Clinical Policy: Thalidomide (Thalomid)

Reference Number: CP.PHAR.78
Effective Date: 09.01.11
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Thalidomide (Thalomid®) is an immunomodulatory agent.

FDA Approved Indication(s)

Thalomid is indicated:

- For the treatment of patients with newly diagnosed multiple myeloma (MM) in combination with dexamethasone
- For the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)
- As maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence

Limitation(s) of use: Thalomid is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Thalomid is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all)**:**

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 12 years;
4. Prescribed in combination with dexamethasone;
5. Thalomid is not prescribed concurrently with lenalidomide or Pomalyst®;
6. For Thalomid requests, member must use generic thalidomide, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 200 mg per day;
      ii. 1 capsule per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Erythema Nodosum Leprosum (must meet all)**:**

1. Diagnosis of ENL;
2. Prescribed by or in consultation with an infectious disease specialist, immunologist, or dermatologist;
3. Age ≥ 12 years;
4. Thalomid is not prescribed concurrently with lenalidomide or Pomalyst;
5. For Thalomid requests, member must use generic thalidomide, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed both of the following (a and b):
   a. 400 mg per day;
   b. 2 capsules per day.

Approval duration: 6 months

C. NCCN Compendium Indications (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a, b, c, or d):
   a. Multicentric Castleman's disease (MCD);
   b. Kaposi sarcoma;
   c. Langerhans cell histiocytosis or Rosai-Dorfman disease;
   d. Pediatric medulloblastoma;
2. Prescribed by or in consultation with one of the following (a, b, or c):
   a. Oncologist;
   b. For Kaposi sarcoma: immunologist;
   c. For Langerhans cell histiocytosis or Rosai-Dorfman disease: hematologist;
3. Age ≥ 12 years;
4. For MCD, one of the following (a or b):
   a. Active idiopathic MCD without organ failure, and all of the following (i, ii, and iii):
      i. Human immunodeficiency virus (HIV) negative;
      ii. Human herpesvirus-8 (HHV-8) negative;
      iii. Prescribed in combination with cyclophosphamide and prednisone;
   b. As subsequent therapy for disease that has progressed following treatment of relapsed/refractory or progressive disease (*see Appendix E*);
5. For Kaposi sarcoma, all of the following (a, b, and c):
   a. If AIDS-related, Thalomid is prescribed in combination with antiretroviral therapy;
   b. Member has corticosteroid-refractory immune reconstitution inflammatory syndrome;
   c. Failure of liposomal doxorubicin and paclitaxel, unless clinically significant adverse effects are experienced or both are contraindicated;*
      **Prior authorization may be required for doxorubicin and paclitaxel*
6. For Langerhans cell histiocytosis or Rosai-Dorfman disease, prescribed as single-agent;
7. For pediatric medulloblastoma, prescribed as part of MEMMAT regimen (thalidomide, celecoxib, fenofibrate, etoposide, cyclophosphamide, bevacizumab);*

**Prior authorization may be required*

8. Thalomid is not prescribed concurrently with lenalidomide or Pomalyst;
9. For Thalomid requests, member must use generic thalidomide, if available, unless contraindicated or clinically significant adverse effects are experienced;
10. Request meets one of the following (a or b):*
    a. Dose does not exceed both of the following (i and ii):
        i. 400 mg per day;
        ii. 2 capsules per day;
    b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

D. Aphthous Stomatitis or Ulcers (off-label) (must meet all)**:**

1. Diagnosis of HIV-associated aphthous ulcers or aphthous stomatitis in immunocompetent members;
2. Age ≥ 12 years;
3. Failure of a systemic corticosteroid, unless clinically significant adverse effects are experienced or all are contraindicated;
4. Thalomid is not prescribed concurrently with lenalidomide or Pomalyst;
5. For Thalomid requests, member must use generic thalidomide, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
    a. Dose does not exceed both of the following (i and ii):
        i. 400 mg per day;
        ii. 2 capsules per day;
    b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

E. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
    a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
    b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Thalomid for oncology and has received this medication for at least 30 days;
   c. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Thalomid is not prescribed concurrently with lenalidomide or Pomalyst;
4. For Thalomid requests, member must use generic thalidomide, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed one of the following (i or ii):
      i. For MM (a and b):
         a) 200 mg per day;
         b) 1 capsule per day
      ii. For all other indications (a and b):
         a) 400 mg per day;
         b) 2 capsules per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ENL: erythema nodosum leprosum
FDA: Food and Drug Administration
MCD: multicentric Castleman's disease
MM: multiple myeloma
EPO: erythropoietin
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
liposomal doxorubicin (Doxil®)	Kaposi sarcoma: 20 mg/m^2 IV every 2-3 weeks with a cumulative lifetime dose of 400-450 mg/m^2 due to cardiotoxicity	20 mg/m^2/dose
paclitaxel	Kaposi sarcoma: 135 mg/m^2 IV every 3 weeks or 100 mg/m^2 IV every 2 weeks	See regimen
Systemic corticosteroids (e.g., prednisone)*	Aphthous stomatitis or ulcers*: 25 mg PO once daily for 15 days, then 12.5 mg PO once daily for 15 days, then 6.25 mg PO once daily for 15 days, and then 6.25 mg PO every other day for 15 days.	See regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
** Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): pregnancy; hypersensitivity
- Boxed warning(s): embryo-fetal toxicity and venous thromboembolism

Appendix D: General Information

- Thalomid is only available under a restricted distribution program called the Thalomid REMS program due to a black box warning for embryo-fetal toxicity. Patient and physician enrollment in the manufacturer's REMS program is required.

Appendix E: Initial Treatment for Relapsed or Progressive MCD per NCCN

- Single-agent therapies of etoposide, vinblastine, liposomal doxorubicin; or
- Combination therapy of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) ± rituximab, CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) ± rituximab, CVP (cyclophosphamide, vincristine, and prednisone) ± rituximab, or liposomal doxorubicin ± rituximab

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	200 mg PO QD	200 mg/day
ENL	100 to 300 mg PO QD	400 mg/day

VI. Product Availability

Capsules: 50 mg, 100 mg, 150 mg, 200 mg

VII. References

1. Thalomid Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; March 2023. Available at https://packageinserts.bms.com/pi/pi_thalomid.pdf. Accessed January 22, 2025.
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3. National Comprehensive Cancer Network Guidelines. Multiple Myeloma, Version 1.2025 Available at https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed February 5, 2025.
4. National Comprehensive Cancer Network Guidelines. Kaposi Sarcoma, Version 2.2025 Available at https://www.nccn.org/professionals/physician_gls/pdf/kaposi.pdf. Accessed February 5, 2025.
5. National Comprehensive Cancer Network Guidelines. Castleman Disease, Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/castleman.pdf. Accessed February 5, 2025.
6. National Comprehensive Cancer Network Guidelines. Histiocytic Neoplasms, Version 3.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed February 5, 2025.
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13. Lau CB, Smith GP. Recurrent aphthous stomatitis: A comprehensive review and recommendations on therapeutic options. *Dermatol Ther.* 2022 Jun;35(6):e15500. doi: 10.1111/dth.15500.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: added hematology specialist option to MM and myeloproliferative neoplasm indications; removed "hyaline vascular histology" requirement from MCD to align with NCCN removal; added criteria for corticosteroid-refractory immune reconstitution inflammatory syndrome in Kaposi sarcoma per NCCN; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	02.19.21	05.21
Added requirement for no concurrent use with Revlimid or Pomalyst since all are thalidomide analogs.	06.29.21	08.21
2Q 2022 annual review: added language for oral oncology generic redirection if available per template; for myeloproliferative neoplasms added notation that Retacrit is the preferred ESA; per NCCN modified KS requirements to allow use in non-AIDs related KS, added off-label criteria set for histiocytic neoplasms; WCG.CP.PHAR.78 to be retired and approval durations consolidated to 6 months initial and 12 months for continuation of therapy; added off-label use for aphthous stomatitis or ulcers per previous coverage in WCG policy; references reviewed and updated.	02.16.22	05.22
Template changes applied to other diagnoses/indications.	10.12.22	
2Q 2023 annual review: for myeloproliferative neoplasms added prescribed in combination with prednisone per NCCN 2A recommendation; for aphthous stomatitis/ulcers, updated dose from 100 to 400 mg per day in initial criteria per Clinical Pharmacology and referenced trial (Jacobson et al); clarified MM dosing in continued therapy criteria; revised oral oncology generic (if available) redirection language to align with template; references reviewed and updated.	02.24.23	05.23
2Q 2024 annual review: removed myeloproliferative neoplasms criteria set as this indication is no longer supported by NCCN compendium; revised Revlimid to generic lenalidomide; references reviewed and updated.	02.05.24	05.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2025 annual review: consolidated criteria for MCD, Kaposi sarcoma, and histiocytic neoplasms into one section of off-label NCCN Compendium Indications; in off-label NCCN compendium indications, added criteria for pediatric medulloblastoma per NCCN 2A recommendation; in continued therapy, clarified continuity of care does not apply to ENL, aphthous stomatitis, or aphthous ulcers and only applies to oncological indications; updated Appendix B per Clinical Pharmacology; references reviewed and updated.	02.05.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.