EAG/Panel/Working Party	EAG MC3
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Deadline for Comment	30 June 2017
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Notes:New Monograph	

Quetiapine Tablets

Quetiapine Preparations

Action and use
Dopamine receptor antagonist; neuroleptic.

DEFINITION

Quetiapine Tablets contain Quetiapine Fumarate.

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

Content of quetiapine, $C_{21}H_{25}N_3O_2S$
95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing the equivalent of 40 mg of quetiapine with 10 mL of *acetonitrile*, filter and discard the filtrate. Extract the residue with 10 mL of *methanol*, filter and evaporate the filtrate to dryness. The *infrared absorption spectrum* of the residue, Appendix IIA, is concordant with the *reference spectrum* of quetiapine fumarate (*RS XXX*).

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 0.01M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 30 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 the equivalent of 0.0028% w/v of quetiapine, at the maximum at 290 nm, Appendix II B using 0.01M *hydrochloric acid* in the reference cell.

(2) Measure the *absorbance* of a solution of 0.0032% w/v of *quetiapine fumarate BPCRS* using 0.01M *hydrochloric acid* in the reference cell.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{25}N_3O_2S$ in the tablets from the absorbance obtained and using the declared content of $C_{46}H_{54}N_6O_8S_2$ in *quetiapine fumarate BPCRS*. Each mg of *quetiapine fumarate BPCRS* is equivalent to 0.869 mg of quetiapine.

LIMITS

The amount of quetiapine 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) Mix with the aid of ultrasound a quantity of powdered tablets containing the equivalent of 25 mg of quetiapine with 20 mL of the mobile phase, dilute to 25 mL with the mobile phase and filter.

(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase. Dilute 1 volume of this solution to 5 volumes with the mobile phase.

(3) 0.02% *quetiapine fumarate*, 0.004% w/v *quetiapine impurity G BPCRS* and 0.004% w/v *quetiapine impurity I BPCRS* in the mobile phase.

(4) 0.04% *fumaric acid* w/v solution in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5µm) (Hypersil Gold C8 is suitable).

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

(c) Use a flow rate of 1.3 mL per minute.

(d) Use column temperature of 25º.

(e) Use a detection wavelength of 230 nm.

(f) Inject 30 µL of each solution.

(g) For solution (1), allow the run time to proceed for 2 times the retention time of quetiapine

MOBILE PHASE

7 volumes of *acetonitrile*, 39 volumes of a 0.26% w/v solution of *diammonium hydrogen orthophosphate* in *water* and 54 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions, the retention times relative to quetiapine (retention time about 14 minutes) are: impurity H, about 0.5; impurity G, about 0.6 and impurity I, about 0.9.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to quetiapine and quetiapine impurity I is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

Identify any peaks due to impurity G using the chromatogram obtained with solution (3) and multiply the peak area by a following correction factor of 0.7;

the area of any *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 all *secondary peaks* is not greater than 5 times the principal peak in the chromatogram obtained with solution (2) (1%).

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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

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

(1) Shake a quantity of powdered tablets containing the equivalent of 50 mg of quetiapine with 200 mL of the mobile phase, dilute to 250 mL with the mobile phase and filter.

(2) 0.023% w/v of *quetiapine fumarate BPCRS* in the mobile phase.

(3) 0.02% w/v *quetiapine fumarate BPCRS*, 0.004% w/v *quetiapine impurity G BPCRS*, 0.006% w/v *quetiapine impurity H BPCRS* and 0.004% w/v *quetiapine impurity I BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to quetiapine and quetiapine impurity I is at least 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{25}N_3O_2S$ in the tablets using the declared content of $C_{46}H_{54}N_6O_8S_2$ in *quetiapine fumarate BPCRS*. Each mg of *quetiapine fumarate BPCRS* is equivalent to 0.434 mg of quetiapine.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities G, H and I listed under Quetiapine Fumarate.