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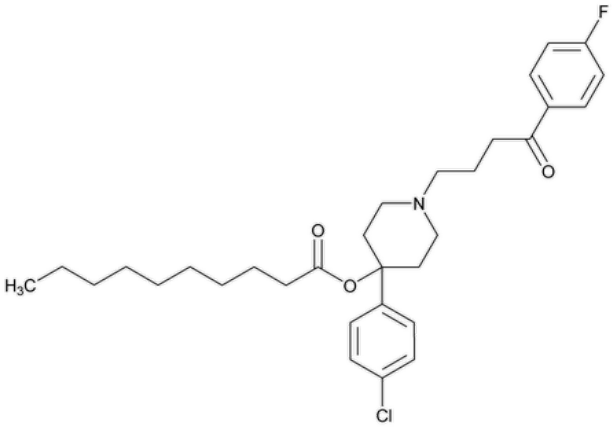
Haloperidol Decanoate

Change to read:



$C_{31}H_{41}ClFNO_3$ ▲530.12▲ (USP 1-May-2021)

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

▲4-(4-Chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate▲ (USP 1-May-2021) CAS RN®: 74050-97-8; UNII: AC20PJ4101.

Change to read:

DEFINITION

Haloperidol Decanoate contains NLT 97.0% and NMT 103.0% of ▲haloperidol decanoate▲ (USP 1-May-2021) ($C_{31}H_{41}ClFNO_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** ▲197A or▲ (USP 1-May-2021) 197M

Change to read:

• **B.** The retention time of the major peak ▲▲ (USP 1-May-2021) of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Delete the following:

▲• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride***

Sample solution: Mix 0.1 g of the sample with 0.5 g of anhydrous sodium carbonate in a porcelain crucible. Heat over open flame for 10 min. Allow to cool. Dissolve the residue in 5 mL of dilute nitric acid, and filter. Dilute 1 mL of the filtrate with 1 mL of water.

Acceptance criteria: Meets the requirements of test *A*▲ (USP 1-May-2021)

ASSAY

Change to read:

• **Procedure**

Solution A: 27 g/L of tetrabutylammonium hydrogen sulfate in water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
30	40	60
35	40	60
40	80	20
45	80	20

Standard solution: 0.2 mg/mL of USP Haloperidol Decanoate RS in methanol

Sample solution: 0.2 mg/mL of Haloperidol Decanoate in methanol

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4-mm × 10-cm; 3-µm packing L1

Flow rate: 1.5 mL/min

Injection ▲volume:▲ (USP 1-May-2021) 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT ▲0.73%▲ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of haloperidol decanoate ($C_{31}H_{41}ClFNO_3$) in the portion of ▲Haloperidol Decanoate▲ (USP 1-May-2021) 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 Haloperidol Decanoate RS in the *Standard solution* (mg/mL)

C_U = concentration of Haloperidol Decanoate in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities**

Solution A, Solution B, Mobile phase, and **▲Chromatographic system:▲** (USP 1-May-2021) Proceed as directed in the *Assay*.

System suitability solution: 0.05 mg/mL each of USP Haloperidol Decanoate RS and USP Bromperidol Decanoate RS in methanol

Standard stock solution: 0.2 mg/mL of USP Haloperidol Decanoate RS in methanol

Standard solution: 0.05 mg/mL of USP Haloperidol Decanoate RS in methanol, from *Standard stock solution*

▲Sensitivity solution: 0.005 mg/mL of USP Haloperidol Decanoate RS in methanol, from *Standard stock solution*▲ (USP 1-May-2021)

Sample solution: 10 mg/mL of Haloperidol Decanoate in methanol

▲▲ (USP 1-May-2021)

System suitability

Samples: *System suitability solution* ▲and *Sensitivity solution*

[NOTE—The relative retention time for bromperidol decanoate is 1.05. See *Table 2* for the other relative retention times.]▲ (USP 1-MAY-2021)

Suitability requirements

Resolution: NLT 1.5 between haloperidol decanoate and bromperidol decanoate, ▲*System suitability solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*▲ (USP 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Haloperidol Decanoate 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 haloperidol decanoate from the *Standard solution*

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

C_U = concentration of Haloperidol Decanoate in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. ▲The reporting threshold is 0.05%.▲ (USP 1-May-2021)

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Haloperidol[a]	0.09	0.50
Haloperidol octanoate[b]	0.6	0.50
Haloperidol nonanoate[c]	0.79	0.50
Haloperidol decanoate-dechloro analog[d]	0.89	0.50
2-Fluorohaloperidol decanoate[e]	0.97	0.50
Haloperidol decanoate	1.0	—
▲▲ (USP 1-May-2021)	▲▲ (USP 1-May-2021)	▲▲ (USP 1-May-2021)
Haloperidol undecanoate[f]	1.10	0.50
Haloperidol decanoate-3-ethyl analog[g]	1.13	0.50
Haloperidol decanoate-4-piperidinol analog[h]	1.17	0.50
Haloperidol dodecanoate[i]	1.21	0.50
Haloperidol decanoate-3-chlorobiphenyl analog[j]	1.22	0.50
Haloperidol decanoate-4-chlorobiphenyl analog[k]	1.24	0.50

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any other individual, unspecified impurity	—	0.10
Total impurities	—	1.0

[a] 4-[4-(4-Chlorophenyl)-4-hydroxypiperidino]-4'▲ (USP 1-May-2021) -fluorobutyrophenone.

[b] 4-(4-Chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl octanoate.

[c] 4-(4-Chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl nonanoate.

[d] 1-[4-(4-Fluorophenyl)-4-oxobutyl]-4-phenylpiperidin-4-yl decanoate.

[e] 4-(4-Chlorophenyl)-1-[4-(2-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

[f] 4-(4-Chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl undecanoate.

[g] 4-(4-Chlorophenyl)-1-[4-(3-ethyl-4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

[h] 4-(4-Chlorophenyl)-1-(4-{4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]phenyl}-4-oxobutyl)piperidin-4-yl decanoate.

[i] 4-(4-Chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl dodecanoate.

[j] 4-(3'-Chlorobiphenyl-4-yl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

[k] 4-(4'-Chlorobiphenyl-4-yl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

SPECIFIC TESTS

Change to read:

• **Loss on Drying** ⟨731⟩

▲**Analysis:** Dry under vacuum over phosphorous pentoxide at 30° to constant weight.

Acceptance criteria: NMT 0.5%▲ (USP 1-May-2021)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in light-resistant, tight containers. Store at room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Bromperidol Decanoate RS

▲4-(4-Bromophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate;
Also known as▲ (USP 1-May-2021) Decanoic acid, 4-(4-bromophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]-4-piperidinyl ester.

$C_{31}H_{41}BrFNO_3$ ▲574.58▲ (USP 1-May-2021)

USP Haloperidol Decanoate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
HALOPERIDOL DECANOATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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