

Contains Nonbinding Recommendations

Draft Guidance on Sorafenib Tosylate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Sorafenib Tosylate

Form/Route: Tablet; Oral

Recommended studies: 1 study

Type of study: Fasting

Design: Single-dose, two-way crossover in vivo

Strength: 200mg (maximum allowed dose of 1x200mg)

Subjects: Healthy males and non-pregnant females, general population

Additional Comments:

1. Due to the relatively long half-life of sorafenib, the firm may wish to conduct this study using a single-dose parallel design. Please refer to the Amiodarone HCl Tablet Guidance for additional information regarding long half-life drugs.
2. Healthy volunteers participating in the study should be informed of the following:
 - While sorafenib is one of several drug products in the general class of kinase inhibitors, it has effect on multiple cellular targets including enzymes and receptors, some of which are not yet fully characterized.
 - Fetal harm is expected from chronic exposure. Sorafenib was teratogenic when given to pregnant rats and rabbits at sub-therapeutic exposures. The teratogenicity potential of the drug when given to mating with female is unknown. All subjects, male and female should use adequate contraceptive methods. Repeat dose toxicology studies showed adverse effects in male and female reproductive organs at sub-therapeutic exposures, although no effect on the reproductive organs of males or females was observed in single-dose toxicology studies under the conditions of the experiments.
 - Carcinogenicity studies have not been performed with sorafenib.
 - Regarding genetic toxicology, sorafenib was clastogenic when tested in an in vitro mammalian cell assay (Chinese Hamster Ovary) but negative in the Ames test and the micronucleus assays.
 - Pregnancy precautions are not infallible. Contraception should be used during the study and for two weeks thereafter.

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

Bioequivalence based on (90% CI): Sorafenib

Waiver request of in-vivo testing: Not Applicable

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.