Clinical Policy: Zanubrutinib (Brukinsa)
Reference Number: CP.PHAR.467
Effective Date: 03.01.20
Last Review Date: 02.21
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Zanubrutinib (Brukinsa™) is a Bruton tyrosine kinase (BTK) inhibitor.

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

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Brukinsa is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Mantle Cell Lymphoma (must meet all):
      1. Diagnosis of MCL;
      2. Prescribed by or in consultation with an oncologist or hematologist;
      3. Age ≥ 18 years;
      4. For brand Brukinsa request, medical justification supports inability to use generic zanubrutinib, if available, (e.g., contraindications to excipients);
      5. Member has received ≥ 1 prior therapy (see Appendix B);
      6. Request meets one of the following (a or b):*
         a. Dose does not exceed 320 mg (4 capsules) per day;
         b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit
B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
A. Mantle Cell Lymphoma (must meet all):
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Brukinsa for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Brukinsa request, medical justification supports inability to use generic zanubrutinib, if available, (e.g., contraindications to excipients);
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 320 mg (4 capsules) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
BTK: Bruton tyrosine kinase
FDA: Food and Drug Administration
MCL: mantle cell lymphoma
NCCN: National Comprehensive Cancer Network
Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CALGB (rituximab + methotrexate + cyclophosphamide, doxorubicin, vincristine, prednisone; etoposide, cytarabine, rituximab; carmustine, etoposide, cyclophosphamide/autologous stem cell rescue; rituximab)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate/ cytarabine) + rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>NORDIC (rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone/rituximab + cytarabine)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>RCHOP/RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, dexamethasone, cisplatin, cytarabine)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>RDHAP (rituximab, dexamethasone, cisplatin, cytarabine)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>RCHOP/RICE (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, ifosfamide, carboplatin, etoposide)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Bendeka® (bendamustine) + Rituxan® (rituximab)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Revlimid® (lenalidomide) + Rituxan® (rituximab)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCL</td>
<td>160 mg PO BID or 320 mg PO QD</td>
<td>320 mg/day</td>
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</table>

VI. Product Availability
Capsule: 80 mg

VII. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Policy created</td>
<td>01.07.20</td>
<td>02.20</td>
</tr>
<tr>
<td>1Q 2021 annual review: oral oncology generic redirection language added; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.</td>
<td>11.09.20</td>
<td>02.21</td>
</tr>
</tbody>
</table>

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to
recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:
**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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