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Draft Guidance on Vandetanib

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: Tablet

Route: Oral

Strengths: 100 mg, 300 mg

Recommended Studies: Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, parallel in vivo
   Strength: 100 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Additional comments: Exclude subjects with QTc interval >450 milliseconds, risk factors or history of Torsades de Pointes, congenital long QT syndrome, bradyarrhythmias, or uncompensated heart failure. Exclude subjects with abnormal electrolyte or thyroid stimulating hormone levels. Monitor electrocardiogram during the study. Exclude subjects who have undergone or plan to undergo elective surgery including dental procedures for at least 2 weeks prior to and at least 1 month after taking the study drug. Instruct subjects to use appropriate sun protection during the study to prevent photosensitivity reactions. Vandetanib is approved under a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU), which restricts its use. All pertinent elements of the REMS/ETASU must be incorporated into the protocol and informed consent. Alternatively, a crossover study design may be considered. Ensure an adequate washout period between treatments in the crossover study due to the long elimination half-life of vandetanib.

2. Type of study: Fed
Design: Single-dose, parallel in vivo
Strength: 100 mg
Subjects: Healthy males and healthy females not of reproductive potential
Additional comments: See comments above.

Analyte to measure: Vandetanib in plasma

Bioequivalence based on (90% CI): Vandetanib

Waiver request of in vivo testing: 300 mg strength based on (i) acceptable bioequivalence studies on the 100 mg strength, (ii) acceptable in vitro dissolution testing of both strengths, and (iii) proportional similarity of the formulations between both 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 each of both strengths of the test and reference products. Specifications will be determined upon evaluation of the abbreviated new drug application.

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 gastrotomy (G) tube. Conduct the in vitro feeding tube studies, including comparative recovery, 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 G tube (12 French)

1. Three different tube materials (e.g., polyvinylchloride, silicone, polyurethane) and/or designs (e.g., various numbers of ports and/or eyes, retention balloons, open or closed distal end) for NG tubes (8 French) and G tubes (12 French), with at least one G tube tested with an inflated balloon design

Reporting of the pH value of the water

Holding times of 0 and 15 minutes

Test strength: 300 mg

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[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.