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5.21.047

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	August 22, 2014
Subject:	Revlimid	**Page:**	1 of 7

Last Review Date: December 13, 2024

Revlimid

Description

Revlimid (lenalidomide)

Background
Revlimid (lenalidomide) is classed as an immunomodulator and is a chemical derivative of thalidomide. Although the exact mechanism of action is unknown, lenalidomide also has anti-inflammatory and anticancer properties. It selectively inhibits secretion of inflammatory cells, enhances the activity of immunity cells, and inhibits the growth of new blood vessels. The medication stops the growth of myeloma cells by causing cell cycle arrest and cell death (1).

Regulatory Status
FDA-approved indications: Revlimid is a thalidomide analogue indicated for the treatment of patients with: (1)

1. Multiple myeloma (MM), in combination with dexamethasone
2. Multiple myeloma (MM), as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT)
3. 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
4. Mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib (Velcade)
5. Previously treated follicular lymphoma (FL), in combination with a rituximab product
6. Previously treated marginal zone lymphoma (MZL), in combination with a rituximab product

Limitations of Use:
Revlimid is not indicated and is not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials (1).

Off-Label Uses: (2-5)

1. Myelodysplastic syndromes (MDS) – without the 5q deletion cytogenic abnormality
2. Systemic light chain amyloidosis
3. Classical Hodgkin lymphoma
4. Relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL) with any of the following histologies:
    a. Mantle cell lymphoma (MCL)
    b. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
    c. Diffuse large B-cell lymphoma
    d. AIDS-related diffuse large B-cell lymphoma
    e. Primary effusion lymphoma
    f. Castleman's disease
    g. Nongastric/gastric mucosa associated lymphoid tissue (MALT) lymphoma
    h. Primary cutaneous B-cell lymphoma

Revlimid includes a boxed warning citing embryo-fetal toxicity, hematologic toxicity and venous and arterial thromboembolism. If Revlimid is used during pregnancy, it may cause birth defects or embryo-fetal death. Pregnancy must be excluded before start of treatment. Pregnancy must be prevented during treatment by the use of two reliable methods of contraception (1).

Revlimid can cause significant neutropenia and thrombocytopenia. For patients with del 5q myelodysplastic syndromes, monitor complete blood counts weekly for the first 8 weeks and monthly thereafter (1).

Revlimid has a significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients with multiple myeloma receiving Revlimid with dexamethasone (1).

Because of the embryo-fetal risk, Revlimid is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS), the Lenalidomide REMS program (1).

The safety and effectiveness of Revlimid in pediatric patients less than 18 years of age have not been established (1).

Related policies
Pomalyst

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Revlimid may be considered **medically necessary** if the conditions indicated below are met.

Revlimid may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Multiple myeloma (MM) with **ONE** of the following:
    a. Must be used in combination with dexamethasone or another corticosteroid
    b. Used as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT)

2. Myelodysplastic syndromes (MDS)
    a. Low- or intermediate-1 risk
    b. Transfusion-dependent anemia

3. Relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL) with any of the following histologies:
    a. Mantle cell lymphoma (MCL)
    b. Follicular lymphoma
    c. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
    d. Diffuse large B-cell lymphoma
    e. AIDS-related diffuse large B-cell lymphoma

f. Primary effusion lymphoma
g. Castleman's disease
h. Nongastric/gastric mucosa associated lymphoid tissue (MALT) lymphoma
i. Primary cutaneous B-cell lymphoma
j. Marginal zone lymphoma

4. Systemic light chain amyloidosis

5. Classical Hodgkin lymphoma

AND the following:

a. Prescriber and patient must be certified with the Lenalidomide REMS program

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Multiple myeloma (MM)

