Contains Nonbinding Recommendations

Draft Guidance on Chlorambucil

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablet/Oral

Recommended studies: 1 study

1. Type of study: Fasting
   Design: Single-dose, two-way crossover *in-vivo*
   Strength: 2 mg
   Subjects: Patients should already be receiving a stable once-daily dose of chlorambucil and should continue the same dose during the study.
   Additional Comments:

   1. Patients should already be on a regimen of oral chlorambucil tables.
   2. The study design should allow for each patient to receive their own established chlorambucil regimen.
   3. No changes in dose or regimen should be made for the purpose of the bioequivalence study.
   4. Ideally, patients should be given the entire daily dose at one time.
   5. Because of the short chlorambucil plasma half-life (about 1½ hours), the two study periods should be conducted on two consecutive days.
   6. Each patient may receive a different dose, but all should use the same dosage strength (only the 2 mg tablet is available).
   7. In a crossover study, the dose that each patient receives should be the same for both study periods. If a change in doses is needed, then that patient should be dropped from the study.
   8. Any concomitant medications taken by each patient should be the same for the two study periods. If a change in concomitant medications is necessary, then that patient should be dropped from the study.
   9. Since patients will be receiving different doses, dose should be included in the statistical model. Correction for differing dosing regimens by dose-normalization is not recommended.

Special Consideration: Submission of an Investigational New Drug Application (IND) is required prior to the conduct of a bioequivalence study for a cytotoxic drug product such as Chlorambucil (see 21 C.F.R § 320.31)

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

Bioequivalence based on (90% CI): Chlorambucil

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.