POLICY NUMBER UM ONC_1377	SUBJECT Brukinsa (zanubrutinib)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATES COMMITTEE REVIEWED 01/08/20	APPROVAL DATE January 8, 2020	EFFECTIVE DATE January 8, 2020	COMMITTEE APPROVAL DATES (latest version listed last) 01/08/20	
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 Brukinsa (zanubrutinib) usage in the treatment of cancer.

II. DEFINITIONS

Brukinsa (zanubrutinib): is a second generation Bruton tyrosine kinase (BTK) inhibitor. BTK is a signaling molecule early within the B-cell antigen receptor (BCR) signaling cascade. Signaling from BCR regulates several pro-survival mechanisms of B-cells, including proliferation, trafficking, chemotaxis, and adhesion. Zanubrutinib forms a covalent bond with a cysteine residue in the BTK active site leading to inhibition of BTK enzymatic activity, inhibition of malignant B-cell proliferation, and reduced tumor growth.

Brukinsa (zanubrutinib) is FDA approved for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

Brukinsa (zanubrutinib) is available in 80 mg capsules.

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: Brukinsa (zanubrutinib) may be considered medically necessary when any of the following selection criteria are met:

1. **PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:**
   a. 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
   b. 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
   c. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways when applicable, otherwise shall follow NCH drug policies: http://pathways.newcenturyhealth.com AND
   d. Continuation requests of previously approved non-preferred medication are not subject to this provision AND
   e. When available, generic alternatives are preferred over brand-name drugs.

f. Mantle Cell Lymphoma

i. The member has mantle cell lymphoma **AND**

ii. Has disease progression on at least one prior treatment regimen **AND**

iii. Brukinsa (zanubrutinib) is being used as a single agent.

Exclusion Criteria: Brukinsa (zanubrutinib) is not considered medically necessary when any of the following selection criteria are met:

1. Brukinsa (zanubrutinib) is being used after disease progression with the same regimen or prior BTK inhibitor (e.g. Ibrutinib).
2. Clinically significant active cardiovascular disease.
3. Uncontrolled systemic infection or infection requiring anti-microbial therapy.
4. Dosing exceeds single dose limit of Brukinsa (zanubrutinib) 320 mg.
5. Treatment exceeds the maximum limit of 120 (80mg) tablets/month.
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 Brukinsa (zanubrutinib) 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:** 160 mg taken orally twice daily, or 320 mg taken orally once daily until disease progression or unacceptable toxicity.
2. **Dosage Adjustments:**
    a. Renal impairment (mild to moderate, CrCl 30 mL/min or greater): No dosage modification necessary.
    b. Renal impairment (severe, CrCl less than 30 mL/min): Monitor patients for adverse reactions.
    c. Hepatic impairment (mild to moderate): No dosage modification necessary; monitor for adverse reactions.
    d. Hepatic impairment (severe): 80 mg orally twice daily; monitor for adverse reactions .
    e. Geriatric: No overall differences in safety or effectiveness were observed between younger and older patients.
    f. Hemodialysis: Monitor patients for adverse reactions.
    g. Asymptomatic lymphocytosis: Continue taking usual dosage.
    h. Febrile neutropenia (Grade 3): Interrupt therapy; once toxicity has resolved to Grade 1 or lower or baseline, resume therapy (first occurrence, 160 mg twice daily or 320 mg once daily; second occurrence, 80 mg twice daily or 160 mg once daily; third occurrence, 80 mg once daily; fourth occurrence, discontinue use).
    i. Neutropenia (Grade 4, lasting more than 10 consecutive days): Interrupt therapy; once toxicity has resolved to Grade 1 or lower or baseline, resume therapy (first occurrence, 160 mg twice daily or 320 mg once daily; second occurrence, 80 mg twice daily or 160 mg once daily; third occurrence, 80 mg once daily; fourth occurrence, discontinue use).

j. Non-hematological toxicity (Grade 3 or greater): Interrupt therapy; once toxicity has resolved to Grade 1 or lower or baseline, resume therapy (first occurrence, 160 mg twice daily or 320 mg once daily; second occurrence, 80 mg twice daily or 160 mg once daily; third occurrence, 80 mg once daily; fourth occurrence, discontinue use).

k. Thrombocytopenia (Grade 3 with significant bleeding): Interrupt therapy; once toxicity has resolved to Grade 1 or lower or baseline, resume therapy (first occurrence, 160 mg twice daily or 320 mg once daily; second occurrence, 80 mg twice daily or 160 mg once daily; third occurrence, 80 mg once daily; fourth occurrence, discontinue use).

l. Thrombocytopenia (Grade 4, lasting more than 10 consecutive days): Interrupt therapy; once toxicity has resolved to Grade 1 or lower or baseline, resume therapy (first occurrence, 160 mg twice daily or 320 mg once daily; second occurrence, 80 mg twice daily or 160 mg once daily; third occurrence, 80 mg once daily; fourth occurrence, discontinue use).

m. Concomitant use (strong CYP3A inhibitor): 80 mg orally once daily; interrupt dose as necessary for adverse reactions. Following discontinuation of the CYP3A inhibitor, resume the previous dose of zanubrutinib.

n. Concomitant use (moderate CYP3A inhibitor): 80 mg orally twice daily; modify dose as necessary for adverse reactions. Following discontinuation of the CYP3A inhibitor, resume the previous dose of zanubrutinib.

o. Concomitant use (moderate or strong CYP3A inducer): Avoid use

3. **Monitoring**

a. Evidence of disease response or stabilization indicates efficacy.

b. CBC: during treatment, including differential

c. Benefit/risk of withholding treatment: For 3 to 7 days pre-and post-surgery depending upon the type of surgery and the risk of bleeding.

d. Signs and symptoms of atrial fibrillation and atrial flutter.

e. Signs and symptoms of bleeding.

f. Signs and symptoms of infection, including fever.

g. Pregnancy test: In females with reproductive potential, prior to initiating therapy.

V. APPROVAL AUTHORITY

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

VI. ATTACHMENTS

None

VII. REFERENCES

1. Brukinsa (zanubrutinib) PI prescribing information. BeiGene USA, Inc. San Mateo, CA 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.