Contains Nonbinding Recommendations

Draft Guidance on Dantrolene Sodium

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Dantrolene sodium

Dosage Form; Route: Suspension; intravenous

Strength: 250 mg/vial

Recommended Studies: In vitro study

I. In vitro study:

To qualify for the in vitro option for this drug product, the following criteria should be met:

i. The test and Reference Listed Drug (RLD) formulations are qualitatively (Q1)[1] and quantitatively (Q2)[2] the same (Q1/Q2).

ii. Acceptable comparative physicochemical characterizations of the test and reference products. Comparative analysis should be performed on at least three batches of both test and reference products and should include:

- Comparable pH, osmolality, and soluble fraction of dantrolene after reconstitution according to label instructions.

- Comparable drug particle size distribution. The particle size distribution should be compared using the population bioequivalence (PBE) statistical analysis procedure (95% upper confidence bound) based on D50 and SPAN [i.e. (D90-D10)/D50)]. Please refer to the Guidance on Budesonide inhalation suspension for additional information regarding PBE. Information on the instrument, analysis mode (if applicable), dilution medium, and level of dilution used for particle size measurements should be submitted along with full profiles of the particle size distribution upon serial dilution.

iii. Acceptable comparative dissolution of dantrolene from the test and reference formulations.

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[1] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the reference product.
[2] Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within ±5% of those used in the reference product.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).