UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 1090-13
Program	Prior Authorization/Notification
Medication	Revlimid® (lenalidomide)
P&T Approval Date	6/2009, 3/2010, 6/2010, 9/2010, 12/2010, 9/2011, 8/2012, 7/2013, 5/2014, 5/2015, 5/2016, 5/2017, 5/2018, 5/2019, 5/2020, 5/2021, 5/2022, 5/2023, 5/2024
Effective Date	8/1/2024

1. Background:

Revlimid® (lenalidomide) is a thalidomide analogue indicated for the treatment of adult patients with the following: multiple myeloma (MM), in combination with dexamethasone; MM, as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT); transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities; mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib; previously treated follicular lymphoma (FL), in combination with a rituximab product; and previously treated marginal zone lymphoma (MZL), in combination with a rituximab product.[1]

The National Cancer Comprehensive Network (NCCN) also recommends use of Revlimid for treatment of the following B-Cell lymphomas: histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma, mantle cell lymphoma, nodal marginal zone lymphoma, classic follicular lymphoma, extranodal marginal zone lymphoma of nongastric sites (noncutaneous), extranodal marginal zone lymphoma (EMZL) of the stomach, high-grade B-cell lymphoma, splenic marginal zone lymphoma, post-transplant lymphoproliferative disorders, diffuse large B-cell lymphoma, and HIV-related B-cell lymphomas. Additionally, NCCN recommends the use of Revlimid for Kaposi Sarcoma, primary CNS lymphoma, castleman disease, chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), MDS/MPN overlap neoplasms, myelofibrosis-associated anemia, systemic light chain amyloidosis, classic hodgkin lymphoma, Langerhans cell histiocytosis, Rosai-Dorfman disease, and the following T-cell lymphomas: hepatosplenic T-cell lymphoma, peripheral T-cell lymphoma, and adult T-cell leukemia/lymphoma.

Because of the risk of serious malformations if given during pregnancy, there is an extensive risk management program requiring registration by patients, prescribers and dispensing pharmacies. Additional information about the lenalidomide Risk Evaluation and Mitigation Strategy (REMS) [Lenalidomide REMS] program may be found at http://www.lenalidomiderems.com/.[4]

Coverage Information:

Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria[a]:

A. Patients less than 19 years of age

1. **Revlimid** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   Authorization will be issued for 12 months.

B. Multiple Myeloma

1. **Initial Authorization**

   a. **Revlimid** will be approved based on the following criterion:

      (1) Diagnosis of multiple myeloma

      Authorization will be issued for 12 months.

2. **Reauthorization**

   a. **Revlimid** will be approved based on the following criterion:

      (1) Patient does not show evidence of progressive disease while on Revlimid therapy

      Authorization will be issued for 12 months.

C. Myelodysplastic Syndromes (MDS)

1. **Initial Authorization**

   a. **Revlimid** will be approved based on **one** of the following criteria:

      (1) Diagnosis of symptomatic anemia due to myelodysplastic syndrome (MDS) associated with a deletion 5q

      -OR-

      (2) **Both** of the following:

         (a) Diagnosis of symptomatic anemia due to myelodysplastic syndrome (MDS) without deletion 5q

         -AND-

         (b) **One** of the following:

            i. **All** of the following:

- Serum erythropoetin levels ≤ 500 mU/mL

- **One** of the following:
  - Ring sideroblasts < 15%
  - Ring sideroblasts < 5% with an SF3B1 mutation

- History of failure, contraindication, or intolerance to **one** of the following:
  - Erythropoietin stimulating agent (ESA) [e.g., Epogen, Procrit, Retacrit (epoetin alfa)] or darbepoetin alfa
  - Reblozyl (luspatercept-aamt)

- Used in combination with an erythropoietin stimulating agent (ESA) [e.g., Epogen, Procrit, Retacrit (epoetin alfa)] or darbepoetin alfa

-OR-

ii. **All** of the following:

- Serum erythropoetin levels ≤ 500 mU/mL

- **One** of the following:
  - Ring sideroblasts ≥ 15%
  - Ring sideroblasts ≥ 5% with an SF3B1 mutation

- History of failure, contraindication, or intolerance to **both** of the following:
  - Erythropoietin stimulating agent (ESA) [e.g., Epogen, Procrit, Retacrit (epoetin alfa)] or darbepoetin alfa
  - Reblozyl (luspatercept-aamt)

-OR-

iii. **All** of the following:

