

Ristol Myers Squibb Access Support >

Reimbursement and Coding for REVLIMID® (lenalidomide) capsules

Indications

REVLIMID $^{\odot}$ (lenalidomide) in combination with dexamethasone (dex) is indicated for the treatment of adult patients with multiple myeloma (MM).

REVLIMID is indicated as maintenance therapy in adult patients with MM following autologous hematopoietic stem cell transplantation (auto-HSCT).

REVLIMID® is indicated for the treatment of adult 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.

REVLIMID® is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

REVLIMID $^{\circ}$ in combination with a rituximab product is indicated for the treatment of adult patients with previously treated follicular lymphoma (FL).

REVLIMID $^{\circ}$ in combination with a rituximab product is indicated for the treatment of adult patients with previously treated marginal zone lymphoma (MZL).

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

REVLIMID is only available through a restricted distribution program, Lenalidomide REMS.

Please see next page for **Boxed WARNINGS**: Embryo-Fetal Toxicity, Hematologic Toxicity, and Venous and Arterial Thromboembolism.

Select Important Safety Information: Boxed WARNINGS

WARNING: EMBRYO-FETAL TOXICITY, HEMATOLOGIC TOXICITY, and VENOUS and ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

Do not use REVLIMID during pregnancy. Lenalidomide, a thalidomide analogue, caused limb abnormalities in a developmental monkey study. Thalidomide is a known human teratogen that causes severe life-threatening human birth defects. If lenalidomide is used during pregnancy, it may cause birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting REVLIMID treatment. Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after REVLIMID treatment. To avoid embryo-fetal exposure to lenalidomide, REVLIMID is only available through a restricted distribution program, the Lenalidomide REMS program.

Information about the Lenalidomide REMS program is available at www.lenalidomiderems.com or by calling the manufacturer's toll-free number 1-888-423-5436.

Hematologic Toxicity (Neutropenia and Thrombocytopenia)

REVLIMID can cause significant neutropenia and thrombocytopenia. Eighty percent of patients with del 5q MDS (myelodysplastic syndromes) had to have a dose delay/reduction during the major study. Thirty-four percent of patients had to have a second dose delay/reduction. Grade 3 or 4 hematologic toxicity was seen in 80% of patients enrolled in the study. Patients on therapy for del 5q MDS should have their complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter. Patients may require dose interruption and/or reduction. Patients may require use of blood product support and/or growth factors.

Venous and Arterial Thromboembolism

REVLIMID has demonstrated a significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), as well as risk of myocardial infarction and stroke in patients with MM (multiple myeloma) who were treated with REVLIMID and dexamethasone therapy. Monitor for and advise patients about signs and symptoms of thromboembolism. Advise patients to seek immediate medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. Thromboprophylaxis is recommended and the choice of regimen should be based on an assessment of the patient's underlying risks.

Bristol Myers Squibb Is Committed to Helping Support Access

This brochure is designed to help appropriate patients get access to our medications by providing helpful reimbursement information for healthcare offices. Healthcare benefits vary significantly; therefore, it is important that healthcare provider offices verify each patient's insurance coverage prior to initiating therapy.

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Healthcare providers should code healthcare claims based upon the service that is rendered, the patient's medical record, the coding requirements of each health insurer, and the best coding practices. The accurate completion of reimbursement- or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

National Drug Code (NDC) Information for REVLIMID® (lenalidomide)

The NDCs for REVLIMID are listed below.

25 m ≥ 55 m =	2.5 mg capsules	REV 5 mg	5 mg capsules
	One bottle containing 28 capsules 59572-0402-28		One bottle containing 28 capsules 59572-0405-28
	One bottle containing 100 capsules 59572-0402-00		One bottle containing 100 capsules 59572-0405-00
REV 10 mg	10 mg capsules	REV 15 mg	15 mg capsules
	One bottle containing 28 capsules 59572-0410-28		One bottle containing 21 capsules 59572-0415-21
	One bottle containing 100 capsules 59572-0410-00		One bottle containing 100 capsules 59572-0415-00
REV 20 mg	20 mg capsules	REV 25 mg	25 mg cαpsules
	One bottle containing 21 capsules 59572-0420-21		One bottle containing 21 capsules 59572-0425-21
	One bottle containing 100 capsules 59572-0420-00		One bottle containing 100 capsules 59572-0425-00

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ICD-10-CM Codes

ICD-10-CM codes are used to identify a patient's diagnosis. On October 1, 2015, the newest version of these codes, ICD-10-CM, was implemented throughout the United States. This version replaces the previous version, ICD-9-CM.²

- The ICD-10-CM diagnosis codes contain **categories**, **subcategories**, and **codes**. Characters for categories, subcategories, and codes may be letters or numerals
- All categories are 3 characters
- **Subcategories** are either 4 or 5 characters
- Codes may be 3, 4, 5, 6, or 7 characters

The ICD-10-CM codes for the labeled indications for REVLIMID® (lenalidomide) capsules are provided on the following pages by Bristol Myers Squibb and should be verified with the payer. Some health plan and Medicare insurers may specify which codes are covered under their policies. Please code to the level of specificity documented in the medical record. For additional coding questions, call BMS Access Support® at **1-800-861-0048** or visit www.BMSAccessSupport.com.

