Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

- **DISSOLUTION,** *Procedure for a Pooled Sample* ⟨**711**⟩
  Medium: Water; 500 mL
  Apparatus 1: 100 rpm
  Time: 45 min
  Standard solution: USP Dextroamphetamine Sulfate RS in *Medium* having a known concentration of USP Dextroamphetamine Sulfate RS similar to the concentration expected in the sample.
  Sample solution: Pass a portion of the solution under test through a suitable filter.
  Diluted acetic acid: 14 mL of glacial acetic acid in 100 mL of water
  Mobile phase: 1.1 g of sodium 1-heptanesulfonate in 575 mL of water. Add 25 mL of *Diluted acetic acid* and 400 mL of methanol. Adjust with glacial acetic acid to a pH of 3.3 ± 0.1.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 254 nm
  Column: 3.9-mm × 30-cm; packing L1
  Flow rate: 1 mL/min
  Injection size: 500 µL
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Relative standard deviation: NMT 2.0%
  Analysis
  Calculate the percentage of the labeled amount of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ dissolved:

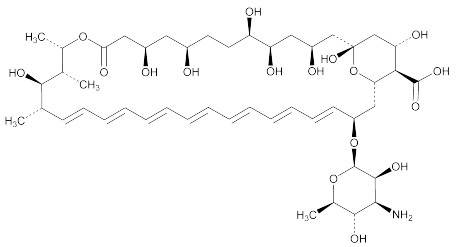
$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

  r_U = peak response from the *Sample solution*
  r_S = peak response from the *Standard solution*
  C_S = concentration of the *Standard solution* (mg/mL)
  L = label claim (mg/Tablet)
  V = volume of *Medium*, 500 mL
  Tolerances: NLT 75% (Q) of amphetamine sulfate $[(C_9H_{13}N)_2 \cdot H_2SO_4]$ is dissolved.
- **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Dextroamphetamine Sulfate RS

Amphotericin B



$C_{47}H_{73}NO_{17}$ 924.08

Amphotericin B.

Amphotericin B.

[1*R*-(1*R**,3*S**,5*R**,6*R**,9*R**,11*R**,15*S**,16*R**,17*R**,18*S**,19*E*,21*E*,23*E*,25*E*,27*E*,29*E*,31*E*,33*R**,35*S**,36*R**,37*S**)]-33-[(3-Amino-3,6-dideoxy-β-D-mannopyranosyl)oxy]-1,3,5,6,9,11,17,37-octahydroxy-15,16,18-trimethyl-13-oxo-14,39-dioxabicyclo[33.3.1]nonatriaconta-19,21,23,25,27,29,31-heptaene-36-carboxylic acid [1397-89-3].

» Amphotericin B has a potency of not less than 750 µg of $C_{47}H_{73}NO_{17}$ per mg, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers, and store in a cold place.

Labeling—Label it to state whether it is intended for use in preparing dermatological and oral dosage forms or parenteral dosage forms.

USP Reference standards ⟨11⟩**—**
USP Amphotericin B RS
USP Nystatin RS

Identification, *Ultraviolet Absorption* ⟨197U⟩**—**

Spectral range 1: 240 to 320 nm.

Solution 1: prepared as directed for *Test preparation* in the *Limit of amphotericin A*, and compare its absorbance to that of the *Amphotericin B standard preparation*. An extra peak may occur at 304 nm in the spectrum of this solution.

Spectral range 2: 320 to 400 nm.

Solution 2: prepared as directed for *Test preparation* in the *Limit of amphotericin A* and then diluted with 9 volumes of methanol. Compare its absorbance to that of a similar dilution of the *Amphotericin B standard preparation*.

Loss on drying ⟨731⟩**—**Dry about 100 mg, accurately weighed, in a capillary-stoppered bottle in vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 hours: it loses not more than 5.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.5%, the charred residue being moistened with 2 mL of nitric acid and 5 drops of sulfuric acid. [NOTE—Amphotericin B intended for use in preparing dermatological creams, lotions, and ointments, and oral suspensions and capsules, yields not more than 3.0%.]

Limit of amphotericin A—

Test preparation—Dissolve about 50 mg of Amphotericin B, accurately weighed, in 10.0 mL of dimethyl sulfoxide in a 50-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 4.0 mL of this solution to a 50-mL volumetric flask, dilute with methanol to volume, and mix.

Nystatin standard preparation—Dissolve about 20 mg of USP Nystatin RS, accurately weighed, in 40.0 mL of dimethyl sulfoxide in a 200-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 4.0 mL of this solution to a 50-mL volumetric flask, dilute with methanol to volume, and mix.

Amphotericin B standard preparation—Dissolve about 50 mg of USP Amphotericin B RS, accurately weighed, in 10.0 mL of dimethyl sulfoxide in a 50-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 4.0 mL of this solution to a 50-mL volumetric flask, dilute with methanol to volume, and mix. Prepare this solution fresh daily.

