PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Oral – Immunomodulator) – Thalomid Prior Authorization Policy
- Thalomid® (thalidomide capsules – Celgene)

REVIEW DATE: 05/14/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Thalomid, an immunomodulatory agent, is indicated for the following uses:[1]
- **Erythema nodosum leprosum (ENL)**, acute treatment of cutaneous manifestations in moderate to severe disease. Thalomid is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis.
- **ENL**, maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence.
- **Multiple myeloma**, newly diagnosed, in combination with dexamethasone.

Other Uses with Supportive Evidence

Discoid Lupus Erythematosus or Cutaneous Lupus Erythematosus

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.[2-12] A retrospective medical review was done that 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.[3] 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.[4] 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., pimecrolimus, tacrolimus, and acitretin).[2,7,12]

Prurigo Nodularis
Thalomid has been studied in patients with prurigo nodularis, most of whom were refractory to other treatments or who have experienced adverse events from the other therapies.[2,13-15] A retrospective review assessed the medical records of 42 patients with prurigo nodularis who were refractory to other therapy and who received Thalomid.[13] 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, calcineurin inhibitors, antihistamines, dapsone, capsaicin, laser therapy, psoralen plus ultraviolet A therapy, ultraviolet B therapy, retinoids, and hydroxyzine. With Thalomid, improvement was noted in approximately one-third of patients.

Aphthous Ulcers or Aphthous Stomatitis
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.[16-27] 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 in Behcet's disease. In general, few adequately powered trials have assessed the efficacy of therapeutic agents for aphthous ulcers or aphthous stomatitis. Although the data are older and limited, Thalomid has led to rapid resolution of symptoms in patients with recurrent aphthous ulcers or aphthous stomatitis.[16-27] 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.[21] 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.[25] 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.[16-27] Due to toxicities, use of Thalomid is generally reserved for patients who have not obtained satisfactory results with other agents.[26,27]

Guidelines
Thalomid is addressed in guidelines from National Comprehensive Cancer Network (NCCN):

- **Castleman Disease:** NCCN guidelines (version 2.2025 – January 28, 2025) recommend use of Thalomid ± rituximab for those who have relapsed/refractory or progressive disease (category 2A).[28] Thalomid is recommended with cyclophosphamide and prednisone for patients with multi-centric Castleman disease who are negative for HIV and human herpesvirus-8 [category 2A].

- **Histiocytic Neoplasms:** NCCN guidelines (version 3.2024 – January 7, 2025) recommend Thalomid in a few clinical scenarios.[29] For Langerhans cell histiocytosis, Thalomid is recommended as first-line or as subsequent therapy for single system multifocal skin disease (including mucosa) and for relapsed/refractory disease (category 2A). Thalomid is also recommended as first-line or subsequent therapy for cutaneous skin disease associated with Rosai-Dorfman disease under "useful in certain circumstances," irrespective of mutation (category 2A) [e.g., those with relapsed/refractory disease, symptomatic multifocal disease, symptomatic unresectable unifocal disease].
- **Kaposi Sarcoma:** NCCN guidelines (version 2.2025 – January 14, 2025) recommended Thalomid as an agent "useful under certain circumstances" for subsequent systemic therapy options for relapsed/refractory therapy (category 2A) [for patients with immune reconstitution inflammatory syndrome].[30] This includes use when given alone (in patients without HIV) or with antiretroviral therapy for patients with HIV. 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], lenalidomide, imatinib).
- **Multiple Myeloma:** NCCN guidelines (version 2.2025 – April 11, 2025) recommend use of Thalomid in various scenarios (category 2A).[31] It is considered "useful in certain circumstances" among patients with previously treated multiple myeloma, as well as for primary therapy for transplant candidates. Thalomid is always recommended to be used with at least two other therapies to comprise the regimen.
- **Pediatric Central Nervous System Cancers:** NCCN guidelines (version 2.2025 – January 17, 2025) recommend Thalomid for recurrent or progressive pediatric medulloblastoma for all risk categories as part of MEMMAT regimen (i.e., thalidomide, celecoxib, fenofibrate, oral etoposide, cyclophosphamide, bevacizumab, intraventricular etoposide) [category 2A].[32]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Thalomid. All approvals are provided for the duration noted below.

- **Thalomid® (thalidomide capsules - Celgene)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. Erythema Nodosum Leprosum. Approve for 1 year.

2. Multiple Myeloma. Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) The medication is used in combination with at least two other medications.
   Note: Examples of medications include bortezomib, dexamethasone, cisplatin, doxorubicin, cyclophosphamide, etoposide, and Kyprolis (carfilzomib intravenous infusion).

