



## PRIOR AUTHORIZATION POLICY

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

**REVIEW DATE:** 05/10/2023

### **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. 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:<sup>1</sup>

- **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.<sup>2-12</sup> 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.<sup>3</sup> 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.<sup>4</sup> 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® [pimecrolimus 1% cream], Protopic® [tacrolimus 0.03% and 0.1% ointment]), and Soriatane® (acitretin capsules).<sup>2,7,12</sup>

### *Prurigo Nodularis*

Thalomid has been studied in patients with prurigo nodularis, most of whom were refractory to other treatments or with adverse events from the other therapies.<sup>2,13-15</sup> A retrospective review assessed the medical records of 42 patients with prurigo nodularis who were refractory to other therapy and who received Thalomid.<sup>13</sup> 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, hydroxyzine, and macrolides. 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.<sup>16-27</sup> 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. Although the data are older and limited, Thalomid has led to rapid resolution of symptoms in patients with recurrent aphthous ulcers or aphthous stomatitis.<sup>16-27</sup> 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.<sup>21</sup> 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.<sup>25</sup> 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.<sup>16-27</sup> Due to toxicities, use of Thalomid is generally reserved for patients who have not obtained satisfactory results with other agents.<sup>26,27</sup>

## **Guidelines**

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

- **Castleman’s Disease:** The NCCN guidelines for B-cell lymphomas (version 2.2023 – February 8, 2023) recommend use of Thalomid, with or without rituximab, for patients with Castleman’s disease for those who have relapsed/refractory or progressive disease (category 2A).<sup>28</sup> Thalomid is cited as an “other recommended therapy” (when given with cyclophosphamide and prednisone) for patients with multi-centric Castleman’s disease who are negative for HIV and human herpesvirus-8 (HHV-8) [category 2A].
- **Histiocytic Neoplasms:** The NCCN guidelines for histiocytic neoplasms (version 1.2022 – May 20, 2022) recommend Thalomid in a few clinical scenarios.<sup>29</sup> 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” (category 2A) [e.g., those with relapsed/refractory disease, symptomatic multifocal disease, symptomatic unresectable unifocal disease].
- **Kaposi Sarcoma:** The NCCN guidelines for Kaposi sarcoma (version 1.2023 – December 20, 2022) recommended Thalomid as an agent “useful under certain conditions” for subsequent systemic therapy options for relapsed/refractory therapy (category 2A) [for patients with corticosteroid-refractory immune reconstitution inflammatory syndrome].<sup>30</sup> 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] {preferred}, lenalidomide, imatinib).
- **Multiple Myeloma:** The NCCN guidelines for multiple myeloma (version 3.2023 – December 8, 2022) recommend use of Thalomid in various scenarios (category 1 for use with bortezomib and dexamethasone; category 2A for others).<sup>31</sup> 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.
- **Myelofibrosis:** The NCCN has guidelines regarding myeloproliferative neoplasms (version 3.2022 – August 11, 2022) discuss myelofibrosis.<sup>32</sup> Thalomid is recommended in the management of anemia associated with myelofibrosis “useful in certain circumstances”, with or without prednisone, for a variety of clinical scenarios (category 2A) including patients with erythropoietin levels  $\geq 500$  mU/mL and with erythropoietin levels  $< 500$  mU/mL and no response or loss of response to erythropoietic stimulating agents.

## 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 the following (A and B):

**A)** Patient is  $\geq$  18 years of age; AND

**B)** Thalomid is being taken 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's 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 the following criteria (i and ii):

**i.** Patient has multi-centric Castleman's 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., Protopic [tacrolimus ointment], Elidel [pimecrolimus cream]), azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, dapsone, and Soriatane (acitretin capsules).

**5. Kaposi Sarcoma.** Approve for 1 year if the patient meets 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.

**6. Langerhans Cell Histiocytosis.** Approve for 1 year if the patient has multifocal skin disease.

**7. Myelofibrosis.** Approve for 1 year if the patient meets one of the following (A or B):

**A)** Patient meets the following criteria (i, ii, and iii):

- i.** Patient is  $\geq 18$  years of age; AND
- ii.** According to the prescriber the patient has anemia; AND
- iii.** Patient has serum erythropoietin levels  $\geq 500$  mU/mL; OR

**B)** Patient meets the following criteria (i, ii, iii, and iv):

- i.** Patient is  $\geq 18$  years of age; AND
- ii.** According to the prescriber the patient has anemia; AND
- iii.** Patient has serum erythropoietin levels  $< 500$  mU/mL; AND
- iv.** Patient has experienced no response or loss of response to an erythropoiesis-stimulating agent.

**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 (Elidel [pimecrolimus cream], Protopic [tacrolimus ointment]), 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.

**10. Rosai-Dorfman Disease.** Approve for 1 year if the patient has cutaneous disease.

## CONDITIONS NOT COVERED

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

**is(are) considered experimental, investigational or unproven 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.<sup>33-37</sup> 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).<sup>34</sup> 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.<sup>34</sup> 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.<sup>37</sup>

**2. Crohn's Disease.** Several publications report use of Thalomid in patients with Crohn's disease.<sup>38-54</sup> 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.<sup>38-54</sup> 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.<sup>49</sup> 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.<sup>55</sup> 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.<sup>49</sup> 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 recommend Thalomid therapy at this juncture.<sup>54</sup> 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.	05/11/2022
Selected Revision	<p><b>Erythema Nodosum Leprosus:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Multiple Myeloma:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Castleman's Disease:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Discoid Lupus Erythematosus or Cutaneous Lupus Erythematosus:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Kaposi Sarcoma:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Langerhans Cell Histiocytosis:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Myelofibrosis:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Prurigo Nodularis:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Recurrent Aphthous Ulcers or Aphthous Stomatitis:</b> The approval duration was changed from 3 years to 1 year.</p> <p><b>Rosai-Dorfman Disease:</b> The approval duration was changed from 3 years to 1 year.</p>	06/22/2022
Annual Revision	No criteria changes	05/10/2023

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