- Serum erythropoetin levels > 500 mU/mL

- **One** of the following:
  - Ring sideroblasts < 15%
  - Ring sideroblasts < 5% with an SF3B1 mutation

- **One** of the following:
  - Poor probability to respond to immunosuppressive therapy (e.g., azacitidine, decitabine)
  - History of failure, contraindication, or intolerance to immunosuppressive therapy (e.g., azacitidine, decitabine)

-OR-

iv. **All** of the following:

- Serum erythropoetin levels > 500 mU/mL
- **One** of the following:
  - Ring sideroblasts ≥ 15%
  - Ring sideroblasts ≥ 5% with an SF3B1 mutation
- History of failure, contraindication, or intolerance to Reblozyl (luspatercept-aamt)

-OR-

(3) **Both** of the following:

(a) Diagnosis of MDS/MPN overlap neoplasm

-AND-

(b) **One** of the following:

i. Patient has SF3B1 mutation and thrombocytosis
ii. Patient has ring sideroblasts and thrombocytosis (MDS/MPN-RS-T)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

D. B-Cell Lymphomas

1. **Initial Authorization**

a. **Revlimid** will be approved based on **one** of the following criteria:

(1) Diagnosis of **one** of the following:

(a) Mantle cell lymphoma (MCL)
(b) Extranodal marginal zone lymphoma of nongastric sites (noncutaneous)
(c) Extranodal marginal zone lymphoma (EMZL) of the stomach
(d) Classic follicular lymphoma
(e) Nodal marginal zone lymphoma
(f) Splenic marginal zone lymphoma

-OR-

(2) **Both** of the following:

(a) **One** of the following diagnoses:

i. HIV-related B-cell lymphoma
ii. Diffuse large B-cell lymphoma
iii. High-grade B-cell lymphoma
iv. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
v. Post-transplant lymphoproliferative disorders

-AND-

(b) Used as second line or subsequent therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

E. Myelofibrosis-Associated Anemia

1. **Initial Authorization**

a. **Revlimid** will be approved based on **all** of the following criteria:

(1) Diagnosis of myelofibrosis-associated anemia

-AND-

(2) Presence of del(5q) mutation

-AND-

(3) No symptomatic splenomegaly and/or constitutional symptoms

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Documentation of positive clinical response while on Revlimid therapy

Authorization will be issued for 12 months.

F. Hodgkin Lymphoma

1. **Initial Authorization**

a. **Revlimid** will be approved based on **both** of the following criteria:

(1) Diagnosis of Hodgkin lymphoma

-AND-

(2) Disease is refractory to at least 3 prior lines of therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

G. Systemic Light Chain Amyloidosis

1. **Initial Authorization**

a. **Revlimid** will be approved based on **both** of the following criteria:

(1) Diagnosis of systemic light chain amyloidosis

-AND-

(2) Used in combination with **one** of the following:

(a) Dexamethasone
(b) Dexamethasone and cyclophosphamide
(c) Dexamethasone and Ninlaro® (ixazomib)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid

therapy

Authorization will be issued for 12 months.

H. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

1. **Initial Authorization**

a. **Revlimid** will be approved based on **all** the following criteria:

(1) Diagnosis of chronic lymphocytic leukemia (CLL) / small lymphocytic lymphoma (SLL)

-AND-

(2) Disease is relapsed or refractory

-AND-

(3) Used after prior therapy with Bruton Tyrosine Kinase (BTK) inhibitor- and venetoclax-based regimens

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

I. T-Cell Lymphomas

1. **Initial Authorization**

a. **Revlimid** will be approved based on **both** of the following criteria:

(1) **One** of the following diagnoses:

(a) Peripheral T-cell lymphoma
(b) T-cell leukemia / lymphoma
(c) Hepatosplenic gamma-delta T-cell lymphoma

-AND-

(2) Used as second-line or subsequent therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

J. Central Nervous System Cancers – Primary CNS Lymphomas

1. **Initial Authorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Diagnosis of primary central nervous system lymphoma

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

K. Kaposi Sarcoma

1. **Initial Authorization**

a. **Revlimid** will be approved based on **both** of the following criteria:

(1) **One** of the following:

(a) Diagnosis of HIV-negative Kaposi Sarcoma

-OR-

(b) **Both** of the following:

i. Diagnosis of HIV-related Kaposi Sarcoma

-AND-

ii. Patient is currently being treated with antiretroviral therapy (ART)

