Pharmacy Medical Necessity Guidelines: Imbruvica® (ibrutinib)

Effective: September 18, 2017

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<th>Prior Authorization Required</th>
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<th>Type of Review – Care Management</th>
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<th>Pharmacy (RX) or Medical (MED) Benefit</th>
<th>Department to Review</th>
<th>Fax Numbers:</th>
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<tr>
<td>RX</td>
<td>RXUM</td>
<td>RXUM: 617.673.0988</td>
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This Pharmacy Medical Necessity Guideline applies to the following:

**Tufts Health Plan Commercial Plans**
- Tufts Health Plan Commercial Plans – large group plans
- Tufts Health Plan Commercial Plans – small group and individual plans

**Tufts Health Public Plans**
- Tufts Health Direct – Health Connector
- Tufts Health Together – A MassHealth Plan
- Tufts Health RITogether – A RIte Care + Rhody Health Partners Plan

**Tufts Health Freedom Plan products**
- Tufts Health Freedom Plan – large group plans
- Tufts Health Freedom Plan – small group plans

**Fax Numbers:**

- RXUM: 617.673.0988

**Note:** For Tufts Health Plan Medicare Preferred Members, please refer to the Tufts Health Plan Medicare Preferred Prior Authorization Criteria. Background, applicable product and disclaimer information can be found on the last page.

**OVERVIEW**

Non-Hodgkin’s lymphomas are a heterogeneous group of lymphoproliferative disorders originating in B-lymphocytes, T-lymphocytes, or natural killer cells. B-cell lymphomas include, but are not limited to, chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), and Waldenstrom macroglobulinemia (WM). The cancer cell in CLL is known as a small lymphocyte and is mainly found in the blood and bone marrow. CLL is a slow growing disease for which standard treatments are not often curative. The cancer cell size in MCL is small to medium. At diagnosis, MCL is usually widespread in the lymph nodes, bone marrow, and spleen. MCL is not a fast growing lymphoma, but it can be challenging to treat. WM, also known as lymphoplasmacytic lymphoma, is not a common type of lymphoma. The cancer cells are small, found primarily in the bone marrow, and make large amounts of macroglobulin, an abnormal protein.

Treatment options for CLL, MCL, and WM include chemotherapy, targeted drugs, biological therapy (immunotherapy), radiation therapy, stem cell transplant, and plasmapheresis (for WM only). Imbruvica (ibrutinib) is considered a targeted therapy and is a first-in-class Bruton tyrosine kinase (BTK) inhibitor. The agent works by blocking the protein BTK inside lymphoma cells resulting in impaired cell growth and survival.

**FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS**

Imbruvica (ibrutinib) is indicated for the treatment of patients with MCL who have received at least one prior therapy, CLL/small lymphocytic lymphoma (SLL), CLL/SLL with 17p deletion, WM, and marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy. Imbruvica (ibrutinib) is also indicated for the treatment of adult patients with chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy.

For MCL, accelerated approval was granted based on overall response rate. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

For MZL, accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

**COVERAGE GUIDELINES**

The plan may authorize coverage of Imbruvica (ibrutinib) for Members, when all of the following criteria are met:
Mantle cell lymphoma
1. Documented diagnosis of mantle cell lymphoma
2. The prescribing physician is an oncologist
3. The Member has been treated with at least one prior therapy

Chronic lymphocytic leukemia and small lymphocytic lymphoma with or without 17p deletion
1. The Member has a diagnosis of chronic lymphocytic leukemia or small lymphocytic lymphoma with or without 17p deletion
2. The prescribing physician is an oncologist

Waldenstrom’s macroglobulinemia
1. Documented diagnosis of Waldenstrom’s macroglobulinemia
2. The prescribing physician is an oncologist

Marginal Zone Lymphoma
1. Documented diagnosis of marginal zone lymphoma with required systemic therapy
2. The Member has been treated with at least one prior anti-CD20-based therapy
3. The prescribing physician is an oncologist

Chronic Graft versus Host Disease
1. Documented diagnosis of chronic graft versus host disease
2. The Member has been treated with at least one systemic therapy

Off-label Use Coverage for Other Cancer Diagnoses
Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia, or in the medical literature, or by the Massachusetts commissioner of Insurance (commissioner) under the provisions of the "Sullivan Law": (M.G.L. c.175, s.47K).

The plan may authorize coverage for use for other cancer diagnoses provided effective treatment with such drug is recognized as a "Medically Accepted Indication" according to the National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium as indicated by a Category 1 or 2A for quality of evidence and level of consensus.

Note: The plan requires prescribers to submit clinical documentation supporting the drug’s effectiveness in treating the intended malignancy, including the applicable NCCN guideline(s).

In cases where the requested off-label use for the diagnosis is not recognized by the NCCN Drugs and Biologics Compendium, the plan will follow the Centers for Medicare and Medicaid Services (CMS) guidance, unless otherwise directed by the commissioner, and accept clinical documentation referenced in one of the other "Standard Reference Compendia” noted below or supported by clinical research that appears in a regular edition of a "Peer-Reviewed Medical Literature" noted below.

"Standard Reference Compendia"
1. American Hospital Formulary Service – Drug Information (AHFS-DI)
2. Thomson Micromedex DrugDex
3. Clinical Pharmacology (Gold Standard)
4. Wolters Kluwer Lexi-Drugs

"Peer Reviewed Medical Literature"
When the plan evaluates the evidence in published, peer-reviewed medical literature, consideration will be given to the following:

1. Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients.
4. Whether the study is appropriate to address the clinical question.
   a. whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question (e.g., in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover);
   b. 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; and,
   c. that case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.

LIMITATIONS
1. The plan will not authorize the use of Imbruvica (ibrutinib) for conditions other than those listed above without appropriate documentation.

CODES
None

REFERENCES

APPROVAL HISTORY
February 11, 2014: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:
- October 7, 2014: Added criteria for chronic lymphocytic leukemia with 17p deletion
- March 10, 2015: Added criteria for Waldenstrom’s Macroglobulinemia (WM)
- January 1, 2016: Administrative change to rebranded template.
- February 9, 2016: No changes.
- April 12, 2016: Updated criteria for chronic lymphocytic leukemia based on Food and Drug Administration labeling to no longer require documentation of at least one previous therapy.
- July 12, 2016: No changes. Effective October 10, 2016 Medical Necessity Guideline applies to Tufts Health Together.
- September 12, 2017: Added coverage criteria for new supplemental indication of chronic graft versus host disease.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION
Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. They are used in conjunction with a Member's benefit document and in coordination with the Member's physician(s). The plan makes coverage decisions on a case-by-case basis considering the individual Member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

This Pharmacy Medical Necessity Guideline does not apply to Uniformed Services Family Health Plan Members or to certain delegated service arrangements. Unless otherwise noted in the Member's benefit document or applicable Pharmacy Medical Necessity Guideline, Pharmacy Medical Necessity Guidelines do not apply to CareLink℠ Members. For self-insured plans, drug coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a coverage guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern. Applicable state or federal mandates will take precedence.

For Tufts Health Plan Medicare Preferred, please refer to Tufts Health Plan Medicare Preferred Prior Authorization Criteria.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to Member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.

Provider Services