*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

**Draft Guidance on Edaravone**

**November 2023**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

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**Active Ingredient:** Edaravone

**Dosage Form:** Suspension

**Route:** Oral

**Strength:** 105 mg/5 mL

**Recommended Study:** One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 105 mg/5 mL
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Exclude subjects with a history of asthma or drug- or sulfite-induced allergic reactions.

**Analyte to measure:** Edaravone in plasma

**Bioequivalence based on (90% CI):** Edaravone

**Waiver request of in vivo testing:** Not applicable

**Dissolution test method and sampling times:** The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units each of the test and reference products. Note that a dosage unit for a suspension is the labeled strength (5 mL). Specifications will be determined upon review of the abbreviated new drug application (ANDA).

**Product-specific testing conditions for in vitro feeding tube studies:** The approved labeling for the reference product states that the product may be administered by a nasogastric (NG) or percutaneous endoscopic gastrotomy (PEG) tube. Conduct the in vitro feeding tube studies, including comparative recovery testing, sedimentation volume and redispersibility testing, and in-use stability in designated dispersion media (i.e., water). For general procedures of in vitro feeding tube studies, refer to the most recent version of the FDA guidance for industry on *Oral Drug Products Administered Via Enteral Feeding Tube: In Vitro Testing and Labeling Recommendations*.[a]

Testing tubes: NG tube (8 French) and PEG tube (12 French)

1. Three types of tube configurations including different materials and/or different designs, with at least one PEG tube tested with an inflated balloon design
2. Holding times of 0 and 15 minutes on Day 0 and Day 15

Sedimentation volume and redispersibility testing

In-use stability test

Test strength: 105 mg/5 mL

For enteral administration (i.e., feeding tube), draw up suspension with an enteral syringe. Flush with water before and after enteral administration. Report the pH value of the water.

**Additional information:**

Device:
The reference listed drug (RLD) is presented in a bottle co-packaged with a bottle adapter and two oral syringes. The oral syringes are the device constituent parts.

FDA recommends that prospective applicants examine the size, shape and volume markings of the RLD device when designing the test device.

User interface assessment:
An ANDA for this product should include complete comparative analyses so FDA can determine whether any differences in design for the user interface of the proposed generic product, as compared to the RLD, are acceptable and whether the product can be expected to have the same clinical effect and safety profile as the RLD when administered to patients under the conditions specified in the labeling. For additional information, refer to the most recent version of the FDA guidance for industry on *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*.[a]

**Document History**: Recommended November 2023

**Unique Agency Identifier:** PSG_215446

[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.