-AND-

(2) Disease has progressed or not responded to two different systemic first-line systemic therapies (e.g., liposomal doxorubicin, sirolimus, paclitaxel)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

L. Histiocytic Neoplasms

1. **Initial Authorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Diagnosis of **one** of the following histiocytic neoplasms:

(a) Langerhans cell histiocytosis
(b) Rosai-Dorfman disease

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

M. Castleman Disease

1. **Initial Authorization**

a. **Revlimid** will be approved based on **both** of the following criteria:

(1) Diagnosis of multicentric castleman disease

-AND-

(2) **One** of the following:

(a) Progressed following treatment of relapsed/refractory disease

(b) Considered progressive disease

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Revlimid** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Revlimid therapy

Authorization will be issued for 12 months.

N. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Revlimid [package insert]. Summit, NJ: Celgene Corporation; March 2023.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at www.nccn.org. Accessed March 26, 2024.
3. Lenalidomide REMS. Available at http://www.lenalidomiderems.com/. Accessed March 26, 2024.

Program	Prior Authorization/Notification - Revlimid (lenalidomide)
Change Control	
5/2014	Annual review. Clarified criteria for MDS. Added coverage for Hodgkin lymphoma per NCCN.
9/2014	Administrative change - Tried/Failed exemption for State of New Jersey removed.
5/2015	Added smoldering myeloma and Castleman's disease. Removed nodal marginal zone lymphoma. Updated mantle cell criteria. Updated

	formatting, background and references.
5/2016	Annual review. Broke out systemic light chain amyloidosis. Removed 'cytogenic abnormality' from MDS. Added criteria for Mycosis Fungoides (MF) / Sezary Syndrome (SS), peripheral T-cell lymphoma, T-cell lymphoma / leukemia, and primary cutaneous CD30+ T-cell lymphoproliferative disorders. Updated formatting, background and references.
5/2017	Annual review. Changed member to patient in criteria A.1.a (patients < 19 years old). Removed try/fail of immunosuppressants from MDS. Added criteria to MF associated anemia per NCCN guidelines. Removed progressive solitary plasmacytoma and smoldering myeloma, added nodal marginal zone lymphoma per NCCN. Reordered NHL diagnoses to separate second line use and first line use. Updated background and references.
5/2018	Annual review. Revised criteria for NHL, added criteria for histological transformation of marginal zone lymphoma to diffuse large B-cell lymphoma, post-transplant lymphoproliferative disorders, and primary CNS lymphoma. Updated background and references.
5/2019	Annual review. Reformatted coverage criteria indications to align with NCCN guidelines. Revised criteria for diffuse large B cell lymphoma, myelodysplastic syndromes and Hodgkin Lymphoma. Added criteria for High-grade B-cell lymphoma, Gamma-delta T-Cell lymphoma. Updated background and references.
5/2020	Annual review. Reformatted coverage criteria indications to align with NCCN guidelines. Added criteria for AIDs related Kaposi Sarcoma and MDS/MPN overlap neoplasm according to NCCN guidelines. Clarified criteria for CLL/SLL, T-cell lymphoma, and primary CNS lymphoma according to NCCN guidelines.
5/2021	Annual review. Added Langerhans cell histiocytosis criteria according to NCCN guidelines. Updated criteria for Kaposi Sarcoma according to NCCN guidelines.
5/2022	Annual review. Formatting changes. Updated background and criteria to remove primary cutaneous lymphoma according to NCCN guidelines. Added criteria to be used in combination with dexamethasone and Ninlaro for systemic light chain amyloidosis. Updated Kaposi Sarcoma according to NCCN guidelines. Updated references.
5/2023	Annual review. Revised the name of gastric and nongastric MALT lymphoma per NCCN guidelines. Updated Systemic Light Chain Amyloidosis criteria per NCCN guidelines. Updated CLL/SLL criteria per NCCN guidelines. Added state mandate and oncology medications footnote. Updated references.
5/2024	Annual review. Updated background to reflect current NCCN guidance and updated the lenalidomide REMS program information. Removed footnote for state mandate for oncology medications. Updated criteria per NCCN for myelodysplastic syndrome, b-cell lymphomas, myelofibrosis-associated anemia, Hodgkin lymphoma, systemic light chain amyloidosis, chronic lymphocytic leukemia/small lymphocytic lymphoma, t-cell lymphoma, and kaposi sarcoma. Renamed and updated criteria for histiocytic neoplasms. Moved castleman disease

	from b-cell lymphoma into its own criteria. Updated references.