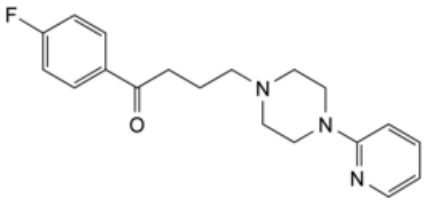
Edition: BP 2025 (Ph. Eur. 11.6 update)

Azaperone

General Notices

(Azaperone for Veterinary Use, Ph. Eur. monograph 1708)



$C_{19}H_{22}FN_3O$ 327.4 *1649-18-9*

Action and use

Dopamine receptor antagonist; neuroleptic (veterinary).

Preparation

Azaperone Injection

Ph Eur

DEFINITION

1-(4-Fluorophenyl)-4-[4-(pyridin-2-yl)piperazin-1-yl]butan-1-one.

Content

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

CHARACTERS

Appearance

White or almost white powder.

Solubility

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

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Preparation Discs.

Comparison azaperone CRS.

If the spectra obtained show differences, dissolve the substance to be examined and the reference substance separately in acetone R, evaporate to dryness and record new spectra using the residues.

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution Y_6 (2.2.2, Method II).

Dissolve 1.0 g in 25 mL of a 14 g/L solution of tartaric acid R.

Related substances

Liquid chromatography (2.2.29).

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 5.0 mg of azaperone CRS and 6.0 mg of benperidol CRS in methanol R and dilute to 200.0 mL with the same solvent.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with methanol R. Dilute 5.0 mL of the solution to 20.0 mL with methanol R.

Column:

— *size*: *l* = 0.10 m, Ø = 4.6 mm;

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

— *temperature*: 25 °C.

Mobile phase:

— *mobile phase A*: dissolve 1.4 g of anhydrous sodium sulfate R in 900 mL of water R, add 16.0 mL of 0.01 M sulfuric acid and dilute to 1000 mL with water R;

— *mobile phase B*: methanol R;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 15	95 → 20	5 → 80
15 - 20	20	80

Flow rate 1.5 mL/min.

Detection Spectrophotometer at 230 nm.

Injection 10 µL.

Relative retention With reference to azaperone (retention time = about 9 min): impurity A = about 0.9; impurity B = about 1.1; impurity C = about 1.15.

System suitability Reference solution (a):

— *resolution*: minimum 8.0 between the peaks due to azaperone and to benperidol.

Limits:

— *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.25 per cent);

— *unspecified impurities*: for each impurity, not more than 0.8 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.20 per cent);

— *sum of impurities B and C*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.75 per cent);

— *total*: not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent);

— *disregard limit*: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (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 60 °C for 4 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.130 g in 70 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.

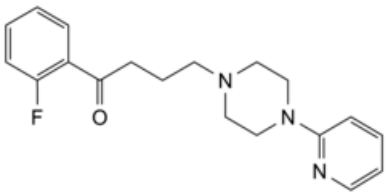
1 mL of *0.1 M perchloric acid* is equivalent to 16.37 mg of $C_{19}H_{22}FN_3O$.

STORAGE

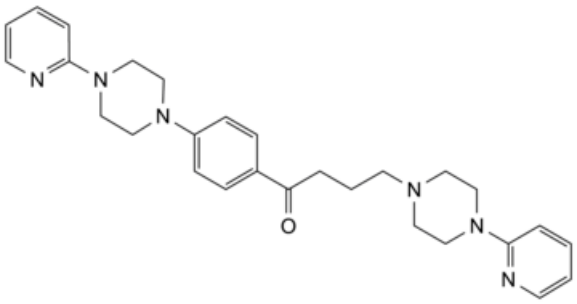
Protected from light.

IMPURITIES

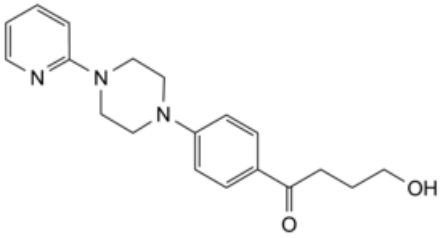
Specified impurities *A, B, C.*



A. 1-(2-fluorophenyl)-4-[4-(pyridin-2-yl)piperazin-1-yl]butan-1-one,



B. 4-[4-(pyridin-2-yl)piperazin-1-yl]-1-[4-[4-(pyridin-2-yl)piperazin-1-yl]phenyl]butan-1-one,



C. 4-hydroxy-1-[4-[4-(pyridin-2-yl)piperazin-1-yl]phenyl]butan-1-one.

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