Medical Policy

Khapzory® (levoleucovorin)	
MEDICAL POLICY NUMBER	Med_Clin_Ops_086
CURRENT VERSION EFFECTIVE DATE	January 1, 2024
APPLICABLE PRODUCT AND MARKET	*Individual Family Plan:* All Plans *Small Group*: All Plans *Medicare Advantage:* All Plans

Brand New Day/Central Health Medicare Plan develops policies and makes coverage determinations using credible scientific evidence including but not limited to MCG™ Health Guidelines, the ASAM Criteria™, and other third party sources, such as peer-reviewed medical literature generally recognized by the relevant medical community, physician specialty society recommendations, and expert opinion as relevant to supplement those sources. Brand New Day/Central Health Medicare Plan Medical Policies, MCG™ Guidelines, and the ASAM Criteria™ are not intended to be used without the independent clinical judgment of a qualified health care provider considering the individual circumstances of each member's case. The treating health care providers are solely responsible for diagnosis, treatment, and medical advice. Members may contact Brand New Day/Central Health Medicare Plan Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Brand New Day/Central Health Medicare Plan Medical Policy may contact the Health Plan. Brand New Day/Central Health Medicare Plan policies and practices are compliant with federal and state requirements, including mental health parity laws.

If there is a difference between this policy and the member specific plan document, the member benefit plan document will govern. For Medicare Advantage members, Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), govern. Refer to the CMS website at http://www.cms.gov for additional information.

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PURPOSE

The purpose of this policy is to establish the clinical review criteria that support the determination of medical necessity for Khapzory® (levoleucovorin) therapy.

POLICY

Prior Authorization and Medical Review is required.

Coverage for Khapzory will be provided for 90 days and may be renewed.

A. Patient is at least 6 years old; **AND**
B. Patient does not have pernicious anemia or vitamin B12 deficiency megaloblastic anemia; **AND**
C. Racemic d,l-leucovorin calcium is not obtainable (in any dosage strength) as confirmed by FDA Drug shortage website located at: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm; **AND**

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Bone Cancer (Osteosarcoma)

A. Patient has a diagnosis of osteosarcoma; **AND**
B. Patient is undergoing high-dose methotrexate chemotherapy treatment; **AND**
C. Khapzory will be used as rescue therapy in combination with chemotherapy regimen containing high dose methotrexate.

Reduction of toxicity due to impaired elimination or inadvertent overdose with folic acid antagonists

A. Patient is undergoing treatment with a folic acid antagonist, such as methotrexate; **AND**
B. Patient has developed toxicity due to impaired elimination or inadvertent overdosage of the folic acid antagonist (i.e., methotrexate).

Colorectal cancer

A. Patient has a diagnosis of metastatic colorectal cancer; **AND**
B. Khapzory will be used in combination with fluorouracil.

LIMITATIONS/EXCLUSIONS

1. Any indication other than those listed above due to insufficient evidence of therapeutic value
2. Patients who have had severe hypersensitivity to leucovorin products, folic acid, or folinic acid
3. Treatment of pernicious anemia and megaloblastic anemia secondary to the lack of vitamin B12

BACKGROUND

Khapzory is a folate analog and the active isomer of 5-formyl tetrahydrofolic acid (THF). It counteracts the therapeutic and toxic effects of folic acid antagonists such as methotrexate, which act by inhibiting dihydrofolate reductase. In colorectal cancer, levoleucovorin enhances the therapeutic and toxic effects of fluorouracil, which is metabolized to 5-fluoro-2'-deoxyuridine-5'-monophosphate (FdUMP).
Levoleucovorin stabilizes the binding of FdUMP to thymidylate synthase, thereby enhancing the inhibition of thymidylate synthase.

DEFINITIONS

1. KHAPZORY (levoleucovorin) for injection, for intravenous use Initial U.S. Approval: 1952 (d,l-leucovorin)
    a. KHAPZORY (levoleucovorin) for injection is a sterile, preservative-free, white to yellowish lyophilized powder in a single-dose vial.

CODING

Applicable NDC Codes	
68152-0112-01	KHAPZORY, levoleucovorin injection vial of 175 mg
68152-0114-01	KHAPZORY, levoleucovorin injection vial of 300 mg

Applicable Procedure Code

Khapzory

J0642	Khapzory (levoleucovorin), for injection.

Applicable Diagnosis Codes	
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.8	Malignant neoplasm of overlapping sites of small intestine
C17.9	Malignant neoplasm of small intestine, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C40.00	Malignant neoplasm of scapula and long bones of unspecified upper limb
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.20	Malignant neoplasm of long bones of unspecified lower limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.30	Malignant neoplasm of short bones of unspecified lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.80	Malignant neoplasm of overlapping sites of bone and articular cartilage of unspecified limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.90	Malignant neoplasm of unspecified bones and articular cartilage of unspecified limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb

C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.068	Personal history of other malignant neoplasm of small intestine
Z85.830	Personal history of malignant neoplasm of bone

EVIDENCE BASED REFERENCES

1. Product Information: KHAPZORY(TM) intravenous injection, levoleucovorin intravenous injection. Acrotech Biopharma LLC (per FDA), East Windsor, NJ, 2020.

POLICY HISTORY

Original Effective Date	November 11, 2021
Revised Date	February 2, 2022 – Annual Review and approval (no policy revisions made) February 28, 2023 – Annual Review and approval (no policy revisions made) March 1, 2023 – Adopted by MA UM Committee (no policy revisions made) January 1, 2024 - Updated to Brand New Day/Central Health Medicare Plan (no policy revisions made)

Approved by Pharmacy and Therapeutics Committee on 2/28/23