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

Diazepam Oral Solution

General Notices

Action and use

Benzodiazepine.

DEFINITION

Diazepam Oral Solution is a solution of Diazepam in a suitable flavoured vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of diazepam, $C_{16}H_{13}ClN_2O$

95.0 to 115.0% of the stated amount.

IDENTIFICATION

A. The *light absorption*, Appendix II B, in the range 320 to 400 nm of the final solution obtained in the Assay exhibits a maximum at 368 nm. The *light absorption* in the range 230 to 330 nm of a solution prepared by diluting 1 volume of the final solution obtained in the Assay to 5 volumes with 0.1M *methanolic sulfuric acid* exhibits two maxima, at 243 nm and 286 nm.
B. Carry out the method described under Related substances applying separately to the plate 10 µL of each of solution (1) and solution (2) and using as solution (2) a 0.4% w/v solution of *diazepam BPCRS* in *ethanol (96%)*. After removal of the plate, allow the solvent to evaporate and examine under *ultraviolet light (254 nm)*. The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

TESTS

Acidity

pH, 4.0 to 6.6, Appendix V L.

Related substances

Carry out in subdued light the method for *thin-layer chromatography*, Appendix III A, using *silica gel GF_{254}* as the coating substance and a mixture of equal volumes of *ethyl acetate* and *hexane* as the mobile phase but allowing the solvent front to ascend 12 cm above the line of application. Apply separately to the plate 25 µL of each of the following solutions. For solution (1) add 40 mL of *water* to a volume of the oral solution containing 8 mg of Diazepam and extract with three 50-mL quantities of *ether*. Wash the combined ether extracts with 30 mL of 1M *sodium hydroxide* followed by two 40 mL quantities of *water*. Shake the extract with *anhydrous sodium sulfate*, filter, evaporate to dryness and dissolve the residue in 2 mL of *ethanol (96%)*. Solution (2) contains 0.0080% w/v of *5-chloro-2-methylaminobenzophenone BPCRS* in *ethanol (96%)*. Solution (3) contains 0.0040% w/v of *3-amino-6-chloro-1-methyl-4-phenylquinolin-2-ol BPCRS* in *ethanol (96%)*. For solution (4) dilute 2 mL of solution (1) to 100 mL with *ethanol (96%)* and dilute 1 mL of the resulting solution to 10 mL with

the same solvent. After removal of the plate, allow it to dry in air and examine under *ultraviolet light (254 nm)*. In the chromatogram obtained with solution (1) any spot corresponding to 5-chloro-2-methylaminobenzophenone is not more intense than the spot in the chromatogram obtained with solution (2) and any spot corresponding to 3-amino-6-chloro-1-methyl-4-phenylquinolin-2-ol is not more intense than the spot in the chromatogram obtained with solution (3). Any other *secondary spot* in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (4).

ASSAY

To a weighed quantity containing 1 mg of Diazepam add 25 mL of a mixture of equal volumes of 1M *sodium hydroxide* and *methanol* and shake for 2 minutes. Extract with five 25 mL quantities of *chloroform*, shaking for 2 minutes each time. Combine the chloroform extracts, shake with 5 g of *anhydrous sodium sulfate* and filter. Evaporate to dryness, dissolve the residue in 25 mL of 0.1M *methanolic sulfuric acid* and filter. Measure the *absorbance* of the filtrate, Appendix II B, at the maximum at 368 nm. Calculate the content of $C_{16}H_{13}ClN_2O$ taking 151 as the value of A(1%, 1 cm) at the maximum at 368 nm. Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_{16}H_{13}ClN_2O$, weight in volume.

STORAGE

Diazepam Oral Solution should be protected from light.