

Draft Guidance on Mercaptopurine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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: Mercaptopurine

Form/Route: Tablet /Oral

Recommended studies: 1 study

Type of study: Fasting

Design: Single-dose, two-treatment, two-period crossover, *in vivo* study in patients

Strength: 50 mg

Subjects: Studies should be conducted in patients receiving mercaptopurine in a stable regimen using the same dosage unit (multiples of the same strength). Mercaptopurine therapy often includes daily oral mercaptopurine and weekly oral methotrexate. Since the pharmacological effect of methotrexate may potentially affect the pharmacokinetics of mercaptopurine differently on different days following the methotrexate administration, the study periods of the bioequivalence study of mercaptopurine tablets should be conducted at weekly intervals (within the daily dosing regimen for mercaptopurine), using the same time interval between methotrexate and study drug administration for each period.

Patients should fast for 10 hours prior to and 4 hours after each study dose.

Additional Comments:

- Patients with inherited deficiency of the enzyme thiopurine methyl transferase must be excluded from these studies.
- The informed consent should include a description of the known genotoxicity of 6-mercaptopurine in human cells and animal models.
- Submission of an Investigational New Drug Application (IND) is required prior to the conduct of a bioequivalence study for a cytotoxic drug product such as mercaptopurine (See 21 C.F.R § 320.31).

Analytes to measure (in appropriate biological fluid): Mercaptopurine in plasma

Bioequivalence based on (90% CI): Mercaptopurine

Waiver request of in-vivo testing: Not Applicable

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution>. Please find the dissolution information for this product at this website. Please 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 application.