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

Erythromycin Lactobionate for Infusion

General Notices

Action and use

Macrolide antibacterial.

DEFINITION

Erythromycin Lactobionate for Infusion is a sterile material consisting of Erythromycin Lactobionate with or without excipients. It is supplied in a sealed container.

The contents of the sealed container comply with the requirements for Powders for Injections or Infusions stated under Parenteral Preparations 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 110.0% of the stated amount of erythromycin.

IDENTIFICATION

The *infrared absorption spectrum*, Appendix II A, of the dry powder, is concordant with the *reference spectrum* of erythromycin lactobionate *(RS 126)*.

TESTS

Acidity or alkalinity

pH of a solution containing the equivalent of 1.34% w/v of erythromycin, 6.5 to 7.5, Appendix V L.

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) Dissolve a quantity of the contents of a sealed container to produce a solution containing the equivalent of 0.4% w/v 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 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 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 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 or F 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 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 (4) (0.2%).

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

ASSAY

Determine the weight of the contents of 10 sealed containers as described in the test for *uniformity of weight*, Appendix XII C1, Powders for Parenteral Administration.

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) Dilute a quantity of the mixed contents of sealed containers 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*.

LABELLING

The label of the sealed container states the quantity of active ingredient contained in it in terms of the equivalent amount of erythromycin.

IMPURITIES

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