BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**1/01/16**
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REVLIMID® (lenalidomide) oral capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Revlimid is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is an Oncologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     - Treatment of multiple myeloma (MM) used in combination with dexamethasone
     - Maintenance of MM after autologous hematopoietic stem cell transplantation (auto-HSCT)
     - Transfusion-dependent anemia in low- or intermediate-1-risk myelodysplastic syndrome (MDS) associated with 5q deletion abnormality with or without additional cytogenetic abnormalities
     - Mantle cell lymphoma (MCL) that has relapsed or progressed after two prior therapies, one of which included Velcade (bortezomib)
     - Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1, 2A, or 2B

  4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - Complete blood count
     - Comprehensive metabolic panel
     - Thyroid function tests

  5. There are **NO** contraindications:
     - Contraindications include:
       - Known hypersensitivity to lenalidomide
       - Pregnancy

  Initial approval duration: 6 months

Criteria for continuation of coverage (renewal request): Revlimid is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

1. Continues to be seen by an Oncologist

2. The condition has not progressed while on therapy

3. Individual has been adherent with the medication

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4. Individual has not developed any contraindications or significant level 4 adverse drug effects that may exclude continued use, such as:
   - Venous thromboembolism (DVT, PE)
   - Arterial thromboembolism (MI, CVA)
   - Allergic reaction (angioedema, skin exfoliation, bullae)
   - Liver failure
   - Tumor lysis syndrome
   - Tumor flare reaction

5. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Revlimid (lenalidomide) is a thalidomide analogue used **in combination with dexamethasone, is indicated for the treatment of patients with multiple myeloma (MM) and as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT); it is also indicated for the treatment of patients with transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities; and it is indicated for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included Velcade (bortezomib).** Revlimid (lenalidomide) is not indicated for the treatment of a patient with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials.

Lenalidomide has immunomodulatory, antiangiogenic, and antineoplastic properties. It inhibits proliferation and induces apoptosis of certain hematopoietic tumor cells including MM, MCL, and del (5q) MDS *in vitro*. Lenalidomide causes a delay in tumor growth in some *in vivo* nonclinical hematopoietic tumor models including MM. The 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-α and IL-6) by monocytes. In MM cells, the combination of lenalidomide and dexamethasone synergizes the inhibition of cell proliferation and the induction of apoptosis.

Use of Revlimid (lenalidomide) is subject to a Risk Evaluation and Mitigation Strategies (REMS) program that requires provider, patient, and dispensing pharmacy be enrolled into the program. Only providers and Pharmacies enrolled into the REMS may prescribe and dispense the drug, respectively, to individuals who are also in the program. A REMS program attempts to manage known or potentially serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) for some drugs to ensure that the benefits of a drug outweigh its risks.

Definitions:

Revlimid (lenalidomide) REMS items
Enrollment and agreement information

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Treatment initiation information
Treatment maintenance information
Pharmacy requirements and responsibilities
Counseling on contraception and avoidance of pregnancy
Pregnancy testing in females of childbearing potential
Counseling on serious risks, warnings, and precautions and safe use

International Prognostic Scoring System (IPSS) in myelodysplastic syndrome

Survival and AML evolution					
	Score value				
Prognostic Variable	**0**	**0.5**	**1.0**	**1.5**	**2.0**
Bone Marrow Blast percentage	< 5	5-10		11-20	21-30
Karyotype	Good	Intermediate	Poor		
Cytopenias	0/1	2/3			
Prognosis					
Score	**IPSS Group**	**Median Survival (Years)**	**25% AML progression (years) in absence of therapy**		
0	Low	5.7	9.4		
0.5-1.0	Intermediate-1	3.5	3.3		
1.5-2.0	Intermediate-2	1.1	1.1		
> 2.5	High	0.4	0.2		

* Cytogenetic definitions:
Good = normal, -Y alone, del(5q) alone, del(20q) alone
Poor = complex (≥3 abnormalities) or chromosome 7 anomalies
Intermediate = other abnormalities (excludes karyotypes t(8;21), inv16, and 5(15;17)
Cytopenias: neutrophil count < 1,800mcL, platelets < 100,000 mcL, Hg < 10 g/dL

Revised international prognostic scoring system (IPSS-R) in myelodysplastic syndrome

