Clinical Policy: Enasidenib (Idhifa)

Reference Number: PA.CP.PHAR.363
Effective Date: 10.17.18
Last Review Date: 10.17.18

Revision Log

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 PA Health & Wellness® 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. Presence of an IDH2 mutation;
4. 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);
5. 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: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
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: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

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 – PA.CP.PMN.53 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.	10/18	