PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Revlimid® (lenalidomide capsules – Celgene)

DATE REVIEWED: 04/01/2020

OVERVIEW

Revlimid, a thalidomide analogue, is indicated in combination with dexamethasone for the treatment of patients with multiple myeloma.[1] It is also indicated as maintenance therapy in patients with multiple myeloma following autologous hematopoietic stem cell transplantation (auto-HSCT). Revlimid is also indicated for the treatment of patients with transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a 5q cytogenetic abnormality with or without additional cytogenetic abnormalities. Revlimid is also indicated for the treatment of patients with mantle cell lymphoma whose disease has relapsed or progressed after two prior therapies, one of which included Velcade® (bortezomib injection). Revlimid is indicated in combination with a rituximab product for the treatment of adults with previously treated follicular lymphoma. Revlimid is indicated in combination with a rituximab product for the treatment of adults with previously-treated marginal zone lymphoma. A limitation of use with Revlimid is that it is not indicated and is not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials.

Guidelines

The NCCN guidelines for acquired immune deficiency syndrome (AIDS)-Related Kaposi Sarcoma (version 1.2020 – February 12, 2020) recommended Revlimid as an Other Recommended Regimen for subsequent systemic therapy options for relapsed/refractory therapy.[2] First-line systemic therapy options include liposomal doxorubicin (preferred), and paclitaxel. Other subsequent systemic therapy options for relapsed/refractory therapy are also cited (e.g., Pomalyst® [pomalidomide capsules] {preferred}, Thalomid® [thalidomide capsules], imatinib).

The National Comprehensive Cancer Network (NCCN) guidelines for B-Cell Lymphomas (version 1.2020 – January 22, 2020) discuss therapeutic options for mantle cell lymphoma.[3] Revlimid, in combination with rituximab, is recommended as a preferred less-aggressive induction therapy (category 2A). Revlimid with or without rituximab is recommended as a preferred second-line therapy (Category 2A). Other recommended second line therapy regimens include Imbruvica, Revlimid, plus rituximab. The NCCN guidelines cited many treatments and medications regimens for mantle cell lymphoma in various clinical scenarios.

The NCCN guidelines for multiple myeloma (version 3.2020 – March 10, 2020) recommend Revlimid in a variety of scenarios.[4] Revlimid is use in various regimens and Revlimid combined with low-dose dexamethasone is cited as a Category 1 agent for primary therapy for non-transplant candidates. As a maintenance therapy, Revlimid also has a Category 1 recommendation. Revlimid, combined with other agents, is also part of a category 1 recommended therapy (preferred) for previously treated multiple myeloma.

The NCCN guidelines for MDS (version 2.2020 – February 28, 2020) recommend Revlimid in a variety of clinical scenarios among patients with symptomatic anemia both with and without 5q deletion abnormalities.[5]

The NCCN guidelines for B-Cell Lymphomas (version 1.2020 – January 22, 2020) recommend Revlimid as an option as subsequent therapy, with or without rituximab, for multi-centric Castleman's disease that has progressed after treatment of relapsed/refractory or progressive disease.[3]

NCCN guidelines for B-Cell Lymphomas (version 1.2020 – January 22, 2020) discuss therapeutic options for diffuse large B-cell lymphoma.[3] Revlimid, with or without rituximab, is mentioned as a second-line therapy. Many examples of first-line therapies are recommended (e.g., RCHOP [Rituximab cyclophosphamide, doxorubicin, vincristine, prednisone] {Category 1}, dose-adjusted EPOCH [etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin] + rituximab {Category 2A}). One examples of a first-line therapy for patients with poor left ventricular function or in those who are frail include RCEPP (rituximab, cyclophosphamide, etoposide, prednisone, procarbazine). NCCN also recommends optional first-line consolidation therapy of Revlimid maintenance (Category 2B) for patients aged 60 to 80 years.

NCCN guidelines for B-Cell Lymphomas (version 1.2020 – January 22, 2020) discuss therapeutic options for follicular lymphoma.[3] Revlimid plus rituximab is a first-line recommended therapy (Category 2A). Many second-line and subsequent therapies are listed, which include Revlimid, with or without rituximab.

