Clinical Policy: Enasidenib (Idhifa)

Reference Number: CP.PHAR.363
Effective Date: 09.05.17
Last Review Date: 11.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

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.

It is the policy of health plans affiliated with Centene Corporation® 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. Idhifa is prescribed as single-agent therapy in members age ≥ 60 years and one of the following (i or ii);
      i. Used for induction therapy when member is not a candidate for intensive induction therapy or declines intensive therapy;
      ii. Used for post-induction therapy with previous lower-intensity therapy (*see Appendix B for examples*);*
      **Prior authorization may be required.*
5. Presence of an IDH2 mutation;
6. For Idhifa requests, member must use generic enasidenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. 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:
Medicaid/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acute Myeloid Leukemia (must meet all)**:**
1. Currently receiving medication via Centene benefit, 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. For Idhifa requests, member must use generic enasidenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. 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:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications(must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid 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.idhifapro.com. Accessed August 2, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 2, 2022.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed August 2, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Combined Commercial and Medicaid policies.	02.12.18	
4Q 2018 annual review: specialist requirement was added; added NCCN Compendium supported use in patients age ≥ 60 years who are not candidates for intensive remission induction therapy or declines intensive therapy; 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; references reviewed and updated.	08.27.19	11.19
Added HIM line of business.	02.13.20	
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; modified reference from HIM.PHAR.21 to HIM.PA.154; added legacy WCG auth durations (WCG.CP.PHAR.363 to be retired); added requirement for use of generic if available; references reviewed and updated.	08.11.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
4Q 2022 annual review: legacy WCG approval duration consolidated; in patients age ≥ 60 years, added Idhifa must be used as a single agent and option to decline intensive therapy per NCCN;	08.02.22	11.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
references reviewed and updated. Template changes applied to other diagnoses/indications.		

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.