Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 5 mg of droperidol, to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

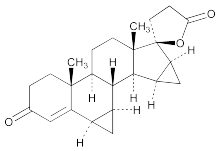
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 25-cm column that contains 10- µm packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the *System suitability preparation* and the *Standard preparation*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between 4′-fluoroacetophenone and droperidol is not less than 5.0; the tailing factor for the analyte peak is not more than 2.0; and the relative standard deviation for replicate injections of the *Standard preparation* is not more than 1.5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of droperidol ($C_{22}H_{22}FN_3O_2$) in each mL of the Injection taken by the formula:

$$100(C / V)(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Droperidol RS in the *Standard preparation; V* is the volume, in mL, of Injection taken; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Drospirenone



$C_{24}H_{30}O_3$ 366.49

(6*R*,7*R*,8*R*,9*S*,10*R*,13*S*,14*S*,15*S*,16*S*,17*S*)-1,3′,4′,6,6a,7,8,9,10,11,12,13,14,15,15a,16-Hexadecahydro-10,13-dimethylspiro-[17*H*-dicyclopropa[6,7:15,16]cyclopenta[*a*]phenanthrene-17,2′(5′*H*)-furan]-3,5′(2*H*)-dione;

17-Hydroxy-6*β*,7*β*:15*β*,16*β*-dimethylene-3-oxo-17 α-pregn-4-ene-21-carboxylic acid, γ-lactone [67392-87-4].

DEFINITION

Drospirenone contains NLT 98.0% and NMT 102.0% of $C_{24}H_{30}O_3$, calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨197M⟩
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

- **Procedure**

▲Solution A: Water
Solution B: Acetonitrile
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	63	37
2.0	63	37
16.0	52	48
23.0	52	48
31.0	20	80
39.0	20	80
39.1	63	37
49.0	63	37

Diluent: Acetonitrile and water (1:1)
System suitability solution: 60 µg/mL of USP Drospirenone RS and 60 µg/mL of USP Drospirenone Related Compound A RS in *Diluent*
Standard solution: 0.6 mg/mL of USP Drospirenone RS in *Diluent*
Sample solution: 0.6 mg/mL of Drospirenone in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 245 nm
Column: 4.6-mm × 25-cm; 3-µm packing L1
Column temperature: 35°
Flow rate: 1 mL/min
Injection size: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 5.0 between drospirenone and drospirenone related compound A, *System suitability solution*
Tailing factor: Between 0.8 and 1.5, *Standard solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled quantity of drospirenone ($C_{24}H_{30}O_3$) in the portion of Drospirenone 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 Drospirenone RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of drospirenone in the *Sample solution* (mg/mL) ▲*USP35*

Acceptance criteria: NLT 98.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

Inorganic Impurities

- **Residue on Ignition** ⟨281⟩**:** NMT 0.1%
- **Heavy Metals,** *Method II* ⟨231⟩**:** 20 ppm

Organic Impurities

- **Procedure 1: Limit of 1,2-Dimethoxyethane and Diisopropyl Ether** (if present)

Standard solution: 0.1 mg/mL of 1,2-dimethoxyethane and 0.05 mg/mL of diisopropyl ether in dimethylformamide
Sample solution: 50 mg/mL of Drospirenone in dimethylformamide

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: GC
Detector: Flame ionization
Column: 0.25-mm × 30-m; 1.4-µm coating of phase G43
Temperature
Injector: 160°
Detector: 250°
Column: See *Table 2*.

Table 2

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	10
40	5	70	0
70	30	220	0

Carrier gas: Helium
Flow rate: 32 ± 8 cm/s. [NOTE—For pressure-controlled systems, a column pressure of about 130 kPa is necessary.]
Injector type: Headspace
Sample volume: 2.0 mL/vial
Vial treatment: Maintain at 80 ° for 60 min before injection.
System suitability
Sample: *Standard solution*
[NOTE—The relative retention times for diisopropyl ether and 1,2-dimethoxyethane are about 0.6 and 1.0, respectively.]
Suitability requirements
Relative standard deviation: NMT 4.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of 1,2-dimethoxyethane and diisopropyl ether in the portion of Drospirenone taken:

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

r_U = peak response of 1,2-dimethoxyethane or diisopropyl ether from the *Sample solution*
r_S = peak response of 1,2-dimethoxyethane or diisopropyl ether from the *Standard solution*
C_S = concentration of 1,2-dimethoxyethane or diisopropyl ether in the *Standard solution* (mg/mL)
C_U = concentration of Drospirenone in the *Sample solution* (mg/mL)

Acceptance criteria
Individual impurities: NMT 0.2% of 1,2-dimethoxyethane and NMT 0.1% of diisopropyl ether

- **PROCEDURE 2**

Solution A: Water
Solution B: Acetonitrile
Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	63	37
2.0	63	37
16.0	52	48
23.0	52	48
31.0	20	80
39.0	20	80
39.1	63	37
49.0	63	37

