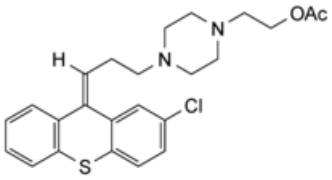
Edition: BP 2025 (Ph. Eur. 11.6 update)

Zuclopenthixol Acetate

General Notices



$C_{24}H_{27}ClN_2O_2S$ 443.0 *85721-05-7*

Action and use

Dopamine receptor antagonist; neuroleptic.

Preparation

Zuclopenthixol Acetate Injection

DEFINITION

Zuclopenthixol Acetate is (*Z*)-2-4-[3-(2-chlorothioxanthene-9-ylidene)propyl]piperazin-1-ylethyl acetate. It contains not less than 98.0% and not more than 102.0% of $C_{24}H_{27}ClN_2O_2S$, calculated with reference to the dried substance.

CHARACTERISTICS

A yellowish, viscous oil.

Very slightly soluble in *water*; very soluble in *dichloromethane*, in *ethanol (96%)* and in *ether*.

IDENTIFICATION

A. The *light absorption* of a 0.0015% w/v solution in *ethanol (96%)*, Appendix II B, in the range 210 to 350 nm exhibits two maxima at 230 and 268 nm. The *absorbances* at the maxima are about 1.18 and 0.51 respectively.
B. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of zuclopenthixol acetate *(RS 363)*.

TESTS

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions protected from light.

(1) 0.250% w/v of the substance being examined in *dichloromethane*.
(2) Dilute 1 volume of solution (1) to 100 volume with *dichloromethane*, further dilute 1 volume of this solution to 10 volumes with the same solvent.
(3) Dilute 1 volume of solution (2) to 2 volumes with *dichloromethane*.
(4) 0.00050% w/v of *2- chlorothioxanthone BPCRS* in *dichloromethane*.
(5) 0.000625% w/v of *zuclopenthixol hydrochloride BPCRS* in a solution containing 3 drops of *diethylamine* in *dichloromethane*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Merck silica gel 60 F254 plates are suitable).

(b) Use an unlined tank and the mobile phase as described below.

(c) Apply 4 µL of each solution.

(d) Develop the plate to 10 cm.

(e) After removal of the plate, allow it to dry in air, spray with a mixture of equal volumes of *sulfuric acid* and *absolute ethanol*, heat at 110° for 5 minutes and examine under *ultraviolet light (365 nm)* immediately.

MOBILE PHASE

10 volumes of *diethylamine*, 40 volumes of *dichloromethane* and 50 volumes of *cyclohexane*.

LIMITS

In the chromatogram obtained with solution (1):

any spot corresponding to 2-chlorothioxanthone is not more intense than the spot in the chromatogram obtained with solution (4) (0.2%);

any spot corresponding to zuclopenthixol is not more intense than the spot in the chromatogram obtained with solution (5) (0.25%);

any other *secondary spot* is not more intense than the spot in the chromatogram obtained with solution (2) (0.1%);

not more than three other secondary spots are more intense than the spot in the chromatogram obtained with solution (3) (0.05%).

***trans*-Isomer**

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *dichloromethane* protected from light.

(1) 0.040% w/v of the substance being examined.
(2) 0.00046% w/v of *trans-clopenthixol acetate dihydrochloride BPCRS* (equivalent to 0.00040% w/v of *trans*-clopenthixol acetate).
(3) 0.020% w/v of the substance being examined and 0.023% w/v of trans-*clopenthixol acetate dihydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use stainless steel column (25 cm x 4.6 mm) packed with *silica gel for chromatography* (5 µm) (Spherisorb S 5W is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use ambient temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 15 µL of each solution.

MOBILE PHASE

0.03 volume of 13.5M *ammonia*, 45 volumes of *dichloromethane*, 45 volumes of *heptane* and 50 volumes of *acetonitrile*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the principal peaks is at least 2.6.

LIMITS

In the chromatogram obtained with solution (1), the area of any peak corresponding to *trans*-clopenthixol acetate is not greater than the area of the peak in the chromatogram obtained with solution (2) (1%).

Loss on drying

When dried at 60° at a pressure not exceeding 0.7 kPa for 3 hours, loses not more than 0.4% of its weight, Appendix XI D. Use 1 g.

Sulfated ash

Not more than 0.1%, Appendix IX A.

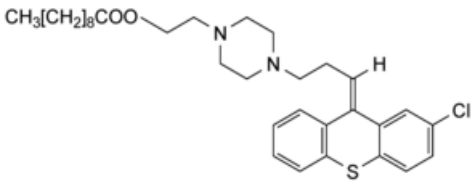
ASSAY

Dissolve 0.2 g in 50 mL of *anhydrous acetic acid* and carry out Method I for *non-aqueous titration*, Appendix VIII A, determining the end point potentiometrically. Each mL of *0.1M perchloric acid VS* is equivalent to 22.15 mg of $C_{24}H_{27}ClN_2O_2S$.

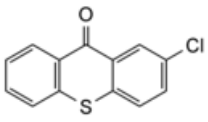
STORAGE

Zuclopenthixol Acetate should be protected from light and stored at a temperature not exceeding -20°.

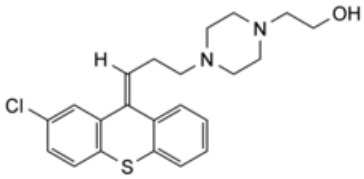
IMPURITIES



A. *trans*-clopenthixol acetate*(*trans-*isomer),*



B. 2-chlorothioxanthone,



C. zuclopenthixol.