Other Uses with Supportive Evidence

3. **Castleman Disease.** Approve for 1 year if the patient meets ONE of the following (A or B):
   A) Patient has relapsed/refractory or progressive disease; OR
   B) Patient meets BOTH of the following (i and ii):
      i. Patient has multi-centric disease; AND
      ii. Patient is negative for the human immunodeficiency virus and human herpesvirus-8.

4. **Discoid Lupus Erythematosus or Cutaneous Lupus Erythematosus.** Approve for 1 year if the patient has tried at least two other medications.
   Note: Examples of medications include corticosteroids (oral, topical, intralesional), antimalarial agents (e.g., hydroxychloroquine), topical calcineurin inhibitors (e.g., tacrolimus, pimecrolimus, azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, dapsone, and acitretin.

5. **Histiocytic Neoplasms:** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. Patient has Langerhans cell histiocytosis and meets ONE of the following (a or b):
         a) Patient has single-system multifocal skin disease; OR
         b) Patient has relapsed or refractory disease; OR
      ii. Patient has Rosai-Dorfman cutaneous disease.

6. **Kaposi Sarcoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient has tried at least one medication; AND
   Note: Examples include liposomal doxorubicin, paclitaxel, Pomalyst (pomalidomide capsules), lenalidomide, and imatinib.
   B) Patient has relapsed or refractory disease.

7. **Medulloblastoma**. Approve for 1 year if the patient meets ALL of the following (A, B and C):
   A) Patient is < 18 years of age; AND
   B) Patient has recurrent or progressive disease; AND
   C) The medication is being used as a part of the MEMMAT regimen (i.e., Thalomid, celecoxib, fenofibrate, oral etoposide, cyclophosphamide, bevacizumab, and intraventricular etoposide).

8. **Prurigo Nodularis.** Approve for 1 year if the patient has tried at least two other medications.
   Note: Examples of medications include topical steroids, intralesional steroids, systemic steroids, topical tar, cyclosporine, macrolides, azathioprine, methotrexate, topical calcineurin inhibitors (e.g., pimecrolimus, tacrolimus) retinoids, antihistamines, hydroxyzine, dapsone, capsaicin, psoralen plus ultraviolet A therapy, and ultraviolet B therapy.

9. **Recurrent Aphthous Ulcers or Aphthous Stomatitis.** Approve for 1 year if the patient has tried at least two other medications.
   Note: Examples of medications 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 COVERED

- **Thalomid® (thalidomide capsules - Celgene)**

is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Cancer Cachexia.** Several small studies are available that have investigated Thalomid in the management of cancer cachexia related to various cancers.[33-37] 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).[34] 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.[34] 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.[37]

2. **Crohn's Disease.** Several publications report use of Thalomid in patients with Crohn's disease.[38-54] 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.[38-54] Guidelines from the American College of Gastroenterology (2018) for the management of Crohn's disease in adults mention that thalidomide may be effective in severe Crohn's disease, but should be used only in exceptional circumstances, given the high risk of serious adverse effects that include sedation, constipation, peripheral neuropathy, and severe birth defects.[49] Also, guidelines from the American Gastroenterological Association (2021) do not mention Thalomid in the guidelines for the medical management of moderate to severe luminal and perianal fistulizing Crohn's Disease.[55] 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.[49] Consensus guidelines of the European Crohn's and Colitis Organization and the European society of Pediatric Gastroenterology, Hepatology and Nutrition (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.[54] Many other therapies are available for the management of Crohn's disease.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes	05/10/2023
Annual Revision	**Histiocytic Neoplasms:** Added new approval condition and criteria. **Langerhans Cell Histiocytosis:** Deleted approval condition since it is now addressed under "Histiocytic Neoplasms" indication. **Rosai-Dorfman Disease:** Deleted approval condition since it is now addressed under "Histiocytic Neoplasms" indication.	05/29/2024
Update	04/08/2025: The policy name was changed from "Oncology – Thalomid PA Policy" to "Oncology (Oral – Immunomodulator) – Thalomid PA Policy".	N/A

Annual Revision	**Castleman Disease:** Previously, this condition of approval was called Castleman's Disease. **Histiocytic Neoplasms:** For a patient with Langerhans cell histiocytosis, an additional option for approval was added for relapsed or refractory disease. **Medulloblastoma**: This condition and criteria for approval were added to Other Uses with Supportive Evidence. **Myelofibrosis**: This condition and criteria for approval were removed.	05/14/2025

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