Diluent: Acetonitrile and water (1:1)
System suitability solution: 60 µg/mL of USP Drospirenone RS and 60 µg/mL of USP Drospirenone Related Compound A RS in *Diluent*
Standard solution: 0.6 µg/mL of USP Drospirenone RS in *Diluent*
Sample solution: 0.6 mg/mL of Drospirenone in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 195 nm and 245 nm
Column: 4.6-mm × 25-cm; 3-µm packing L1
Column temperature: 35 ± 5°
Flow rate: 1 mL/min
Injection size: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
Suitability requirements
Resolution: NLT 5.0 between drospirenone and drospirenone related compound A, *System suitability solution*
Tailing factor: Between 0.8 and 1.5, *Standard solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Drospirenone taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*
r_S = peak response of drospirenone from the *Standard solution*
C_S = concentration of USP Drospirenone RS in the *Standard solution* (µg/mL)
C_U = concentration of Drospirenone in the *Sample solution* (µg/mL)
F = relative response factor for each individual impurity (see *Table 4*)

[NOTE—The percentage of hydroxydrospirenone is calculated at 195 nm.]
Acceptance criteria
[NOTE—Disregard any peaks that are less than 0.05% of the drospirenone peak.]
Individual impurities: See *Table 4*.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
7-Hydroxymethyl drospirenone at 245 nm[a]	0.43	1.9	0.1
5-Hydroxydrospirenone at 195 nm[b]	0.57	0.57	0.1
17-Keto drospirenone at 245 nm[c]	0.77	1.2	0.1
Drospirenone at 245 and 195 nm	1.00	—	—
Drospirenone 6-ene at 245 nm[d]	1.04	0.30	0.1
Drospirenone related compound A at 245 nm[e]	1.11	1.0	0.1
6,7-Epidrospirenone at 245 nm[f]	1.14	1.3	0.1
6,7-Desmethylene drospirenone at 245 nm[g]	1.18	2.2	0.1
15-Methyl drospirenone at 245 nm[h]	1.34	0.99	0.1
7-Chloromethyl drospirenone at 245 nm[i]	1.38	1.6	0.1
7-Chloromethyl 17-epidrospirenone at 245 nm[j]	1.51	1.9	0.1
7-Hydroxymethyl 3,5(6)-diene drospirenone at 245 nm[k]	1.55	1.4	0.1
Any unspecified impurity at 245 nm	—	1.0	0.1
Total impurities	—	—	0.4

[a] 17-Hydroxy-7β-hydroxymethyl-15β,16β-methylene-3-oxo-17α-pregn-4-ene-21-carboxylic acid, γ-lactone.
[b] 5β,17β-Dihydroxy-6β,7β:15β,16β-dimethylene-17α-pregnan-21-carboxylic acid, γ-lactone.
[c] 6β,7β:15β,16β-Dimethyleneandrost-4-ene-3,17-dione.
[d] 17-Hydroxy-15β,16β-methylene-3-oxo-17α-pregn-4,6-diene-21-carboxylic acid, γ-lactone.
[e] 17-Hydroxy-6β,7β:15β,16β-dimethylene-3-oxo-17β-pregn-4-ene-21-carboxylic acid, γ-lactone; 17-epidrospirenone.
[f] 17-Hydroxy-6α,7α:15β,16β-dimethylene-3-oxo-17α-pregn-4-ene-21-carboxylic acid, γ-lactone.
[g] 17-Hydroxy-15β,16β-methylene-3-oxo-17α-pregn-4-ene-21-carboxylic acid, γ-lactone.
[h] 17-Hydroxy-15β-methyl-6β,7β-methylene-3-oxo-17α-pregn-4-ene-21-carboxylic acid, γ-lactone.
[i] 17-Hydroxy-7β-chloromethyl-15β,16β-methylene-3-oxo-17α-pregn-4-ene-21-carboxylic acid, γ-lactone.
[j] 17-Hydroxy-7β-chloromethyl-15β,16β-methylene-3-oxo-17β-pregn-4-ene-21-carboxylic acid, γ-lactone.
[k] 17-Hydroxy-7β-hydroxymethyl-15β,16β-methylene-17α-pregn-3,5(6)-diene-21-carboxylic acid, γ-lactone.

SPECIFIC TESTS

- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩
  Sample solution: 10 mg/mL in methanol
  Acceptance criteria: –187° to –193° at 20° on the anhydrous and solvent-free basis
- **MELTING RANGE OR TEMPERATURE,** *Class 1* ⟨**741**⟩**:** 198°–203°. [NOTE—Dry over silica gel for NL T 24 h before testing.]
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 0.2%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Drospirenone RS
  USP Drospirenone Related Compound A RS
  17-Hydroxy-6β,7β:15β,16β-dimethylene-3-oxo-17β-pregn-4-ene-21-carboxylic acid, γ-lactone.
  $C_{24}H_{30}O_3$ 366.49

Absorbable Dusting Powder

» Absorbable Dusting Powder is an absorbable powder prepared by processing cornstar ch and intended for use as a lubricant for surgical gloves. It contains not more than 2.0 per cent of magnesium oxide.

Packaging and storage—Preserve in well-closed containers. It may be preser ved in sealed paper packets.

Identification—A 1 in 10 suspension is colored purplish blue to deep blue by iodine TS.

Stability to autoclaving—Transfer about 2 g to a suitable paper packet, and seal or close the packet with a double fold. Wrap the paper packet in muslin, transfer to an autoclave, heat to 121° for 30 minutes, and cool: the powder is not caked, and any lumps are easily crushed between the fingers.

Sedimentation—Boil 100 mL of a 1 in 10 suspension in water for 20 minutes. Cool, transfer to a 100-mL graduated cylinder,