*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

**Draft Guidance on Mirdametinib**

**May 2026**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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| **Active Ingredient:** | Mirdametinib |
| **Dosage Form:** | Capsule |
| **Route:** | Oral |
| **Strengths:** | 1 mg \| 2 mg |
| **Reference Listed Drug:** | NDA 219389 |
| **Recommended Studies:** | Two options: (I) Biopharmaceutics Classification System (BCS)-based biowaiver or (II) one in vivo bioequivalence study with pharmacokinetic endpoints |

**Option I: BCS Class I-based biowaiver**

**BCS-I waiver:** A waiver request of in vivo testing for this product may be considered provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution of the test product and reference listed drug (RLD) as detailed in the guidance for industry *M9 Biopharmaceutics Classification System-Based Biowaivers*[a] is submitted in the application. Applicants may use the information contained in the approved labeling of the RLD. Peer-reviewed articles may not contain the necessary details of the testing for the FDA to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request will be made upon assessment of the data submitted in the application.

**Option II: One in vivo bioequivalence study with pharmacokinetic endpoints**

1. Class of study: Bioequivalence
   Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 2 mg
   Subjects: Healthy males and healthy females not of reproductive potential
   Safety recommendations:
   - Exclude subjects with abnormal findings from ophthalmic exam.
   - Males with female partners of reproductive potential should use effective contraception during the study and for three months after the last dose.

   Study design recommendation:
   - $AUC_{(0\text{-}72h)}$ may be used in place of $AUC_{(0\text{-}t)}$ for comparing the extent of absorption due to mirdametinib's long half-life. Ensure adequate washout periods between treatments in the crossover study.
   - Alternatively, a parallel study design may be considered.

**Analyte to measure:** Mirdametinib in plasma

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

**Waiver request of in vivo testing of additional strength:** Justification based on (i) an acceptable bioequivalence study on the 2 mg strength, (ii) acceptable comparative in vitro dissolution studies between the additional strength and the 2 mg strength using 12 units per strength, and (iii) proportional similarity of the formulations between both strengths

**Dissolution**: Dissolution test(s) should be included for quality control and to support a waiver request of in vivo testing of an additional strength. For the quality control dissolution method, provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method[1] and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

For drug products containing high solubility drug substances that meet the rapidly dissolving criteria, demonstration of discriminating ability may not be needed. For additional information, refer to the guidance for industry *Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances*.[a]

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**Document History:** Recommended May 2026

[a] We update guidances periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[1] Applicant-developed, United States Pharmacopeia drug product monograph or Dissolution Methods database, https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm