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# Ketamine Injection

General Notices

**Action and use**

Intravenous general anaesthetic.

## DEFINITION

Ketamine Injection is a sterile solution of Ketamine Hydrochloride in Water for Injections.

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

**Content of ketamine, $C_{13}H_{16}ClNO$**

95.0 to 105.0% of the stated amount.

## IDENTIFICATION

A. Dilute a volume of the injection with a mixture of 1 volume of 1M *sodium hydroxide* and 49 volumes of *methanol* to produce a solution containing the equivalent of 0.07% w/v of ketamine. The *light absorption*, Appendix II B, in the range 230 to 350 nm of this solution exhibits a maximum at 301 nm and shoulders at 274, 268 and 261 nm.
B. Dilute a volume of the injection with *0.1M hydrochloric acid* to produce a solution containing the equivalent of 0.025% w/v of ketamine. The *light absorption*, Appendix II B, in the range 230 to 350 nm of this solution exhibits two maxima at 276 nm and at 269 nm and a shoulder at 260 nm.

## TESTS

**Acidity**

pH, 3.5 to 5.5, Appendix V L.

**Related substances**

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

(1) Dilute the injection, if necessary, to produce a solution containing the equivalent of 0.1% w/v of ketamine.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) Dilute 1 volume of solution (2) to 2 volumes.
(4) Add 2 volumes of a 0.05% w/v solution of *ketamine impurity A EPCRS* in the mobile phase to 1 volume of solution (1) and dilute the resulting solution to 100 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.0 mm) and a stainless steel pre-column (4 mm × 4.0 mm), both packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Lichrosorb RP18 is suitable).

(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 215 nm.
(f) Inject 20 µL of each solution.
(g) For solutions (1), (2) and (3), continue the chromatography for 10 times the retention time of ketamine.

MOBILE PHASE

Dissolve 0.95 g of *sodium hexanesulfonate* in 1 litre of a mixture of 25 volumes of *acetonitrile R1* and 75 volumes of *water*. To the resulting solution add 4 mL of 6M *acetic acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution factor* between the peaks due to ketamine and ketamine impurity A is at least 1.5 and the retention time for ketamine is about 3 to 4.5 minutes. If necessary, adjust the concentrations of water and *acetonitrile* in the mobile phase.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of not more than one such peak is greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.25%);

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 0.4 times the area of the principal peak in the chromatogram obtained with solution (3) (0.1%).

## ASSAY

Dilute a volume of the injection containing the equivalent of 20 mg of ketamine to 100 mL with 0.05M *hydrochloric acid* and mix. Measure the *absorbance* of the resulting solution at the maximum at 269 nm, Appendix II B. Measure the *absorbance* of a 0.023% w/v solution of *ketamine hydrochloride BPCRS* in 0.05M *hydrochloric acid* at the same wavelength. Calculate the content of $C_{13}H_{16}ClNO$, using the declared content of $C_{13}H_{16}ClNO$, in *ketamine hydrochloride BPCRS*.

## IMPURITIES

The impurities limited by the requirements of this monograph include impurity A, listed under Ketamine Hydrochloride.

## STORAGE

Ketamine Injection should be protected from light and stored at a temperature not exceeding 30°.

## LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of ketamine.