Clinical Policy: Thalidomide (Thalomid)

Reference Number: ERX.SPA.44
Effective Date: 07.01.16
Last Review Date: 08.21
Line of Business: Commercial, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 Revlimid® or Pomalyst®;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 200 mg (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:
Commercial – Length of Benefit
Medicaid – 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 Revlimid or Pomalyst;
5. Dose does not exceed 400 mg (2 capsules) per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

C. Myeloproliferative Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of myeloproliferative neoplasms (myelofibrosis) with associated anemia;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 12 years;
4. Member meets one of the following (a or b):
   a. Serum EPO ≥ 500 mU/mL;
   b. Serum EPO < 500 mU/mL, and no response or loss of response to erythropoietic stimulating agents;
6. Thalomid is not prescribed concurrently with Revlimid or Pomalyst;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (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:
Commercial – Length of Benefit
Medicaid – 6 months

D. Castleman's Disease (off-label) (must meet all)**:**
1. Diagnosis of multicentric Castleman's disease;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 12 years;
4. For active idiopathic MCD without organ failure, all of the following (a, b, and c):
   a. Human immunodeficiency virus (HIV) negative;
   b. Human herpesvirus-8 (HHV-8) negative;
   c. Prescribed in combination with cyclophosphamide and prednisone;
5. For disease that has progressed following treatment of relapsed/refractory or progressive disease, Thalomid is prescribed as subsequent therapy with or without rituximab (*see Appendix E);*
6. Thalomid is not prescribed concurrently with Revlimid or Pomalyst;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (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:
Commercial – Length of Benefit
Medicaid – 6 months

E. Kaposi Sarcoma (off-label) (must meet all)**:**
1. Diagnosis of AIDS-related Kaposi sarcoma;
2. Prescribed by or in consultation with an oncologist or immunologist;
3. Age ≥ 12 years;
4. Thalomid is prescribed in combination with antiretroviral therapy;
5. Member has corticosteroid-refractory immune reconstitution inflammatory syndrome;
6. Failure of liposomal doxorubicin and paclitaxel, unless clinically significant adverse effects are experienced or both are contraindicated;
7. Thalomid is not prescribed concurrently with Revlimid or Pomalyst;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (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:
Commercial – Length of Benefit
Medicaid – 6 months

F. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or documentation supports that member is currently receiving Thalomid for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Thalomid is not prescribed concurrently with Revlimid or Pomalyst;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 400 mg 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:
Commercial – Length of Benefit
Medicaid – 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ENL: erythema nodosum leprosum
EPO: erythropoietin
MCD: multicentric Castleman's disease
FDA: Food and Drug Administration
MM: multiple myeloma
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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
liposomal doxorubicin (Doxil®, Lipodox® 50)	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

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.

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. Summit, NJ: Celgene Corporation; February 2021. Available at http://media.celgene.com/content/uploads/thalomid-pi.pdf. Accessed June 29, 2021.
2. Thalidomide. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 19, 2021.
3. Multiple Myeloma (Version 2.2020). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed February 19, 2021.
4. AIDS-Related Kaposi Sarcoma (Version 1.2021). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed February 19, 2021.
5. B-cell Lymphomas (Version 2.2021). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed February February 19, 2021.
6. Myeloproliferative Neoplasms (Version 1.2020). In: National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed February February 19, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Increased approval durations from 3/6 months to 6/12 months. Updated off-label NCCN recommendations for MM. Split NCCN off-label uses into their own criteria sets per updated template.	04.17	05.17
2Q 2018 annual review: age added; removed off label indication for systemic light chain amyloidosis that is no longer included in NCCN Compendium; added off-label use for Kaposi Sarcoma; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; added continuity of care statement; approval durations changed to length of benefit; references reviewed and updated.	01.22.18	05.18
2Q 2019 annual review: myeloproliferative neoplasms – removed requirement for use in combination with prednisone to align with NCCN compendium; ENL	02.04.19	05.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
– removed disease specific requirements as specialist prescribing is required; removed off-label use for Waldenstrom macroglobulinemia/ lymphoplasmacytic lymphoma criteria set as this indication is no longer supported by NCCN compendium; references reviewed and updated.		
2Q 2020 annual review: added NCCN compendium-supported indication of active idiopathic MCD in section I.D.; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	02.15.20	05.20
AIDS-related KS: specified that the liposomal form of doxorubicin should be tried; added bypass of trial requirements if member is intolerant or contraindicated; all indications: added quantity limits associated with max FDA dose.	06.29.20	11.20
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 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

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.