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Erythromycin Gastro-resistant Tablets

General Notices

Erythromycin Tablets
Gastro-resistant Erythromycin Tablets

Action and use

Macrolide antibacterial.

DEFINITION

Erythromycin Gastro-resistant Tablets contain Erythromycin. They are made gastro-resistant by enteric-coating or by other means.

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

Content of erythromycins, calculated as the sum of erythromycin A ($C_{37}H_{67}NO_{13}$), erythromycin B ($C_{37}H_{67}NO_{12}$) and erythromycin C ($C_{36}H_{65}NO_{13}$)

90.0 to 110.0% of the stated amount of Erythromycin.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 0.1 g of Erythromycin with 5 mL of *dichloromethane*, decolourise, if necessary, with *activated charcoal*, filter through a 0.45-µm PTFE filter and evaporate the filtrate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, after drying *in vacuo* at 60° for 10 minutes, is concordant with the *reference spectrum* of erythromycin *(RS 123)*.

TESTS

Dissolution

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

Solution A A solution containing 0.68% w/v of *potassium dihydrogen orthophosphate* and 0.09% w/v of *sodium hydroxide* in water. Adjust the solution to pH 6.8, if necessary, using *orthophosphoric acid* or *sodium hydroxide*.

First stage

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 50 revolutions per minute.
(b) Use 900 mL of 0.06M *hydrochloric acid*, at a temperature of 37° as the medium.

PROCEDURE

After 1 hour remove the basket from the dissolution medium, and immediately lower the basket into the second dissolution medium.

Final stage

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 50 revolutions per minute.
(b) Use 900 mL of solution A, at a temperature of 37°.

PROCEDURE

After 1 hour remove the basket from the dissolution medium. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions, in solution A. *Prepare the solutions immediately before use and protect from light.*

(1) Withdraw a sample of the second medium and filter. Use the filtered medium, diluted with solution A, if necessary, to produce a solution expected to contain 0.028% w/v of Erythromycin.
(2) 0.028% w/v of *erythromycin BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions under Related substances may be used with isocratic elution using mobile phase A. Continue the chromatography for twice the retention time of erythromycin A.

When the chromatograms are recorded under the prescribed conditions, the retention time of erythromycin A is about 23 minutes.

DETERMINATION OF CONTENT

Calculate the content of erythromycin A, $C_{37}H_{67}NO_{13}$, using the declared content of $C_{37}H_{67}NO_{13}$ in *erythromycin BPCRS*.

The amount of erythromycin A released in the final stage is not less than 75% of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in solution B. *Prepare the solutions immediately before use and protect from light.*

Solution B 40 volumes of a 1.15% w/v solution of *dipotassium hydrogen orthophosphate* adjusted to pH 8.0 using *dilute phosphoric acid* and 60 volumes of *methanol*.

(1) Dissolve a quantity of powdered tablets in solution B and dilute to produce a solution containing 0.4% w/v of Erythromycin.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.4% w/v of *erythromycin for system suitability EPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped polar-embedded octadecylsilyl amorphous organosilica polymer* (3.5 µm) (X-Terra RP18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 65°.
(e) Use a detection wavelength of 210 nm.
(f) Inject 100 µL of each solution.

MOBILE PHASE

Mobile phase A 5 volumes of a 3.5% w/v solution of *dipotassium hydrogen orthophosphate* previously adjusted to pH 7.0 using *dilute phosphoric acid*, 35 volumes of *acetonitrile R1* and 60 volumes of *water*.

Mobile phase B 5 volumes of a 3.5% w/v solution of *dipotassium hydrogen orthophosphate* previously adjusted to pH 7.0 using *dilute phosphoric acid*, 50 volumes of *acetonitrile R1* and 45 volumes of *water*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-44	100	0	isocratic
44-46	100→0	0→100	linear gradient
46-61	0	100	isocratic
61-63	0→100	100→0	linear gradient
63-80	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to erythromycin A (retention time about 23 minutes) are: impurity H, about 0.3; impurity A, about 0.4; impurity B, about 0.5; erythromycin C, about 0.55; impurity M, about 0.58; impurity L, about 0.63; impurity C, about 0.9; impurity D, about 1.6; erythromycin B, about 1.75; impurity F, about 1.8 and impurity E, about 2.3.

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 erythromycin C is at least 1.2;

the *peak-to-valley ratio* is at least 2.0, where *Hp* is the height above the baseline of the peak due to impurity C and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to erythromycin A;

the *peak-to-valley ratio* is at least 1.5, where *Hp* is the height above the baseline of the peak due to impurity F and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to erythromycin B.

LIMITS

Identify any peaks corresponding to impurities D, E, F and L in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the areas of these peaks by the corresponding correction factors: impurity D, 2.0; impurity E, 0.08; impurity F, 0.08; impurity L, 0.11.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity C is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (3%);

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

the area of any peak corresponding to impurity D, E, F or H is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1% of each);

the area of any peak corresponding to impurity L is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

the area of any other *secondary peak*, other than the peaks due to erythromycin B and C is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

the sum of the areas of any *secondary peaks*, other than the peaks due to erythromycin B and C is not greater than 7 times the principal peak in the chromatogram obtained with solution (2) (7%).

Disregard any peak due to erythromycin B and erythromycin C and any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.2%).

The content of each of erythromycin B and erythromycin C, as determined under Assay, is not more than 5%.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in solution B. *Prepare the solutions immediately before use and protect from light.*

Solution B 40 volumes of a 1.15% w/v solution of *dipotassium hydrogen orthophosphate* adjusted to pH 8.0 using *dilute phosphoric acid* and 60 volumes of *methanol*.

(1) Dissolve a quantity of the powdered tablets with solution B and dilute to produce a solution containing 0.4% w/v of Erythromycin.
(2) 0.4% w/v of *erythromycin BPCRS*.
(3) 0.4% w/v of *erythromycin for system suitability EPCRS*.

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 impurity B and erythromycin C is at least 1.2;

the *peak-to-valley ratio* is at least 2.0, where *Hp* is the height above the baseline of the peak due to impurity C and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to erythromycin A;

the *peak-to-valley ratio* is at least 1.5, where *Hp* is the height above the baseline of the peak due to impurity F and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to erythromycin B.

DETERMINATION OF CONTENT

Calculate the percentage content of erythromycin A ($C_{37}H_{67}NO_{13}$), erythromycin B ($C_{37}H_{67}NO_{12}$) and erythromycin C ($C_{36}H_{65}NO_{13}$) using the chromatograms obtained with solutions (1) and (2) and the declared contents of $C_{37}H_{67}NO_{13}$, $C_{37}H_{67}NO_{12}$ and $C_{36}H_{65}NO_{13}$ respectively in *erythromycin BPCRS*.

STORAGE

Erythromycin Gastro-resistant Tablets should be protected from light.

IMPURITIES

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