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ICD-10-CM Codes for REVLIMID® (lenalidomide): Multiple Myeloma (MM)

ICD-10-CM Codes for Multiple Myelomα ³	
C90.0	Multiple Myelomα
C90.00	Multiple Myeloma Not Having Achieved Remission
C90.01	Multiple Myelomα in Remission
C90.02	Multiple Myeloma in Relapse

ICD-10-CM Codes for REVLIMID® (lenalidomide): Follicular Lymphoma (FL)

ICD-10-CM C	odes for Follicular Lymphoma³
C82.0	Follicular Lymphoma Grade I
C82.00	Follicular Lymphoma Grade I, Unspecified Site
C82.01	Follicular Lymphoma Grade I, Lymph Nodes of Head, Face, and Neck
C82.02	Follicular Lymphoma Grade I, Intrathoracic Lymph Nodes
C82.03	Follicular Lymphoma Grade I, Intra-Abdominal Lymph Nodes
C82.04	Follicular Lymphoma Grade I, Lymph Nodes of Axilla and Upper Limb
C82.05	Follicular Lymphoma Grade I, Lymph Nodes of Inguinal Region and Lower Limb
C82.06	Follicular Lymphoma Grade I, Intrapelvic Lymph Nodes
C82.07	Follicular Lymphoma Grade I, Spleen
C82.08	Follicular Lymphoma Grade I, Lymph Nodes of Multiple Sites
C82.09	Follicular Lymphoma Grade I, Extranodal and Solid Organ Sites
C82.1	Follicular Lymphoma Grade II
C82.10	Follicular Lymphoma Grade II, Unspecified Site
C82.11	Follicular Lymphoma Grade II, Lymph Nodes of Head, Face, and Neck
C82.12	Follicular Lymphoma Grade II, Intrathoracic Lymph Nodes
C82.13	Follicular Lymphoma Grade II, Intra-Abdominal Lymph Nodes
C82.14	Follicular Lymphoma Grade II, Lymph Nodes of Axilla and Upper Limb
C82.15	Follicular Lymphoma Grade II, Lymph Nodes of Inguinal Region and Lower Limb

The accurate completion of reimbursement- or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

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ICD-10-CM Codes for REVLIMID® (lenalidomide): Follicular Lymphoma (FL), (cont'd)

ICD-10-CM C	odes for Follicular Lymphoma³
C82.16	Follicular Lymphoma Grade II, Intrapelvic Lymph Nodes
C82.17	Follicular Lymphoma Grade II, Spleen
C82.18	Follicular Lymphoma Grade II, Lymph Nodes of Multiple Sites
C82.19	Follicular Lymphoma Grade II, Extranodal and Solid Organ Sites
C82.2	Follicular Lymphoma Grade III, Unspecified
C82.20	Follicular Lymphoma Grade III, Unspecified, Unspecified Site
C82.21	Follicular Lymphoma Grade III, Unspecified, Lymph Nodes of Head, Face, and Neck
C82.22	Follicular Lymphoma Grade III, Unspecified, Intrathoracic Lymph Nodes
C82.23	Follicular Lymphoma Grade III, Unspecified, Intra-Abdominal Lymph Nodes
C82.24	Follicular Lymphoma Grade III, Unspecified, Lymph Nodes of Axilla and Upper Limb
C82.25	Follicular Lymphoma Grade III, Unspecified, Lymph Nodes of Inguinal Region and Lower Limb
C82.26	Follicular Lymphoma Grade III, Unspecified, Intrapelvic Lymph Nodes
C82.27	Follicular Lymphoma Grade III, Unspecified, Spleen
C82.28	Follicular Lymphoma Grade III, Unspecified, Lymph Nodes of Multiple Sites
C82.29	Follicular Lymphoma Grade III, Unspecified, Extranodal and Solid Organ Sites
C82.3	Follicular Lymphoma Grade IIIA
C82.30	Follicular Lymphoma Grade IIIA, Unspecified Site
C82.31	Follicular Lymphoma Grade IIIA, Lymph Nodes of Head, Face, and Neck
C82.32	Follicular Lymphoma Grade IIIA, Intrathoracic Lymph Nodes
C82.33	Follicular Lymphoma Grade IIIA, Intra-Abdominal Lymph Nodes
C82.34	Follicular Lymphoma Grade IIIA, Lymph Nodes of Axilla and Upper Limb
C82.35	Follicular Lymphoma Grade IIIA, Lymph Nodes of Inguinal Region and Lower Limb
C82.36	Follicular Lymphoma Grade IIIA, Intrapelvic Lymph Nodes
C82.37	Follicular Lymphoma Grade IIIA, Spleen
C82.38	Follicular Lymphoma Grade IIIA, Lymph Nodes of Multiple Sites
C82.39	Follicular Lymphoma Grade IIIA, Extranodal and Solid Organ Sites

The accurate completion of reimbursement- or coverage-related documentation is the responsibility of the healthcare provider and patient. Bristol Myers Squibb and its agents make no guarantee regarding reimbursement for any service or item.

