

USP Reference standards (11)—

USP Haloperidol RS

USP Haloperidol Related Compound A RS

4,4'-Bis[4-*p*-chlorophenyl]-4-hydroxypiperidino] butyrophenone.C₃₂H₃₆Cl₂N₂O₃ 567.56**Identification**—**A:** Infrared Absorption (197K).**B:** Ultraviolet Absorption (197U)—

Solution: 20 µg per mL.

Medium: dilute hydrochloric acid (1 in 100) in isopropyl alcohol (1 in 9).

Absorptivities at 245 nm, calculated on the dried basis, do not differ by more than 3.0%.

Melting range (741): between 149° and 155°, determined after drying in vacuum at 60° for 3 hours.**Loss on drying** (731)—Dry it in vacuum at 60° for 3 hours: it loses not more than 0.5% of its weight.**Residue on ignition** (281): not more than 0.1%.**Limit of haloperidol related compound A**—**Test solution**—Dissolve about 80 mg of Haloperidol, accurately weighed, in 80 mL of isopropyl alcohol in a 100-mL volumetric flask. Add 10 mL of dilute hydrochloric acid (1 in 100), dilute with isopropyl alcohol to volume, and mix.**Standard solution**—Prepare a solution containing 800 µg per mL of USP Haloperidol RS and 8 µg per mL of USP Haloperidol Related Compound A RS in isopropyl alcohol containing 10 mL of dilute hydrochloric acid (1 in 100) in each 100 mL of solution.**Procedure**—Concomitantly determine the absorbances of the *Test solution* and the *Standard solution* at the wavelength of maximum absorbance at about 335 nm, with a suitable spectrophotometer, using isopropyl alcohol containing 10 mL of dilute hydrochloric acid (1 in 100) in each 100 mL of solution as the blank. The absorbance of the *Test solution* is not greater than that of the *Standard solution*, corresponding to not more than 1.0%.**Assay**—Dissolve about 125 mg of Haloperidol, accurately weighed, in 25 mL of glacial acetic acid, add 3 drops of *p*-naphtholbenzein TS, and titrate with 0.05 N per chloric acid VS. Perform a blank determination, and make any necessary correction. Each mL of 0.05 N per chloric acid is equivalent to 18.79 mg of C₂₁H₂₃ClFNO₂.**Haloperidol Injection**» Haloperidol Injection is a sterile solution of Haloperidol in Water for Injection, prepared with the aid of Lactic Acid. It may contain a suitable preservative. It contains not less than 90.0 per cent and not more than 110.0 per cent of the labeled amount of C₂₁H₂₃ClFNO₂.**Packaging and storage**—Preserve in single-dose or in multiple-dose containers, preferably of T type I glass, protected from light.**USP Reference standards** (11)—

USP Haloperidol RS

USP Endotoxin RS

Identification—The solution prepared for measurement of absorbance in the *Assay* exhibits a maximum at 245 ± 2 nm.**Bacterial endotoxins** (85)—It contains not more than 71.4 USP Endotoxin Units per mg of haloperidol.**pH** (791): between 3.0 and 3.8.**Other requirements**—It meets the requirements under *Injections* (1).**Assay**—Transfer an accurately measured volume of Injection, equivalent to about 10 mg of haloperidol, to a separator, and add 20 mL of dilute hydrochloric acid (1 in 20). Extract the solution with four 25-mL portions of ether, and wash the combined ether extracts with four 5-mL portions of dilute hydrochloric acid (1 in 20). Proceed as directed in the *Assay* under *Haloperidol Solution*, beginning with "Discard the ether." Calculate the quantity, in mg, of C₂₁H₂₃ClFNO₂ in each mL of Injection taken by the formula:

$$0.5(C/V)(A_U/A_S)$$

in which C is the concentration, in µg per mL, of USP Haloperidol RS in the Standard solution; V is the volume, in mL, of Injection taken; and A_U and A_S are the absorbances of the solution from the Injection and the Standard solution, respectively.**Haloperidol Oral Solution**» Haloperidol Oral Solution is a solution of Haloperidol in Water, prepared with the aid of Lactic Acid. It contains not less than 90.0 per cent and not more than 110.0 per cent of the labeled amount of haloperidol (C₂₁H₂₃ClFNO₂).**Packaging and storage**—Preserve in tight, light-resistant containers.**USP Reference standards** (11)—

USP Haloperidol RS

Identification—The solution prepared for measurement of absorbance in the *Assay* exhibits a maximum at 245 ± 2 nm.**Uniformity of dosage units** (905)—

FOR ORAL SOLUTION PACKAGED IN SINGLE-UNIT CONTAINERS: meets the requirements.

