

Draft Guidance on Nitisinone

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover *in-vivo*
Strength: 10 mg
Subjects: Healthy males and non-pregnant, non-lactating females.
Additional Comments: Nitisinone has a long half-life. Ensure adequate washout periods between treatments in all crossover studies. An AUC truncated to 72 hours may be used in place of AUC_{0-t} or AUC_{0-inf} for long half-life drugs. Collect sufficient blood samples in the bioequivalence studies to adequately characterize the peak concentration (C_{max}) and time to reach the peak concentration (T_{max}).

2. Type of study: Fed
Design: Single-dose, two-way crossover *in-vivo*
Strength: 10 mg
Subjects: Healthy males and non-pregnant, non-lactating females.
Additional comments: See comments above.

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

Bioequivalence based on (90% CI): Nitisinone

Waiver request of in-vivo testing: The 2 mg and 5 mg strength tablet strengths based on (i) acceptable bioequivalence studies on the 10 mg strength tablet, (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.