



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

## Indapamide Prolonged-release Tablets

### [General Notices](#)

Prolonged-release Indapamide Tablets

*Indapamide Prolonged-release Tablets from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.*

### Action and use

Thiazide-like diuretic.

## DEFINITION

Indapamide Prolonged-release Tablets contain Indapamide. They are formulated so that the medicament is released over a period of several hours.

## PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Indapamide. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

A suitable test is carried out to demonstrate that the content of (2*RS*)-2-methyl-2,3-dihydro-1*H*-indol-1-amine (impurity C) is not more than 600 ppm.

*The tablets comply with the requirements stated under Tablets and with the following requirements.*

### Content of indapamide, $C_{16}H_{16}ClN_3O_3S$

95.0 to 105.0% of the stated amount.

## IDENTIFICATION

A. Carry out the method for [thin-layer chromatography](#), [Appendix III A](#), using the following solutions.

- (1) Grind a quantity of the powdered tablets containing 50 mg of Indapamide with 10 mL of [acetone](#), mix for 15 minutes, filter (Whatman 42 is suitable) and use the filtrate.
- (2) 0.5% w/v of [indapamide BPCRS](#) in [acetone](#).

### CHROMATOGRAPHIC CONDITIONS

- (a) Use as the coating TLC [silica gel](#)  $F_{254}$  (Merck [silica gel 60  \$F\_{254}\$](#)  plates are suitable).
- (b) Use the mobile phase as described below.
- (c) Apply 20  $\mu$ L of each solution.
- (d) Develop the plate to 12 cm.
- (e) After removal of the plate, allow it to dry until the solvent has evaporated and examine under [ultraviolet light \(254 nm\)](#). Spray the plate with a solution prepared by mixing 10 volumes of [potassium iodobismuthate solution](#) and 20 volumes of [glacial acetic acid](#) and diluting to 100 volumes with [water](#) and examine again. Finally, spray the plate with a 5% w/v solution of [sodium nitrite](#) in a mixture of equal volumes of [water](#) and [ethanol \(96%\)](#) and examine again.

### MOBILE PHASE

20 volumes of [acetone](#) and 80 volumes of [toluene](#).

#### CONFIRMATION

By each method of visualisation, the principal spot in the chromatogram obtained with solution (1) is similar in position, colour and intensity to that in the chromatogram obtained with solution (2).

B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

## TESTS

#### Related substances

Carry out the method for [liquid chromatography, Appendix III D](#), protected from light, using the following solutions prepared immediately before use.

- (1) To a quantity of the powdered tablets containing 25 mg of Indapamide add 70 mL of [ethanol \(96%\)](#) and mix mechanically for 2 hours. Add sufficient [ethanol \(96%\)](#) to produce 100 mL, mix and centrifuge. Dilute the supernatant liquid with the mobile phase to produce a solution containing 0.005% w/v of Indapamide.
- (2) Dilute 1 volume of solution (1) to 10 volumes with the mobile phase and further dilute 1 volume of this solution to 100 volumes with the mobile phase.
- (3) Dilute 1 volume of a 0.00025% w/v solution of [indapamide impurity B BPCRS](#) in [ethanol \(96%\)](#) to 10 volumes with the mobile phase.
- (4) Dilute 1 volume of a 0.00025% w/v solution of *4-chloro-3-sulfamoylbenzoic acid* in [ethanol \(96%\)](#) to 10 volumes with the mobile phase.
- (5) Mix 1 volume of solution (1), 1 volume of a 0.00025% w/v solution of [indapamide impurity B BPCRS](#) in [ethanol \(96%\)](#) and 1 volume of a 0.00025% w/v solution of *4-chloro-3-sulfamoylbenzoic acid* in [ethanol \(96%\)](#) and add 7 volumes of the mobile phase.

#### CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (15 cm × 4.6 mm) packed with [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 1.6 mL per minute.
- (d) Use an ambient column temperature.
- (e) Use a detection wavelength of 240 nm.
- (f) Inject 20 µL of each solution.

#### MOBILE PHASE

6 volumes of a solution containing 5% w/v of [sodium dodecyl sulfate](#) and 3% v/v of [glacial acetic acid](#), 10 volumes of [triethylamine](#), 20 volumes of [butan-2-ol](#), 310 volumes of [acetonitrile](#) and 690 volumes of [water](#), the mixture being adjusted to pH 3.0 with [orthophosphoric acid](#).

#### SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5), the retention time of impurity B relative to indapamide is about 1.7 and the retention time of 4-chloro-3-sulfamoylbenzoic acid relative to indapamide is about 0.3.

#### LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than twice the area of the peak in the chromatogram obtained with solution (3) (1.0%);

the area of any peak corresponding to 4-chloro-3-sulfamoylbenzoic acid is not greater than the area of the peak in the chromatogram obtained with solution (4) (0.5%);

the area of any other [secondary peak](#) is not greater than 5 times the area of the peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the impurities is not greater than 1.5%.

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

#### Uniformity of Content

Tablets containing less than 2 mg of Indapamide comply with the requirement stated under [Tablets](#) using the following method of analysis. Carry out the method for *liquid chromatography*, [Appendix III D](#), protected from light, using the following solutions.

- (1) Add 5 mL of [ethanol \(96%\)](#) to one whole tablet and mix mechanically for 2 hours and centrifuge. Dilute 1 volume of the supernatant liquid to 5 volumes with the mobile phase.
- (2) Dilute 1 volume of a 0.03% w/v solution of [indapamide BPCRS](#) in [ethanol \(96%\)](#) to 5 volumes with the mobile phase.

#### CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

#### DETERMINATION OF CONTENT

Calculate the content of  $C_{16}H_{16}ClN_3O_3S$  in each tablet using the declared content of  $C_{16}H_{16}ClN_3O_3S$  in [indapamide BPCRS](#).

## ASSAY

### ***For tablets containing less than 2 mg and/or less than 2% w/w of Indapamide***

Use the average of the individual results determined in the test for Uniformity of content.

### ***For tablets containing 2 mg or more and 2% w/w or more of Indapamide***

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, [Appendix III D](#), protected from light, using the following solutions.

- (1) To a quantity of the powdered tablets containing 25 mg of Indapamide add 70 mL of [ethanol \(96%\)](#) and mix mechanically for 2 hours. Add sufficient [ethanol \(96%\)](#) to produce 100 mL, mix and centrifuge. Dilute the supernatant liquid with the mobile phase to produce a solution containing 0.005% w/v of Indapamide.
- (2) Dilute 1 volume of a 0.025% w/v solution of [indapamide BPCRS](#) in [ethanol \(96%\)](#) to 5 volumes with the mobile phase.

#### CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

#### DETERMINATION OF CONTENT

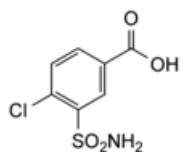
Calculate the content of  $C_{16}H_{16}ClN_3O_3S$  in each tablet using the declared content of  $C_{16}H_{16}ClN_3O_3S$  in [indapamide BPCRS](#).

## STORAGE

Indapamide Prolonged-release Tablets should be protected from light.

## IMPURITIES

The impurities limited by the requirements of this monograph include impurities B and C listed under Indapamide and the following:



1. 4-chloro-3-sulfamoylbenzoic acid