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ICD-10-CM Codes for REVLIMID® (lenalidomide): Follicular Lymphoma (FL), (cont'd)

ICD-10-CM Codes for Follicular Lymphoma³		
C82.8	Other Types of Follicular Lymphoma	
C82.80	Other Types of Follicular Lymphoma, Unspecified Site	
C82.81	Other Types of Follicular Lymphoma, Lymph Nodes of Head, Face, and Neck	
C82.82	Other Types of Follicular Lymphoma, Intrathoracic Lymph Nodes	
C82.83	Other Types of Follicular Lymphoma, Intra-Abdominal Lymph Nodes	
C82.84	Other Types of Follicular Lymphoma, Lymph Nodes of Axilla and Upper Limb	
C82.85	Other Types of Follicular Lymphoma, Lymph Nodes of Inguinal Region and Lower Limb	
C82.86	Other Types of Follicular Lymphoma, Intrapelvic Lymph Nodes	
C82.87	Other Types of Follicular Lymphoma, Spleen	
C82.88	Other Types of Follicular Lymphoma, Lymph Nodes of Multiple Sites	
C82.89	Other Types of Follicular Lymphoma, Extranodal and Solid Organ Sites	
C82.9	Follicular Lymphoma, Unspecified	
C82.90	Follicular Lymphoma, Unspecified, Unspecified Site	
C82.91	Follicular Lymphoma, Unspecified, Lymph Nodes of Head, Face, and Neck	
C82.92	Follicular Lymphoma, Unspecified, Intrathoracic Lymph Nodes	
C82.93	Follicular Lymphoma, Unspecified, Intra-Abdominal Lymph Nodes	
C82.94	Follicular Lymphoma, Unspecified, Lymph Nodes of Axilla and Upper Limb	
C82.95	Follicular Lymphoma, Unspecified, Lymph Nodes of Inguinal Region and Lower Limb	
C82.96	Follicular Lymphoma, Unspecified, Intrapelvic Lymph Nodes	
C82.97	Follicular Lymphoma, Unspecified, Spleen	
C82.98	Follicular Lymphoma, Unspecified, Lymph Nodes of Multiple Sites	
C82.99	Follicular Lymphoma, Unspecified, Extranodal and Solid Organ Sites	

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ICD-10-CM Codes for REVLIMID® (lenalidomide): Marginal Zone Lymphoma (MZL)

ICD-10-CM Codes for Marginal Zone Lymphoma³

C88.4 Extranodal Marginal Zone B-Cell Lymphoma of Mucosa-Associated Lymphoid Tissue

(MALT)

ICD-10-CM Codes for REVLIMID® (lenalidomide): Mantle Cell Lymphoma (MCL)

ICD-10-CM Codes for Mantle Cell Lymphoma³		
C83.1	Mantle Cell Lymphoma	
C83.10	Mantle Cell Lymphoma, Unspecified Site	
C83.11	Mantle Cell Lymphoma, Lymph Nodes of Head, Face, and Neck	
C83.12	Mantle Cell Lymphoma, Intrathoracic Lymph Nodes	
C83.13	Mantle Cell Lymphoma, Intra-Abdominal Lymph Nodes	
C83.14	Mantle Cell Lymphoma, Lymph Nodes of Axilla and Upper Limb	
C83.15	Mantle Cell Lymphoma, Lymph Nodes of Inguinal Region and Lower Limb	
C83.16	Mantle Cell Lymphoma, Intrapelvic Lymph Nodes	
C83.17	Mantle Cell Lymphoma, Spleen	
C83.18	Mantle Cell Lymphoma, Lymph Nodes of Multiple Sites	
C83.19	Mantle Cell Lymphoma, Extranodal and Solid Organ Sites	

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ICD-10-CM Codes for REVLIMID® (lenalidomide): Myelodysplastic Syndromes (MDS)

ICD-10-CM Codes for Myelodysplastic Syndromes ³		
D46 Myelodysplastic Syndromes		
D46.0	Refractory Anemia without Ring Sideroblasts, so stated	
D46.1	Refractory Anemia with Ring Sideroblasts	
D46.2	Refractory Anemia with Excess of Blasts [RAEB]	
D46.20	Refractory Anemia with Excess of Blasts, Unspecified	
D46.21	Refractory Anemia with Excess of Blasts 1	
D46.22	Refractory Anemia with Excess of Blasts 2	
D46.A	Refractory Cytopenia with Multilineage Dysplasia	
D46.B	Refractory Cytopenia with Multilineage Dysplasia and Ring Sideroblasts	
D46.C	Myelodysplastic Syndrome with Isolated Del(5q) Chromosomal Abnormality	
D46.4	Refractory Anemia, Unspecified	
D46.Z	Other Myelodysplastic Syndromes	
D46.9	Myelodysplastic Syndrome, Unspecified	

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Dosage and Administration for REVLIMID® (lenalidomide): MM Combination Therapy¹

REVLIMID in combination with dexamethasone (dex) is indicated for the treatment of adult patients with MM.

25 mg on Days 1-21 of repeated 28-day cycles

Continue treatment until disease progression or unacceptable toxicity

For patients who are auto-HSCT eligible, hematopoietic stem cell mobilization should occur within 4 cycles of receiving REVLIMID-containing therapy.