The NCCN Hodgkin Lymphoma clinical practice guidelines (version 1.2020 – January 30, 2020) recommend Revlimid as an additional therapy option for treatment of classical Hodgkin lymphoma as a single agent for refractory or relapsed disease.[6]

The NCCN guidelines for B-Cell Lymphomas (version 1.2020 – January 22, 2020) discuss marginal zone lymphomas.[3] Revlimid plus rituximab has a Category 2B recommendation for first-line therapy. Revlimid with or without rituximab is also recommended as a second-line and subsequent therapy.

The NCCN has guidelines regarding myeloproliferative neoplasms (version 2.2019 – October 29, 2018) that discuss myelofibrosis with related anemia.[7] Revlimid is recommended, with or without prednisone, for patients with serum epoetin alfa levels > 500 mU/mL.

The NCCN guidelines for T-Cell Lymphomas (version 1.2020 – January 6, 2020) makes several recommendations that include Revlimid.[8] For peripheral T-cell lymphomas, Revlimid is recommended as second-line and subsequent therapy as a monotherapy. Similarily, Revlimid is recommended as a second-line and subsequent therapy for adult T-cell leukemia/lymphoma.

NCCN guidelines for systemic light chain amyloidosis (version 1.2020 – December 6, 2019) cite Revlimid as a therapeutic option used in combination with other agents in several clinical scenarios, including newly diagnosed disease.[9] The NCCN guidelines state that Phase II studies have noted that Revlimid in combination with dexamethasone is active in the treatment of patients with systemic light chain amyloidosis, including patients with relapsed/refractory disease.

The NCCN guidelines for Central Nervous System (CNS) Cancers (version 1.2020 – March 10, 2020) recommend Revlimid, with or without rituximab, as one of the options for patients with relapsed or refractory disease.[10]

Safety
In a prospective randomized clinical study in the first-line treatment of patients with CLL, use of Revlimid as a single agent increased the risk of death compared with chlorambucil given as a single agent.[1] The trial was stopped for safety in July 2013. In an interim analysis, 34 deaths occurred in 210 patients in the Revlimid treatment arm compared with 18 deaths among the 211 patients in the chlorambucil treatment arm (hazard ratio for overall survival was 1.92 [95% confidence interval {CI}: 1.08, 3.41]), which was consistent with a 92% increase in the risk of death. Also, serious adverse cardiovascular (CV) events, including atrial fibrillation, myocardial infarction, and cardiac failure, occurred more frequently in patients receiving Revlimid. Revlimid has a Boxed Warning regarding embryofetal toxicity, hematologic toxicity, and venous thromboembolism. Revlimid is only available through a restricted distribution program called the Revlimid Risk Evaluation Mitigation Strategy (REMS®). Males and females must follow the required reproductive precautions.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Revlimid. All approvals are provided for 3 years in duration.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Revlimid is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Follicular Lymphoma.** Approve for 3 years if the patient meets one of the following (A or B):
   A) The patient is using Revlimid in combination with rituximab; OR
   B) The patient has tried at least one prior therapy.
   Note: Examples include Treanda® (bendamustine injection) plus rituximab; Treanda plus Gazyva® (obinutuzumab injection for intravenous use); CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) plus Gazyva or rituximab; CVP (cyclophosphamide, vincristine, prednisone) plus Gazyva or rituximab; chlorambucil with or without rituximab; cyclophosphamide with or without rituximab; Gazyva; Copiktra™ (duvelisib capsules); Aliqopa® (copanlisib injection for intravenous use); or Zydelig® (idelalisib capsules).

2. **Mantle Cell Lymphoma**. Approve for 3 years.

3. **Marginal Zone Lymphoma.** Approve for 3 years.

4. **Multiple Myeloma.** Approve for 3 years.

5. **Myelodysplastic Syndrome (MDS).** Approve for 3 years if the patient meets ONE of the following (A, B, or C):
   A) The patient has symptomatic anemia; OR
   B) The patient has transfusion-dependent anemia; OR
   C) The patient has anemia that is not controlled with an erythroid stimulating agent (ESA) [e.g., Epogen®/Procrit® {epoetin alfa injection}, Aranesp® {darbepoetin alfa injection}].

