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Erythromycin and Zinc Acetate Lotion

General Notices

Erythromycin and Zinc Acetate Cutaneous Solution

Action and use

Macrolide antibacterial.

DEFINITION

Erythromycin and Zinc Acetate Lotion is a *cutaneous solution*. It contains 4% w/v of Erythromycin and 1.2% w/v of Zinc Acetate in a suitable ethanolic vehicle. It is prepared by dissolving the dry ingredients in the requisite volume of the vehicle provided before use.

The lotion complies with the requirements stated under Liquids for Cutaneous Application.

The dry ingredients comply with the requirements for Powders for Lotions stated under Liquids for Cutaneous Application 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.

Content of zinc acetate, $C_4H_6O_4Zn,2H_2O$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. In the Assay for erythromycin, the retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).
B. Mix a quantity of the powder with sufficient *water* to produce a 5% w/v solution and filter. Add 0.5 mL of a 0.25M solution of *potassium hexacyanoferrate(II)* to 5 mL of the resulting solution and mix; a white precipitate is produced. Add 5 mL of 4M *hydrochloric acid*; the precipitate does not dissolve.

TESTS

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 powder in solution A 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 volumes 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 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

For erythromycin

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*.

(1) Dissolve a quantity of the powder containing 0.4 g of Erythromycin in 75 mL of solution A and shake. Dilute to 100 mL.
(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*.

For zinc acetate

To a quantity of the powder containing 0.2 g of Zinc Acetate add 5 mL of *dilute acetic acid*. Carry out the *complexometric titration of zinc*, Appendix VIII D. Each mL of *0.1M disodium edetate VS* is equivalent to 21.95 mg of $C_4H_6O_4Zn,2H_2O$.

For the following tests prepare the lotion as directed on the label. The lotion complies with the requirements stated under Liquids for Cutaneous Application 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.

Content of zinc acetate, $C_4H_6O_4Zn,2H_2O$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. In the Assay for erythromycin, the retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).
B. Evaporate a suitable volume of the lotion to dryness on a water bath, add 20 mL of water to the residue, mix, with shaking, and filter. Add 1 mL of a 0.25M solution of *potassium hexacyanoferrate(II)* to the resulting filtrate and mix; a white precipitate is produced. Add 10 mL of 4M *hydrochloric acid*; the precipitate does not dissolve.

TESTS

Clarity and colour of solution

The solution is *clear*, Appendix IV A, and *colourless*, Appendix IV B, Method I.

ASSAY

For erythromycin

Carry out the Assay for erythromycin described in the requirements for the dry ingredients. For solution (1) use a volume of the lotion containing 80 mg of Erythromycin in place of the powder.

For zinc acetate

To a volume of the lotion containing 0.2 g of Zinc Acetate add 5 mL of *dilute acetic acid*. Carry out the *complexometric titration of zinc*, Appendix VIII D. Each mL of 0.1M *disodium edetate VS* is equivalent to 21.95 mg of $C_4H_6O_4Zn,2H_2O$.

STORAGE

Erythromycin and Zinc Acetate Lotion should be stored at the temperature and used within the period stated on the label.

IMPURITIES

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