Clinical Policy Title:	Enasidenib
Policy Number:	RxA.176
Drug(s) Applied:	Idhifa®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Enasidenib (Idhifa®) is an isocitrate dehydrogenase-2 (IDH2) inhibitor. It is indicated for the 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
enasidenib (Idhifa®)	AML	100 mg by mouth once daily	100 mg/day

Dosage Forms

- Tablets: 50 mg, 100 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 $\geq$ 18 years;
4. Member meets one of the following (a orb):
   a. Age is 60 years or older s and member meets i or ii:
      i. Member is not a candidate for intensive remission induction therapy;
      ii. Idhifa is prescribed as post-induction therapy following response to previous lower intensity therapy with same regimen;
   b. Members with relapsed/refractory disease disease must meet i or ii:
      i. Prescribed as monotherapy;

ii. Prescribed as a component of repeating the initial successful induction regimen;

5. Presence of an IDH2 mutation;
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).*

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

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications 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).*

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

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug	Dosing Regimen	Dose Limit/Maximum Dose
Low intensity therapy (azacytidine (Vidaza®), decitabine (Dacogen®)) Venclexta® (venetoclax)-based therapy (in combination with azacytidine (Vidaza®), decitabine (Dacogen®), or low-dose cytarabine)	Varies	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

- Differentiation syndrome is a condition that affects blood cells which may be life-threatening or lead to death if not treated. Differentiation syndrome has happened within 1 day and up to 5 months after starting Idhifa®.

References

1. Idhifa® Prescribing Information. Summit, NJ: Celgene Corporation; November 2020. Available at: www.idhifa.com. Accessed February 24, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed March 22, 2021.
3. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 2.2021-March 2, 2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf . Accessed March 22, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4. Commercial approval duration was updated from “Length of benefit to 6 months for initial approval criteria & 12 months for continued therapy approval. 5. Therapeutic alternatives updated based on NCCN V3.2020 guidelines for AML IDH2 mutation. 6. References were reviewed and updated.	07/08/2020	09/14/2020
Policy was reviewed: 1. Dosing information Abbreviated form PO changed to “by mouth” 2. Therapeutic Alternatives verbiage changed to “Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management	02/24/2021	06/10/2021

requirements.” 3. Updated Appendix D. 4. References were updated. 5. Initial approval criteria has been updated per NCCN AML guideline recommendation under section I.A.4.		