

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Imbruvica® (ibrutinib tablets and capsules – Pharmacyclics/Janssen)

TAC APPROVAL DATE: 06/05/2019

OVERVIEW

Imbruvica, a Bruton kinase inhibitor, is indicated for the treatment of adults patients with mantle cell lymphoma who have received at least one prior therapy.¹ Accelerated approval for this indication was granted based on overall response rate. Continued approval for this condition may be contingent on verification of clinical benefit in confirmatory trials. Imbruvica is also indicated for use in adult patients with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). Regarding CLL and SLL, Imbruvica is also indicated for the treatment of adult patients with 17p deletion CLL and SLL. Imbruvica is also indicated for the treatment of adult patients with Waldenström’s macroglobulinemia. Imbruvica is indicated in adult patients with marginal zone lymphoma who require systemic therapy and have received at least one prior anti-CD20-based therapy. Accelerated approval was granted for this indication was based on the overall response rate. Continued approval may be based contingent upon verification and description of clinical benefit in a confirmatory trial. Imbruvica is also indicated for the treatment of adult patients with chronic graft-versus-host disease after failure of one or more lines of systemic therapy.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for CLL/SLL (version 5.2019 – May 23, 2019) recommend Imbruvica as a treatment option in various scenarios (e.g., first-line therapy for patients with or without deletion 17p/TP53 mutation; and as relapsed/refractory therapy [category 1 recommendations for many scenarios]).² Imbruvica plays a vital role in the management of CLL/SLL and many trials describe its efficacy.

The NCCN guidelines for B-Cell Lymphomas (version 3.2019 – May 6, 2019) address mantle cell lymphoma.³ Imbruvica is recommended as a one of the preferred second-line therapies, with or without rituximab (Category 2A).

The NCCN guidelines for B-Cell Lymphomas (version 3.2019 – May 6, 2019) address marginal zone lymphoma.³ Preferred first-line regimens include use of rituximab with other agents. Imbruvica is cited as an option as a second-line and subsequent therapy.

The NCCN guidelines for Waldenstrom’s macroglobulinemia/lymphoplasmacytic lymphomas (version 2.2019 – September 14, 2018) recommend Imbruvica, with or without rituximab, as a primary therapy option (Category 2).⁴ For previously treated patients Imbruvica, with or without rituximab, is also cited as a preferred regimen.

The NCCN guidelines for Central Nervous System (CNS) Cancers B-Cell Lymphomas (version 1.2019 – March 5, 2019) recommend Imbruvica as one of the options for patients with relapsed or refractory disease.⁵

The NCCN guidelines for Hairy Cell Leukemia (version 3.2019 – January 31, 2019) recommend Imbruvica as one of the options for patients with relapsed or refractory disease following progression.⁶

The NCCN guidelines for B-Cell Lymphomas (version 3.2019 – May 6, 2019) address diffuse large B-cell lymphoma.² Imbruvica is cited as a second-line and subsequent therapy. Other therapy regimens are recommended first-line, many of which are rituximab-based.

Other Uses with Supportive Evidence

Imbruvica is indicated for the treatment of adult patients with chronic graft versus host disease after failure of one or more lines of systemic therapy.^{1,8} Imbruvica was evaluated in patients with chronic graft versus host disease in an open-label, single-arm trial involving patients with graft-versus-host disease following failure of first-line corticosteroid therapy and requiring additional treatment (n = 42). Patients had received a median number of two prior treatments for chronic graft-versus-host disease.^{1,8} All patients had received corticosteroids and other medications used included tacrolimus (50%), rituximab (26%), mycophenolate mofetil (24%), cyclosporine (19%), and sirolimus (17%).⁸ Most patients (88%) had at least two organs involved at baseline.^{1,8} The median corticosteroid dose (prednisone or equivalent) at baseline was 0.3 mg/kg/day, and 52% of patients were receiving ongoing immunosuppressants in addition to systemic corticosteroids at baseline. The best overall response rate was 67% (n = 28/42) [21% complete response rate and 45% partial response rate]. The sustained response rate (patients who achieved a complete response or a partial response that was sustained for at least 20 weeks) was 48% (n = 20/42). Responses were noted across all organs involved.^{1,8} Imbruvica is not addressed yet in current recommendations for the management of chronic graft versus host disease.⁹

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Imbruvica. All approvals are provided for 3 years in duration unless otherwise noted below.

Automation: When available, the ICD-9/ICD-10 codes for chronic lymphocytic leukemia (CLL) (ICD-9: 204.1* [lymphoid leukemia chronic] and ICD-10: C91.1* [chronic lymphocytic leukemia of B-cell type]), Mantle Cell Lymphoma (ICD-9: 200.4* and ICD-10: C83.1*), Small Lymphocytic Lymphoma (ICD-10: C83.0* [small cell B-cell lymphoma]) and Waldenström’s macroglobulinemia (ICD-9: 273.3* [macroglobulinemia] and ICD-10: C88.0*) will be used as part of automation to allow approval of the requested medication.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Imbruvica is recommended in those who meet the following criteria:

FDA-Approved Indications

- 1. Chronic Lymphocytic Leukemia (CLL).** Approve for 3 years.
- 2. Mantle Cell Lymphoma.** Approve for 3 years.
- 3. Marginal Zone Lymphoma.** Approve for 3 years.
- 4. Small Lymphocytic Lymphoma (SLL).** Approve for 3 years.
- 5. Waldenström’s Macroglobulinemia.** Approve for 3 years.

