Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Dofetilide

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Dofetilide

Dosage Form: Capsules

Route: Oral

Strengths: 0.125 mg, 0.25 mg, 0.5 mg

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: 0.5 mg
   Subjects: Healthy males and non-pregnant, non-lactating females.
   Additional comments: A Black Box warning concerns the risk of drug-induced arrhythmia. The study should be conducted in a facility that can provide continuous cardiac monitoring in the presence of personnel trained in management of serious ventricular arrhythmias. Any subject that develops a prolonged QTc interval should be monitored until the QTc is within limits. Females of reproductive potential should use effective contraception during the study.

Analyte to measure: Dofetilide in plasma

Bioequivalence based on (90% CI): Dofetilide

Waiver request of in vivo testing: 0.25 mg, 0.125 mg based on (i) acceptable bioequivalence study on the 0.5 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

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 for each of all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended May 2007; Finalized May 2008; Revised October 2024

Unique Agency Identifier: PSG_020931

[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.