramipril are 0.8 and 1.0, respectively.]▲ (USP 1-Aug-2022)

Suitability requirements

Resolution: NLT 2.0 between ramipril and ramipril related compound A, *System suitability solution*

▲▲ (USP 1-Aug-2022)

Relative standard deviation: NMT ▲0.73%, *Standard solution* ▲ (USP 1-Aug-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

▲ Calculate the percentage of ramipril ($C_{23}H_{32}N_2O_5$) in the portion of Ramipril taken: ▲ (USP 1-Aug-2022)

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

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

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

C_S = concentration of [USP Ramipril RS](#) in the *Standard solution* (mg/mL)

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

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

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Delete the following:

▲• **LIMIT OF PALLADIUM**

Diluent: Water and nitric acid (997:3)

Standard stock solution: Dissolve 50 mg of palladium metal taken in a 100-mL volumetric flask, in 9 mL of hydrochloric acid, and dilute with water to volume.

Standard solutions: 0.02, 0.03, and 0.05 µg/mL of palladium in *Diluent* from *Standard stock solution*

Sample solution: 2 mg/mL of Ramipril in *Diluent*

Blank solution: 1.5 mg/mL of magnesium nitrate in *Diluent*

Instrumental conditions

(See [Atomic Absorption Spectroscopy \(852\)](#).)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: 247.6 nm palladium emission line

Lamp: Palladium hollow-cathode

Flame: Air–acetylene

Injection volume: 20 µL each for the *Standard solutions* and *Sample solution*, and 10 µL for the *Blank solution*

Analysis: Concomitantly determine the absorbances of the *Standard solutions*, *Sample solution*, and the *Blank solution*. Plot the absorbances of the *Standard solutions* versus the concentration, in µg/mL, of palladium, and draw the straight line best fitting the three plotted points.

From the graph so obtained, determine the concentration, C_P , in µg/mL, of palladium in the *Sample solution*.

Calculate the percentage of palladium in the portion of Ramipril taken:

$$\text{Result} = (C_P/C_R) \times 100$$

C_P = concentration of palladium in the *Sample solution* (µg/mL)

C_R = concentration of Ramipril in the *Sample solution* (µg/mL)

Acceptance criteria: 20 ppm ▲ (USP 1-Aug-2022)

Change to read:

• **ORGANIC IMPURITIES**

Solution A: 2.0 g of [sodium perchlorate](#) in a mixture of 800 mL of [water](#) and 0.5 mL of [triethylamine](#). Adjust with [phosphoric acid](#) to a pH of about 3.6 ± 0.1 , and add 200 mL of [acetonitrile](#).

Solution B: 2.0 g of [sodium perchlorate](#) in a mixture of 300 mL of [water](#) and 0.5 mL of [triethylamine](#). Adjust with [phosphoric acid](#) to a pH of about 2.6 ± 0.1 , and add 700 mL of [acetonitrile](#).

System suitability solution: 0.5 mg/mL each of [USP Ramipril RS](#), [USP Ramipril Related Compound A RS](#), [USP Ramipril Related Compound B RS](#), [USP Ramipril Related Compound C RS](#), and [USP Ramipril Related Compound D RS](#) in *Solution B*

Standard solution: 5 µg/mL of [USP Ramipril RS](#) in *Solution B*



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