Deliverable volume (698)—

FOR ORAL SOLUTION PACKAGED IN MULTIPLE-UNIT CONTAINERS: meets the requirements.

pH (791): between 2.75 and 3.75.**Assay**—Transfer an accurately measured volume of Oral Solution, equivalent to about 10 mg of haloperidol, to a separator, and add 20 mL of dilute hydrochloric acid (1 in 20). Extract the solution with four 20-mL portions of ether, and wash the combined ether extracts with four 5-mL portions of dilute hydrochloric acid (1 in 20). Discard the ether, and add the acid washings to the aqueous phase. Filter the aqueous phase through a pledget of cotton into a 50-mL volumetric flask, add dilute hydrochloric acid (1 in 20) to volume, and mix. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, dilute with methanol to volume, and mix. Concomitantly determine the absorbances of this solution and of a solution of USP Haloperidol RS in the same medium having a known concentration of about 20 µg per mL, in 1-cm cells at the wavelength of maximum absorbance at about 245 nm, with a suitable spectrophotometer, using a 1 in 10 solution of dilute hydrochloric acid (1 in 20) in methanol as the blank. Calculate the quantity, in mg, of haloperidol (C₂₁H₂₃ClFNO₂) in each mL of Oral Solution taken by the formula:

$$0.5(C/V)(A_U/A_S)$$

in which C is the concentration, in µg per mL, of USP Haloperidol RS in the Standard solution; V is the volume, in mL, of Oral Solution taken; and A_U and A_S are the absorbances of the solution from the Oral Solution and the Standard solution, respectively.

Haloperidol Tablets

DEFINITION

Haloperidol Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of haloperidol ($C_{21}H_{23}ClFNO_2$).

IDENTIFICATION

- A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

PROCEDURE

Mobile phase: Methanol and 0.05 M monobasic potassium phosphate buffer (60:40). Adjust with 1 N sodium hydroxide or phosphoric acid to a pH of 4.0.

Standard solution: 0.1 mg/mL of USP Haloperidol RS in *Mobile phase*

Sample solution: Nominally 0.1 mg/mL of Haloperidol prepared as follows. Transfer an equivalent of about 10 mg of haloperidol from NLT 20 finely powdered Tablets to a 100-mL volumetric flask. Add 60 mL of *Mobile phase*, sonicate for 10 min, and shake by mechanical means for about 1 h.

Dilute with *Mobile phase* to volume, mix, and filter, discarding the first 20 mL of the filtrate.

Chromatographic system

(See *Chromatography* <621>, *System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 25-cm; packing L1

Flow rate: 1 mL/min

Injection size: 15 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of haloperidol ($C_{21}H_{23}ClFNO_2$) in the portion of Tablets taken:

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

r_U = peak response of the *Sample solution*

r_S = peak response of the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

DISSOLUTION <711>

Medium: Simulated gastric fluid TS without enzyme; 900 mL

Apparatus 1: 100 rpm

Time: 60 min

Mobile phase: Prepare as directed in the *Assay*.

Standard solution: A known concentration of USP Haloperidol RS in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary, to a concentration that is similar to that of the *Standard solution*.

Chromatographic system

(See *Chromatography* <621>, *System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 25-cm; packing L1

Flow rate: 1 mL/min

Injection size: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 3.0%

Tolerances: NLT 80% (Q) of the labeled amount of haloperidol ($C_{21}H_{23}ClFNO_2$) is dissolved.

UNIFORMITY OF DOSAGE UNITS <905>

Procedure for content uniformity

Standard solution: 20 µg/mL of USP Haloperidol RS in warm methanol

Sample solution: 20 µg/mL of haloperidol from 1 finely powdered Tablet in warm methanol. Shake for 15 min and filter, discarding the first 20 mL of the filtrate.

Instrumental conditions

(See *Spectrophotometry and Light-Scattering* <851>.)

Mode: UV

Analytical wavelength: 245 nm

Cell: 1 cm

Blank: Methanol

Analysis: Concomitantly determine the absorbances of the *Standard solution* and *Sample solution* at the wavelength of maximum absorbance.

Calculate the percentage of the labeled amount of haloperidol ($C_{21}H_{23}ClFNO_2$) in the portion of Tablets taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Haloperidol RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of haloperidol in the *Sample solution* (µg/mL)

Acceptance criteria: Meet the requirements

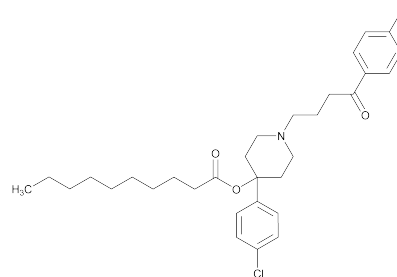
ADDITIONAL REQUIREMENTS

- PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.

USP REFERENCE STANDARDS <11>

USP Haloperidol RS

Haloperidol Decanoate



$C_{31}H_{41}ClFNO_3$ 530.11

Decanoic acid, 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]-4-piperidinyl ester;

Decanoic acid, ester with 4-[4-(p-chlorophenyl)-4-hydroxypiperidino]-4'-fluorobutyrophenone [74050-97-8].

DEFINITION

Haloperidol Decanoate contains NLT 97.0% and NMT 103.0% of $C_{31}H_{41}ClFNO_3$, calculated on the dried basis.