PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Thalomid® (thalidomide capsules – Celgene)

DATE REVIEWED: 04/01/2020

OVERVIEW

Thalomid is indicated for use in combination with dexamethasone for the treatment of patients with newly diagnosed multiple myeloma.[1] It is also indicated for the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL). It is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis. Thalomid is also indicated as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for multiple myeloma (version 3.2020 – March 10, 2020) recommend use of Thalomid in various scenarios.[2] It is considered useful in certain circumstances among patients with previously treated multiple myeloma, as well as for primary therapy for transplant candidates.

The National Comprehensive Cancer Network (NCCN) has guidelines regarding myeloproliferative neoplasms (version 3.2019 – September 4, 2019) that discuss myelofibrosis.[3] Thalomid is recommended in the management of anemia associated with myelofibrosis, with or without prednisone, for patients with erythropoietin levels ≥ 500 mU/mL.

The NCCN guidelines for acquired immune deficiency syndrome (AIDS)-Related Kaposi Sarcoma (version 1.2020 – February 12, 2020) recommended Thalomid as an agent useful under certain conditions for subsequent systemic therapy options for relapsed/refractory therapy.[4] First-line systemic therapy options include liposomal doxorubicin (preferred), and paclitaxel. Other subsequent systemic therapy options for relapsed/refractory therapy are also cited (e.g., Pomalyst® [pomalidomide capsules] {preferred}, Revlimid® [lenalidomide], imatinib).

The National Comprehensive Cancer Network (NCCN) guidelines for B-Cell Lymphomas (version 1.2020 – January 22, 2020) recommend use of Thalomid, with or without rituximab, for patients with Castleman's disease who have relapsed/refractory or progressive disease.[5] Thalomid is cited as an other recommended therapy (when given with cyclophosphamide and prednisone) for hyaline vascular histology for patients with multicentric Castleman's disease who are negative for the human immunodeficiency virus (HIV) and human herpesvirus-8 (HHV-8).

Other Uses with Supportive Evidence

Some data support the use of Thalomid for ENL, although the condition is not common and data are limited.[6,7] Data indicates that Thalomid does successfully and quickly improve the cutaneous manifestations of ENL and in some patients the steroid requirement was reduced.

Thalomid has been used for discoid lupus erythematosus and cutaneous lupus erythematosus. Patients usually had refractory disease after trial of other therapies and good responses were achieved for many patients given Thalomid.[8-17] A retrospective medical review was done and involved 29 patients with refractory cutaneous manifestations of cutaneous lupus erythematosus who received Thalomid. Of the 23 patients who took Thalomid for 1 month, 74% of patients (n = 17/23) had complete resolution of

the cutaneous manifestations and 13% of patients (n = 3/23) had a 75% or greater partial improvement.[11] Another report involving patients with discoid lupus (n = 18), subacute cutaneous lupus (n = 6), and systemic lupus erythematosus with skin involvement (n = 24) who had been resistant to at least two other treatments found a response rate of 81% (n = 39/48) with use of Thalomid with 60% of patients (n = 29/48) achieving a complete cutaneous remission.[12] Other therapies used for these conditions include antimalarial agents (e.g. hydroxychloroquine), corticosteroids (oral, topical, intralesional), methotrexate, azathioprine, cyclosporine, dapsone, mycophenolate mofetil, topical calcineurin inhibitors (e.g., Elidel, Protopic) and Soriatane.[10,15]

Thalomid has been studied in patients with prurigo nodularis, most of whom were refractory to other treatments or with adverse events (AEs) from the other therapies.[8,18,19] A retrospective review assessed the medical records of 42 patients with prurigo nodularis who were refractory to other therapy and who received Thalomid.[18] Patients received Thalomid for an average of 105 weeks. Previous therapies tried included topical steroids, intralesional steroids, systemic steroids, topical tar, macrolides, cyclosporine, azathioprine, methotrexate, calcineurnin inhibitors, antihistamines, dapsone, capsaicin, laser therapy, PUVA, UVB, retinoids, hydroxyzine, and macrolides. With Thalomid, improvement was noted in approximately one-third of patients.

Recurrent aphthous ulcers and recurrent aphthous stomatitis are associated with frequent and recurring symptoms that are painful and can lead to difficulty in speaking, eating, and swallowing.[20-23] Ulcers are larger and may persist for weeks to months. The conditions are noted in certain disease states such as in patients who are human immunodeficiency virus (HIV)-positive and Bechet's disease. In general, few adequately powered trials have assessed the efficacy of therapeutic agents for aphthous ulcers or aphthous stomatitis.[20] Although the data are older and limited, Thalomid has led to rapid resolution of symptoms in patients with recurrent aphthous ulcers or aphthous stomatitis.[24-29] A double-blind, randomized, placebo-controlled study assessed Thalomid as a therapy for oral aphthous ulcers in patients infected with HIV. In total, 55% of patients (n = 16/29) given Thalomid had complete healing of their aphthous ulcers after 4 weeks compared with only 7% of patients (n = 2/28) who received placebo. Patients given Thalomid had symptom improvements in regards to discomfort that occurred while eating.[25] A retrospective cohort study involving patients with recurrent aphthous stomatitis found that Thalomid was rapidly effective as 85% of patients (n = 78/92) achieved a complete remission of the condition within 14 days.[29] Many other agents have been used for recurrent aphthous ulcers or stomatitis including topical or intralesional corticosteroids, systemic corticosteroids, topical anesthetics/analgesics (lidocaine 2% viscous solution, benzocaine lozenges), antimicrobial mouth washes (tetracycline, chlorhexidine), topical sucralfate, acyclovir, pentoxifylline, dapsone, colchicine, and azathioprine.[20-23] Due to toxicities, use of Thalomid is generally reserved for patients who have not obtained satisfactory results with other agents.[30,31]

