PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Revlimid Prior Authorization Policy
- Revlimid® (lenalidomide capsules – Celgene)

REVIEW DATE: 04/14/2021

OVERVIEW

Revlimid, a thalidomide analog, is indicated for the following uses in adults:[1]

- **Follicular lymphoma**, previously treated, in combination with a rituximab product.
- **Mantle cell lymphoma**, in patients whose disease has relapsed or progressed after two prior therapies, one of which included Velcade® (bortezomib injection for subcutaneous or intravenous use).
- **Marginal zone lymphoma**, previously treated, in combination with a rituximab product.
- **Multiple myeloma**, as maintenance following autologous hematopoietic stem cell transplantation.
- **Multiple myeloma**, treatment, in combination with dexamethasone.
- **Myelodysplastic syndrome**, for transfusion-dependent anemia due to low- or intermediate-risk disease, associated with a deletion 5q abnormality with or without cytogenetic abnormalities.

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 outside of controlled clinical trials.[1]

Guidelines

Revlimid is incorporated into various guidelines by the National Comprehensive Cancer Network (NCCN).[2-11]

- **B-Cell Lymphomas (Other):** The NCCN guidelines for B-Cell lymphomas (version 3.2021 – March 16, 2021), discuss therapeutic options for diffuse large B-cell lymphoma (DLBCL), the most common type of other B-cell lymphoma (other).[2] Revlimid, with or without rituximab, is mentioned as a second-line therapy that is useful in certain circumstances (category 2A). 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 example of a first-line therapy for patients with poor left ventricular function or in those who are frail is RCEPP (rituximab, cyclophosphamide, etoposide, prednisone, procarbazine). NCCN also recommends optional first-line consolidation therapy of Revlimid maintenance (category 2B) for patients 60 to 80 years of age. Other types of B-cell lymphomas (high grade B-cell lymphomas [not otherwise specified], post-transplant lymphoproliferative disorders, acquired immunodeficiency [AIDS]-related B-cell lymphomas, high-grade B-cell lymphomas with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma]) are also cited in the guidelines and note a place in therapy of Revlimid. Regimens recommended in these clinical scenarios are similar to those used in DLBCL.
- **Castleman's Disease:** The NCCN guidelines for B-Cell lymphomas (version 3.2021 – March 16, 2021) recommend Revlimid as an option as second-line and subsequent therapy, with or without rituximab, for multi-centric Castleman's disease that is relapsed/refractory or progressive disease.[2]

- **Central Nervous System (CNS) Lymphoma:** The NCCN guidelines for 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.[3]
- **Follicular Lymphomas:** The NCCN guidelines for B-Cell lymphomas (version 3.2021 – March 16, 2021) discuss agents for follicular lymphoma.[2] Revlimid plus rituximab is a first-line recommended therapy (category 2A). Many second-line and subsequent therapies are listed, usually with or without rituximab. Revlimid with Gazyva® (obinutuzumab injection for intravenous use) is an other recommended regimen in this setting (category 2A).
- **Histiocytic Neoplasms:** The NCCN guidelines for histiocytic neoplasms (version 1.2021 – March 1, 2021) recommend Revlimid for Langerhans cell histiocytosis as first-line or as subsequent therapy for single system multifocal skin disease (including mucosa) and for relapsed/refractory disease (category 2A).[4]
- **Hodgkin Lymphoma:** The NCCN Hodgkin lymphoma guidelines (version 3.2021 – March 12, 2021) recommend Revlimid as a subsequent option for treatment of classical Hodgkin lymphoma as a single agent for refractory or relapsed disease in patients ≥ 18 years of age (category 2A). Many other therapies are recommended as primary systemic therapy regimens before Revlimid is recommended.[5]
- **Mantle Cell Lymphoma:** The NCCN guidelines for B-Cell lymphomas (version 3.2021 – March 16, 2021) discuss mantle cell lymphoma.[2] Revlimid, in combination with rituximab, is recommended as a preferred, less aggressive induction therapy (category 2A). Revlimid with rituximab is recommended as a preferred second-line and subsequent therapy (category 2A). Other recommended second-line therapy regimens useful in certain circumstances include Imbruvica® (ibrutinib tablets and capsules) with or without rituximab, Calquence® (acalabrutinib capsules), Brukinsa™ (zanubrutinib capsules) [all category 2A]. The regimen of Revlimid, rituximabm and Imbruvica is cited as and second-line and subsequent therapy that is useful in certain circumstances (category 2B). The NCCN guidelines cites many other regimens and medications for mantle cell lymphoma in various clinical scenarios.
- **Marginal Zone Lymphoma:** The NCCN guidelines for B-Cell lymphomas (version 3.2021 – March 16, 2021) discuss marginal zone lymphomas.[2] Revlimid plus rituximab has a category 2B recommendation for first-line therapy as an other recommended regimen and a category 2A recommendation for second-line and subsequent therapy in certain clinical scenarios. It is also an other recommended regimen for second-line and subsequent therapy when given with Gazyva (category 2B). Many other regimens are recommended for this condition.
- **Multiple Myeloma:** The NCCN guidelines for multiple myeloma (version 6.2021 – April 12, 2021) feature Revlimid prominently in a variety of scenarios with several category 1 recommendations (e.g., Revlimid with dexamethasone for other recommended regimens for primary therapy, monotherapy for maintenance therapy).[6] The agent is also cited in other regimens with category 2A and 2B recommendations. Revlimid is also indicated for treatment in combination with dexamethasone for the management of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome as induction therapy for transplant eligible patients and for transplant ineligible patients (category 2A).
- **Myelodysplastic Syndrome (MDS)**: The NCCN guidelines for MDS (version 3.2021 – January 15, 2021) recommend Revlimid in a variety of clinical scenarios among patients with symptomatic anemia both with and without 5q deletion abnormalities (category 2A).[7]
- **Myelofibrosis:** The NCCN has guidelines regarding myeloproliferative neoplasms (version 1.2020 – May 21, 2020) discuss myelofibrosis with related anemia.[8] Revlimid is recommended in the management of anemia associated with myelofibrosis (useful in certain circumstances), with or without prednisone, for a variety of clinical scenarios (category 2A) including patients with erythropoietin levels ≥ 500 mU/mL and with erythropoietin levels < 500 mU/mL and no response or loss of response to erythropoietic stimulating agents.

