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Notes:	

Tolterodine Tablets

Tolterodine Preparations

Action and use
Anticholinergic.

DEFINITION

Tolterodine Tablets contain Tolterodine Tartrate.

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

Content of tolterodine tartrate, $C_{26}H_{37}NO_7$
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) Mix with the aid of ultrasound a quantity of the powdered tablets containing 12.5 mg of Tolterodine Tartrate with 5 mL of *methanol*, centrifuge and use the supernatant liquid.

(2) 0.25% w/v solution of *tolterodine tartrate BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* F_{254} (Merck silica gel 60 F_{254} plates are suitable).

(b) Use the mobile phase as described below.

(c) Apply 10 µL of each solution.

(d) Develop the plate to 15 cm.

(e) After removal of the plate, dry in air and examine under ultraviolet light (254 nm).

MOBILE PHASE

2 volumes of *triethylamine* 30 volumes of *ethyl acetate* and 70 volumes of n-*pentane*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position to that in the chromatogram obtained with solution (2).

B. In the test for Dissolution, the chromatogram obtained with solution (1) exhibits a peak with the same retention time as 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 a 0.68% w/v solution of *potassium dihydrogen orthophosphate* in 0.0224M *sodium hydroxide* at a temperature of 37°, as the dissolution medium.

PROCEDURE

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

(1) After 30 minutes withdraw a sample of the medium and filter. Use the filtrate, diluted with the dissolution medium if necessary, to produce a solution expected to contain 0.0001% w/v of Tolterodine Tartrate.

(2) 0.0001% w/v of *tolterodine tartrate BPCRS* in the dissolution medium.

(3) 0.02% w/v of *tolterodine tartrate BPCRS* and 0.004% w/v of *tolterodine impurity E EPCRS* in the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column 25 cm × 4.6 mm packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil BDS C18 is suitable).

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

(c) Use a flow rate of 1.5 mL per minute.

(d) Use an ambient column temperature.

(e) Use a detection wavelength of 220 nm.

(f) Inject 100 µL of each solution.

MOBILE PHASE

To 450 volumes of 0.288% w/v *ammonium dihydrogen orthophosphate* add 5 volumes of *triethylamine R2*. Adjust the mixture to pH 5.9 with a 50% v/v solution of *orthophosphoric acid* and add 550 volumes of *methanol R1*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity E and tolterodine tartrate is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{26}H_{37}NO_7$ in the medium using the declared content of $C_{26}H_{37}NO_7$ in *tolterodine tartrate BPCRS*.

LIMITS

The amount of tolterodine tartrate 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 the powdered tablets containing 10 mg of Tolterodine Tartrate with 7 mL of *methanol R1*, add sufficient *methanol R1* to produce 10mL and filter.

(2) Dilute 1 volume of solution (1) to 200 volumes with *methanol R1*.

(3) 0.02% w/v of *tolterodine tartrate BPCRS* and 0.004% w/v of *tolterodine impurity E EPCRS* in *methanol R1*.

(4) Dilute 1 volume of solution (2) to 5 volumes with *methanol R1*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column 25 cm × 4.6 mm packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil BDS C18 is suitable).

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

(c) Use a flow rate of 1.5 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

mobile phase A To 450 volumes of 0.288% w/v *ammonium dihydrogen orthophosphate* add 5 volumes of *triethylamine R2*. Adjust the mixture to pH 5.9 with a 50% v/v solution of *orthophosphoric acid* and add 550 volumes of *methanol R1*.

mobile phase B *methanol R1*.

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Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0 - 25	100	0	isocratic
25 - 45	100→80	0→20	linear gradient
45 - 46	80	20	isocratic
46 - 50	80→100	20→0	linear gradient
50 - 60	100	0	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity E and tolterodine tartrate is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

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

the sum of the areas of all *secondary peaks* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1%).

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

Uniformity of content
Tablets containing less than 2 mg and/or less than 2% w/w of Tolterodine Tartrate comply with the requirements stated under Tablets using the following method of analysis.

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

(1) Shake one tablet in sufficient *methanol R1* to obtain a solution containing 0.01% w/v of Tolterodine Tartrate and filter.

(2) 0.01% w/v of *tolterodine tartrate BPCRS* in *methanol R1*.

(3) 0.02% w/v of *tolterodine tartrate BPCRS* and 0.004% w/v of *tolterodine impurity E EPCRS* in *methanol R1*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used with an injection volume of 10 µL.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity E and tolterodine tartrate is at least 1.5.

DETERMINATION OF CONTENT

Calculate the total content of $C_{26}H_{37}NO_7$ in the tablets using the declared content of $C_{26}H_{37}NO_7$ in *tolterodine tartrate BPCRS*.

ASSAY

For tablets containing less than 2 mg and/or less than 2% w/w of Tolterodine Tartrate
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 Tolterodine Tartrate
Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Weigh and powder 20 tablets. Shake a quantity of powdered tablets containing 10 mg of Tolterodine Tartrate with 80 mL of *methanol R1*, dilute to 100 mL with the same solvent and filter.

(2) 0.01% w/v of *tolterodine tartrate BPCRS* in *methanol R1*.

(3) 0.02% w/v of *tolterodine tartrate BPCRS* and 0.004% w/v of *tolterodine impurity E EPCRS* in *methanol R1*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used with an injection volume of 10 µL.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity E and tolterodine tartrate is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{26}H_{37}NO_7$ in the tablets using the declared content of $C_{26}H_{37}NO_7$ in *tolterodine tartrate BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Tolterodine Tartrate.