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Notes: New monograph.	

Telmisartan Tablets

Telmisartan Preparations

Action and use
Angiotensin II (AT_1) receptor antagonist.

DEFINITION

Telmisartan Tablets contain Telmisartan.

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

Content of telmisartan, $C_{33}H_{30}N_4O_2$
95.0 to 105.0% of the stated amount.

Identification

A. Shake a quantity of powdered tablets containing 80 mg of Telmisartan with 15 mL of *water*, filter and add 15 mL of *dichloromethane* to the filtrate, mixing with the aid of ultrasound. Separate the dichloromethane layer and evaporate to dryness under a stream of nitrogen. To the residue, add 10 mL of *acetonitrile* and filter. Repeat the evaporation process under a stream of nitrogen and dry the residue at 105° for 1 hour. The *infrared absorption spectrum* of the dried residue, Appendix IIA, is concordant with the *reference spectrum* of telmisartan (*RS XXX*).

TESTS

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

TEST CONDITIONS

(a) Use Apparatus 2, and rotate the paddle at 75 revolutions per minute.

(b) Use 900 mL of a pH 7.5 phosphate buffer solution, prepared by dissolving 13.61 g of *potassium dihydrogen phosphate* in 800 mL of *water*, adjusted to pH 7.5 using 2M *sodium hydroxide* and diluted to 1000 mL, 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 expected to contain 0.001% w/v of Telmisartan, at the maximum at 296 nm, Appendix II B using the dissolution medium in the reference cell.

(2) To 40 mg of *telmisartan BPCRS* add 1 mL of 0.1M *sodium hydroxide* and dilute to 100 mL with *methanol*. Dilute 1 volume of this solution to 4 volumes with the dissolution medium. Measure the *absorbance* of this solution using the dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of telmisartan, $C_{33}H_{30}N_4O_2$, in the medium from the absorbances obtained and using the declared content of $C_{33}H_{30}N_4O_2$, in *telmisartan BPCRS*.

LIMITS

The amount of telmisartan 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.

(1) Dissolve a quantity of the powdered tablets containing 25 mg of Telmisartan in 5 mL of *methanol* and 100 µL of a 4% w/v solution of *sodium hydroxide* and mix with the aid of ultrasound. Add sufficient *methanol* to produce a solution containing 0.05% w/v of Telmisartan.

(2) Dilute 1 volume of solution (1) to 10 volumes with *methanol*. Dilute 1 volume of this solution to 100 volumes with *methanol*.

(3) Dissolve the contents of a vial of *telmisartan for system suitability EPCRS* (containing impurities A, B, C, E and F) in 2 mL of *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12 cm × 4.0 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Kromasil C18 is suitable).

(b) Use gradient elution and the mobile phase described below.

(c) Use a flow rate of 1 mL per minute.

(d) Use a column temperature of 40°.

(e) Use a detection wavelength of 230 nm.

(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A Dissolve 2.0 g of *potassium dihydrogen phosphate* and 3.8 g of *sodium pentanesulphonate monohydrate R1* in 950 mL water, adjust to pH 3.0 with dilute *orthophosphoric acid* and dilute to 1000 mL with *water*.

Mobile phase B 20 volumes of *methanol R2* and 80 volumes of *acetonitrile R1*.

Time (Minutes)	Mobile phase A%	Mobile phase B%	Comment
0-3	70	30	isocratic
3-28	70→20	30→80	linear gradient
28-30	20→70	80→30	linear gradient
30-35	70	30	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to telmisartan (retention time about 15 minutes) are:

impurity A, about 0.2; impurity E, about 0.6; impurity F, about 0.7; impurity B, about 0.9; impurity C, about 1.5.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) is similar to the chromatogram supplied with *telmisartan for system suitability EPCRS* and the *resolution factor* between the peaks due to impurity B and telmisartan is at least 3.0.

LIMITS

Use the chromatogram supplied with *telmisartan for system suitability EPCRS* and the chromatogram obtained with solution (3) to identify the peaks due to impurities A, B, C, E and F.
In the chromatogram obtained with solution (1):

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

the area of any peak corresponding to impurity A or B is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.15% of each);

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

the sum of the areas of all the *secondary peaks* is not greater than 10 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

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

ASSAY

Weigh and power 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dissolve a quantity of the powdered tablets containing 25 mg of Telmisartan in 5 mL of *methanol* and 100 µL of a 4% w/v solution of *sodium hydroxide*. Mix with the aid of ultrasound, dilute to 50 mL with *methanol* and filter. To the filtrate, add sufficient *methanol* to produce a solution containing 0.0005% w/v of Telmisartan.

(2) 0.0005% w/v of *telmisartan BPCRS* in *methanol*.

(3) Dissolve the contents of a vial of *telmisartan for system suitability EPCRS* (containing impurities A, B, C, E and F) in 2 mL of *methanol.*

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) is similar to the chromatogram supplied with *telmisartan for system suitability EPCRS* and the *resolution factor* between the peaks due to impurity B and telmisartan is at least 3.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{33}H_{30}N_4O_2$, in the tablets using the declared content of $C_{33}H_{30}N_4O_2$ in *telmisartan BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, C, E and F listed under Telmisartan.