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

Irbesartan Tablets

General Notices

Action and use

Angiotensin II (AT_1) receptor antagonist.

DEFINITION

Irbesartan Tablets contain Irbesartan.

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

Content of irbesartan, $C_{25}H_{28}N_6O$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Dissolve a quantity of the powdered tablets containing 0.3 g of Irbesartan in 10 mL of *methanol* with the aid of ultrasound. Filter through a Whatman GF/C filter and then through a 0.45-µm filter. Evaporate the filtrate to dryness under a stream of nitrogen and dry the residue at 60° for 1 hour. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of Irbesartan (*RS 467*). Disregard any bands occurring between 1125 and 1000 cm^{-1}.
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

Dissolution

Comply with the requirements in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a 10 mL sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary to produce a solution containing 0.0083% w/v of Irbesartan, at the maximum at 254 nm, Appendix II B using 0.1M *hydrochloric acid* in the reference cell.
(2) Measure the *absorbance* of a 0.0083% w/v solution of *irbesartan BPCRS* using 0.1M *hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of irbesartan, $C_{25}H_{28}N_6O$ in the medium from the absorbances obtained and using the declared content of $C_{25}H_{28}N_6O$ in *irbesartan BPCRS*.

LIMITS

The amount of irbesartan released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Prepare a 0.025M solution of *sodium dihydrogen orthophosphate monohydrate*, adjusted to pH 3.2 with *orthophosphoric acid* (solvent A).

(1) To a quantity of the powdered tablets containing 62.5 mg of Irbesartan, add 125 mL of *methanol* and mix with the aid of ultrasound. Add 100 mL of solvent A and shake. Dilute to 250 mL with solvent A, mix and filter (a 0.45-µm filter is suitable).
(2) Dilute 1 volume of solution (1) to 50 volumes with equal volumes of *methanol* and solvent A. Dilute 1 volume of this solution to 10 volumes with solvent A.
(3) 0.025% w/v of *irbesartan impurity A BPCRS* in *methanol*.
(4) To 25 mg of *irbesartan BPCRS*, add 50 mL of *methanol* and mix with the aid of ultrasound, add sufficient solvent A to produce 100 mL.
(5) Dilute 1 volume of solution (3) to 200 volumes with solution (4).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 3.0 mm) packed with *octadecylsilyl silica gel for chromatography* (3.5 µm) (Waters SunFire C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 0.6 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 10 µL of solutions 1, 2 and 5.

MOBILE PHASE

Mobile phase A 42 volumes of *acetonitrile R1* and 58 volumes of solvent A.

Mobile phase B 20 volumes of solvent A and 80 volumes of *acetonitrile R1*.

Time (Minutes)	Mobile phase A%	Mobile phase B%	Comment
0-6	100	0	isocratic
6-11	100→0	0→100	linear gradient
11-12	0	100	isocratic
12-13	0→100	100→0	linear gradient
13-15	100	0	Re-equilibration

When the chromatograms are recorded under the prescribed conditions the relative retention, with reference to Irbesartan (retention time = about 5 minutes), of impurity A is about 0.8.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5), the *resolution factor* between the peaks due to irbesartan and irbesartan impurity A is at least 4.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to irbesartan impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any other *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

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

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Prepare a 0.025M solution of *sodium dihydrogen orthophosphate monohydrate*, adjusted to pH 3.2 with *orthophosphoric acid* (solvent B).

(1) To a quantity of the powdered tablets containing 62.5 mg of irbesartan, add 125 mL of *methanol* and mix with the aid of ultrasound. Add 100 mL of solvent B and shake. Dilute to 250 mL with solvent B, mix and filter (a 0.45-µm filter is suitable).
(2) To 25 mg of *irbesartan BPCRS*, add 50 mL of *methanol* and mix with the aid of ultrasound. Dilute to 100 mL with solvent B.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used with a detection wavelength of 250 nm.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *symmetry factor* of the peak due to irbesartan is between 0.8 and 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{25}H_{28}N_6O$ in the tablets using the declared content of $C_{25}H_{28}N_6O$ in *irbesartan BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurity A listed under Irbesartan.