- NDMM clinical trials: dexamethasone was dosed at 40 mg on Days 1, 8, 15, and 22 of repeated 28-day cycles. Patients >75 years received 20 mg of dexamethasone once daily on Days 1, 8, 15, and 22 of repeated 28-day cycles
- **RRMM clinical trials:** dexamethasone was dosed at 40 mg on Days 1-4, 9-12, and 17-20 of each 28-day cycle for the first 4 cycles, and reduced to 40 mg once daily on Days 1-4 for subsequent 28-day cycles
- Monitor complete blood counts every 7 days for the first 2 cycles, on Days 1 and 15 of Cycle 3, and every 28 days thereafter
- Permanently discontinue REVLIMID for angioedema, anaphylaxis, Grade 4 rash, skin exfoliation, bullae, or any other severe dermatologic reactions, such as SJS, TEN, or DRESS

NDMM=newly diagnosed multiple myeloma; RRMM=relapsed/refractory multiple myeloma.

Important Dosing Information

The capsules should not be opened, broken, or chewed.

REVLIMID is primarily excreted unchanged by the kidney. Since elderly patients are more likely to have decreased renal function, care should be taken in dose selection. Monitor renal function.

Monitor CBCs every 7 days (weekly) for the first 2 cycles, on Days 1 and 15 of Cycle 3, and every 28 days (4 weeks) thereafter.

Treatment is continued or modified based on clinical and laboratory findings.

Dose modification guidelines are recommended to manage Grade 3/4 neutropenia or thrombocytopenia.

For non-hematologic Grade 3/4 toxicities judged to be related to REVLIMID, hold treatment and restart at next lower dose level when toxicity has resolved to ≤Grade 2.

Patients may require dose interruption and/or reduction.

Patients may require the use of blood product support and/or growth factors.

Please see Section 2, DOSAGE AND ADMINISTRATION, of the U.S. Full Prescribing Information for additional information on dose adjustments for hematologic toxicities, dose modifications for non-hematologic adverse reactions, and recommended dosage for patients with renal impairment.

Please see <u>Important Safety Information</u> on pages 17–21 and <u>U.S. Full Prescribing Information</u>, including **Boxed WARNINGS**, for REVLIMID.



Dosage and Administration for REVLIMID® (lenalidomide): MM Post Auto-HSCT¹

REVLIMID is indicated as maintenance therapy in adult patients with MM following auto-HSCT.

Induction Therapy

Auto-HSCT

Adequate
Hematologic Recovery

10 mg on Days 1-28
of repeated 28-day cycles

Continue treatment until disease progression or unacceptable toxicity

- Hematologic recovery: absolute neutrophil count (ANC) ≥1000/mcL and/or platelet counts ≥75,000/mcL
- If tolerated, dose can be increased to 15 mg after 3 cycles
- Monitor complete blood counts every 7 days for the first 2 cycles, on Days 1 and 15 of Cycle 3, and every 28 days thereafter
- Permanently discontinue REVLIMID for angioedema, anaphylaxis, Grade 4 rash, skin exfoliation, bullae, or any other severe dermatologic reactions, such as SJS, TEN, or DRESS

Important Dosing Information

The capsules should not be opened, broken, or chewed.

REVLIMID is primarily excreted unchanged by the kidney. Since elderly patients are more likely to have decreased renal function, care should be taken in dose selection. Monitor renal function.

Monitor CBCs every 7 days (weekly) for the first 2 cycles, on Days 1 and 15 of Cycle 3, and every 28 days (4 weeks) thereafter.

Treatment is continued or modified based on clinical and laboratory findings.

Dose modification guidelines are recommended to manage Grade 3/4 neutropenia or thrombocytopenia.

For non-hematologic Grade 3/4 toxicities judged to be related to REVLIMID, hold treatment and restart at next lower dose level when toxicity has resolved to \leq Grade 2.

Patients may require dose interruption and/or reduction.

Patients may require the use of blood product support and/or growth factors.

Please see Section 2, DOSAGE AND ADMINISTRATION, of the U.S. Full Prescribing Information for additional information on dose adjustments for hematologic toxicities, dose modifications for non-hematologic adverse reactions, and recommended dosage for patients with renal impairment.

Please see Important Safety Information on pages 17–21 and U.S. Full Prescribing Information, including **Boxed WARNINGS**, for REVLIMID.



Dosage and Administration for REVLIMID® (lenalidomide): FL/MZL¹

REVLIMID in combination with a rituximab product is indicated for the treatment of adult patients with previously treated FL.

REVLIMID in combination with a rituximab product is indicated for the treatment of adult patients with previously treated MZL.

REVLIMID + a rituximab product is administered for up to 12 cycles or until acceptable toxicity. For dose adjustments due to toxicity with rituximab, refer to the product prescribing information.

20 mg on Days 1-21 of up to 12 repeated 28-day cycles

- Rituximab 375 mg/m^{2*} on Days 1, 8, 15, and 22 of Cycle 1 and on Day 1 of Cycles 2-5: 28-day cycles
- Monitor complete blood counts weekly for the first 3 weeks of Cycle 1 (28 days), every 2 weeks during Cycles 2-4, and then monthly thereafter
- Permanently discontinue REVLIMID for angioedema, anaphylaxis, Grade 4 rash, skin exfoliation, bullae, or any other severe dermatologic reactions, such as SJS, TEN, or DRESS

Important Dosing Information

The capsules should not be opened, broken, or chewed.

