

**THALOMID
(thalidomide)****RATIONALE FOR INCLUSION IN PA PROGRAM****Background**

Thalomid (thalidomide) possesses immunomodulatory, anti-inflammatory, and antiangiogenic properties. Studies suggest that the immunologic effects of Thalomid can vary substantially under different conditions but may be related to suppression of excessive tumor necrosis factor-alpha (TNF- α) production and down-regulation of selected cell surface adhesion molecules involved in leukocyte migration. For example, administration of thalidomide has been reported to decrease circulating levels of TNF- α in patients with erythema nodosum leprosum (ENL); however, it has been shown to increase plasma TNF- α level in HIV-seropositive patients. Thalidomide treatment of multiple myeloma patients is accompanied by an increase in the number of circulating natural killer cells, and an increase in plasma levels of interleukin-2 and interferon-gamma. Thalidomide was found to inhibit angiogenesis *in vitro* (1).

Regulatory Status

FDA-approved indications: Thalomid is indicated: (1)

1. For the treatment of patients with newly diagnosed multiple myeloma (MM), in combination with dexamethasone
2. For the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)
 - a. Thalomid is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis.
 - b. Thalomid is also indicated as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence.

Off-Label Uses: (2)

1. Castleman disease
2. Langerhans cell histiocytosis
3. Rosai-Dorfman disease
4. Kaposi sarcoma
5. Relapsed, or progressive multiple myeloma (MM)
6. Myelofibrosis

Thalomid includes a boxed warning citing embryo-fetal toxicity. If Thalomid is used during



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pregnancy, it may cause birth defects or embryo-fetal death. Thalomid should never be used by females who are pregnant or who could become pregnant while taking the drug. Because of this toxicity and in an effort to make the chance of embryo-fetal exposure to Thalomid as negligible as possible, Thalomid is approved for marketing only through a special restricted distribution program: Thalomid REMS program (1).

Thalomid also contains a boxed warning regarding the increased risk of venous thromboembolism. This risk increases significantly when Thalomid is used in combination with standard chemotherapeutic agents including dexamethasone. Patients and physicians are advised to be observant for the signs and symptoms of thromboembolism (1).

Additional warnings for Thalomid are increased mortality in patients with MM when pembrolizumab is added to a thalidomide analogue and dexamethasone, drowsiness and somnolence, peripheral neuropathy, dizziness and orthostatic hypotension, neutropenia, thrombocytopenia, increased HIV viral load, bradycardia, severe cutaneous reactions, seizures, tumor lysis syndrome, contraceptive risks, and hypersensitivity (1).

The safety and effectiveness of Thalomid in pediatric patients less than 12 years of age have not been established (1).

Summary

Thalomid (thalidomide) is an immunomodulatory, anti-inflammatory, and antiangiogenic medication. It is indicated for use in newly diagnosed multiple myeloma and erythema nodosum leprosum (ENL). Thalomid is also used off-label for Castleman disease, Langerhans cell histiocytosis, Rosai-Dorfman disease, Kaposi sarcoma, relapsed or progressive multiple myeloma, and myelofibrosis. Thalomid has a boxed warning regarding embryo-fetal toxicity and venous thromboembolism. Thalomid is approved for marketing only through a special restricted distribution program, the Thalomid REMS program. The safety and effectiveness of Thalomid in pediatric patients less than 12 years of age have not been established (1-2).

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



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References

1. Thalomid [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2023.
2. NCCN Drugs & Biologics Compendium® Thalidomide 2024. National Comprehensive Cancer Network, Inc. Accessed on April 24, 2024.