Clinical Policy: Enasidenib (Idhifa)

Reference Number: ERX.SPA.218
Effective Date: 12.01.17
Last Review Date: 11.21 Revision Log
Line of Business: Commercial, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Enasidenib (Idhifa®) is an isocitrate dehydrogenase-2 (IDH2) inhibitor.

FDA Approved Indication(s)
Idhifa is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an IDH2 mutation as detected by an FDA-approved test.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Idhifa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Myeloid Leukemia (must meet all)**:**

1. Diagnosis of AML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Disease is relapsed or refractory;
   b. Age ≥ 60 years and one of the following (i or ii):
      i. Member is not a candidate for intensive induction therapy;
      ii. Used for post-induction therapy with previous lower-intensive therapy (*see Appendix B for examples*);*

   **Prior authorization may be required.*
5. Presence of an IDH2 mutation;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 100 mg (1 tablet) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Acute Myeloid Leukemia (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Idhifa for AML and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 100 mg (1 tablet) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myeloid leukemia
FDA: Food and Drug Administration
IDH2: isocitrate dehydrogenase-2
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cytarabine with idarubicin or daunorubicin	Age < 60 years: example of intensive induction therapy: cytarabine 100 – 200 mg/m^2 continuous IV infusion x 7 days with idarubicin 12 mg/m^2 IV or daunorubicin 60-90 mg/m^2 IV x 3 days	Varies
cytarabine with idarubicin or daunorubicin or mitoxantrone	Age ≥ 60 years: example of intensive induction therapy: cytarabine 100 – 200 mg/m^2 continuous IV infusion x 7 days with idarubicin 12 mg/m^2 IV or daunorubicin 60-90 mg/m^2 IV x 3 days or mitoxantrone 12 mg/m^2 x 3 days	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/ Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): differentiation syndrome. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AML	100 mg PO QD	100 mg/day

VI. Product Availability

Tablets: 50 mg, 100 mg

VII. References

1. Idhifa Prescribing Information. Summit, NJ: Celgene Corporation; November 2020. Available at: www.idhifa.com. Accessed August 11, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 11, 2021.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 11, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.05.17	11.17
4Q 2018 annual review: added specialist requirement; added NCCN supported use in patients age ≥ 60 years who are not candidates for intensive remission induction therapy or declines intensive therapy; increased approval durations to length of benefit; references reviewed and updated.	08.21.18	11.18
4Q 2019 annual review: NCCN use added - relapse/remission post Idhifa therapy; FDA/NCCN dosing limitation added; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	08.27.19	11.19
4Q 2020 annual review: no significant changes; updated Appendix C; references reviewed and updated.	08.04.20	11.20
4Q 2021 annual review: added coverage for age ≥ 60 with either not candidate for induction therapy or used for post-induction therapy with previous lower intensity therapy per NCCN; references reviewed and updated.	08.11.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.