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Dantrolene Sodium for Injection

» Dantrolene Sodium for Injection is a sterile, non-pyrogenic, lyophilized formulation containing Dantrolene Sodium, and one or more suitable buffering or sequestering agents. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{14}H_9N_4NaO_5 \cdot 3½H_2O$.

Packaging and storage—Preserve in tight containers. Store at controlled room temperature, protected from light.

USP Reference standards ⟨11⟩—
USP Dantrolene RS
USP Dantrolene Related Compound B RS
5-(4-Nitrophenyl)-2-furaldehyde-2-carboxymethyl semicarbazone.
$C_{14}H_{12}N_4O_6$

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests ⟨197⟩, Infrared Spectroscopy: 197K*▲ (CN 1-May-2020) —

Test specimen—To 0.5 g of Dantrolene Sodium for Injection, add 10 mL of 0.1 N hydrochloric acid and 10 mL of ethyl acetate, and mix. Allow the phases to separate, and transfer the upper ethyl acetate phase to a suitable glass container. Evaporate the solvent, dry the residue at 105° for 10 minutes, and use the residue.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Bacterial Endotoxins Test ⟨85⟩ —It contains not more than 0.5 USP Endotoxin Unit per mg of dantrolene sodium.

Sterility Tests ⟨71⟩ : meets the requirements.

Uniformity of dosage units ⟨905⟩: meets the requirements.

pH ⟨791⟩—Dissolve the contents of 1 vial in 60 mL of USP Water for Injection: the pH is between 8.8 and 11.0.

Water Determination, *Method Ia* ⟨921⟩ : not more than 3.0%.

Related compounds—

Mobile phase and *Diluent*—Proceed as directed in the *Assay.*

Standard solution—Transfer 10 mg of USP Dantrolene Related Compound B RS, accurately weighed, into a 50-mL volumetric flask, and dissolve in 2.5 mL of dimethylformamide. Add 2.5 mL of glacial acetic acid, and dilute with acetone to volume to obtain a solution having a known concentration of about 0.2 mg per mL. Dilute with *Diluent* to obtain a solution having a known concentration of about 0.002 mg per mL of dantrolene related compound B.

Test solution—Use the *Assay preparation.*

Chromatographic system—Proceed as directed in the *Assay.* Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections for dantrolene related compound B is not more than 5.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of dantrolene related compound B in the portion of Dantrolene Sodium for Injection taken by the formula:

$$100(r_U/r_S)(C_S/C_T)$$

in which r_U is the peak response for dantrolene related compound B obtained from the *Test solution;* r_S is the corresponding peak response in the *Standard solution*; C_S is the concentration, in mg per mL, of dantrolene related compound B in the *Standard solution*; and C_T is the concentration, in mg per mL, of dantrolene sodium hydrate in the *Test solution*. Not more than 8% of dantrolene related compound B is found.

Other requirements: meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*.

Assay—

Buffer—Dissolve 3.3 g of ammonium acetate in 1 L of water, and adjust with acetic acid to a pH of 4.5 ± 0.1.

Solution A—Prepare a filtered and degassed mixture of *Buffer,* acetonitrile, and glacial acetic acid (120:80:7).

Solution B—Prepare a filtered and degassed mixture of acetonitrile and water (70:30).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B,* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Diluent—Prepare a mixture of acetonitrile and water (60:40).

Standard preparation—Transfer 40 mg of USP Dantrolene RS, accurately weighed, into a 50-mL volumetric flask, and dissolve in 2.5 mL of dimethylformamide. Add 2.5 mL of glacial acetic acid, and dilute with acetone to volume to obtain a solution having a known concentration of about 0.8 mg per mL. Dilute this solution with *Diluent* to obtain a solution having a known concentration of about 0.08 mg per mL of dantrolene.

Assay preparation—Using 70 mL of water for each vial, transfer the entire contents of the required number of vials to a suitable flask necessary to obtain a solution having a known concentration of about 0.1 mg of dantrolene sodium hydrate per mL. Sonicate for 2 to 5 minutes to dissolve the sample. Dilute with *Diluent* to volume.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 365-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–8	100	0	isocratic
8–8.1	100→0	0→100	linear gradient
8.1–13	0	100	isocratic
13–13.1	0→100	100→0	linear gradient
13.1–20	100	0	re-equilibration

Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections for dantrolene is not more than 1.5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak responses for dantrolene. Calculate the percentage of $C_{14}H_9N_4NaO_5 \cdot 3½H_2O$ in the portion of Dantrolene Sodium for Injection taken by the formula:

$$(399.29/314.25)(r_U/r_S)(C_S/C_U)$$

in which 399.29 and 314.25 are the molecular weights of dantrolene sodium hydrate and dantrolene, respectively; r_U and r_S are the peak responses for dantrolene obtained from the *Assay preparation* and the *Standard preparation*, respectively; C_S is the concentration, in mg per mL, of dantrolene in the *Standard preparation*; and C_U is the concentration, in mg per mL, of dantrolene sodium hydrate in the *Assay preparation*.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
DANTROLENE SODIUM FOR INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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