Contains Nonbinding Recommendations

Draft Guidance on Estramustine Phosphate Sodium

Active ingredient: Estramustine Phosphate Sodium

Form/Route: Capsule/Oral

Recommended studies: 1 study

1. Type of study: Steady-state
   Design: Randomized, parallel, steady state, in vivo
   Strength: 140 mg
   Subjects: Prostatic cancer patients who are already on established treatment regimens involving monotherapy or combination therapy with estramustine phosphate sodium.

   Additional Comments:

   1. For a parallel design study, the Test and Reference groups should be well-balanced (including factors such as gender, age, and body mass) with respect to patient disease progression, treatment history, and treatment regimen.

   2. Steady-state conditions for estromustine should be confirmed by measuring concentrations of estromustine in three consecutive plasma samples taken during dosing and prior to receiving the dose for the pharmacokinetic measurements, at 24-hour intervals.

   3. Since the labeling recommends that estramustine be taken on an empty stomach to improve bioavailability, patients should take no food for 2 hours before and 1 hour after dosing each day.

   4. Since this is a cytotoxic drug, an Investigational New Drug Application (IND) should be submitted prior to conducting the bioequivalence study as indicated in 21 CFR 320.31.

Analytes to measure (in appropriate biological fluid): Estromustine and estramustine in plasma

Bioequivalence based on (90% CI): Estromustine

Waiver request of *in-vivo* testing: Not applicable

Dissolution test method and sampling times: Please note that **Dissolution Method Database** is available to the public at the OGD website at: http://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of the test and reference products. Specifications will be determined upon review of the application.