Safety

Thalomid has a Boxed Warning regarding embryofetal toxicity and venous thromboembolism. The safety and effectiveness in pediatric patients < 12 years of age have not been established. Thalomid is available only through the THALOMID Risk Evaluation Mitigation Strategy (REMS™) program. Males and females must follow the required reproductive precautions.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Thalomid. All approvals are provided for 3 years in duration.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Thalomid is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Erythema Nodosum Leprosum (ENL).** Approve for 3 years.

2. **Multiple Myeloma.** Approve for 3 years.

Other Uses with Supportive Evidence

3. **Acquired Immune Deficiency Syndrome (AIDS)-Related Kaposi's Sarcoma.** Approve for 3 years if the patient meets the following (A and B):
   - **A)** The patient has tried at least one regimen or therapy; AND
     Note: Examples include liposomal doxorubicin, paclitaxel, Pomalyst® (pomalidomide capsules), Revlimid® [lenalidomide], and imatinib.
   - **B)** The patient has relapsed or refractory disease.

4. **Castleman's Disease.** Approve for 3 years if the patient meets one of the following (A or B):
   - **A)** The patient has relapsed/refractory or progressive disease; OR
   - **B)** The patient meets all of the following (i, ii, and iii):
     - **i.** The patient has multicentric Castleman's disease; AND
     - **ii.** The patient is negative for the human immunodeficiency virus (HIV) and human herpesvirus-8 (HHV-8); AND
     - **iii.** The patient has hyaline vascular histology.

5. **Discoid Lupus Erythematosus or Cutaneous Lupus Erythematosus.** Approve for 3 years if the patient has tried at least two other therapies.
   Note: Examples of therapies include corticosteroids (oral, topical, intralesional), antimalarial agents (e.g., hydroxychloroquine), topical calcineurin inhibitors (e.g., Protopic® [tacrolimus ointment], Elidel® [pimecrolimus cream]), azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, dapsone, and Soriatane® (acitretin capsules).

6. **Myelofibrosis.** Approve for 3 years if the patient meets the following criteria (A and B):
   - **A)** According to the prescriber the patient has anemia; AND
   - **B)** The patient has serum erythropoietin levels ≥ 500 mU/mL.

7. **Prurigo Nodularis.** Approve for 3 years if the patient has tried at least two other therapies.
   Note: Examples of therapies include topical steroids, intralesional steroids, systemic steroids, topical tar, cyclosporine, macrolides, azathioprine, methotrexate, topical calcineurin inhibitors (Elidel, Protopic), retinoids, antihistamines, hydroxyzine, dapsone, capsaicin, psoralen plus ultraviolet A (PUVA) therapy, and ultraviolet B (UVB) therapy.

8. **Recurrent Aphthous Ulcers or Aphthous Stomatitis.** Approve for 3 years if the patient has tried at least two other therapies.

Note: Examples include topical or intralesional corticosteroids, systemic corticosteroids, topical anesthetics/analgesics (e.g., lidocaine 2% viscous solution, benzocaine lozenges), antimicrobial mouthwashes (e.g., tetracycline, chlorhexidine), topical sucralfate, acyclovir, pentoxifylline, dapsone, colchicine, and azathioprine.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Thalomid has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Cancer Cachexia.** Several small studies are available that have investigated Thalomid in the management of cancer cachexia related to various cancers.[32-36] A single center double-blind, controlled trial randomized patients with pancreatic cancer who had lost at least 10% of their body weight to receive Thalomid or placebo for 24 weeks (n = 50).[33] Of the 33 patients evaluable at 4 weeks, patients given Thalomid had gained an average of 0.37 kg compared with a loss of 2.21 kg in the patients given placebo.[33] A published review of data regarding use of Thalomid for the management of cancer cachexia concluded that there is inadequate evidence to recommend Thalomid in clinical practice.[36]

2. **Crohn's Disease.** Several publications report use of Thalomid in patients with Crohn's disease.[37-53] Thalomid was used as an adjunctive therapy, or in those refractory to other therapy, and usually involved children. The data were not of high quality and primarily consisted of open-label designs or retrospective reviews, without a placebo control, and involved very few patients.[37-53] Guidelines from the American College of Gastroenterology (2018) for the management of Crohn's disease in adults do not mention Thalomid as a therapeutic alternative.[48] Although some improvements were noted in published data with Thalomid, more definite data from randomized, controlled trials are required before this is a recommended therapy.[48] Consensus guidelines of the European Crohn's and Colitis Organization (ECCO) and the European society of Pediatric Gastroenterology, Hepatology and Nutrition (ESOGGAN) [2014] state that even though some data are available that suggest efficacy of Thalomid in refractory pediatric Crohn's disease, there are insufficient data to recommended Thalomid therapy at this juncture.[53] Many other therapies are available for the management of Crohn's disease.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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