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

# Haloperidol Injection

General Notices

**Action and use**

Dopamine receptor antagonist; neuroleptic.

## DEFINITION

Haloperidol Injection is a sterile solution of Haloperidol in Lactic Acid diluted with Water for Injections.

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

**Content of haloperidol, $C_{21}H_{23}ClFNO_2$**

95.0 to 105.0% of the stated amount.

## IDENTIFICATION

To a volume containing 20 mg of Haloperidol add 5 mL of *water* and 1 mL of 1M *sodium hydroxide* and extract with 10 mL of *dichloromethane*. Filter and evaporate the filtrate to dryness. Dry the residue at 60° at a pressure not exceeding 0.7 kPa. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of haloperidol *(RS 173)*.

## TESTS

**Acidity**

pH, 2.8 to 3.6, Appendix V L.

**Related substances**

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 1 volume of mobile phase A and 9 volumes of mobile phase B (solution A). Prepare the solutions immediately before use and protect from light.

(1) Dilute a volume of the injection with sufficient solution A to produce a solution containing 0.05% w/v of Haloperidol.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.05% w/v of *haloperidol for system suitability EPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Hypersil BDS is suitable).
(b) Use gradient elution and the mobile phase described below.

(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 230 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

*Mobile phase A* 1.7% w/v of *tetrabutylammonium hydrogen sulfate*.

*Mobile phase B* *acetonitrile*.

| Time (Minutes) | Mobile phase A (% v/v) | Mobile phase B (% v/v) | Comment |
|---|---|---|---|
| 0-2 | 90 | 10 | isocratic |
| 2-17 | 90→50 | 10→50 | linear gradient |
| 17-22 | 50 | 50 | isocratic |
| 22-23 | 50→90 | 50→10 | linear gradient |
| 23-28 | 90 | 10 | re-equilibration |

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to haloperidol (retention time about 8 minutes) are: impurity B, about 0.9 and impurity D, about 1.6.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and haloperidol is at least 3.0.

LIMITS

Identify any peak corresponding to impurity B in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the area of this peak by a correction factor of 0.7.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity D or impurity B is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5% of each);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of all *secondary peaks* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

## ASSAY

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

(1) Dilute a volume of the injection with sufficient mobile phase to produce a solution containing 0.005% w/v of Haloperidol.
(2) 0.005% w/v of *haloperidol BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 5 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil ODS 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 247 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

45 volumes of *acetonitrile* and 55 volumes of a 1% w/v solution of *ammonium acetate*.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{23}ClFNO_2$ in the injection using the declared content of $C_{21}H_{23}ClFNO_2$ in *haloperidol BPCRS*.

## STORAGE

Haloperidol Injection should be protected from light.

## IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Haloperidol.