Edition: BP 2025 (Ph. Eur. 11.6 update)

Erythromycin Stearate Tablets

General Notices

Action and use

Macrolide antibacterial.

DEFINITION

Erythromycin Stearate Tablets contain Erythromycin Stearate.

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 ($C_{36}H_{65}NO_{13}$)

95.0 to 105.0% of the stated amount of erythromycin.

IDENTIFICATION

Shake a quantity of the powdered tablets containing the equivalent of 0.1 g of erythromycin with 10 mL of *water*, allow to settle and discard the supernatant liquid. Add 10 mL of *methanol* to the residue, filter and evaporate the filtrate to dryness. The *infrared absorption spectrum*, Appendix II A, of the residue after drying at a pressure not exceeding 0.7 kPa is concordant with the *reference spectrum* of erythromycin stearate *(RS 127)*.

TESTS

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 2.722% w/v solution of *sodium acetate*, adjusted to pH 5.0 with *glacial acetic acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes transfer 5 mL of a filtered sample of the medium to a graduated flask, add 40 mL of *glacial acetic acid* and 10 mL of a 0.5% w/v solution of *4-dimethylaminobenzaldehyde* in *glacial acetic acid* and dilute to 100 mL with a mixture of 35 volumes of *glacial acetic acid* and 70 volumes of *hydrochloric acid*. Allow to stand for 15 minutes and measure the absorbance of the resulting solution at the maximum at 485 nm, Appendix II B, using dissolution medium that has been subjected to the conditions of the test in the reference cell
(2) Prepare a suitable solution of *erythromycin stearate BPCRS* in the dissolution medium and filter. Transfer 5 mL of the filtered solution to a graduated flask, add 40 mL of *glacial acetic acid* and 10 mL of a 0.5% w/v solution of *4-*

dimethylaminobenzaldehyde in *glacial acetic acid* and dilute to 100 mL with a mixture of 35 volumes of *glacial acetic acid* and 70 volumes of *hydrochloric acid*. Allow to stand for 15 minutes and measure the *absorbance* of the resulting solution at the maximum at 485 nm, Appendix II B, using dissolution medium that has been subjected to the conditions of the test in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of erythromycins, ($C_{37}H_{67}NO_{13}$), in the medium from the absorbances obtained and using the declared content of $C_{37}H_{67}NO_{13}$ in *erythromycin stearate BPCRS*.

The amount of erythromycin 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 in solution A. *Prepare the solutions immediately before use and protect from light.*

Solution A 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 R1*.

(1) Disperse a quantity of powdered tablets in solution A and shake for a minimum of 30 minutes, using ultrasound where necessary. Dilute to produce a solution containing the equivalent of 0.4% w/v of erythromycin and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) 0.4% w/v of *erythromycin for system suitability EPCRS*.
(4) 0.4% w/v of *erythromycin stearate for impurity S identification EPCRS*.
(5) 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 A, about 0.4; impurity B, about 0.5; erythromycin C, about 0.55; 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; impurity S, about 2.1; 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 twice 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 S 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 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 area of 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 (5) (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 A. *Prepare the solutions immediately before use and protect from light.*

Solution A 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 R1*.

(1) Dissolve a quantity of the powdered tablets in solution A and shake for a minimum of 30 minutes, using ultrasound where necessary. Dilute to produce a solution containing the equivalent of 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 described 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 Stearate Tablets should be protected from light.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of Erythromycin.

IMPURITIES

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