2. Myelodysplastic syndromes (MDS)

3. Relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL) with any of the following histologies:
   a. Mantle cell lymphoma (MCL)
   b. Follicular lymphoma
   c. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
   d. Diffuse large B-cell lymphoma
   e. AIDS-related diffuse large B-cell lymphoma
   f. Primary effusion lymphoma
   g. Castleman's disease

h. Nongastric/gastric mucosa associated lymphoid tissue (MALT) lymphoma
i. Primary cutaneous B-cell lymphoma
j. Marginal zone lymphoma

4. Systemic light chain amyloidosis

5. Classical Hodgkin lymphoma

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 25 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Revlimid is a thalidomide analogue used for the treatment of multiple myeloma, myelodysplastic syndromes (MDS), non-Hodgkin lymphoma (NHL) with certain histologies, systemic light chain amyloidosis and classical Hodgkin lymphoma. Revlimid includes a boxed warning citing embryo-fetal toxicity, hematologic toxicity and venous and arterial thromboembolism. Because of the embryo-fetal risk, Revlimid is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS), the Lenalidomide REMS program. The safety and effectiveness of Revlimid in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Revlimid while maintaining optimal therapeutic outcomes.

References

1. Revlimid [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2023.
2. NCCN Drugs & Biologics Compendium® Lenalidomide 2024. National Comprehensive Cancer Network, Inc. Accessed on October 1, 2024.
3. NCCN Clinical Practice Guidelines in Oncology® Multiple Myeloma (Version 1.2025). National Comprehensive Cancer Network, Inc. September 2024. Accessed on October 1, 2024.
4. NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 3.2024). National Comprehensive Cancer Network, Inc. August 2024. Accessed on October 1, 2024.
5. NCCN Clinical Practice Guidelines in Oncology® Hodgkin's Lymphoma (Version 3.2024). National Comprehensive Cancer Network, Inc. March 2024. Accessed on October 1, 2024.

Policy History

Date	Action
August 2014	New addition to PA
September 2014	Annual review Removal of Multiple Myeloma one prior therapy requirement
October 2014	Removal of the requirement combination with dexamethasone or another corticosteroid in the Multiple Myeloma renewal section
November 2014	Rewording of the Myelodysplastic syndromes (MDS)
December 2014	Annual review and reference update
February 2015	Addition of follicular lymphoma, chronic lymphocytic leukemia (CLL), and diffuse large B-cell lymphoma. Change to mantle cell lymphoma to only require 1 prior therapy instead of 2 and removal of requirement of Velcade being tried and failed
June 2015	Annual review and reference update
September 2016	Annual editorial review and reference update Removal of laboratory confirmation of the deletion 5q cytogenetic abnormality and complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter and removal of used in combination with Rituxan (rituximab) Addition of indications: relapsed, refractory, or progressive non-Hodgkin lymphoma (NHL) with any of the following histologies: mantle cell lymphoma (MCL), follicular lymphoma, chronic lymphocytic leukemia (CLL) /small lymphocytic lymphoma (SLL), diffuse large B-cell lymphoma, AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma,

	Castleman's disease, non-gastric/gastric mucosa associated lymphoid tissue (MALT) lymphoma, primary cutaneous B-cell lymphoma, or splenic marginal zone lymphoma; and for the treatment of systemic light chain amyloidosis and classical Hodgkin lymphoma Policy number change from 5.04.47 to 5.21.47
March 2017	Addition of multiple myeloma when used as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT)
September 2017	Annual review
June 2018	Annual editorial review and reference update
June 2019	Annual review and reference update. Removed splenic from the diagnosis of marginal zone lymphoma
September 2019	Annual review
June 2020	Annual editorial review and reference update. Addition of PA quantity limit per FEP
December 2020	Annual review
September 2021	Annual review and reference update
April 2022	Quantity limit changed from 28 capsules per 28 days to 25 mg per day to allow dosing flexibility. Revised the name of the REMS program to Lenalidomide REMS per PI
June 2022	Annual review
December 2022	Annual review and reference update. Changed policy number to 5.21.047
September 2023	Annual review and reference update
September 2024	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.