r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Mefloquine Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of Mefloquine Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **DISSOLUTION** ⟨**711**⟩

Medium: 0.1 N Hydrochloric acid; 900 mL
Apparatus 2: 50 rpm
Time: 30 min
Standard stock solution: 0.2 mg/mL of USP Mefloquine Hydrochloride RS in *Medium*. [NOTE—Use 5% of the flask volume of methanol to facilitate dissolution before solubilization with *Medium*.]
Standard solution: 0.04 mg/mL of USP Mefloquine Hydrochloride RS in *Medium* from the *Standard stock solution*
Sample solution: Dilute a portion of the solution under test with *Medium* (1:5), and pass a portion through a suitable filter of 0.8-µm pore size.
Spectrometric conditions
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
Mode: UV absorption spectroscopy
Analytical wavelength: UV 285 nm
Cell length: 1 cm
Blank: *Medium*
Analysis
Calculate the percentage of $C_{17}H_{16}F_6N_2O \cdot HCl$ dissolved:

$$\text{Result} = (A_U/A_S) \times (C_S/L) \times D \times V \times 100$$

A_U = absorbance of mefloquine from the *Sample solution*
A_S = absorbance of mefloquine from the *Standard solution*
C_S = concentration of USP Mefloquine Hydrochloride RS in the *Standard solution* (mg/mL)
D = dilution factor of the *Sample solution*
L = label claim (mg/Tablet)
V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (Q) of the labeled amount of $C_{17}H_{16}F_6N_2O \cdot HCl$ is dissolved.

• **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

IMPURITIES

Organic Impurities

• **PROCEDURE**

Buffer, Diluent, Mobile phase, Standard solution, Sensitivity solution, Sample stock solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response of each impurity from the *Sample solution*
r_S = peak response of mefloquine hydrochloride from the *Standard solution*
C_S = concentration of USP Mefloquine Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of Mefloquine Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria
Individual impurities: See *Impurity Table 1*.
[NOTE—Do not include the threo isomer, a process impurity monitored in the drug substance, in the calculation of total impurities. Disregard any peak less than 0.05%.]

Total impurities: NMT 0.50%

Impurity Table 1

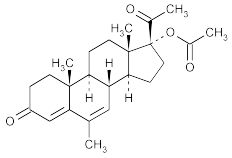
Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Specified (unidentified)	0.67	0.15
Specified (unidentified)	0.70	0.15
threo-Mefloquine (DL-*threo*-α-2-piperidyl-2,8-bis(trifluoromethyl)-4-quinolinemethanol)	0.75	—
Specified (unidentified)	0.84	0.25
Mefloquine hydrochloride	1.0	—
Any other unknown individual impurity	—	0.15

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Mefloquine Hydrochloride RS

Megestrol Acetate



$C_{24}H_{32}O_4$ 384.51
Pregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl-.
17-Hydroxy-6-methylpregna-4,6-diene-3,20-dione acetate [595-33-5].

» Megestrol Acetate contains not less than 97.0 percent and not more than 103.0 percent of $C_{24}H_{32}O_4$, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers, protected from light.

USP Reference standards ⟨11⟩**—**
USP Megestrol Acetate RS

Completeness of solution ⟨641⟩: meets the requirements, 500 mg being dissolved in 10 mL of acetone.

Identification, *Infrared Absorption* ⟨197K⟩.

Melting range ⟨741⟩: between 213° and 220°, but the range between beginning and end of melting does not exceed 3°.

Specific rotation ⟨781S⟩: between +8.8° and +12.0° (*t* = 20°).
Test solution: 20 mg per mL, in chloroform.

Water, *Method I* ⟨921⟩: not more than 0.5%.

Residue on ignition ⟨281⟩: not more than 0.2%, a platinum dish being used, with ignition at 600 ± 25°.

Heavy metals, *Method II* ⟨231⟩: not more than 0.002%.

Assay—

Mobile phase—Prepare a solution of acetonitrile and water (55:45), mix, and degas. The acetonitrile concentration may be varied slightly to meet system suitability test requirements and to provide a suitable elution time.

Solvent mixture—Mix 60 volumes of water and 40 volumes of acetonitrile.

Internal standard solution—Transfer about 80 mg of propylparaben to a 100-mL volumetric flask, dissolve in acetonitrile, add acetonitrile to volume, and mix.

Standard preparation—Using an accurately weighed quantity of USP Megestrol Acetate RS, prepare a solution in acetonitrile containing about 1 mg per mL. Transfer 4.0 mL of this solution and 5.0 mL of *Internal standard solution* to a 50-mL volumetric flask, dilute with *Solvent mixture* to volume, and mix. The *Standard preparation* has a known concentration of about 80 µg of megestrol acetate per mL.

