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Erythromycin Ointment

» Erythromycin Ointment is Erythromycin in a suitable ointment base. It contains not less than 90.0 percent and not more than 125.0 percent of the labeled amount of erythromycin ($C_{37}H_{67}NO_{13}$).

Packaging and storage—Preserve in collapsible tubes or in other tight containers, preferably at controlled room temperature.

USP Reference standards ⟨11⟩—

USP Erythromycin RS
USP Erythromycin B RS
USP Erythromycin C RS
USP Erythromycin Related Compound N RS
N-Demethylerythromycin A.
$C_{36}H_{65}NO_{13}$ 719.91

Identification—

A: Transfer a quantity of Ointment, equivalent to about 5 mg of erythromycin, to a separator containing 50 mL of solvent hexane. Shake until dissolved. Extract with three separate 20-mL portions of methanol. Combine the methanol extracts in a beaker, and evaporate to dryness. Dissolve the residue in 2 mL of methanol (test solution). Proceed as directed in the *Identification* test under *Erythromycin Delayed-Release Capsules*, beginning with "Prepare a Standard solution of USP Erythromycin RS."

B: The retention times of the peaks for erythromycin A, erythromycin B, and erythromycin C in the chromatogram of the *Assay preparation* correspond to those in the chromatograms of the *Standard preparation* and *Erythromycins B and C standard preparation*, as obtained in the *Assay*.

Minimum fill ⟨755⟩: meets the requirements.

Water Determination, *Method I* ⟨921⟩: not more than 1.0%, 20 mL of a mixture of toluene and methanol (7:3) being used in place of methanol in the titration vessel.

Assay—

Solution A—Prepare a degassed mixture of acetonitrile and water (90:10). Store in a reservoir protected from air by sparging with helium.

Solution B—To 1000 mL of degassed water add 0.5 mL of sodium hydroxide solution (1 in 2), using a suitable syringe and needle to minimize exposure to air. Degas, and store in a reservoir protected from air by sparging with helium.

Solution C—Use degassed water, and store in a reservoir protected from air by sparging with helium.

Mobile phase—Using a suitable pumping system, pump *Solution A*, *Solution C*, and *Solution B* from the respective reservoirs in the ratio of 56:37:7. Make any necessary adjustments (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a mixture of methanol and water (50:50).

Standard preparation—Quantitatively prepare a solution of USP Erythromycin RS in *Diluent* having a known concentration of about 0.66 mg per mL.

Erythromycins B and C standard preparation—Quantitatively prepare a solution in *Diluent* having known concentrations of about 34 µg each of USP Erythromycin B RS and USP Erythromycin C RS per mL.

System suitability solution—Transfer about 2 mg of USP Erythromycin Related Compound N RS to a 10-mL volumetric flask, add 0.4 mL of the *Standard preparation* and 6 mL of *Erythromycins B and C standard preparation*, and mix. Dilute with *Erythromycins B and C standard preparation* to volume, and mix.

Assay preparation—Transfer an accurately weighed portion of Ointment, equivalent to about 60 mg of erythromycin, to a 125-mL separator. Add 50 mL of solvent hexane, and shake until dissolved. Extract with four separate 20-mL portions of *Diluent*, collecting the extracts in a 100-mL volumetric flask. Dilute the combined extracts with *Diluent* to volume, mix, and pass a portion of the solution through a filter having a 0.45-µm porosity. Use the clear filtrate as the *Assay preparation*.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with an electrochemical detector, a glassy carbon electrode fitted with three gaskets, a 4-mm × 5-cm guard column that contains 8-µm packing L50, and a 4-mm × 25-cm analytical column that contains 8-µm packing L50. The electrochemical detector is used in the pulsed integrated amperometric mode with a range of 10 nC, an output of 1 V full scale, a rise time of 0.6 second, positive polarity, E = 0.9 V; t1 = 400 ms; E2 = 0.9 V; t2 = 100 ms; E3 = −0.9 V; t3 = 100

ms. The flow rate is about 1 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.4 for erythromycin related compound N, 0.5 for erythromycin C, 1.0 for erythromycin A, and 1.6 for erythromycin B; the resolution, *R*, between erythromycin related compound N and erythromycin C is not less than 0.6, between erythromycin C and erythromycin A not less than 2.5, and between erythromycin A and erythromycin B not less than 2.5. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2; and the relative standard deviation for replicate injections is not more than 3%.

[NOTE—Turn off the electrochemical detector before stopping the flow of the *Mobile phase*.]

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation*, *Erythromycins B and C standard preparation*, and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak areas. Calculate the percentage of erythromycin A in the portion of Ointment taken by the formula:

$$0.1(CP/W)(r_U/r_S)$$

in which *C* is the concentration, in mg per mL, of USP Erythromycin RS in the *Standard preparation; P* is the designated percentage of erythromycin A in USP Erythromycin RS; *W* is the quantity, in g, of Ointment taken to prepare the *Assay preparation;* and r_U and r_S are the erythromycin A peak areas obtained from the *Assay preparation* and the *Standard preparation*, respectively. Calculate the percentages of erythromycin B and erythromycin C in the portion of Ointment taken by the formula:

$$0.0001(CP/W)(r_U/r_S)$$

in which *C* is the concentration, in µg per mL, of the relevant USP Reference Standard in the *Erythromycins B and C standard preparation; P* is the designated percentage of erythromycin B or erythromycin C in the relevant USP Reference Standard; *W* is the quantity, in g, of Ointment taken to prepare the *Assay preparation;* and r_U and r_S are the peak areas for the relevant analyte obtained from the *Assay preparation* and the *Erythromycins B and C standard preparation*, respectively. Calculate the percentage content of erythromycin in the Ointment by adding the percentages of erythromycin A, erythromycin B, and erythromycin C found.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ERYTHROMYCIN OINTMENT	Rebecca C. Potts Associate Scientific Liaison	BIO42020 Biologics Monographs 4 - Antibiotics

Chromatographic Database Information: Chromatographic Database

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