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

Zuclopenthixol Acetate Injection

General Notices

Action and use

Dopamine receptor antagonist; neuroleptic.

DEFINITION

Zuclopenthixol Acetate Injection is a sterile solution of Zuclopenthixol Acetate in a suitable vegetable oil.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

Content of zuclopenthixol acetate, $C_{24}H_{27}ClN_2O_2S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, protected from light, using the following solutions.
(1) Dilute a volume of the injection with *ethanol* (*96%*) to contain 0.5% w/v of Zuclopenthixol Acetate.
(2) 0.5% w/v of *zuclopenthixol acetate dihydrochloride BPCRS* in *ethanol* (*96%*).
(3) 0.5% w/v each of *zuclopenthixol acetate dihydrochloride BPCRS* and *zuclopenthixol decanoate dihydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a *silica gel F_{254}* precoated plate (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, spray with a 1% w/v solution of *sodium molybdate* in *sulfuric acid*, heat at 110° for 20 minutes and examine in daylight.

MOBILE PHASE

3 volumes of *diethylamine* and 90 volumes of *cyclohexane*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Dissolve a quantity of the injection containing 0.10 g of Zuclopenthixol Acetate in sufficient *dichloromethane* to produce 50 mL.
(2) 0.0010% w/v of *2-chlorothioxanthone BPCRS* in *dichloromethane*.
(3) 0.0020% w/v of *zuclopenthixol hydrochloride BPCRS* in *dichloromethane* containing a few drops of *diethylamine*.
(4) 0.00040% w/v of *zuclopenthixol hydrochloride BPCRS* in *dichloromethane* containing a few drops of *diethylamine*.
(5) 0.00020% w/v of *zuclopenthixol hydrochloride BPCRS* in *dichloromethane* containing a few drops of *diethylamine*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a silica gel F_{254} precoated plate (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, 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*).

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 (2) (0.5%);

any spot corresponding to zuclopenthixol is not more intense than the spot in the chromatogram obtained with solution (3) (1%);

any other *secondary spot* is not more intense than the spot in the chromatogram obtained with solution (4) (0.2%);

and not more than one other *secondary spot* spot is more intense than the spot in the chromatogram obtained with solution (5) (0.1%).

trans-Isomer

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

(1) Dissolve a quantity of the injection containing 20 mg of Zuclopenthixol Acetate in 25 mL of *dichloromethane* and dilute to 50 mL with *dichloromethane*.
(2) Dissolve 23 mg of trans-*clopenthixol acetate dihydrochloride BPCRS* (equivalent to 20 mg of *trans*-clopenthixol acetate) in sufficient *dichloromethane* containing a few drops of *diethylamine* to produce 50 mL; dilute 1 mL of the resulting solution to 100 mL with *dichloromethane*.
(3) Mix equal volumes of solution (1) and undiluted solution (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 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 an ambient column temperature.
(e) Use a detection wavelength of 254 nm.

(f) Inject 50 µL of each solution.

MOBILE PHASE

0.08 of a volume of 13.5M *ammonia*, 45 volumes of *dichloromethane*, 45 volumes of n-*heptane* and 50 volumes of *acetonitrile*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* 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%).

ASSAY

Prepare a 0.2% w/v solution of cis-*flupenthixol propionate dihydrochloride BPCRS* (internal standard) in *dichloromethane*. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dissolve a quantity of the injection containing 20 mg of Zuclopenthixol Acetate in 25 mL of *dichloromethane*, add 5 mL of the internal standard solution and dilute to 50 mL with *dichloromethane*.
(2) Dissolve 20 mg of *zuclopenthixol acetate dihydrochloride BPCRS* in 25 mL of *dichloromethane* containing a few drops of *diethylamine*, add 5 mL of the internal standard solution and dilute to 50 mL with *dichloromethane*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under *trans*-Isomer may be used.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the injection, Appendix V G, and calculate the content of $C_{24}H_{27}ClN_2O_2S$ using the declared content of $C_{24}H_{27}ClN_2O_2S$ in *zuclopenthixol acetate dihydrochloride BPCRS*.

STORAGE

Zuclopenthixol Acetate Injection should be protected from light.