Pharmacy Policy Bulletin: J-0610 Idhifa (enasidenib) – Commercial and Healthcare Reform	
Number: J-0610	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization** 1. Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0610-011	**Original Date:** 08/09/2017
Effective Date: 10/08/2025	**Review Date: 09/17/2025**

Drugs Product(s):	• Idhifa (enasidenib)
FDA-Approved Indication(s):	• Treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.

Background:	• Idhifa is an IDH2 inhibitor. Inhibition results in decreased 2-hydroxyglutarate (2-HG) levels and induced myeloid differentiation, reduced blast counts and increased percentages of mature myeloid cells.
	• Mutations in IDH2 occur in approximately 8% to 19% of adult patients with AML. Prognosis of AML with IDH mutations is dependent upon various factors including the specific location of the mutation at diagnosis, the dynamics of the mutation burden during disease course, and computational status.
	• Companion diagnostic tests FDA-approved for genetic testing include for Idhifa the Abbott RealTi*me* IDH2 test. For additional information regarding FDA-approved companion diagnostics, please visit: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools
	• Prescribing Considerations:
	  ○ Idhifa carries a black box warning differentiation syndrome. If differentiation syndrome is suspected, initiate systemic corticosteroids and hemodynamic monitoring until symptom resolution. Taper corticosteroids only after resolution of symptoms. Differentiation syndrome symptoms may recur with premature discontinuation of corticosteroids.
	  ○ Safety and effectiveness have not been established in pediatric patients.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Idhifa may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member is 18 years of age or older.

B. The member has a diagnosis of relapsed or refractory acute myeloid leukemia (AML, ICD-10: C92.5).

C. The member is isocitrate dehydrogenase-2 (IDH2) mutation-positive as detected by an FDA approved test.

II. Reauthorization

When a benefit, reauthorization of Idhifa may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as one (1) of the following **(1. or 2.)**:

1. Disease improvement

2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Idhifa is indicated for members with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation. Idhifa should not be used for treatment in any other mutation type.

II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

III. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Idhifa [package insert]. Summit, NJ: Celgene Corporation; January 2025.
2. Ravandi F, et al. Characteristics and outcome of patients with acute myeloid leukemia refractory to 1 cycle of high-dose cytarabine-based induction chemotherapy. *Blood*. 2010;116(26):5818-23.
3. Medeiros B, et al. Isocitrate dehydrogenase mutations in myeloid malignancies. *Leukemia*. 2017; 31:272-281.
4. Zarnegar-Lumley S, Alonzo TA, Gerbing RB, et al. Characteristics and prognostic impact of *IDH* mutations in AML: a COG, SWOG, and ECOG analysis. *Blood Adv.* 2023; 7(19): 5941-5953.
5. Bill M, Jentzsch M, Bischof L, et al. Impact of IDH1 and IDH2 mutation detection at diagnosis and in remission in patients with AML receiving allogeneic transplantation. *Blood Adv.* 2023; 7(3): 436-444.
6. U.S Food & Drug Administration. List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools). Available at: https://www.fda.gov/medical-devices/vitro-diagnostics/list-

cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools. Accessed July 29, 2025.