Prognostic variable	**Score value**						
	0	**0.5**	**1.0**	**1.5**	**2.0**	**3.0**	**4.0**
Cytogenetics*	Very good		Good		Intermediate	Poor	Very poor
Bone marrow blast (percent)	≤ 2		> 2 to < 5		5 to 10	> 10	
Hemoglobin (g/dL)	≥ 10		8 to < 10	<8			
Platelets (cells/microL)	≥ 100	50 to 100	< 50				
Absolute neutrophil count (cells/microL)	≥ 0.8	< 0.8					

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This scoring system was applied to an initial group of 7012 patients with primary MDS by the French-American-British classification who had at least two months of stable blood counts, ≤ 30 percent bone marrow blasts and ≤19 percent peripheral blood blasts, and who were observed until progression to AML transformation or death (did not receive disease-modifying agents for MDS). Patients could be stratified into five groups with the following estimated overall survival and progression to AML.

Risk group	IPSS-R score	Median overall survival (years)	Median time to 25 percent AML evolution (years)
Very low	≤ 1.5	8.8	> 14.5
Low	> 1.5 to 3.0	5.3	10.8
Intermediate	> 3 to 4.5	3.0	3.2
High	> 4.5 to 6	1.6	1.4
Very high	> 6	0.8	0.7

The prognostic value of the IPSS-R was validated in an external cohort of 200 patients with MDS

AML: acute myeloid leukemia; MDS: myelodysplastic syndrome.
* Cytogenetic definitions:
Very good: -Y, del(11q).
Good: Normal, del(5q), del(12p), del(20q), double including del(5q).
Intermediate: del(7q), +8, +19, i(17q), any other single, double not including del(5q) or -7/del(7q), or independent clones.
Poor: -7, inv(3)/t(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities.
Very poor: Complex: > 3 abnormalities

Resources:

Revlimid. Package Insert. Revised by manufacturer 02/2015. Accessed 08-04-2015, 07-22-2016.

Revlimid. Package Insert. Revised by manufacturer 02/2017. Accessed 08-24-2017.
Revlimid. Package Insert. Revised by manufacturer 12/2017. Accessed 07-19-2018.

NCCN Clinical Practice Guidelines in Oncology: Multiple myeloma. Version 3.2017, November 28, 2016. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic syndromes. Version 1.2018, August 29, 2017. https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

NCCN Clinical Practice Guidelines in Oncology: B-cell lymphomas. Version 4.2017, Sept 8, 2017. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

NCCN Clinical Practice Guidelines in Oncology: Multiple myeloma. Version 1.2019, July 20, 2018. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

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NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic syndromes. Version 1.2019, July 16, 2018. https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

NCCN Clinical Practice Guidelines in Oncology: B-cell lymphomas. Version 4.2018, May 15, 2018. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

UpToDate: Treatment of refractory multiple myeloma. Current through Aug 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-relapsed-or-refractory-multiple-myeloma?source=search_result&search=multiple%20myeloma&selectedTitle=4~150#H22

UpToDate: Selection of initial chemotherapy for symptomatic multiple myeloma. Current through Aug 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/selection-of-initial-chemotherapy-for-symptomatic-multiple-myeloma?source=search_result&search=multiple%20myeloma&selectedTitle=5~150

UpToDate: Overview of the treatment of myelodysplastic syndromes. Current through Aug 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/overview-of-the-treatment-of-myelodysplastic-syndromes?source=search_result&search=myelodysplastic%20syndrome&selectedTitle=2~150#H516101

UpToDate: Treatment of intermediate, low, or very low risk myelodysplastic syndromes. Current through Aug 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-intermediate-low-or-very-low-risk-myelodysplastic-syndromes?source=see_link&sectionName=Choice%20of%20therapy&anchor=H519324#H48

UpToDate: Initial treatment of mantle cell lymphoma. Current through Aug 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/initial-treatment-of-mantle-cell-lymphoma?source=see_link&sectionName=Conventional%20chemoimmunotherapy&anchor=H7#H14

UpToDate: Treatment of refractory mantle cell lymphoma. Current through Aug 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-relapsed-or-refractory-mantle-cell-lymphoma?source=search_result&search=mantle%20cell%20lymphoma&selectedTitle=3~68

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.