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

Dantrolene Oral Suspension

General Notices

NOTE: This monograph has been developed to cover unlicensed formulations.

Action and use

Skeletal muscle relaxant.

DEFINITION

Dantrolene Oral Suspension is a suspension of Dantrolene Sodium in a suitable flavoured vehicle.

The oral suspension complies with the requirements stated under Oral Liquids and with the following requirements. Where appropriate, the oral suspension also complies with the requirements stated under Unlicensed Medicines.

Content of dantrolene sodium, $C_{14}H_9N_4NaO_5,3½H_2O$

95.0 to 105.0% of the stated amount.

Shake the oral suspension vigorously before carrying out the following tests.

IDENTIFICATION

A. Shake a quantity of the oral suspension containing 0.1 g of Dantrolene Sodium with sufficient 0.01M *sodium hydroxide* to produce 100 mL, dilute 1 mL to 100 mL with 0.01M *sodium hydroxide*, filter and use the filtrate. The *light absorption*, Appendix II B, in the range 230 nm to 350 nm, of the final solution, exhibits a maximum at 314 nm.
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

Acidity

pH, 4.5 to 5.5, Appendix V L.

Dissolution

Complies with the requirements stated under Unlicensed Medicines, Oral Suspensions. Use a volume of the oral suspension containing one dose.

Related substances

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

(1) Dissolve a quantity of the oral suspension containing 50 mg of Dantrolene Sodium in 20 mL of *tetrahydrofuran* and 2 mL of *glacial acetic acid* and dilute with sufficient *absolute ethanol* to produce 100 mL.
(2) Dilute 1 mL of solution (1) to 100 mL with *absolute ethanol*.
(3) Dissolve 5 mg of *dantrolene sodium BPCRS* and 0.1 g of *theophylline BPCRS* in 20 mL of *tetrahydrofuran* and 2 mL of *glacial acetic acid* and dilute with sufficient *absolute ethanol* to produce 100 mL. Dilute 10 mL of the resulting solution to

100 mL with *absolute ethanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *silica gel for chromatography* (5 µm) (Zorbax Sil is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Adjust the flow rate of the mobile phase so that the retention time of the peak corresponding to dantrolene sodium is about 8 minutes.
(d) Use a column temperature of 30°.
(e) Use a detection wavelength of 300 nm.
(f) Inject 10 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for at least twice the retention time of the principal peak.

MOBILE PHASE

9 volumes of *absolute ethanol*, 10 volumes of *glacial acetic acid* and 90 volumes of *hexane*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks corresponding to theophylline and dantrolene is at least 6.0.

LIMITS

In the chromatogram obtained with solution (1):

the total area of all the *secondary peaks* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%).

ASSAY

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

(1) Add 50 mL of *dimethylformamide* to a weighed quantity of the oral suspension containing 60 mg of Dantrolene Sodium and dilute 1 volume of this solution to 100 volumes with the mobile phase.
(2) Dilute 1 volume of a 0.12% w/v solution of *dantrolene sodium BPCRS* in *dimethylformamide* to 100 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with spherical particles of silica, 5 µm in diameter, the surface of which has been modified with chemically-bonded nitrile groups (Spherisorb CN is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 262 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

15 volumes of *acetonitrile* and 85 volumes of a phosphate buffer pH 6.8 prepared by dissolving 11.88 g of *disodium hydrogen orthophosphate* and 9.08 g of *potassium dihydrogen orthophosphate* in 1000 mL of *water*.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{14}H_9N_4NaO_5$,3½H_2O, weight in volume, using the declared content of $C_{14}H_9N_4NaO_5$ in *dantrolene sodium BPCRS*. Each mg of $C_{14}H_9N_4NaO_5$ is equivalent to 1.1873 mg of $C_{14}H_9N_4NaO_5$,3½H_2O.

STORAGE

Dantrolene Oral Suspension should be protected from light.