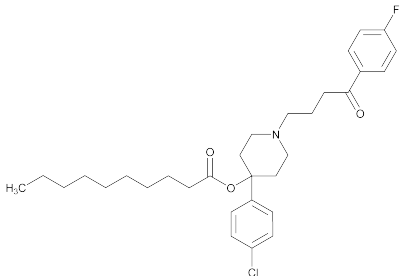


Haloperidol Decanoate

Change to read:



C₃₁H₄₁ClFNO₃ [▲]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) (C₃₁H₄₁ClFNO₃), 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

Table 1 (continued)

Time (min)	Solution A (%)	Solution B (%)
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 (C₃₁H₄₁ClFNO₃) in the portion of ▲Haloperidol Decanoate▲ (USP 1-May-2021) taken:

Result = (r_U/r_S) × (C_S/C_U) × 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

Table 2 (continued)

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-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