Edition: BP 2025 (Ph. Eur. 11.6 update)

Captopril Oral Solution

General Notices

NOTE: *This monograph has been developed to cover unlicensed formulations.*

Action and use

Angiotensin-converting enzyme inhibitor.

DEFINITION

Captopril Oral Solution is a solution containing Captopril in a suitable flavoured vehicle. It is supplied as a ready-to-use solution or it is prepared by dissolving Captopril Powder for Oral Solution in the requisite volume of the vehicle provided just before issue for use.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements. Where appropriate the oral solution also complies with the requirements stated under Unlicensed Medicines.

STORAGE

The oral solution should be stored at the temperature and used within the period stated on the label.

When supplied as a ready-to-use solution, the oral solution complies with the following requirements.

Content of captopril, $C_9H_{15}NO_3S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Add 10 mL of *dichloromethane* to a quantity of the oral solution containing 0.1 g of Captopril and shake gently (take care to avoid forming an emulsion). Remove the lower organic layer, repeat the extraction with two further 10-mL quantities of *dichloromethane*, combine the organic extracts and filter through *anhydrous sodium sulfate*. Mix 1 mL of the filtrate with 0.5 g of *potassium bromide*, dry at room temperature at a pressure of 2 kPa, grind to a uniform mixture and prepare a disc. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of captopril (*RS 038*).

TESTS

Captopril disulfide

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute a quantity of the oral solution containing 25 mg of Captopril to 50 mL with *methanol* and mix.
(2) Dilute 1 volume of solution (1) to 100 volumes with *methanol*.
(3) Dissolve 5 mg of *captopril BPCRS* in 1 mL *methanol* and add 230 µL of 0.05M *iodine*. If the solution is not colourless, add 0.1M *sodium thiosulfate* dropwise until it becomes colourless, and dilute to 50 mL with *methanol* (generation of captopril disulfide). Further dilute 3 volumes to 20 volumes with *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

0.5 volume of *orthophosphoric acid*, 450 volumes of *water* and 550 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions, the relative retention of captopril disulfide (impurity A) with reference to captopril (retention time about 4 minutes) is 1.5.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to captopril and captopril disulfide is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1), the area of any peak corresponding to captopril disulfide is not greater than three times the area of the peak in the chromatogram obtained with solution (2) (3%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase.

(1) Dilute a weighed quantity of the oral solution containing 25 mg of Captopril to 50 mL with mobile phase, mix and dilute 1 volume of the resulting solution to 5 volumes with the mobile phase.
(2) 0.01% w/v of *captopril BPCRS*.
(3) Dissolve 5 mg of *captopril BPCRS* in 1 mL of the mobile phase and add 230 µL of 0.05M *iodine*. If the solution is not colourless, add 0.1M *sodium thiosulfate* dropwise until it becomes colourless, and dilute to 50 mL (generation of captopril disulfide). Dilute 1 volume to 20 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (10 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

0.5 volume of *orthophosphoric acid*, 450 volumes of *water* and 550 volumes of *methanol*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to captopril and captopril disulfide is at least 2.0.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_9H_{15}NO_3S$, weight in volume, using the declared content of $C_9H_{15}NO_3S$ in *captopril BPCRS*.

CAPTOPRIL POWDER FOR ORAL SOLUTION

DEFINITION

Captopril Powder for Oral Solution is a dry powder consisting of Captopril with or without excipients. It is supplied in a sealed container.

The dry ingredients comply with the requirements for Powders and Granules for Oral Solutions and Oral Suspensions stated under Oral Liquids. Where appropriate, the dry ingredients also comply with the requirements stated under Unlicensed Medicines.

Content of captopril, $C_9H_{15}NO_3S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of captopril (*RS 038*).

TESTS

Acidity

pH of a solution containing 2% w/v of Captopril, 2.0 to 2.6, Appendix V L.

Clarity of solution

A solution containing 2% w/v of Captopril in *carbon dioxide-free water* is *clear*, Appendix IV A, and *colourless*, Appendix IV B, Method II.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dissolve a quantity of the contents of the sealed container containing 50 mg of Captopril in the mobile phase and add sufficient mobile phase to produce 100 mL.
(2) Dilute 1 volume of solution (1) to 50 volumes with the mobile phase.
(3) Dissolve a quantity of the mixed contents of the sealed containers containing 10 mg of Captopril in mobile phase, add 0.25 mL of 0.05M *iodine* and sufficient mobile phase to produce 100 mL. Dilute 1 volume of the resulting solution to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Nucleosil C8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 3 times the retention time of Captopril.

MOBILE PHASE

0.5 volume of *orthophosphoric acid*, 500 volumes of *methanol* and 500 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows three principal peaks and the *resolution* between the last two eluting principal peaks is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the sum of the areas of all such peaks is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (2%).

Disregard any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%) and any peak with a retention time less than 1.4 minutes.

ASSAY

Mix the contents of 10 containers and dissolve a quantity of the mixed contents containing 0.15 g of Captopril in 30 mL of *water*. Titrate with 0.05M *iodine*, determining the end-point potentiometrically, Appendix VIII B, using a combined platinum electrode.

Each mL of 0.05M *iodine* is equivalent to 21.73 mg of $C_9H_{15}NO_3S$.