Drug Policy:

Idhifa™ (enasidenib)

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, 08/12/20, 08/11/21, 11/15/21, 05/11/22, 07/13/22	**APPROVAL DATE** July 13, 2022	**EFFECTIVE DATE** July 29, 2022	**COMMITTEE APPROVAL DATES** 09/13/17, 09/21/18, 08/14/19, 12/11/19, 08/12/20, 08/11/21, 11/15/21, 05/11/22, 07/13/22	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM v8: UM 1-2; UM 2-1	**NCQA STANDARDS** UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Idhifa (enasidenib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines OR
2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines OR

3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways (http://pathways.newcenturyhealth.com/) when applicable, otherwise shall follow NCH drug policies AND
4. Continuation requests of previously approved, non-preferred medication are not subject to this provision AND
5. When applicable, generic alternatives are preferred over brand-name drugs AND
6. When there is a documented drug shortage, disease progression, contraindication, or confirmed intolerance to a Preferred drug/regimen, per NCH Policy and Pathway, the available alternative product may be used if deemed medically appropriate and the indication is listed in a standard reference compendia or accepted peer review literature. For a list of current drug shortages, please refer to FDA drug shortage website in the reference section.

B. Acute Myeloid Leukemia (AML) with Positive IDH-2 Mutation

1. The member has a confirmed diagnosed of IDH-2 mutation positive AML (confirmed with any FDA approved test) and Idhifa (enasidenib) may be used either as a single agent for relapsed or refractory disease OR
2. Idhifa(enasidenib) may be used as first line therapy in IDH2 mutation positive AML in combination with either azacitidine or decitabine, in a member who is not a suitable candidate for standard induction chemotherapy.

III. EXCLUSION CRITERIA

A. Idhifa (enasidenib) is being used after disease progression with the Idhifa or an Idhifa-containing regimen.

B. Dosing exceeds single dose limit of Idhifa (enasidenib) 100 mg.

C. Treatment exceeds the maximum limit of 60 (50 mg) tablets/month or 30 (100 mg) tablets/month.

D. Investigational use of Idhifa (enasidenib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
3. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
4. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
5. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
6. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.

7. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
8. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. DiNardo CD, et al. Enasidenib plus azacitidine versus azacitidine alone in patients with newly diagnosed, mutant-IDH2 acute myeloid leukaemia (AG221-AML-005): a single-arm, phase 1b and randomised, phase 2 trial. Lancet Oncol. 2021 Nov;22(11):1597-1608.

B. Venugopal S, et al. Efficacy and safety of enasidenib and azacitidine combination in patients with IDH2 mutated acute myeloid leukemia and not eligible for intensive chemotherapy. Blood Cancer J. 2022 Jan 25;12(1):10.

C. Idhifa prescribing information. Celgene Corporation. Summit, NJ 2020.

D. Clinical Pharmacology Elsevier Gold Standard 2022.

E. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2022.

F. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2022.

G. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2022.

H. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

I. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.

J. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.