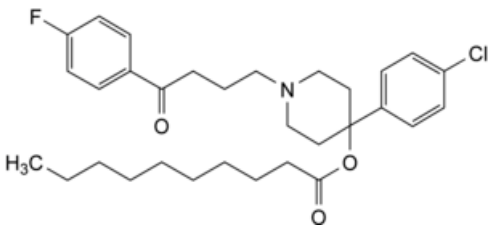
Edition: BP 2025 (Ph. Eur. 11.6 update)

Haloperidol Decanoate

General Notices

(Ph. Eur. monograph 1431)



$C_{31}H_{41}ClFNO_3$ 530.1 *74050-97-8*

Action and use

Dopamine receptor antagonist; neuroleptic.

Ph Eur

DEFINITION

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

Content

98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white powder.

Solubility

Practically insoluble in water, very soluble in ethanol (96 per cent), in methanol and in methylene chloride.

mp

About 42 °C.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison haloperidol decanoate CRS.

B. To 0.1 g in a porcelain crucible add 0.5 g of anhydrous sodium carbonate R. Heat over an open flame for 10 min. Allow to cool. Take up the residue with 5 mL of dilute nitric acid R and filter. To 1 mL of the filtrate add 1 mL of water R. The solution gives reaction (a) of chlorides (2.3.1).

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution B_5 (2.2.2, Method II).

Dissolve 2.0 g in methylene chloride R and dilute to 20 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use and protect from light*.

Test solution Dissolve 0.100 g of the substance to be examined in methanol R and dilute to 10.0 mL with the same solvent.

Reference solution (a) Dissolve 10 mg of haloperidol decanoate for system suitability CRS (containing impurities B, D and I) in methanol R and dilute to 1 mL with the same solvent.

Reference solution (b) Dissolve the contents of a vial of haloperidol decanoate impurity mixture CRS (impurities H, J and K) in 1 mL of methanol R.

Reference solution (c) Dilute 1.0 mL of the test solution to 100.0 mL with methanol R. Dilute 1.0 mL of this solution to 10.0 mL with methanol R.

Column:

— *size*: *l* = 0.10 m, Ø = 4.0 mm;

— *stationary phase*: base-deactivated end-capped octadecylsilyl silica gel for chromatography R (3 µm).

Mobile phase:

— *mobile phase A*: 27 g/L solution of tetrabutylammonium hydrogen sulfate R;

— *mobile phase B*: acetonitrile for chromatography R;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 30	80 → 40	20 → 60
30 - 35	40	60

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 10 µL.

Identification of impurities Use the chromatogram supplied with haloperidol decanoate for system suitability CRS and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities B, D and I; use the

chromatogram supplied with *haloperidol decanoate impurity mixture CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities H, J and K.

Relative retention With reference to haloperidol decanoate (retention time = about 24 min): impurity H = about 0.80; impurity I =about 0.88; impurity B = about 0.98; impurity J = about 1.1; impurity D = about 1.20; impurity K = about 1.22.

System suitability Reference solution (a):

— *peak-to-valley ratio*: minimum 1.5, where H_p = height above the baseline of the peak due to impurity B and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to haloperidol decanoate.

Calculation of percentage contents:

— for each impurity, use the concentration of haloperidol decanoate in reference solution (c).

Limits:

— *impurity D*: maximum 0.5 per cent;

— *impurities B, H, I, J, K*: for each impurity, maximum 0.3 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 1.0 per cent;

— *reporting threshold*: 0.05 per cent.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* at 30 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Dissolve 0.425 g in 50 mL of a mixture of 1 volume of *anhydrous acetic acid R* and 7 volumes of *methyl ethyl ketone R*. Titrate with *0.1 M perchloric acid*, using 0.2 mL of *naphtholbenzein solution R* as indicator.

1 mL of *0.1 M perchloric acid* is equivalent to 53.01 mg of $C_{31}H_{41}ClFNO_3$.

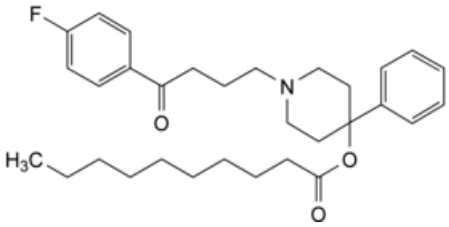
STORAGE

Protected from light, at a temperature below 25 °C.

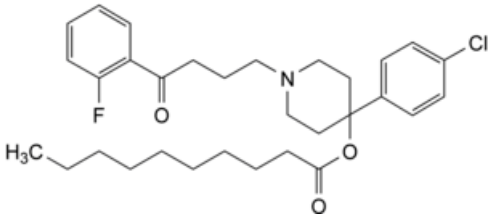
IMPURITIES

Specified impurities *B, D, H, I, J, K*.

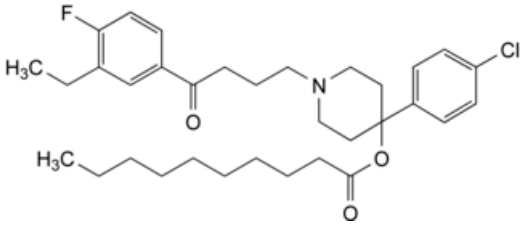
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *A, C, E, F, G, L*.



