

## Draft Guidance on Ketorolac Tromethamine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

**Active ingredient:** Ketorolac Tromethamine

**Form/Route:** Metered Spray/Nasal

**Recommended studies:** 2 options: In-Vivo or In Vitro

### I. In-Vivo Option:

If the test product is **not** qualitatively (Q1) and quantitatively (Q2) the same as the reference product, the following study is recommended to document bioequivalence of the test product to the reference product:

Type of study: Fasting

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

Strength: 15.75 mg/spray x 2 sprays (one spray/nostril resulting in 31.5 mg total dose)

Subjects: Healthy males and nonpregnant females, general population.

Additional Comments: None

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

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

**Waiver request of in-vivo testing:** Not Applicable

**Dissolution test method and sampling times:** Not Applicable

**Additional information:** While comparative in vitro studies are not required, in vitro studies outlined in the 2002 Guidance for Industry, *Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products – Chemistry, Manufacturing, and Controls Documentation* (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070575.pdf>) should be submitted for Chemistry, Manufacturing, and Controls evaluation.

### II. In-Vitro Option:

If the test product is qualitatively (Q1) and quantitatively (Q2) the same as the reference product, then bioequivalence may be documented by an in vitro approach in lieu of an in vivo approach.

Equivalent in vitro performance of the test product to the reference product should be established. The current FDA recommendations for documenting bioequivalence of nasally-administered products via in vitro testing may be found in the draft guidance “Bioavailability and Bioequivalence Studies for Nasal Aerosols and Nasal Sprays for Local Action”. The guidance is available at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070111.pdf> under Biopharmaceutics Draft (April 2003).

**Waiver request of in-vitro testing:** Not Applicable.

**Dissolution test method and sampling times:** Not Applicable.

**Additional information:** Not Applicable.