Drug Therapy Guidelines	Applicable	Imbruvica® (ibrutinib)
Medical Benefit		**Effective:** 8/15/18
Pharmacy- Formulary 1	x	**Next Review:** 6/19
Pharmacy- Formulary 2	x	**Date of Origin:** 3/14
Pharmacy- Formulary 3/Exclusive	x	**Review Dates:** 12/13, 12/14, 6/15, 6/16, 6/17, 6/18
Pharmacy- Formulary 4/AON	x	

I. Medication Description

Ibrutinib is an oral inhibitor of Bruton's tyrosine kinase (BTK). It works by inhibiting BTK, an enzyme responsible for proliferation, differentiation, apoptosis, and cell migration of B-cells.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage of Imbruvica is available when the following criteria have been met:

- Member is at least 18 years of age **AND**
- The medication is prescribed by a hematologist/oncologist **AND**
- The requested use is supported by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (NCCN Guidelines®) and/or NCCN Drugs & Biologics Compendium (NCCN Compendium®) with a recommendation of category level 1 or 2A.

Coverage of Imbruvica is also available for the treatment of Chronic Graft-versus-Host Disease (cGVHD) when the following criteria have been met:

- Member is at least 18 years of age **AND**
- The medication is prescribed by a hematologist/oncologist **AND**
- The member has failed first-line therapy with corticosteroids and requires additional treatment **OR**
- If corticosteroids are medically contraindicated, the member has failed therapy with at least one line of systemic therapy (ex. mycophenolate, tacrolimus, cyclosporine, etc) and requires additional treatment

IV. Quantity Limitations

Coverage is available as follows:

- 70 mg capsules: up to 120 capsules per 30 days
- 140 mg capsules: up to 120 capsules per 30 days
- 140 mg tablets: up to 28 tablets per 28 days
- 280 mg tablets: up to 28 tablets per 28 days
- 420 mg tablets: up to 28 tablets per 28 days
- 560 mg tablets: up to 28 tablets per 28 days

V. Coverage Duration

Coverage is available for 6 months and may be renewed

VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Stabilization of disease or in absence of disease progression **AND**
- Absence of unacceptable toxicity from the drug

VII. Billing/Coding Information

Imbruvica is available as:

- Capsules: 70mg and 140mg
- Tablets: 140mg, 280mg, 420mg, and 560 mg

VIII. Summary of Policy Changes

- 3/15/14: new policy
- 3/15/15: Addition of indication for CLL with 17p deletion
- 4/30/15: updated based on NCCN treatment guideline update for use in Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma
- 7/1/15: formulary distinctions made
- 9/15/15: updated to reflect current NCCN treatment guidelines
- 7/19/16: updated to reflect current NCCN treatment guidelines
- 6/21/17: coverage criteria updated to allow use as supported by current NCCN guidelines
- 4/11/18: addition of new capsule/tablet strengths and quantity limits updated
- 8/15/18: addition of indication for cGVHD and corresponding coverage criteria

IX. References

1. Imbruvica [prescribing information]. Horseham, PA 19044: Janssen Biotech, Inc; Revised 2/2018.
2. Clinical Pharmacology Online. Imbruvica. Elsevier/Gold Standard. Accessed 5/2018.
3. Wang M, Rule S, Martin P, et al, Targeting BTK with Ibrutinib in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med. 2013;369(6):507-516.
4. Byrd JC, Furman RR, Coutre SE, et al. Targeting BTK with Ibrutinib in Relapsed Chronic Lymphocytic Leukemia. N Engl J Med. 2013;369:32-42
5. National Comprehensive Cancer Network® (NCCN) Clinical Guidelines in Oncology. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 4.2018. Accessed 3/2018.
6. National Comprehensive Cancer Network® (NCCN) Clinical Guidelines in Oncology. B-cell Lymphomas. Version 2.2018. Accessed 3/2018.
7. National Comprehensive Cancer Network® (NCCN) Clinical Guidelines in Oncology. Hairy Cell Leukemia. Version 2.2018. Accessed 3/2018.

8. National Comprehensive Cancer Network® (NCCN) Compendium: Ibrutinib. Accessed 3/2018.
9. National Comprehensive Cancer Network ® (NCCN) Clinical Guidelines in Oncology. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 1.2018. Accessed 3/2018.
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11. Chao N, Negrin R, Rosmarin A et al. Treatment of chronic graft-versus-host disease. UpToDate, Waltham, MA. Accessed May 3, 2018.
12. Dignan F, Amrolia P, Clark A, et al. Diagnosis and management of chronic graft-versus-host disease. *Br J Haematol*. 2012; 158: 46-61.
13. Wolff D, Schleuning M, Von Harsdorf S, et al. Consensus Conference on Clinical Practice in Chronic HvHD: Second-line Treatment of Chronic Graft-versus-Host Disease. ASBMT, 2011; 17(1):1-17.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.