UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2023 P 1090-12
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
Effective Date	8/1/2023; Oxford only: 8/1/2023

1. **Background:**
Revlimid® (lenalidomide) is a thalidomide analogue indicated for the treatment of adult patients with 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 nodal marginal zone lymphoma to diffuse large B-cell lymphoma, mantle cell lymphoma, nodal marginal zone lymphoma, follicular lymphoma (grade 1-2), extranodal marginal zone lymphoma of nongastric sites (noncutaneous), Castleman's Disease, 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 AIDS-related B-cell lymphomas. NCCN additionally recommends the use of Revlimid in treatment for Kaposi Sarcoma, primary CNS lymphoma, chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), MDS/MPN overlap neoplasms, myelofibrosis, systemic light chain amyloidosis, classic Hodgkin lymphoma, Langerhans cell histiocytosis, and the following T-cell lymphomas: hepatosplenic gamma-delta T-cell lymphoma, peripheral T-cell lymphoma, and Adult T-cell leukemia/lymphoma.
Because of the risk of serious malformations if given during pregnancy, the manufacturer has an extensive risk management program requiring registration by patients, prescribers and dispensing pharmacies. Additional information about the Revlimid Risk Evaluation and Mitigation Strategy (REMS) [Revlimid REMS ®] program may be found at http://www.revlimidrems.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,b] :

A. <u>Patients less than 19 years of age</u>

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. <u>Multiple Myeloma</u>

1. **<u>Initial Authorization</u>**

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

      (1) Diagnosis of multiple myeloma

      Authorization will be issued for 12 months.

2. **<u>Reauthorization</u>**

   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. <u>Myelodysplastic Syndromes (MDS)</u>

1. **<u>Initial Authorization</u>**

   a. **Revlimid** will be approved based on **<u>one</u>** of the following criteria:

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

      -OR-

      (2) **<u>Both</u>** of the following:

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

         -AND-

         (b) **<u>One</u>** of the following:

            i. Serum erythropoetin levels >500 mU/mL

-OR-

ii. **Both** of the following:

- **Both** of the following:
  - Serum erythropoetin levels ≤ 500 mU/mL
  - Ring sideroblasts < 15%

-AND-

- **One** of the following:
  - Revlimid therapy is in combination with an erythropoietin [e.g., Epogen, Procrit, Retacrit (epoetin alfa)
  - History of failure, contraindication, or intolerance to erythropoietins [e.g., Epogen, Procrit, Retacrit (epoetin alfa)]

-OR-

iii. **All** of the following:

- Serum erythropoetin levels ≤ 500 mU/mL
- Ring sideroblasts ≥15%
- No response to an erythropoietin in combination with a granulocyte-colony stimulating factor (G-CSF)

-OR-

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

(a) Diagnosis of MDS/MPN overlap neoplasm

-AND-

(b) 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) Diffuse large B-cell lymphoma (patients 60 to 80 years old)
(c) Extranodal marginal zone lymphoma of nongastric sites (noncutaneous)
(d) Extranodal marginal zone lymphoma (EMZL) of the stomach
(e) Follicular lymphoma
(f) Nodal marginal zone lymphoma
(g) Splenic marginal zone lymphoma

-OR-

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

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

i. AIDS-related B-cell lymphoma
ii. Castleman's Disease (CD)
iii. Diffuse large B-cell lymphoma (patients who are < 60 years old)
iv. High-grade B-cell lymphoma
v. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
vi. Post-transplant lymphoproliferative disorders

-AND-

(b) **Not** used as first line 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 **both** of the following criteria:

(1) Diagnosis of myelofibrosis

-AND-

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

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

i. Serum erythropoietin levels <500 mU/mL

-AND-

ii. History of failure, contraindication, or intolerance to erythropoietins [e.g., Procrit (epoetin alfa)]

-OR-

(b) Serum erythropoietin levels ≥ 500 mU/mL

Authorization will be issued for 12 months.

2. **Reauthorization**

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

(1) Documentation that member has evidence of symptom improvement or reduction in spleen/liver volume while on Revlimid

Authorization will be issued for 12 months.

F. Hodgkin Lymphoma

1. **Initial Authorization**

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

(1) Diagnosis of Hodgkin lymphoma

-AND-

(2) Disease is **one** of the following:

(a) Relapsed
(b) Refractory

-AND-

(3) Used as third-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.

G. Systemic Light Chain Amyloidosis

1. **Initial Authorization**

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

(1) Diagnosis of systemic light chain amyloidosis

-AND-

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

(a) Used in combination with dexamethasone
(b) Used in combination with dexamethasone and bortezomib
(c) Used in combination with dexamethasone and cyclophosphamide
(d) Used in combination with 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 the following criteria:

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

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

-AND-

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

i. Used for relapsed or refractory disease after prior therapy with Bruton Tyrosine Kinase (BTK) inhibitor- and venetoclax-based regimens without del(17p)/TP53 mutation
ii. Used for Second-line and subsequent therapy with del(17p)/TP53 mutation.

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 the following criteria:

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

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

i. Peripheral T-cell lymphoma
ii. T-cell leukemia / lymphoma
iii. Hepatosplenic gamma-delta T-cell lymphoma

-AND-

(b) **Not** used as first line 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 AIDS-related Kaposi Sarcoma

            -AND-

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

         -AND-

      (2) **Not** used as first line 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.

L. Langerhans Cell Histiocytosis

1. **Initial Authorization**

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

(1) Diagnosis of Langerhans cell histiocytosis

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. 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

[b] Coverage of oncology medications may be approved based on state mandates.

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; December 2022.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at www.nccn.org. Accessed March 21, 2023.
3. Revlimid REMS®. Available at http://www.revlimidrems.com/. Accessed March 21, 2023.

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.