Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Hydromorphone Hydrochloride

October 2024

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient: Hydromorphone hydrochloride

Dosage Form: Tablet

Route: Oral

Strengths: 2 mg, 4 mg, 8 mg

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 8 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: A clear plan for continuous respiratory monitoring from the time of dosing past the time of expected peak effect of the drug (i.e., at least 3 hours from dosing) should be included. Standard operating procedures should be in place for assessing and treating ventilatory depression, and personnel qualified to treat ventilatory emergencies should be immediately available. Hydromorphone hydrochloride tablet is under a Risk Evaluation and Mitigation Strategy (REMS) with Elements to Assure Safe Use (ETASU). All pertinent elements of the REMS/ETASU are recommended to be incorporated into the protocol and informed consent.

Analyte to measure: Hydromorphone in plasma

Bioequivalence based on (90% CI): Hydromorphone

Waiver request of in vivo testing: 2 mg and 4 mg strengths based on (i) acceptable bioequivalence study on the 8 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

Dissolution test method and sampling times: The dissolution information for this drug product can be found in the FDA's Dissolution Methods database, http://www.accessdata.fda.gov/scripts/cder/dissolution/. Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test product and reference listed drug (RLD).[1] Specifications will be determined upon review of the abbreviated new drug application.

Document History: Recommended February 2010; Finalized August 2017; Revised October 2024

Unique Agency Identifier: PSG_019892

[1] If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.