POLICY NUMBER UM ONC_1323	SUBJECT Idhifa™ (enasidenib)		DEPT/PROGRAM UM Dept	PAGE 1 OF 3
DATES COMMITTEE REVIEWED 09/13/17, 09/21/18, 08/14/19, 12/11/19	APPROVAL DATE December 11, 2019	EFFECTIVE DATE December 11, 2019	COMMITTEE APPROVAL DATES (latest version listed last) 09/13/17, 09/21/18, 08/14/19	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		NCQA STANDARDS UM 2	ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

To define and describe the accepted indications for Idhifa (enasidenib) usage in the treatment of cancer.

II. DEFINITIONS

Idhifa (enasidenib): is an oral isocitrate dehydrogenase-2 (IDH2) inhibitor that targets the mutant IDH2 variants including R140Q, R172S, and R172K; IDH2 inhibition decreases levels of the oncologic metabolite, 2-hydroxyglutarate (2-HG), and causes increased myeloid differentiation, increased mature myeloid cell count, and reduced blast counts in IDH2-mutated acute myelogenous leukemia. This is the first FDA approval for relapsed or refractory AML specifically with an IDH2 mutation. The FDA concurrently approved a companion diagnostic, the RealTime IDH2 Assay, used to detect the IDH2 mutation.

Idhifa (enasidenib) is FDA approved for the treatment of adult patients with relapsed or refractory acute myeloid leukemia with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.

Idhifa (enasidenib) is available as 50mg and 100 mg tablets.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Idhifa (enasidenib) may be considered medically necessary when any of the following selection criteria is met:

1. **Acute Myeloid Leukemia (AML)**
    a. The member has a confirmed diagnosed of AML by bone marrow aspiration and/or biopsy and **ONE** of the following:
        i. As treatment induction when not a candidate for intensive remission induction therapy or declines intensive therapy **OR**
        ii. As post-remission therapy following response to previous lower intensity therapy **OR**
        iii. For relapse or refractory disease **AND**

iv. Documented IDH2 gene-mutation as detected by an FDA approved test, Real Time IDH2 Assay.

Exclusion Criteria: Idhifa (enasidenib) is not considered medically necessary when any of the following selection criteria is met:

1. Idhifa (enasidenib) is being used after disease progression with the same regimen.
2. Concurrent use with other systemic anticancer therapy or radiotherapy.
3. Dosing exceeds single dose limit of Idhifa (enasidenib) 100 mg.
4. Treatment exceeds the maximum limit of 60 (50 mg) tablets/month or 30 (100 mg) tablets/month.
5. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Idhifa (enasidenib) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration**: 100 mg PO once daily until disease progression. Treat patients without disease progression for a minimum of 6 months to allow time for clinical response. Therapy interruption, dose reduction, or drug discontinuation may be necessary in patients who develop toxicity.
2. **Dosage Adjustments:**
    a. Geriatric: No dose adjustment necessary based on age.
    b. Differentiation syndrome: Interrupt therapy if severe pulmonary symptoms occur requiring intubation or ventilator support or renal dysfunction persisting for over 48 hours following corticosteroid initiation; resume therapy with improvement to Grade 2 or below.
    c. Noninfectious leukocytosis (WBC greater than 30 x 10^9/L): Interrupt therapy if no improvement with hydroxyurea is seen; resume at 100 mg orally once daily when WBC is less than 30 x 10^9/L.
    d. Bilirubin greater than 3 times ULN for 2 weeks or more without elevated transaminases or other hepatic disorders: Reduce dose to 50 mg orally daily; resume at 100 mg orally daily if bilirubin elevation resolves to less than 2 times ULN.
    e. Other Grade 3 or higher toxicity, including tumor lysis syndrome: Interrupt therapy until toxicity resolves to Grade 2 or lower; resume at 50 mg orally daily and increase to 100 mg orally daily if toxicities resolve to Grade 1 or lower; discontinue if grade 3 or higher toxicity recurs.
3. **Monitoring**
    a. Screen for presence of IDH2 mutations prior to initiation of treatment.
    b. Disease response or stabilization may indicate efficacy.
    c. Blood counts and blood chemistries: Prior to treatment and at least every 2 weeks for the first 3 months during treatment.

d. Pregnancy test prior to treatment: May cause fetal harm when administered to pregnant women; avoid pregnancy during use regardless of which partner is receiving treatment and for a minimum of 1 month after therapy.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Idhifa prescribing information. Celgene Corporation. Summit, NJ 2017.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.