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Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl for Oral Suspension

DEFINITION

Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl for Oral Suspension is a dry mixture of Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl with one or more suitable buffers, colors, flavors, surfactants, and suspending agents. It contains the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of erythromycin ($C_{37}H_{67}NO_{13}$) and the equivalent of NLT 90.0% and NMT 115.0% of the labeled amount of sulfisoxazole ($C_{11}H_{13}N_3O_3S$).

[Note—Where Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl for Oral Suspension is prescribed, without reference to the quantity of erythromycin or sulfisoxazole contained therein, a product containing 40 mg/mL of erythromycin and 120 mg/mL of sulfisoxazole when constituted as directed in the labeling shall be dispensed.]

IDENTIFICATION

Change to read:

• **▲A.▲ (USP 1-May-2019) Thin-Layer Chromatographic Identification Test**

Standard solution A: 3 mg/mL of USP Erythromycin Ethylsuccinate RS in methanol

Standard solution B: 8.7 mg/mL of USP Sulfisoxazole Acetyl RS in methanol

Sample solution: Nominally 2.5 mg/mL of erythromycin from Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl for Oral Suspension in methanol. Shake this mixture by mechanical means for about 30 min. Centrifuge a portion of this mixture, and use the clear supernatant.

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Methanol and chloroform (85:15)

Spray reagent: Dehydrated alcohol, *p*-methoxybenzaldehyde, and sulfuric acid (90:5:5)

Analysis

Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

Place the plate in an unlined chromatographic chamber, and develop the plate in the *Developing solvent system* until the solvent front has moved about 9 cm. Remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Spray the plate with *Spray reagent*. Heat the plate at 100° for 10 min, and examine the chromatograms, in which the erythromycin and succinic acid moieties appear as black-to-purple spots and the sulfisoxazole acetyl appears as a yellow spot.

Acceptance criteria: The R_F values of the principal black-to-purple spots of the *Sample solution* correspond to those of *Standard solution A*; and the R_F value of the principal yellow spot of the *Sample solution* corresponds to that of *Standard solution B*.

ASSAY

• **Erythromycin**

(See *Antibiotics—Microbial Assays* ⟨81⟩.)

Sample stock solution: Constitute Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl for Oral Suspension as directed in the labeling, and allow to stand for 1 h. Gently shake the suspension, transfer 5.0 mL to a high-speed blender jar containing 195.0 mL of methanol, and blend for 4 ± 1 min.

Sample solution: Dilute the *Sample stock solution* quantitatively with *Buffer B.3* to obtain a *Sample solution* having a concentration assumed to be equal to the median dose level of the Standard (1.0 µg/mL of erythromycin).

Analysis: Proceed as directed in *Antibiotics—Microbial Assays* ⟨81⟩.

Acceptance criteria: 90.0%–120.0%

Change to read:

• **Sulfisoxazole**

Mobile phase: Acetonitrile and water (40:60) ▲▲ (USP 1-May-2019)

Internal standard solution: 0.33 mg/mL of benzanilide in acetonitrile▲▲ (USP 1-May-2019)

Standard solution: 1 mg/mL of USP Sulfisoxazole Acetyl RS in *Internal standard solution*

Sample stock solution: Constitute Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl for Oral Suspension as directed in the labeling, and allow to stand for 1 h. Gently shake Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl for Oral Suspension, transfer a volume equivalent to 600 mg of sulfisoxazole to a 125-mL separator, and extract with three 75-mL portions of chloroform. Collect the extracts in a 250-mL volumetric flask and dilute with chloroform to volume. Pass a portion of this solution through a suitable filter of 1-µm or finer pore size.

Sample solution: Pipet 4 mL of the filtrate from the *Sample stock solution* into a glass-stoppered, 25-mL conical flask, and evaporate with the aid of a current of dry air to dryness. Add 10.0 mL of *Internal standard solution*, and mix.

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 30-cm; ▲5-µm▲ (USP 1-May-2019) packing L1

Flow rate: 1.2 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 3.0 between sulfisoxazole acetyl and benzanilide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of sulfisoxazole ($C_{11}H_{13}N_3O_3S$) in the portion of Erythromycin Ethylsuccinate and Sulfisoxazole Acetyl for Oral Suspension taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

R_U = peak response ratio of sulfisoxazole acetyl to benzanilide from the *Sample solution*

R_S = peak response ratio of sulfisoxazole acetyl to benzanilide from the *Standard solution*

C_S = concentration of USP Sulfisoxazole Acetyl RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of the *Sample solution* (mg/mL)

M_{r1} = molecular weight of sulfisoxazole, 267.31

M_{r2} = molecular weight of sulfisoxazole acetyl, 309.35

Acceptance criteria: 90.0%–115.0%

PERFORMANCE TESTS

- **Uniformity of Dosage Units** ⟨905⟩, *Content Uniformity*

For solids packaged in single-unit containers: Meets the requirements with respect to erythromycin and sulfisoxazole

- **Deliverable Volume** ⟨698⟩**:** Meets the requirements

SPECIFIC TESTS

- **pH** ⟨791⟩

Sample solution: Suspension constituted as directed in the labeling

Acceptance criteria: 5.0–7.2

- **Loss on Drying** ⟨731⟩

Analysis: Dry about 100 mg in a capillary-stoppered bottle under vacuum at 60° for 3 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards** ⟨11⟩

USP Erythromycin RS

USP Erythromycin Ethylsuccinate RS

USP Sulfisoxazole Acetyl RS

Topic/Question	Contact	Expert Committee
ERYTHROMYCIN ETHYLSUCCINATE AND SULFISOXAZOLE ACETYL FOR ORAL SUSPENSION	Julie Zhang Associate Science & Standards Liaison	BIO42020 Biologics Monographs 4 - Antibiotics

Chromatographic Database Information: Chromatographic Database

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