

## Draft Guidance on Panobinostat Lactate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

**Dosage Form; Route:** Capsule; oral

**Recommended Studies:** Two studies

1. Type of study: Fasting

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

Strength: EQ 20 mg base

Subjects: Multiple myeloma patients with a well-established dosing regimen (once every other day for 3 doses per week (Mondays, Wednesdays, and Fridays) in Weeks 1 and 2 of each 21-day cycle) who have already taken panobinostat lactate capsules orally for one or more cycles.

Additional comments: 1. Due to the undesired drug interaction between panobinostat and dexamethasone, the test and reference products should be dosed in patients with one or more therapeutic cycles. 2. To avoid pre-dose plasma concentrations, full pharmacokinetic (PK) profiles of BE studies for the test and reference treatments are recommended from all patients dosed on Day 1 (Monday) of each therapeutic cycle. The test and reference pharmacokinetics of panobinostat can be evaluated during the sampling period of 48 hrs.

2. Type of study: Fed

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

Strength: EQ 20 mg base

Subjects: Multiple myeloma patients with an well-established dosing regimen (once every other day for 3 doses per week (Mondays, Wednesdays, and Fridays) in Weeks 1 and 2 of each 21-day cycle) who have already taken panobinostat lactate capsules orally for one or more cycles.

Additional comments: See comments above.

Submission of a Bio Investigational New Drug Application (BioIND) is required prior to the conduct of a bioequivalence study for a cytotoxic drug product such as Panobinostat (see 21CFR § 320.31).

**Analytes to measure (in appropriate biological fluid):** Panobinostat in plasma

**Bioequivalence based on (90% CI):** Panobinostat

**Waiver request of in vivo testing:** EQ 10 mg and 15 mg base strength based on (i) acceptable bioequivalence studies on the 20 mg strength, (ii) proportional similarity of the formulations 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).