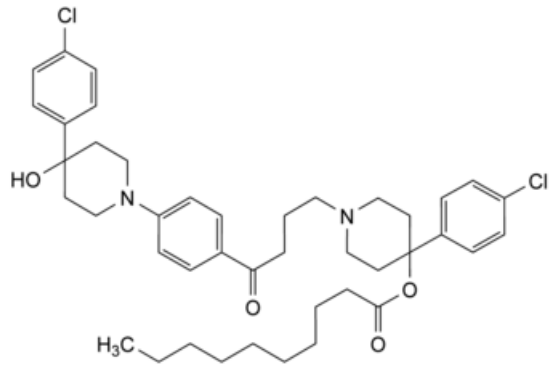
A. 1-[4-(4-fluorophenyl)-4-oxobutyl]-4-phenylpiperidin-4-yl decanoate,



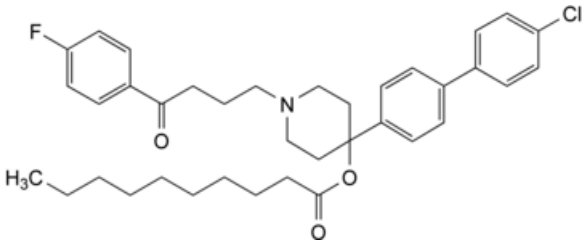
B. 4-(4-chlorophenyl)-1-[4-(2-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate,



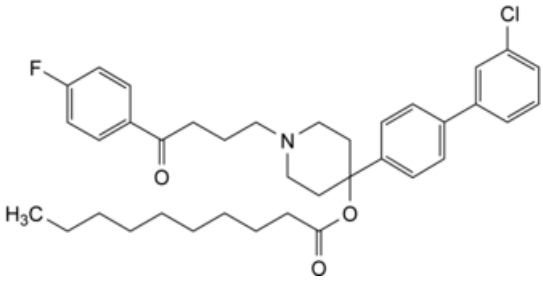
C. 4-(4-chlorophenyl)-1-[4-(3-ethyl-4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate,



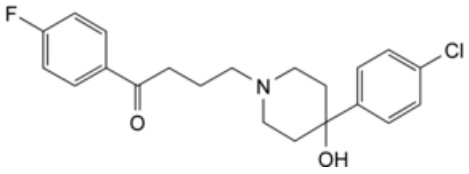
D. 1^4,9^4-dichloro-2^4-hydroxy-4-oxo-2(4,1),8(1,4)-piperidina-1,9(1),3(1,4)-tribenzenanonaphan-8^4-yl decanoate,



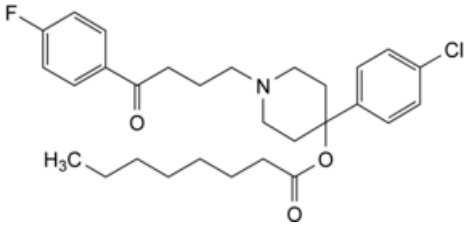
E. 1^4-chloro-8^4-fluoro-7-oxo-3(4,1)-piperidina-1,8(1),2(1,4)-tribenzenaoctaphan-3^4-yl decanoate,



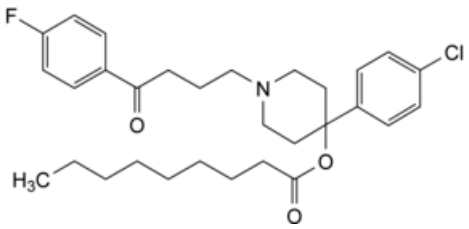
F. 1^{3}-chloro-8^{4}-fluoro-7-oxo-3(4,1)-piperidina-1,8(1),2(1,4)-tribenzenaoctaphan-3^{4}-yl decanoate,



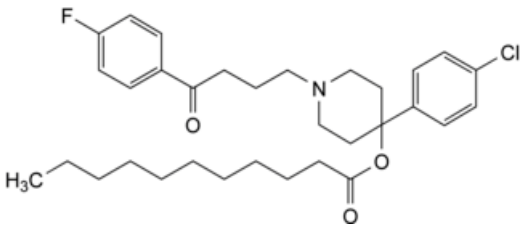
G. 4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)butan-1-one (haloperidol),



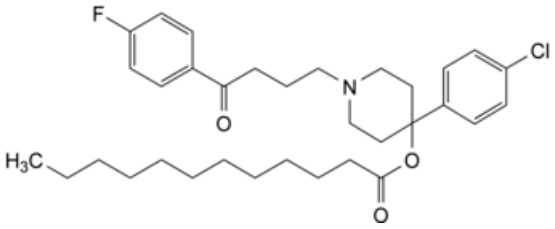
H. 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl octanoate,



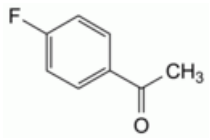
I. 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl nonanoate,



J. 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl undecanoate,



K. 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl dodecanoate,



L. 1-(4-fluorophenyl)ethan-1-one.

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