Clinical Policy: Ibrutinib (Imbruvica)

Reference Number: ERX.SPA.08
Effective Date: 04.01.17
Last Review Date: 11.17 Revision Log

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

Description
Ibrutinib (Imbruvica®) is a kinase inhibitor.

FDA Approved Indication(s)
Imbruvica is indicated:

- For the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy
  - 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
- For the treatment of adult patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
- For the treatment of adult patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with 17p deletion
- For the treatment of adult patients with Waldenström's macroglobulinemia (WM)
- For the treatment of adult patients with marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy
  - 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
- For the treatment of adult patients with chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Imbruvica 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. Previously received at least one prior therapy;
3. Dose does not exceed 560 mg/day.

Approval duration: 6 months

B. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all)**:**
1. Diagnosis of CLL or SLL;
2. Dose does not exceed 420 mg/day.

Approval duration: 6 months

C. Waldenstrom's Macroglobulinemia (must meet all)**:**
1. Diagnosis of WM;
2. Dose does not exceed 420 mg/day.

Approval duration: 6 months

D. Marginal Zone Lymphoma (must meet all)**:**

1. Diagnosis of MZL;
2. Previously received at least one prior anti-CD20-based therapy, unless contraindicated;
3. Dose does not exceed 560 mg/day.

Approval duration: 6 months

E. Chronic Graft-Versus-Host Disease (must meet all)**:**

1. Diagnosis of cGVHD;
2. Member has a history of bone marrow/stem cell transplant;
3. Prescribed by or in consultation with an oncologist, hematologist, or bone marrow transplant specialist;
4. Age ≥ 18 years;
5. One of the following (a or b):
   a. Member has failed to respond, has progressed (see Appendix B), or has experienced clinically significant adverse effects to systemic corticosteroid treatment (e.g., prednisone);
   b. If member has contraindication(s) to corticosteroid treatment, failure of at least one prior line of systemic therapy for cGVHD (see Appendix B), unless all are contraindicated;
6. Dose does not exceed 420 mg per day (3 capsules per day).

Approval duration: 6 months

F. Hairy Cell Leukemia (off-label) (must meet all)**:**

1. Diagnosis of hairy cell leukemia;
2. Used as a single-agent therapy for member with disease progression;
3. Documentation supports failure of or presence of clinically significant adverse effects or contraindication to at least two FDA approved medications for hairy cell leukemia (e.g., cladribine, pentostatin, interferon alfa);
4. Request meets one of the following (a or b):
   a. Dose does not exceed 560 mg per day (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*).

Approval duration: 6 months

G. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. MCL, CLL/SLL, WM, MZL and cGVHD (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Imbruvica for MCL, CLL/SLL, WM, MZL, or cGVHD and has received this medication for at least 30 days;
2. Member is responding positively to therapy (e.g., no disease progression or unacceptable toxicity);
3. If request is for a dose increase, new dose does not exceed the following:
   a. For MCL and MZL: 560 mg per day (4 capsules per day);
   b. For CLL/SLL, WM, and cGVHD: 420 mg per day (3 capsules per day).

Approval duration: 12 months

B. Hairy Cell Leukemia (off-label) (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 560 mg per day (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).

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents;

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

cGVHD: chronic graft-versus-host disease
CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
MCL: mantle cell lymphoma
MZL: marginal zone lymphoma
SLL: small lymphocytic lymphoma
WM: Waldenström's macroglobulinemia

Appendix B: General Information

- Prior therapies for MCL include: R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), BR (bendamustine, rituximab), R-CVP (rituximab, cyclophosphamide, vincristine, prednisone), R-DHAP (rituximab, dexamethasone, high dose cytarabine, and cisplatin), and Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone, alternating with high-dose methotrexate and cytarabine, with or without rituximab).
- cGVHD:
  - The National Institutes of Health Working Group recommends that the diagnosis of cGVHD require at least 1 diagnostic manifestation of cGVHD (e.g., poikiloderma or esophageal web) or at least 1 distinctive manifestation (e.g., keratoconjunctivitis sicca) confirmed by pertinent biopsy or other relevant tests in the same or another organ.
  - Corticosteroids are the mainstay of initial systemic treatment for patients with cGVHD. In addition to corticosteroids, components of second-line pharmacologic treatments include, but are not limited to, mycophenolate mofetil, calcineurin inhibitors (e.g., cyclosporine, tacrolimus), sirolimus, and rituximab.
  - Steroid-refractory chronic GVHD is defined as either failure to improve after at least 2 months, or progression after 1 month of standard immunosuppressive therapy, including corticosteroids and cyclosporine.

Appendix C: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
rituximab (Rituxan)*	MZL: Varies	Can be used alone or as part of RCHOP depending on MZL subtype, histology, and stage of disease
Prednisone†	cGVHD Adults: Prednisone alternating with cyclosporine has been recommended at doses of prednisone 1 mg/kg/day PO plus cyclosporine (10 mg/kg/day PO in 2 divided doses) based on actual or ideal body weight, whichever is lower. After 2 weeks if no disease progression is noted, the prednisone dose	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	is tapered by 25% per week to 1 mg/kg of prednisone on alternate days. Once the prednisone taper is completed without a flare, the cyclosporine dose is tapered to alternate day dosing such that the patient is taking prednisone one day and cyclosporine the next day. Once patients reach their maximal response, therapy is continued for another 3 months and then tapered.	

**Requires prior authorization*
†Off-label indication

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MCL and MZL	560 mg (four 140 mg capsules) PO once daily until disease progression or unacceptable toxicity	560 mg/day
CLL/SLL, WM, and cGVHD	420 mg (three 140 mg capsules) PO once daily until disease progression or unacceptable toxicity (for CLL/SLL and WM) or until cGVHD progression, recurrence of an underlying malignancy, or unacceptable toxicity	420 mg/day

VI. Product Availability
Capsule: 140 mg

VII. References
1. Imbruvica Prescribing Information. Sunnyvale, CA: Pharmacyclics, Inc.; August 2017. Available at www.imbruvica.com. Accessed August 9, 2017.
2. Ibrutinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed August 21, 2017.
3. National Comprehensive Cancer Network. Hairy Cell Leukemia Version 2.2017. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed August 21, 2017.
4. ClinicalTrials.Gov. clinicaltrials.gov. Accessed January 23, 2017.
5. Ruutu T, Gratwohl A, de Witte T, et al. Prophylaxis and treatment of GVHD: EBMT-ELN working group recommendations for a standardized practice. Bone Marrow Transplant. 2014 Feb;49(2):168-73.
6. Lee SJ, Vogelsang G, Flowers ME. Chronic graft-versus-host disease. Biol Blood Marrow Transplant 2003; 9:215-233.
7. Filipovich, AH, Weisdorf D, Pavletic S., et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. Diagnosis and Staging Working Group Report. Biol Blood Marrow Transplant. 2005 Dec;11(12):945-56.
8. Prednisone Drug Monograph. Clinical Pharmacology. Accessed August 2017. http://www.clinicalpharmacology-ip.com.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.17	02.17
Added new FDA approved indication: cGVHD. Added criteria for hairy cell leukemia per NCCN guidelines/compendium. Re-auth: updated to include cGVHD; added requirement for positive response to therapy.	08.29.17	11.17

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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