Draft Guidance on Nitisinone

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

Active Ingredient: Nitisinone

Dosage Form; Route: Capsule; oral

Recommended Studies: One study

Type of study: Fasting

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

Strength: 20 mg

Subjects: Healthy males and non-lactating, non-pregnant females

Additional comments: Nitisinone has a long terminal half- life. Ensure adequate washout periods between treatments in all crossover studies. An AUC truncated to 72 hours may be used in place of AUC0-t or AUC∞ for long half-life drug products. Collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration (Cmax) and time to reach peak concentration (Tmax).

Analytes to measure (in appropriate biological fluid): Nitisinone in serum

Bioequivalence based on (90% CI): Nitisinone

Waiver request of in-vivo testing: 2 mg, 5 mg and 10 mg strength capsules based on (i) acceptable bioequivalence studies on the 20 mg strength, (ii) proportionally similar across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website available to the public at the following location: http://www.accessdata.fda.gov/scripts/cder/dissolution/. 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 abbreviated new drug application (ANDA).