Clinical Policy: Lenalidomide (Revlimid)

Reference Number: PA.CP.PHAR.71
Effective Date: 01/18
Last Review Date: 04/18

Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for lenalidomide (Revlimid®) capsules for oral use.

FDA Approved Indication
Revlimid is indicated for the treatment of patients with:

- Transfusion-dependent anemia due to low- or intermediate-risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities
- Multiple myeloma (MM), in combination with dexamethasone
- MM as maintenance following autologous hematopoietic stem cell transplantation
- Mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib (Velcade)

Limitation of use: Revlimid is not indicated and is not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness® that Revlimid is **medically necessary** when one of the following criteria is met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of multiple myeloma (MM);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Will be used for one of the following indications (a, b, or c):
   a. In combination with dexamethasone;
   b. As maintenance therapy as a single agent following autologous hematopoietic stem cell transplantation;
   c. As maintenance therapy as a single agent for active (symptomatic) myeloma after response to primary myeloma therapy;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 25 mg/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

B. Myelodysplastic Syndrome (must meet all):
1. Diagnosis of myelodysplastic syndrome (MDS);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member has symptomatic or transfusion-dependent anemia due to MDS;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/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

C. Mantle Cell Lymphoma (must meet all):
1. Diagnosis of mantle cell lymphoma (MCL);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Will be used for one of the following indications (a, b, or c):
   a. Relapsed or progressive disease after two prior therapies, one of which included bortezomib;
   b. In combination with rituximab;
   c. Second-line therapy as a single agent;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 25 mg/day;
   b. Requested 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

D. Other diagnoses/indications (must meet all):
1. The following NCCN recommended use(s) meeting NCCN categories 1, 2a may be covered provided that member meets the off-label criteria defined in the Global Biopharm policy (PA.CP.PHAR.57):
   a. Myelofibrosis-associated anemia;
   b. Systemic light chain amyloidosis in combination with dexamethasone;
   c. Classic Hodgkin lymphoma as subsequent therapy for relapsed or refractory disease, or as palliative therapy;
   d. Any of the following non-Hodgkin lymphoma subtypes:
      i. T-cell leukemia/lymphoma as second-line therapy;
      ii. AIDS-related B-cell lymphoma as second-line or subsequent therapy;
      iii. Castleman's disease (CD) as subsequent therapy following treatment of relapsed, refractory, or progressive disease;
      iv. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) as first or second-line maintenance therapy, or for relapsed or refractory disease;
      v. Diffuse large B-cell lymphoma;

vi. Follicular lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
vii. Gastric MALT lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
viii. Mycosis fungoides /Sezary syndrome;
ix. Nodal marginal zone lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
x. Nongastric MALT lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
xi. Peripheral T-cell lymphoma as second-line and subsequent therapy;
xii. Primary cutaneous CD30+ T-cell lymphoproliferative disorders as therapy for relapsed or refractory anaplastic large cell lymphoma with multifocal lesions or regional nodes;
xiii. Splenic marginal zone lymphoma as first-line therapy in combination with rituximab or as second-line or subsequent therapy;
xiv. Post-transplant lymphoproliferative disorders of B-cell lymphomas as second-line or subsequent therapy

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 25 mg/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

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. No disease progression or unacceptable toxicity;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 25 mg/day for MM and MCL and 10 mg/day for MDS;
   b. Requested new 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

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PHAR.57 – Global Biopharm Policy.

Background

Description/Mechanism of Action:

Lenalidomide is an analogue of thalidomide with immunomodulatory, antiangiogenic, and antineoplastic properties. Lenalidomide inhibits proliferation and induces apoptosis of certain hematopoietic tumor cells including multiple myeloma, mantle cell lymphoma, and del (5q) myelodysplastic syndromes *in vitro*. Lenalidomide causes a delay in tumor growth in some *in vivo* nonclinical hematopoietic tumor models including multiple myeloma. Immunomodulatory properties of lenalidomide include activation of T cells and natural killer (NK) cells, increased numbers of NKT cells, and inhibition of pro-inflammatory cytokines (e.g., TNF-a and IL-6) by monocytes. In multiple myeloma cells, the combination of lenalidomide and dexamethasone synergizes the inhibition of cell proliferation and the induction of apoptosis.

Formulations:

Revlimid oral capsules: 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg

FDA Approved Indications:

Revlimid is a thalidomide analogue/oral capsule formulation indicated for the treatment of patients with:

- Multiple myeloma (MM) in combination with dexamethasone.
- Transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities.
- Mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

Limitations of use:

- Revlimid is not indicated and is not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials.

Safety information: REMS Program

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

Appendices

Appendix A: Abbreviation Key

MDSCD: Castleman's disease
CLL: chronic lymphocytic leukemia
MALT: mucosa associated lymphoid tissue
MCL: mantle cell lymphoma
MDS: myelodysplastic syndromes
MM: multiple myeloma
SLL: small lymphocytic lymphoma

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: MDS: removed criteria requirements for low-risk disease and deletion 5q cytogenetic abnormality; MCL: removed disease staging; removed off-label use for primary cutaneous B-cell lymphoma; references reviewed and updated.	1.22.18	4.18

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