Assay preparation—Transfer about 100 mg of Megestrol Acetate, accurately weighed, to a 100-mL volumetric flask. Dissolve in acetonitrile, add acetonitrile to volume, and mix. Transfer 4.0 mL of this solution and 5.0 mL of *Internal standard solution* to a 50-mL volumetric flask, dilute with *Solvent mixture* to volume, and mix.

Chromatographic system (see Chromatography ⟨621⟩)—The liquid chromatograph is equipped with an UV detector that monitors absorption at 280 nm and 3.9-mm × 30-cm column containing packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.4 for propylparaben and 1.0 for megestrol acetate; the resolution factor, *R* (see *Chromatography* ⟨621⟩), between the peaks for propylparaben and megestrol acetate is not less than 8.0; and the relative standard deviation of the peak response ratio, R_S, for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak responses of the major peaks. Calculate the quantity, in mg, of $C_{24}H_{32}O_4$ in the portion of Megestrol Acetate taken by the formula:

$$1.25C(R_U / R_S)$$

in which *C* is the concentration, in µg per mL, of USP Megestrol Acetate RS in the *Standard preparation*; and R_U and R_S are the ratios of the peak responses of megestrol acetate and propylparaben obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Megestrol Acetate Oral Suspension

DEFINITION

Megestrol Acetate Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of megestrol acetate ($C_{24}H_{32}O_4$).

IDENTIFICATION

• **THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST ⟨201⟩**

Standard solution: 4.0 mg/mL of USP Megestrol Acetate RS in chloroform

Sample solution: Transfer Oral Suspension, equivalent to 160 mg of megestrol acetate, to a separatory funnel, add 50 mL of water and 40 mL of chloroform, and shake. Allow the phases to separate, and discard the aqueous layer.

Developing solvent system: Chloroform and ethyl acetate (4:1)

ASSAY

• **PROCEDURE**

Mobile phase: Acetonitrile and water (11:9)

Standard solution: 80 µg/mL of USP Megestrol Acetate RS in *Mobile phase*

Sample solution: A volume of Oral Suspension diluted with *Mobile phase* to obtain nominally 80 µg/mL of megestrol acetate

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 280 nm
Column: 3.9-mm × 30-cm; packing L1
Flow rate: 1.5 mL/min
Injection size: 25 µL

System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 2500 theoretical plates
Tailing factor: NMT 1.4
Relative standard deviation: NMT 2.0%

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{24}H_{32}O_4$ in the portion of Oral Suspension taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Megestrol Acetate RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **DISSOLUTION ⟨711⟩**

Test 1
Medium: 0.5% sodium lauryl sulfate in water; 900 mL
Apparatus 2: 25 rpm
Time: 30 min
Detector: UV 292 nm
Standard solution: 45 mg of USP Megestrol Acetate RS in a 250-mL volumetric flask. Add 12 mL of methanol, and place the flask in a warm water bath until the solid is dissolved. Dilute with *Medium* to volume. The final concentration is 180 µg/mL of megestrol acetate. Dilute with *Medium*, if necessary.
Sample solution: Transfer to the surface of the *Medium* in the dissolution vessel an accurately measured volume of Oral Suspension, freshly mixed and free from air bubbles, equivalent to 160 mg of megestrol acetate. At the sampling time, withdraw a volume of the solution under test and pass through a suitable filter with 0.45-µm pore size. Dilute with *Medium*, if necessary.

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_{24}H_{32}O_4$ released:

$$\text{Result} = (A_U/A_S) \times (C_S/V) \times V_D \times (100/L)$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
V = volume of Oral Suspension taken
V_D = volume of *Medium*, 900 mL
L = label claim (mg/mL)

Tolerances: NLT 80% (Q) of the labeled amount of $C_{24}H_{32}O_4$ is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.
Medium: 0.5% sodium lauryl sulfate in water; 900 mL
Apparatus 2: 25 rpm
Time: 30 min
Detector: UV 292 nm, using 0.5-cm pathlength cuvettes
Standard solution: 45 mg of USP Megestrol Acetate RS in a 250-mL volumetric flask. Add 5 mL of methanol. Dilute with *Medium* to volume. Transfer 10 mL of this solution to a 100-mL volumetric flask, and dilute with *Medium* to volume. The final concentration is 18 µg/mL.
Sample solution: [NOTE—Use a separate syringe for each vessel.] Withdraw more than 10 mL of the Oral Suspension,