Other Uses with Supportive Evidence

6. **Acquired Immune Deficiency Syndrome (AIDS)-Related Kaposi's Sarcoma.** Approve for 3 years if the patient meets the following (A and B):
   A) The patient has tried at least one regimen or therapy; AND
   B) The patient has relapsed or refractory disease.
   Note: Examples include liposomal doxorubicin, paclitaxel, Pomalyst® (pomalidomide capsules), Thalomid® [thalidomide capsules], and imatinib.

7. **Castleman's Disease.** Approve for 3 years in patients with relapsed/refractory or progressive disease.

8. **Central Nervous System (CNS) Cancer (Primary).** Approve for 3 years if according to the prescriber the patient has relapsed or refractory disease.

9. **Diffuse, Large B Cell Lymphoma (DLBCL) [Non-Hodgkin's Lymphoma].** Approve for 3 years if the patient has tried at least one prior therapy
   Note: Examples include RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, predisone); dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab; RCEPP (rituximab, cyclophosphamide, etoposide, prednisone, procarbazine); DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab; ICE (Ifex, carboplatin, etoposide) ± rituximab; or Treanda ± rituximab.

10. **Hodgkin Lymphoma, Classical (nodular sclerosis, mixed cellularity, lymphocyte depleted, and lymphocyte-rich subtypes of Hodgkin lymphoma).** Approve for 3 years in patients with relapsed or refractory disease.

11. **Myelofibrosis.** Approve for 3 years if the patient meets the following criteria (A and B):
    A) According to the prescriber the patient has anemia; AND
    B) The patient has serum erythropoietin levels ≥ 500 mU/mL.

12. **Peripheral T-Cell Lymphomas.** Approve for 3 years if the patient has tried at least one other therapy or regimen.
    Note: Examples of therapies or regimens include Beleodaq® (belinostat injection for intravenous infusion); Adcetris® (brentuximab vedotin injection for intravenous use); DHAP (dexamethasone, cisplatin, cytarabine); ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin); GDP (gemcitabine, dexamethasone, cisplatin); GemOX (gemcitabine, oxaliplatin); ICE (ifosfamide, carboplatin, etoposide); or Istodax® (romidepsin injection for intravenous infusion). Indications regarding peripheral T-cell lymphomas include peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL); enteropathy-associated T-cell lymphoma (EATL); monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL); nodal peripheral T-cell lymphoma (nodal PTCL) with TFH phenotype (TFH); follicular T-cell lymphoma (FTCL); and hepatosplenic gamma-delta T-cell lymphomas.

13. **Systemic Light Chain Amyloidosis.** Approve for 3 years.

14. **T-Cell Leukemia/Lymphoma.** Approve for 3 years if the patient has tried at least one other therapy or regimen.

Note: Examples include Adcetris® (brentuximab vedotin injection for intravenous use) plus CHP (cyclophosphamide, doxorubicin, and prednisone); CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone); CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone); dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin); HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine; or Beleodaq® (belinostat injection for intravenous infusion).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Revlimid 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. Rationale for non-coverage for these specific conditions is provided below. (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. Revlimid® capsules [prescribing information]. Summit, NJ: Celgene; October 2019.
2. The NCCN AIDS-Related Kaposi Sarcoma Clinical Practice Guidelines in Oncology (Version 1.2020 – February 12, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 13, 2020.
3. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 1.2020 – January 22, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 13, 2020.
4. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (Version 3.2020 – March 10, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 13, 2020.
5. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (Version 2.2020 – February 28, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 13, 2020.
6. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (Version 1.2020 – January 30, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 13, 2020.
7. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (Version 2.2019 – October 29, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 14, 2019.
8. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 1.2020 – January 6, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 13, 2020.
9. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (Version 1.2020 – December 6, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 13, 2020.
10. The NCCN Central Nervous System Cancers Guidelines in Oncology (Version 1.2020 – March 10, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 13, 2020.