- **Kaposi Sarcoma:** The NCCN guidelines for Kaposi sarcoma (version 1.2021 – February 12, 2021) recommended Revlimid as an agent useful under certain conditions for subsequent systemic therapy options for relapsed/refractory therapy (category 2A) [for patients with corticosteroid-refractory immune reconstitution inflammatory syndrome].[9] This includes use when given alone (in patients without human immunodeficiency virus [HIV]) or with antiretroviral therapy for patients with HIV. 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).
- **Systemic Light Chain Amyloidosis:** The NCCN guidelines for systemic light chain amyloidosis (version 2.2021 – February 8, 2021) cite Revlimid as a therapeutic option used in combination dexamethasone, and in some circumstances with additional medications, in several clinical scenarios, including as primary therapy (category 2A).[10] Also, Revlimid in combination with dexamethasone, and an additional medication recommended in some situations, is also recommended in patients with previously treated disease (category 2A).
- **T-Cell Lymphomas:** The NCCN guidelines for T-cell lymphomas (version 1.2021 – October 5, 2020) make several recommendations that include Revlimid.[11] Revlimid is recommended as a second-line and subsequent therapy for adult T-cell leukemia/lymphoma (category 2A). For peripheral T-cell lymphomas, Revlimid is recommended as second-line and subsequent therapy (other recommended regimens) as a monotherapy (category 2A). Indications regarding peripheral T-cell lymphomas include the following: peripheral T-cell lymphoma not otherwise specified, angioimmunoblastic T-cell lymphoma; enteropathy-associated T-cell lymphoma; monomorphic epitheliotropic intestinal T-cell lymphoma; nodal peripheral T-cell lymphoma with T-follicular helper (TFH) phenotype; follicular T-cell lymphoma; and hepatosplenic gamma-delta T-cell lymphomas. Other regimens are recommended as first-line or preferred for in both of these clinical scenarios.

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: 1.08, 3.41]), which was consistent with a 92% increase in the risk of death. Also, serious adverse cardiovascular 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. 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 the duration noted below.

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 the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets one of the following (i or ii)
     - **i.** Patient is using Revlimid in combination with rituximab; OR
     - **ii.** Patient has tried at least one other regimen.
       Note: Examples include bendamustine plus rituximab; bendamustine 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 if the patient meets the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets one of the following (i or ii).
     - **i.** Patient is using Revlimid in combination with rituximab; OR
     - **ii.** Patient has tried at least two other regimens.
       Note: Examples include HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) + rituximab; the NORDIC regimen (dose-intensified induction immunochemotherapy with rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone alternating with rituximab and high-dose cytarabine); RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone); bendamustine injection plus rituximab; RDHA (rituximab, dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin); Imbruvica (ibrutinib capsules and tablets); Calquence (acalabrutinib capsules); or Brukinsa (zanubrutinib capsules).

3. **Marginal Zone Lymphoma.** Approve for 3 years if the patient meets the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets one of the following (i or ii).
     - **i.** Patient is using Revlimid in combination with rituximab; OR
     - **ii.** Patient has tried least one other regimen.
       Note: Examples include CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab; bendamustine + rituximab; CVP (cyclophosphamide, vincristine, prednisone) + rituximab; rituximab; chlorambucil with or without rituximab; cyclophosphamide with or without rituximab; bendamustine + Gazyva (obinutuzumab injection for intravenous use); Copiktra (duvelisib capsules); Aliqopa (copanlisib injection for intravenous use); or Zydelig (idelalisib capsules).

