Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Risperidone

November 2021

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency's regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

In July 2010, FDA issued a draft product-specific guidance for industry on generic risperidone. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

Active Ingredient: Risperidone

Dosage Form; Route: Tablet, orally disintegrating; oral

Recommended Studies: Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 1 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: The orally disintegrating tablet should be placed on the tongue, allowed to disintegrate, and swallowed without water. Exclude geriatric subject due to higher incidences of falls, orthostatic hypotension, and central nervous system and musculoskeletal adverse events. Subjects should be instructed not to engage in potentially hazardous activities requiring complete mental alertness, such as driving a motor vehicle or operating machinery until they have completely returned to their level of baseline

cognitive functioning after taking risperidone. Subjects should be monitored for vital sign changes and/or orthostatic symptoms during the study.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: 1 mg
Subjects: Males and non-pregnant, non-lactating females, general population
Additional comments: See comments above

Analyte to measure: Risperidone in plasma

Bioequivalence based on (90% CI): Risperidone

Waiver request of in vivo testing: 0.5 mg, 2 mg, 3 mg and 4 mg based on (i) acceptable bioequivalence studies on the 1 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 each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

Revision History: Recommended July 2010; Revised November 2021

Unique Agency Identifier: PSG_021444