

Draft Guidance on Temozolomide

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Capsules/Oral

I. BCS Waiver option:

It may be possible to request a waiver of in vivo testing for all the strengths of this product provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution as detailed in the Guidance for Industry: *Waiver of In Vivo Bioavailability and Bioequivalence for Immediate – Release Solid Oral Dosage Forms Based on the Biopharmaceutics Classification System* is submitted in the application. Peer reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon review of the data submitted in the application.

II. In Vivo option:

Recommended studies: 1 study

Type of study: Fasting

Design: Single-dose, two-way crossover in vivo with dosing on the first 2 days of a treatment cycle (i.e., Period I and Period II of the study are Day 1 and Day 2, respectively, of the treatment cycle)

Strength: 250 mg (dose 1x250 mg)

Subjects: Cancer patients who are already receiving or are about to start receiving temozolomide 250 mg once daily as their calculated individualized dose (e.g. based upon factors such as tumor type, body surface area, cycle number and toxicity). All subjects who received at least one dose of the investigational drug (i.e., the safety population) should be included in the assessments of safety and tolerability.

Additional Comments: Submission of an Investigational New Drug Application (IND) is required prior to conducting a bioequivalence study for a cytotoxic drug product such as temozolomide (see 21 C.F.R § 320.31).

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

Bioequivalence based on (90% CI): Temozolomide

Waiver request of in vivo testing: 5 mg, 20 mg, 100 mg, 140 mg and 180 mg based on (i) acceptable bioequivalence study on the 250 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:

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.