Contains Nonbinding Recommendations

Draft Guidance on Colestipol Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: In vitro equilibrium binding study
   Design: With and without acid pre-treatment at pH 6.8
   Strength: 1 gm
   Subjects: Not Applicable
   Additional Comments: The equilibrium binding study is the pivotal bioequivalence study. This study should be conducted on whole tablets by incubating the Test and Reference products with at least eight different concentrations of total bile salts, with and without acid pretreatment. Each bile salt-containing incubation medium should contain glycocholic acid (GCA), glycochenodeoxycholic acid (GCDA) and taurodeoxycholic acid (TDCA). Total bile salt concentrations should be spaced along the spectrum until the maximum binding is clearly established. All incubations should be conducted at 37°C. Each binding study should be repeated at least 12 times. In addition, data should be provided demonstrating that the length of time selected for incubation with the total bile salt-containing medium yields maximum binding.

   For additional details on the study design, please see the Cholestyramine Powder/Oral guidance.

---

2. Type of study: In vitro kinetic binding study
   Design: without acid pre-treatment
   Strength: 1 gm
   Subjects: Not Applicable
   Additional Comments: The kinetic binding study should be used to support the pivotal equilibrium binding study. This study should be conducted on whole tablets by incubating the Test and Reference products for at least eight different lengths of time, with two different constant total bile salt concentrations, without acid pre-treatment. The total bile acid concentrations used should be 5 mM and 15 mM. Times should be selected along the spectrum until the maximum binding is clearly established. All incubations should be conducted at 37°C. Each binding study should be repeated at least 12 times.

   For additional details on the study design, please see the Cholestyramine Powder/Oral guidance

Analytes to measure (in appropriate biological fluid): Unbound bile salts in filtrate (to calculate bile salts bound to resin).

For the in vitro equilibrium binding study, the Langmuir binding constants k_1 and k_2 should be determined based on total bile salt binding (GC+GCDC+TDC). The test/reference ratio should be calculated for k_1. The 90% confidence interval should be calculated for k_2 with the acceptance criteria of 80% to 120%.

For the in vitro kinetic binding study, the test/reference bound bile acid salt ratios at the various times should be compared but not subjected to the 90% confidence interval criteria.

Bioequivalence based on (90% CI): The Langmuir binding constant k_2 from the equilibrium binding study

Waiver request of in vivo testing: Not Applicable

Dissolution test method and sampling times: Not Applicable

Disintegration Test:
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 disintegration information for this product at this website. Please conduct comparative disintegration testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.