Procedure—Concomitantly determine the absorbances of the *Nystatin* and *Amphotericin B standard preparations* and the *Test preparation* in 1-cm cells at 304 nm and at 282 nm, with a suitable spectrophotometer, using a 1 in 62.5 solution of dimethyl sulfoxide in methanol as the blank. Calculate the percentage of amphotericin A taken by the formula:

$$25W_N[(A_{B_{282}} \times A_{U_{304}}) - (A_{B_{304}} \times A_{U_{282}})]/[(A_{B_{282}} \times A_{N_{304}}) - (A_{B_{304}} \times A_{N_{282}})]W_U$$

in which W_N is the weight, in mg, of USP Nystatin RS taken, A_{B282} and A_{B304} are the absorbances of the *Amphotericin B standard preparation* at 282 nm and 304 nm, respectively, A_{N282} and A_{N304} are the absorbances of the *Nystatin standard*

preparation at 282 nm and 304 nm, respectively, A_{U282} and A_{U304} are the absorbances of the *Test preparation* at 282 nm and 304 nm, respectively, and W_U is the weight, in mg, of the Amphotericin B taken: not more than 5%, calculated on the dried basis, is found. [NOTE—Amphotericin B intended for use in preparing dermatological creams, lotions, and ointments, and oral suspensions and capsules, contains not more than 15% of amphotericin A, calculated on the dried basis.]

Assay—Proceed with amphotericin B as directed under *Antibiotics—Microbial Assays* ⟨81⟩.

Amphotericin B Cream

» Amphotericin B Cream contains not less than 90.0 percent and not more than 125.0 percent of the labeled amount of Amphotericin B.

Packaging and storage—Preserve in collapsible tubes, or other well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Amphotericin B RS

Minimum fill ⟨755⟩: meets the requirements.

Change to read:

Assay—Proceed as directed for amphotericin B under *Antibiotics—Microbial Assays* ⟨81⟩, blending a suitable accurately weighed portion of Cream in a high-speed blender with a sufficient accurately measured volume of dimethyl sulfoxide to give a convenient concentration. Quantitatively dilute an accurately measured volume of this solution with dimethyl sulfoxide to obtain a stock solution having a concentration of about 20 µg of amphotericin B per mL. Quantitatively dilute an accurately measured volume of this stock solution with •*Buffer B.10*• (CN 1-May-2017) to obtain a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

Amphotericin B for Injection

» Amphotericin B for Injection is a sterile complex of Amphotericin B and deoxycholate sodium and one or more suitable buffers. It contains not less than 90.0 percent and not more than 120.0 percent of the labeled amount of $C_{47}H_{73}NO_{17}$.

Change to read:

Packaging and storage—Preserve as described in •*Packaging and Storage Requirements* ⟨659⟩*, Injection Packaging, Packaging for constitution*• (CN 1-May-2017), in a refrigerator and protected from light.

Labeling—Label it to indicate that it is intended for use by intravenous infusion to hospitalized patients only, and that the solution should be protected from light during administration.

USP Reference standards ⟨11⟩**—**
USP Amphotericin B RS
USP Endotoxin RS

Bacterial Endotoxins Test ⟨85⟩**—**It contains not more than 5.0 USP Endotoxin Units per mg of amphotericin B. For products used or labeled for intrathecal injection, it contains not more than 0.9 USP Endotoxin Unit per mg of amphotericin B.

Sterility Tests ⟨71⟩**—**It meets the requirements when tested as directed in the section *Membrane Filtration* under *Test for Sterility of the Product to be Examined*, 50 mg from each container being tested.

pH ⟨791⟩: between 7.2 and 8.0, in an aqueous solution containing 10 mg of amphotericin B per mL.

Loss on drying ⟨731⟩**—**Dry about 100 mg in a capillary-stoppered bottle in vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 hours: it loses not more than 8.0% of its weight.

Other requirements—It meets the requirements for *Uniformity of Dosage Units* ⟨905⟩ and for *Labeling* ⟨7⟩*, Labels and Labeling for Injectable Products*.

Change to read:

Assay—

Assay preparation 1 (where it is packaged as a single-dose container)—Constitute Amphotericin B for Injection as directed in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and dilute quantitatively and stepwise with dimethyl sulfoxide to obtain a solution containing about 20 µg of amphotericin B per mL.

Assay preparation 2 (where the labeling states the quantity of amphotericin B in a given volume of constituted solution)—Constitute Amphotericin B for Injection as directed in the labeling. Withdraw an accurately measured volume of the resultant solution, using a suitable hypodermic needle and syringe, and dilute quantitatively and stepwise with dimethyl sulfoxide to obtain a solution containing about 20 µg of amphotericin B per mL.

Procedure—Proceed as directed for amphotericin B under *Antibiotics—Microbial Assays* ⟨81⟩, using an accurately measured volume of *Assay preparation* diluted quantitatively and stepwise with •*Buffer B.10*• (CN 1-May-2017) to obtain a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

Amphotericin B Lotion

» Amphotericin B Lotion contains not less than 90.0 percent and not more than 125.0 percent of the labeled amount of amphotericin B.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Amphotericin B RS

Minimum fill ⟨755⟩: meets the requirements.

pH ⟨791⟩: between 5.0 and 7.0.

Change to read:

Assay—Proceed as directed for amphotericin B under *Antibiotics—Microbial Assays* ⟨81⟩, quantitatively dissolving a suitable accurately measured volume of Lotion in sufficient dimethyl sulfoxide to give a convenient concentration. Quantitatively dilute an accurately measured volume of this solution with dimethyl sulfoxide to obtain a stock solution having a concentration of about 20 µg of amphotericin B per mL. Quantitatively dilute an accurately measured vol-