REVLIMID is primarily excreted unchanged by the kidney. Since elderly patients are more likely to have decreased renal function, care should be taken in dose selection. Monitor renal function.

Monitor CBCs weekly for the first 3 weeks of Cycle 1 (28 days), every 2 weeks during Cycles 2-4, and then monthly thereafter.

Treatment is continued or modified based on clinical and laboratory findings.

Dose modification guidelines are recommended to manage Grade 3/4 neutropenia or thrombocytopenia. For non-hematologic Grade 3/4 toxicities judged to be related to REVLIMID, hold treatment and restart at next lower dose level when toxicity has resolved to ≤Grade 2.

For Grade 3 or 4 TFR, it is recommended to withhold treatment with REVLIMID until TFR resolves to ≤Grade 1.

Patients may require dose interruption and/or reduction.

Patients may require the use of blood product support and/or growth factors.

Please see Section 2, DOSAGE AND ADMINISTRATION, of the U.S. Full Prescribing Information for additional information on dose adjustments for hematologic toxicities, dose modifications for non-hematologic adverse reactions, and recommended dosage for patients with renal impairment.

Please see <u>Important Safety Information</u> on pages 17–21 and <u>U.S. Full Prescribing Information</u>, including **Boxed WARNINGS**, for REVLIMID.

^{*}Dosage calculations for rituximab were based on the patient's body surface area, using actual patient weight.



Dosage and Administration for REVLIMID® (lenalidomide): MCL1

REVLIMID is indicated for the treatment of adult patients with MCL whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

25 mg on Days 1-21 of repeated 28-day cycles

Continue treatment until disease progression or unacceptable toxicity

- Monitor complete blood counts weekly for the first cycle (28 days), every 2 weeks during Cycles 2-4, and then monthly thereafter
- Permanently discontinue REVLIMID for angioedema, anaphylaxis, Grade 4 rash, skin exfoliation, bullae, or any other severe dermatologic reactions, such as SJS, TEN, or DRESS

Important Dosing Information

The capsules should not be opened, broken, or chewed.

REVLIMID is primarily excreted unchanged by the kidney. Since elderly patients are more likely to have decreased renal function, care should be taken in dose selection. Monitor renal function.

Monitor CBCs weekly for the first cycle (28 days), every 2 weeks during cycles 2-4, then monthly thereafter.

Treatment is continued or modified based on clinical and laboratory findings.

Dose modification guidelines are recommended to manage Grade 3/4 neutropenia or thrombocytopenia. For non-hematologic Grade 3/4 toxicities judged to be related to REVLIMID, hold treatment and restart at next lower dose level when toxicity has resolved to ≤Grade 2.

For Grade 3 or 4 tumor flare reaction (TFR), it is recommended to withhold treatment with REVLIMID until TFR resolves to SGrade 1.

Patients may require dose interruption and/or reduction.

Patients may require the use of blood product support and/or growth factors.

Please see Section 2, DOSAGE AND ADMINISTRATION, of the U.S. Full Prescribing Information for additional information on dose adjustments for hematologic toxicities, dose modifications for non-hematologic adverse reactions, and recommended dosage for patients with renal impairment.

Please see <u>Important Safety Information</u> on pages 17–21 and <u>U.S. Full Prescribing Information</u>, including **Boxed WARNINGS**, for REVLIMID.



Dosage and Administration for REVLIMID® (lenalidomide): MDS¹

REVLIMID is indicated for the treatment of adult patients with transfusion-dependent anemia due to low- or intermediate-1-risk MDS associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.

10 mg once daily

Continue treatment until disease progression or unacceptable toxicity

- Monitor complete blood counts weekly for the first 8 weeks of therapy and at least monthly thereafter.
 See Boxed WARNINGS
- Permanently discontinue REVLIMID for angioedema, anaphylaxis, Grade 4 rash, skin exfoliation, bullae, or any other severe dermatologic reactions, such as SJS, TEN, or DRESS

Important Dosing Information

The capsules should not be opened, broken, or chewed.

REVLIMID is primarily excreted unchanged by the kidney. Since elderly patients are more likely to have decreased renal function, care should be taken in dose selection. Monitor renal function.

Treatment is continued or modified based on clinical and laboratory findings.

Dose modification guidelines are recommended to manage Grade 3/4 neutropenia or thrombocytopenia. For non-hematologic Grade 3/4 toxicities judged to be related to REVLIMID, hold treatment and restart at the physician's discretion at next lower dose level when toxicity has resolved to ≤Grade 2.

For Grade 3 or 4 TFR, it is recommended to withhold treatment with REVLIMID until TFR resolves to ≤Grade 1.

Patients may require dose interruption and/or reduction.

Patients may require the use of blood product support and/or growth factors.

Monitor CBCs weekly for the first 8 weeks, and at least monthly thereafter.

Please see Section 2, DOSAGE AND ADMINISTRATION, of the U.S. Full Prescribing Information for additional information on dose adjustments for hematologic toxicities, dose modifications for non-hematologic adverse reactions, and recommended dosage for patients with renal impairment.

Please see <u>Important Safety Information</u> on pages 17–21 and <u>U.S. Full Prescribing Information</u>, including **Boxed WARNINGS**, for REVLIMID.

