POLICY NUMBER UM ONC_1225	SUBJECT Voraxaze™ (glucarpidase)		DEPT/PROGRAM UM Department	PAGE 1 OF 3
DATES COMMITTEE REVIEWED 10/03/12, 11/13/13, 04/02/15, 05/24/16, 03/08/17, 11/14/18, 11/13/19, 12/11/19	APPROVAL DATE December 11, 2019	EFFECTIVE DATE December 11, 2019	COMMITTEE APPROVAL DATES (latest version listed last) 10/03/12, 11/13/13, 04/02/15, 05/24/16, 03/08/17, 11/14/18, 11/13/19, 12/11/19	
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 Voraxaze (glucarpidase) usage in the treatment of cancer.

II. DEFINITIONS

Voraxaze (glucarpidase): is a recombinant carboxypeptidase that hydrolyzes the carboxyl-terminal glutamate residue from folic acid and antifolates such as methotrexate. Glucarpidase converts methotrexate to its inactive metabolites, 4-deoxy-4-amino-N10-methylpteroic acid (DAMPA) and glutamate, providing a non-renal route of elimination.

Voraxaze (glucarpidase) is FDA approved for the treatment of toxic plasma methotrexate concentrations (>1 micromole per liter) in patients with delayed methotrexate clearance due to impaired renal function.

Voraxaze (glucarpidase) is available in intravenous powder for solution: 1,000 units.

III. POLICY

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

Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must be supported by, at minimum, two peer reviewed citations. If references are not produced, delays may occur to the processing of such request.

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

1. **Methotrexate Toxicity**
    a. Voraxaze (glucarpidase) is being used in members with ALL of the following conditions:
        i. Delayed methotrexate clearance due to renal impairment (i.e. creatinine clearance is 60 ml/min or less)
        ii. Plasma concentration of methotrexate is > 1 micromole per liter prior to the first dose of glucarpidase (patients who received a second dose failed to achieve efficacy).
        iii. Administered with IV hydration, urinary alkalinization, and leucovorin therapy (not given within 2 hours before or after glucarpidase).

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

1. The member has normal or mildly impaired renal function (i.e. creatinine clearance greater than 60 mL/min).
2. Voraxaze (glucarpidase) is not used in members with expected clearance of methotrexate (i.e. the plasma methotrexate concentrations are within 2 standard deviations of the mean methotrexate excretion curve, specific for methotrexate dose).
3. The member does not have toxic levels of methotrexate of > 1 mcmol/L.
4. Dosing exceeds single dose limit of Voraxaze (glucarpidase) 50 units/kg.
5. Treatment with Voraxaze (glucarpidase) exceeds the maximum duration limit of one dose (patients who received a second dose failed to achieve efficacy).
6. 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 Voraxaze (glucarpidase) 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:** 50 units/kg as a single IV bolus injection over 5 minutes. While leucovorin rescue should continue in conjunction with glucarpidase, leucovorin is a glucarpidase substrate and should not be given within 2 hours before or after glucarpidase. For leucovorin use within 48 hours of glucarpidase administration, administer the previous leucovorin dose. Beyond 48 hours following glucarpidase injection, leucovorin should be dosed on the methotrexate concentration, and leucovorin rescue continued until the plasma methotrexate level remains below the intervention limit for 3 days.
2. **Dosage Adjustments:** Dosage adjustments are not required for renal or hepatic impairment.
3. **Monitoring:**
    a. Normalization of methotrexate concentrations may be indicative of efficacy.
    b. Monitor methotrexate concentrations using a chromatographic method for 48 hours following administration of glucarpidase. Measurement using immunoassays may result in overestimated methotrexate concentrations.
    c. Serum creatinine/BUN.

V. APPROVAL AUTHORITY

1. Review – Utilization Management Department
2. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Voraxaze prescribing information. BTG International Inc, West Conshohocken, PA 2019
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.