- 6. Graft versus Host Disease, Chronic:** Approve for 1 year if the patient has tried one conventional systemic treatment for graft versus host disease (e.g., corticosteroids [methylprednisolone, prednisone], cyclosporine, tacrolimus, mycophenolate mofetil, imatinib, Jakafi® [ruxolitinib tablets]).

Other Uses with Supportive Evidence

- 1. Central Nervous System (CNS) Lymphoma (Primary).** Approve for 3 years if according to the prescribing physician the patient has relapsed or refractory disease.
- 2. B-Cell Lymphoma (e.g., follicular lymphoma, gastric mucosa-associated lymphoid tissue [MALT] lymphoma, nongastric MALT lymphoma, Acquired Immune Deficiency Syndrome (AIDS)-related, post-transplant lymphoproliferative disorders).** Approve for 3 years if according the prescribing physician the patient is using as second-line or subsequent therapy.
- 3. Hairy Cell Leukemia.** Approve for 3 years if the according to the prescribing physician the patient has relapsed or refractory disease.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Imbruvica has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Imbruvica® tablets and capsules [prescribing information]. Sunnyvale, CA and Horsham, PA: Pharmacyclics and Janssen Biotech; January 2019.
2. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (Version 5.2019 – May 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at <http://www.nccn.org>. Accessed on May 28, 2019.
3. The NCCN B-cell Lymphomas Guidelines in Oncology (Version 3.2019 – May 6, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on May 31, 2019.
4. The NCCN Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (Version 2.2019 – September 14, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on May 31, 2019.
5. The NCCN Central Nervous System Cancers Guidelines in Oncology (Version 1.2019 – March 5, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on May 31, 2019.
6. The NCCN Hairy Cell Leukemia Guidelines in Oncology (Version 3.2019 – January 31, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on May 31, 2019.
7. Treon SP, Tripsas CK, Meid K, et al. Ibrutinib in previously treated Waldenström’s Macroglobulinemia. *N Engl J Med*. 2015;372(15):1430-1440.
8. Miklos D, Cutler CS, Arora M, et al. Ibrutinib for chronic graft-versus-host disease after failure or prior therapy. *Blood*. 2017;130(21):2243-2250.
9. Dignan FL, Amrolia P, Clark A, et al, on behalf of the Haemato-oncology Task Force of the British Committee for Standards in Haematology and British Society for Blood and Marrow Transplantation. Diagnosis and management of chronic graft-versus-host disease. *Br J Haematol*. 2012;158(1):46-61.

HISTORY

Type of Revision	Summary of Changes [†]	TAC Approval Date
Selected revision by the DEU	Added approval for patients with marginal zone lymphoma if the patient has tried Rituxan® (rituximab for intravenous infusion) or according to the prescribing physician, Rituxan is contraindicated for use in this patient.	01/25/2017
Annual revision	No criteria changes.	04/19/2017
Selected revision	Added criteria for Imbruvica for its new indication in chronic graft versus host disease to approve for 1 year if the patient has tried one conventional systemic treatment for graft versus host disease (e.g., corticosteroids [methylprednisolone, prednisone], cyclosporine, tacrolimus, mycophenolate mofetil, imatinib).	08/16/2017
Annual revision	Added approvals under the “Other Uses with Supportive Evidence” section, for hairy cell leukemia, DLBCL, and central nervous system lymphoma (primary) per recommendations by the respective NCCN guidelines.	05/16/2018
Annual revision	<p>The following changes were made:</p> <ol style="list-style-type: none"> 1. Marginal Zone Lymphoma: The requirement that the patient has tried rituximab, or according to the prescribing physician rituximab is contraindicated, was removed. 2. Graft Versus Host Disease, Chronic: For clarity, Jakafi was added to the list of examples of conventional systemic agents, one of which must be tried prior to approval of Imbruvica. 3. B-Cell Lymphoma: The condition was changed to as listed; previously listed as “Diffuse Large B-Cell Lymphoma”. Autoimmune Deficiency Syndrome (AIDS)-related and post-transplant lymphoproliferative disorder were added to the examples of B-Cell Lymphoma. The listing of primary diffuse large B-cell lymphoma of the central nervous system (CNS) was deleted as it is addressed in a different criterion. 	06/05/2019

[†] For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; TAC – Therapeutic Assessment Committee; CLL – Chronic lymphocytic leukemia; DEU – Drug Evaluation Unit; SLL – Small lymphocytic lymphoma; DLBCL – Diffuse large B-cell lymphoma; NCCN – National Comprehensive Cancer Network.