For reimbursement assistance, call BMS Access Support® at 1-800-861-0048, 8 AM to 8 PM ET, Monday–Friday, or visit www.BMSAccessSupport.com.



WARNING: EMBRYO-FETAL TOXICITY, HEMATOLOGIC TOXICITY, and VENOUS and ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

Do not use REVLIMID during pregnancy. Lenalidomide, a thalidomide analogue, caused limb abnormalities in a developmental monkey study. Thalidomide is a known human teratogen that causes severe life-threatening human birth defects. If lenalidomide is used during pregnancy, it may cause birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting REVLIMID treatment. Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after REVLIMID treatment. To avoid embryo-fetal exposure to lenalidomide, REVLIMID is only available through a restricted distribution program, the Lenalidomide REMS program.

Information about the Lenalidomide REMS program is available at www.lenalidomiderems.com or by calling the manufacturer's toll-free number 1-888-423-5436.

Hematologic Toxicity (Neutropenia and Thrombocytopenia)

REVLIMID can cause significant neutropenia and thrombocytopenia. Eighty percent of patients with del 5q MDS (myelodysplastic syndromes) had to have a dose delay/reduction during the major study. Thirty-four percent of patients had to have a second dose delay/reduction. Grade 3 or 4 hematologic toxicity was seen in 80% of patients enrolled in the study. Patients on therapy for del 5q MDS should have their complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter. Patients may require dose interruption and/or reduction. Patients may require use of blood product support and/or growth factors.

Venous and Arterial Thromboembolism

REVLIMID has demonstrated a significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), as well as risk of myocardial infarction and stroke in patients with MM (multiple myeloma) who were treated with REVLIMID and dexamethasone therapy. Monitor for and advise patients about signs and symptoms of thromboembolism. Advise patients to seek immediate medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. Thromboprophylaxis is recommended and the choice of regimen should be based on an assessment of the patient's underlying risks.

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CONTRAINDICATIONS

Pregnancy: REVLIMID can cause fetal harm when administered to a pregnant female and is contraindicated in females who are pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to the fetus.

Severe Hypersensitivity Reactions: REVLIMID is contraindicated in patients who have demonstrated severe hypersensitivity (e.g., angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis) to lenalidomide.

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity: See Boxed WARNINGS.

- Females of Reproductive Potential: See Boxed WARNINGS.
- <u>Males</u>: Lenalidomide is present in the semen of patients receiving the drug. Males must always use a latex or synthetic condom during any sexual contact with females of reproductive potential while taking REVLIMID and for up to 4 weeks after discontinuing REVLIMID, even if they have undergone a successful vasectomy. Male patients taking REVLIMID must not donate sperm while taking REVLIMID and for up to 4 weeks after discontinuing REVLIMID.
- <u>Blood Donation</u>: Patients must not donate blood during treatment with REVLIMID and for 4 weeks following discontinuation of the drug because the blood might be given to a pregnant female patient whose fetus must not be exposed to REVLIMID.

Lenalidomide REMS Program: See Boxed WARNINGS. Prescribers and pharmacies must be certified with the Lenalidomide REMS program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive REVLIMID. Patients must sign a Patient-Physician Agreement Form and comply with REMS requirements; female patients of reproductive potential who are not pregnant must comply with the pregnancy testing and contraception requirements and males must comply with contraception requirements.

Hematologic Toxicity: REVLIMID can cause significant neutropenia and thrombocytopenia. Monitor patients with neutropenia for signs of infection. Advise patients to observe for bleeding or bruising, especially with use of concomitant medications that may increase risk of bleeding. Patients may require a dose interruption and/or dose reduction. MM: Monitor complete blood counts (CBC) in patients taking REVLIMID + dexamethasone or REVLIMID as maintenance therapy, every 7 days for the first 2 cycles, on days 1 and 15 of cycle 3, and every 28 days thereafter. MDS: Monitor CBC in patients on therapy for del 5q MDS, weekly for the first 8 weeks of therapy and at least monthly thereafter. See Boxed WARNINGS for further information. MCL: Monitor CBC in patients taking REVLIMID for MCL weekly for the first cycle (28 days), every 2 weeks during cycles 2-4, and then monthly thereafter. FL/MZL: Monitor CBC in patients taking REVLIMID for FL or MZL weekly for the first 3 weeks of Cycle 1 (28 days), every 2 weeks during Cycles 2-4, and then monthly thereafter.

Venous and Arterial Thromboembolism: See Boxed WARNINGS. Venous thromboembolic events (DVT and PE) and arterial thromboses (MI and CVA) are increased in patients treated with REVLIMID. Patients with known risk factors, including prior thrombosis, may be at greater risk and actions should be taken to try to minimize all modifiable factors (e.g., hyperlipidemia, hypertension, smoking). Thromboprophylaxis is recommended and the regimen should be based on the patient's underlying risks. Erythropoietin-stimulating agents (ESAs) and estrogens may further increase the risk of thrombosis and their use should be based on a benefit-risk decision.

Increased Mortality in Patients With CLL: In a clinical trial in the first-line treatment of patients with CLL, single-agent REVLIMID therapy increased the risk of death as compared to single-agent chlorambucil. Serious adverse cardiovascular reactions, including atrial fibrillation, myocardial infarction, and cardiac failure, occurred more frequently in the REVLIMID arm. REVLIMID is not indicated and not recommended for use in CLL outside of controlled clinical trials.

