Clinical Policy: Enasidenib (Idhifa)

Reference Number: CP.PHAR.363
Effective Date: 09.05.17
Last Review Date: 11.18
Line of Business: Commercial, 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. Presence of an IDH2 mutation;
5. One of the following (a or b):
   a. Disease has relapsed or is refractory following treatment with first line agents (e.g., cytarabine, idarubicin, daunorubicin, Vyxeos®, cladribine, Rydapt®, Mylotarg®);
      **Prior authorization may be required for Mylotarg, Rydapt, and Vyxeos*
   b. Age ≥ 60 years (off-label);
6. Request meets one of the following (a or b):
   a. Dose does not exceed 100 mg per day (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*).

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

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial 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. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 100 mg per day (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*).

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

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial 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 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

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	Various combination regimens (e.g., with one or more of the following: idarubicin (Idamycin), daunorubicin (Vyxeos), Rydapt (midostaurin), Mylotarg (gemtuzumab ozogamicin))	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

Appendix D: General Information

- In clinical trials, refractory disease was defined as disease which was refractory to initial induction or re-induction treatment. Relapsed disease was defined as the reappearance of > 5% blasts in the bone marrow.
- Factors in decisions about fitness for induction chemotherapy include age, performance status, functional status, and comorbid conditions.
- Idhifa has a black box warning for differentiation syndrome, which can be fatal if not treated. If differentiation syndrome is suspected, corticosteroid therapy and hemodynamic monitoring should be initiated until symptom resolution.
- The Abbott RealTime™ IDH2 assay is an FDA-approved test to detect presence of IDH2 mutations.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AML	100 mg PO QD; may reduce to 50 mg PO QD for toxicities	100 mg/day

VI. Product Availability

Tablets: 50 mg, 100 mg

VII. References

1. Idhifa Prescribing Information. Summit, NJ: Celgene Corporation; August 2017. Available at: www.idhifa.com. Accessed July 30, 2018.
2. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 1.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed July 30, 2018.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 30, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.05.17	11.17

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

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.