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# Olmesartan Tablets

General Notices

*Details for the public consultation of this monograph are as follows:*

| EAG/Panel/Working Party | Medicinal Chemicals 2 |
|---|---|
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| **Deadline for Comment** | 31st March 2025 |
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| **Notes** | Revised monograph<br>If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.<br>**Related substances** Limits restated to align with UK licences. |



**Action and use**

Angiotensin II ($AT_1$) receptor antagonist.

## DEFINITION

Olmesartan Tablets contain Olmesartan Medoxomil.

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

**Content of olmesartan medoxomil, $C_{29}H_{30}N_6O_6$**

95.0 to 105.0% of the stated amount.

## IDENTIFICATION

A. Shake a tablet in sufficient of 60% v/v of *acetonitrile* to prepare a solution containing 0.02% w/v of Olmesartan Medoxomil and mix with the aid of ultrasound. Centrifuge and dilute 5 mL of the supernatant liquid to 100 mL with 60% v/v of *acetonitrile*. The light absorption of the resulting solution, Appendix II B, in the range 200 to 360 nm exhibits a maximum at about 258 nm.

B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

**Dissolution**

Comply with 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 a solution prepared by dissolving 6.80 g of *potassium dihydrogen orthophosphate* and 0.944 g of *sodium hydroxide* in *water* and diluted to 1000 mL with *water*, at a temperature of 37°, as the dissolution medium.

PROCEDURE

(1) After 45 minutes, withdraw a sample of the medium, filter and dilute the filtrate with sufficient of the dissolution medium to give a solution expected to contain about 0.001% w/v of Olmesartan Medoxomil. Measure the *absorbance* of this solution, Appendix II B, at 258 nm using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.001% w/v solution of *olmesartan medoxomil BPCRS* using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of olmesartan medoxomil, $C_{29}H_{30}N_6O_6$, in the medium from the absorbances obtained and using the declared content of $C_{29}H_{30}N_6O_6$, in *olmesartan medoxomil BPCRS*.

LIMITS

The amount of olmesartan medoxomil 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) Shake a quantity of tablets in a sufficient volume of 90% v/v of *acetonitrile* to produce a solution containing 0.1% w/v of Olmesartan Medoxomil, mix with the aid of ultrasound, centrifuge and filter the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 50 volumes with 90% v/v of *acetonitrile*.
(3) Dissolve 5 mg of *olmesartan medoxomil for system suitability EPCRS* in 90% v/v of *acetonitrile* and dilute to 5 mL with the same solvent.
(4) Dilute 1 volume of solution (2) to 10 volumes with 90% v/v of *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

(a) A stainless steel column (10 cm × 4.6 mm) packed with *end-capped octylsilyl silica gel for chromatography* (3.5 µm) (Waters Symmetry C8 is suitable).
(b) Use gradient elution and the mobile phases described below.
(c) Use a flow rate of 1.0 mL per minute.

(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 250 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

*Mobile phase A* 20 volumes of *acetonitrile* and 80 volumes of a 0.015M potassium dihydrogen orthophosphate buffer solution prepared in the following manner. Dissolve 4.08 g of *potassium dihydrogen orthophosphate* in *water*, dilute to 2000 mL and adjust the pH to 3.4 with a 0.173% w/v solution of *orthophosphoric acid*.

*Mobile phase B* 20 volumes of a 0.015M potassium dihydrogen orthophosphate buffer solution prepared as described under mobile phase A, and 80 volumes of *acetonitrile*.

| Time (Minutes) | Mobile phase A (% v/v) | Mobile phase B (% v/v) | Comment |
|---|---|---|---|
| 0-10 | 75 | 25 | isocratic |
| 10-35 | 75→0 | 25→100 | linear gradient |
| 35-45 | 0 | 100 | isocratic |
| 45-60 | 0→75 | 100→25 | re-equilibration |

When the chromatograms are recorded under the prescribed conditions the retention times relative to olmesartan medoxomil (retention time, about 10 minutes) are: impurity A, about 0.2; impurity B, about 0.7; impurity C, about 1.5.

SYSTEM SUITABILITY

The test is not valid unless in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and olmesartan medoxomil is at least 3.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (2.5%);

the area of any peak corresponding to impurity C is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (4) (0.3%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (4) (0.2%);

the sum of the areas of any *secondary peaks*, excluding impurity A, is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (4) (0.8%).

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

## ASSAY

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

(1) To 10 whole tablets add 80 mL of 60% v/v *acetonitrile* and shake. Dilute to 100 mL with 60% v/v *acetonitrile* and disperse with the aid of ultrasound. Centrifuge the resulting solution and dilute a suitable quantity of the supernatant with 60% v/v *acetonitrile* to produce a solution containing 0.004% w/v of Olmesartan Medoxomil.
(2) 0.004% w/v of *olmesartan medoxomil BPCRS* in 60% v/v of *acetonitrile*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (L-Column ODS is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 249 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

34 volumes of *acetonitrile* and 66 volumes of a 0.015M *potassium dihydrogen orthophosphate* buffer solution prepared in the following manner. Dissolve 4.08 g of *potassium dihydrogen orthophosphate* in *water*, dilute to 2000 mL and adjust the pH to 3.4 with a 0.173% w/v solution of *orthophosphoric acid*.

DETERMINATION OF CONTENT

Calculate the content of $C_{29}H_{30}N_6O_6$ in the tablets from the chromatograms obtained using the declared content of $C_{29}H_{30}N_6O_6$ in *olmesartan medoxomil BPCRS*

## IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Olmesartan Medoxomil.