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Please see <u>U.S. Full Prescribing Information</u>, including **Boxed WARNINGS**, for REVLIMID.



Second Primary Malignancies (SPM): In clinical trials in patients with MM receiving REVLIMID and in patients with FL or MZL receiving REVLIMID + rituximab therapy, an increase of hematologic plus solid tumor SPM, notably AML, have been observed. In patients with MM, MDS was also observed. Monitor patients for the development of SPM. Take into account both the potential benefit of REVLIMID and risk of SPM when considering treatment.

Increased Mortality With Pembrolizumab: In clinical trials in patients with MM, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with MM with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.

Hepatotoxicity: Hepatic failure, including fatal cases, has occurred in patients treated with REVLIMID + dexamethasone. Pre-existing viral liver disease, elevated baseline liver enzymes, and concomitant medications may be risk factors. Monitor liver enzymes periodically. Stop REVLIMID upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.

Severe Cutaneous Reactions: Severe cutaneous reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. These events can be fatal. Patients with a prior history of Grade 4 rash associated with thalidomide treatment should not receive REVLIMID. Consider REVLIMID interruption or discontinuation for Grade 2-3 skin rash. Permanently discontinue REVLIMID for Grade 4 rash, exfoliative or bullous rash, or for other severe cutaneous reactions such as SJS, TEN, or DRESS.

Tumor Lysis Syndrome (TLS): Fatal instances of TLS have been reported during treatment with REVLIMID. The patients at risk of TLS are those with high tumor burden prior to treatment. Closely monitor patients at risk and take appropriate preventive approaches.

Tumor Flare Reaction (TFR): TFR, including fatal reactions, have occurred during investigational use of REVLIMID for CLL and lymphoma. Monitoring and evaluation for TFR is recommended in patients with MCL, FL, or MZL. Tumor flare may mimic the progression of disease (PD). In patients with Grade 3 or 4 TFR, it is recommended to withhold treatment with REVLIMID until TFR resolves to ≤Grade 1. REVLIMID may be continued in patients with Grade 1 and 2 TFR without interruption or modification, at the physician's discretion.

Impaired Stem Cell Mobilization: A decrease in the number of CD34+ cells collected after treatment (>4 cycles) with REVLIMID has been reported. Consider early referral to transplant center to optimize timing of the stem cell collection.

Thyroid Disorders: Both hypothyroidism and hyperthyroidism have been reported. Measure thyroid function before starting REVLIMID treatment and during therapy.

Early Mortality in Patients With MCL: In another MCL study, there was an increase in early deaths (within 20 weeks); 12.9% in the REVLIMID arm versus 7.1% in the control arm. Risk factors for early deaths include high tumor burden, MIPI score at diagnosis, and high WBC at baseline ($\ge 10 \times 10^9$ /L).

Hypersensitivity: Hypersensitivity, including angioedema, anaphylaxis, and anaphylactic reactions to REVLIMID has been reported. Permanently discontinue REVLIMID for angioedema and anaphylaxis.

ADVERSE REACTIONS

Multiple Myeloma

• In newly diagnosed: The most frequently reported Grade 3 or 4 reactions included neutropenia, anemia, thrombocytopenia, pneumonia, asthenia, fatigue, back pain, hypokalemia, rash, cataract, lymphopenia, dyspnea, DVT, hyperglycemia, and leukopenia. The highest frequency of infections occurred in Arm Rd Continuous (75%) compared to Arm MPT (56%). There were more Grade 3 and 4 and serious adverse reactions of infection in Arm Rd Continuous than either Arm MPT or Rd18.

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- The most common adverse reactions reported in ≥20% (Arm Rd Continuous): diarrhea (45%), anemia (44%), neutropenia (35%), fatigue (33%), back pain (32%), asthenia (28%), insomnia (28%), rash (26%), decreased appetite (23%), cough (23%), dyspnea (22%), pyrexia (21%), abdominal pain (20%), muscle spasms (20%), and thrombocytopenia (20%).
- Maintenance Therapy Post Auto-HSCT: The most frequently reported Grade 3 or 4 reactions in ≥20% (REVLIMID arm) included neutropenia, thrombocytopenia, and leukopenia. The serious adverse reactions of lung infection and neutropenia (more than 4.5%) occurred in the REVLIMID arm.
- The most frequently reported adverse reactions in ≥20% (REVLIMID arm) across both maintenance studies (Study 1, Study 2) were neutropenia (79%, 61%), thrombocytopenia (72%, 24%), leukopenia (23%, 32%), anemia (21%, 9%), upper respiratory tract infection (27%, 11%), bronchitis (4%, 47%), nasopharyngitis (2%, 35%), cough (10%, 27%), gastroenteritis (0%, 23%), diarrhea (54%, 39%), rash (32%, 8%), fatigue (23%, 11%), asthenia (0%, 30%), muscle spasm (0%, 33%), and pyrexia (8%, 20%).
- After at least one prior therapy: The most common adverse reactions reported in ≥20% (REVLIMID/dex vs dex/placebo): fatigue (44% vs 42%), neutropenia (42% vs 6%), constipation (41% vs 21%), diarrhea (39% vs 27%), muscle cramp (33% vs 21%), anemia (31% vs 24%), pyrexia (27% vs 23%), peripheral edema (26% vs 21%), nausea (26% vs 21%), back pain (26% vs 19%), upper respiratory tract infection (25% vs 16%), dyspnea (24% vs 17%), dizziness (23% vs 17%), thrombocytopenia (22% vs 11%), rash (21% vs 9%), tremor (21% vs 7%), and weight decreased (20% vs 15%).