4. **Multiple Myeloma.** Approve for 3 years if the patient is ≥ 18 years of age.

5. **Myelodysplastic Syndrome.** Approve for 3 years if the patient meets the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets one of the following (i, ii, or iii):
     - **i.** Patient has symptomatic anemia; OR
     - **ii.** Patient has transfusion-dependent anemia; OR
     - **iii.** Patient has anemia that is not controlled with an erythroid stimulating agent (e.g., Epogen/Procrit [epoetin alfa injection], Aranesp [darbepoetin alfa injection]).

Other Uses with Supportive Evidence

6. **B-Cell-Lymphomas (Other):** Approve for 3 years if the patient meets the following criteria (A and B):
   Note: Examples include diffuse large B-cell lymphoma (DLBCL); high grade B-cell lymphomas (not otherwise specified), post-transplant lymphoproliferative disorders, AIDS-related B-cell lymphomas, high-grade B-cell lymphomas with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma).
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried at least one other regimen.
   Note: Examples include RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone); 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; RCVP (rituximab cyclophosphamide, vincristine, prednisone); CVD (cyclophosphamide, vincristine, prednisone); R-HyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine); or bendamustine ± rituximab.

7. **Kaposi Sarcoma.** Approve for 3 years if the patient meets the following (A and B):
   A) Patient has relapsed or refractory disease; AND
   B) Patient has tried at least one other medication; AND
   Note: Examples include liposomal doxorubicin, paclitaxel, Pomalyst (pomalidomide capsules), Thalomid (thalidomide capsules), and imatinib.

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

9. **Central Nervous System Lymphoma.** Approve for 3 years if according to the prescriber the patient has relapsed or refractory disease.

10. **Hodgkin Lymphoma, Classical.** Approve for 3 years if the patient meets the following (A and B):
    A) Patient is ≥ 18 years of age; AND
    B) Patient has tried at least one other regimen.
    Note: Examples include ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine); BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone); Adcetris (brentuximab vedotin injection for intravenous use); Adcetris + AVD (doxorubicin, vinblastine, and dacarbazine); DHAP (dexamethasone, cisplatin, high-dose cytarabine); ESHAP (etoposide, methylprednisolone, high-dose cytarabine, cisplatin); ICE (ifosfamide, carboplatin, etoposide); or GVD (gemcitabine, vinorelbine, liposomal doxorubicin).

11. **Langerhans Cell Histiocytosis:** Approve for 3 years for patients with multifocal skin disease.

12. **Myelofibrosis.** Approve for 3 years if the patient meets the following (A or B):
    A) Patient meets the following (i, ii, and iii):
       i. Patient is ≥ 18 years of age; AND
       ii. According to the prescriber the patient has anemia; AND
       iii. Patient has serum erythropoietin levels ≥ 500 mU/mL.
    B) Patient meets the following (i, ii, iii, and iv):
       i. Patient is ≥ 18 years of age; AND
       ii. According to the prescriber the patient has anemia; AND
       iii. Patient has serum erythropoietin levels < 500 mU/mL; AND

iv. Patient has experienced no response or loss of response to an erythropoiesis-stimulating stimulating agent.

13. Peripheral T-Cell Lymphomas. Approve for 3 years if the patient meets the following (A and B):
Note: 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 T-follicular helper (TFH) phenotype; follicular T-cell lymphoma (FTCL); and hepatosplenic gamma-delta T-cell lymphomas.
A) Patient is ≥ 18 years of age; AND
B) Patient has tried at least one other regimen.
Note: Examples of 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).

14. POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) Syndrome. Approve for 3 years if the patient meets the following (A and B):
A) Patient is ≥ 18 years of age; AND
B) Use of Revlimid is in combination with dexamethasone.

15. Systemic Light Chain Amyloidosis. Approve for 3 years if the patient meets the following (A and B):
A) Patient is ≥ 18 years of age; AND
B) Use of Revlimid is in combination with dexamethasone.

16. T-Cell Leukemia/Lymphoma. Approve for 3 years if the patient meets the following (A and B):
A) Patient is ≥ 18 years of age; AND
B) Patient has tried at least one other 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

Coverage of Revlimid is not recommended in the following situations:

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 B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 3.2021 – March 16, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 9, 2021.

3. 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 April 9, 2021.
4. The NCCN Histiocytic Neoplasms (version 1.2021 – March 1, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 10, 2021.
5. The NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (version 3.2021 – March 12, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 9, 2021.
6. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 6.2021 – April 12, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 9, 2021.
7. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 3.2021 – January 15, 2021). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 9, 2021.
8. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (version 1.2020 – May 21, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 9, 2021.
9. The NCCN 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 April 9, 2021.
10. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2021 – February 8, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 9, 2021.
11. The NCCN T-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2021 – October 5, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 9, 2021.