Contains Nonbinding Recommendation

Draft Guidance on Nilotinib Hydrochloride Monohydrate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Nilotinib Hydrochloride Monohydrate

Form/Route: Capsules/Oral

Recommended studies: 1 study

Type of study: Fasting
Design: Single-dose, two-way, crossover in vivo
Strength: 200 mg
Subjects: Healthy males and nonpregnant females, general population

Additional Comments:

1) Females should not be lactating, and if applicable, should practice abstention or contraception during the study.
2) Patients with hypokalemia, hypomagnesemia, or long QT syndrome, or a history of cardiac disease should be excluded.
3) Drugs known to prolong the QT interval should be avoided within 4 weeks prior to study. Please see http://www.azcert.org/medical-pros/drug-lists.cfm for a list of agents that prolong the QT interval.
4) Strong CYP3A4 inhibitors or inducers should be avoided within 4 weeks prior to study. Please see http://medicine.iupui.edu/flockhart for a list of inhibitors and/or inducers.
5) Grapefruit, pomegranate, star fruit and Seville oranges should be avoided for 7 days prior to dosing. The juices and products containing these fruits should also to be avoided. Subjects should also refrain from taking St. John's Wort.
6) Caution should be exercised if co-administered with drugs that are substrates or inhibitors of P-glycoprotein.
7) Caution should be exercised if co-administered with narrow therapeutic index drugs that are substrates of CYP3A4, CYP2B6, CYP2C8, CYP2C9, CYP2D6 or UGT1A1.
8) Subjects should have normal renal and hepatic function.
9) Males and their female partners need to practice adequate contraception for at least 1 week after the last nilotinib dose.

Analytes to measure (in appropriate biological fluid): Nilotinib in plasma

Bioequivalence based on (90% CI): Nilotinib

Waiver request of in vivo testing: 150 mg based on (i) acceptable bioequivalence studies on the 200 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times:
Please note that a **Dissolution Methods Database** is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please 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 application.