Myelodysplastic Syndromes

- Grade 3 and 4 adverse events reported in ≥ 5% of patients with del 5q MDS were neutropenia (53%), thrombocytopenia (50%), pneumonia (7%), rash (7%), anemia (6%), leukopenia (5%), fatigue (5%), dyspnea (5%), and back pain (5%).
- Adverse events reported in ≥15% of del 5q MDS patients (REVLIMID): thrombocytopenia (61.5%), neutropenia (58.8%), diarrhea (49%), pruritus (42%), rash (36%), fatigue (31%), constipation (24%), nausea (24%), nasopharyngitis (23%), arthralgia (22%), pyrexia (21%), back pain (21%), peripheral edema (20%), cough (20%), dizziness (20%), headache (20%), muscle cramp (18%), dyspnea (17%), pharyngitis (16%), epistaxis (15%), asthenia (15%), upper respiratory tract infection (15%).

Mantle Cell Lymphoma

- Grade 3 and 4 adverse events reported in ≥5% of patients treated with REVLIMID in the MCL trial (N=134) included neutropenia (43%), thrombocytopenia (28%), anemia (11%), pneumonia (9%), leukopenia (7%), fatigue (7%), diarrhea (6%), dyspnea (6%), and febrile neutropenia (6%).
- Adverse events reported in ≥15% of patients treated with REVLIMID in the MCL trial included neutropenia (49%), thrombocytopenia (36%), fatigue (34%), anemia (31%), diarrhea (31%), nausea (30%), cough (28%), pyrexia (23%), rash (22%), dyspnea (18%), pruritus (17%), peripheral edema (16%), constipation (16%), and leukopenia (15%).

Follicular Lymphoma/Marginal Zone Lymphoma

• Fatal adverse reactions occurred in 6 patients (1.5%) receiving REVLIMID + rituximab across both trials. Fatal adverse reactions (1 each) included: cardio-respiratory arrest, arrhythmia, cardiopulmonary failure, multiple organ dysfunction syndrome, sepsis, and acute kidney injury. The most frequent serious adverse reaction that occurred in the REVLIMID + rituximab arm was febrile neutropenia (3.0%).

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- Grade 3 and 4 adverse reactions reported in ≥5% of patients treated in the FL/MZL trial with REVLIMID + rituximab were: neutropenia (50%) and leukopenia (7%).
- Adverse reactions reported in ≥15% of patients with FL/MZL treated with REVLIMID + rituximab were: neutropenia (58%), diarrhea (31%), constipation (26%), cough (24%), fatigue (22%), rash (22%), pyrexia (21%), leukopenia (20%), pruritus (20%), upper respiratory tract infections (18%), abdominal pain (18%), anemia (16%), headache (15%), thrombocytopenia (15%).

DRUG INTERACTIONS

Periodically monitor digoxin plasma levels due to increased C_{max} and AUC with concomitant REVLIMID therapy. Patients taking concomitant therapies such as ESAs or estrogen-containing therapies may have an increased risk of thrombosis. It is not known whether there is an interaction between dexamethasone and warfarin. Close monitoring of PT and INR is recommended in patients with MM taking concomitant warfarin.

USE IN SPECIFIC POPULATIONS

Pregnancy: See Boxed WARNINGS: If pregnancy does occur during treatment, immediately discontinue the drug and refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. There is a REVLIMID pregnancy exposure registry that monitors pregnancy outcomes in females exposed to REVLIMID during pregnancy as well as female partners of male patients who are exposed to REVLIMID. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to REVLIMID to the FDA via the MedWatch program at 1-800-FDA-1088 and also to REMS Call Center at 1-888-423-5436.

- Lactation: There is no information regarding the presence of lenalidomide in human milk, the effects of REVLIMID on the breastfed infant, or the effects of REVLIMID on milk production. Because many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed infants from REVLIMID, advise women not to breastfeed during treatment with REVLIMID.
- Renal Impairment: Adjust the starting dose of REVLIMID based on the creatinine clearance value and for patients on dialysis.

Please see the rituximab full Prescribing Information for Important Safety Information at www.rituxan.com

References

- 1. REVLIMID [package insert]. Princeton, NJ: Bristol-Myers Squibb Company.
- 2. eHealth University, Centers for Medicare & Medicaid Services. The ICD-10-transition: an introduction. Updated August 2014. Accessed December 15, 2021. https://www.cms.gov/Medicare/Coding/ICD10/Downloads/ICD10Introduction20140819.pdf
- 3. Centers for Medicare & Medicaid Services. ICD-10-CM tabular list of diseases and injuries. Accessed December 15, 2021. https://www.cms.gov/medicare/icd-10/2021-icd-10-cm

Please see <u>Important Safety Information</u> on pages 17–21 and <u>U.S. Full Prescribing Information</u>, including **Boxed WARNINGS**, for REVLIMID.



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