FIRST TIME GENERIC APPROVAL

Brand Name	Revlimid®
Generic Name	lenalidomide
Drug Manufacturer	Teva Pharmaceuticals, Inc.

New Drug Approval

TYPE OF CLINICAL UPDATE

First Time Generic

FDA APPROVAL DATE

August 5, 2021

LAUNCH DATE

March 7, 2022

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

Abbreviated New Drug Application (ANDA): 201452

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION FOR USE

Lenalidomide is a thalidomide analogue indicated for the treatment of adult patients with:

- Multiple myeloma (MM), in combination with dexamethasone
- Multiple myeloma (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.
- Previously treated marginal zone lymphoma (MZL), in combination with a rituximab product.

Limitations of Use:

- Lenalidomide capsules are not indicated and are not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials.

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MECHANISMS OF ACTION

Lenalidomide is an analogue of thalidomide with immunomodulatory, antiangiogenic, and antineoplastic properties. Cellular activities of lenalidomide are mediated through its target cereblon, a component of a cullin ring E3 ubiquitin ligase enzyme complex. *In vitro*, in the presence of drug, substrate proteins (including Aiolos, Ikaros, and CK1α) are targeted for ubiquitination and subsequent degradation leading to direct cytotoxic and immunomodulatory effects. Lenalidomide inhibits proliferation and induces apoptosis of certain hematopoietic tumor cells including MM, mantle cell lymphoma, and del (5q) myelodysplastic syndromes *in vitro*. Lenalidomide causes a delay in tumor growth in some *in vivo* nonclinical hematopoietic tumor models including MM. Immunomodulatory properties of lenalidomide include increased number and activation of T cells and natural killer (NK) cells leading to direct and enhanced antibody-dependent cell-mediated cytotoxicity (ADCC) via increased secretion of interleukin-2 and interferon-gamma, increased numbers of NKT cells, and inhibition of pro-inflammatory cytokines (e.g., TNF-α and IL-6) by monocytes. In MM cells, the combination of lenalidomide and dexamethasone synergizes the inhibition of cell proliferation and the induction of apoptosis.

DOSE FORM AND STRENGTH

Capsules: 5 mg, 10 mg, 15 mg, and 25 m

DOSE & ADMINISTRATION

- MM combination therapy: 25 mg once daily orally on Days 1 to 21 of repeated 28-day cycles.
- MDS: 10 mg once daily.
- MCL: 25 mg once daily orally on Days 1 to 21 of repeated 28-day cycles.
- Renal impairment: Adjust starting dose based on the creatinine clearance value.