REVLIMID Dosing Guide
Convenient Once-Daily Oral Dosing for MM, MCL, and MDS

REVLIMID® (lenalidomide) in combination with dexamethasone (dex) is indicated for the treatment of patients with multiple myeloma (MM).

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

REVLIMID® is 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.

REVLIMID® 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 bortezomib.

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

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

See page 3 and full prescribing information for complete boxed warning.

EMBRYO-FETAL TOXICITY

- Lenalidomide, a thalidomide analogue, caused limb abnormalities in a developmental monkey study similar to birth defects caused by thalidomide in humans. If lenalidomide is used during pregnancy, it may cause birth defects or embryo-fetal death.
- Pregnancy must be excluded before start of treatment. Prevent pregnancy during treatment by the use of two reliable methods of contraception.

REVLIMID is available only through a restricted distribution program called the REVLIMID REMS® program.

HEMATOLOGIC TOXICITY. REVLIMID can cause significant neutropenia and thrombocytopenia.

- For patients with del 5q myelodysplastic syndromes, monitor complete blood counts weekly for the first 8 weeks and monthly thereafter.

VENOUS AND ARTERIAL THROMBOEMBOLISM

- Significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), as well as risk of myocardial infarction and stroke in patients with multiple myeloma receiving REVLIMID with dexamethasone. Anti-thrombotic prophylaxis is recommended.

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.

REVLIMID is only available through a restricted distribution program, REVLIMID REMS®.
Important information about REVLIMID® (lenalidomide) and the Risk Evaluation and Mitigation Strategy (REMS) program

- REVLIMID can cause fetal harm when administered to a pregnant woman, and is contraindicated in pregnant females or females capable of becoming pregnant.
- To avoid embryo-fetal exposure, REVLIMID is only available under a restricted distribution program called “REVLIMID Risk Evaluation and Mitigation Strategy.”
- Prescribers and pharmacies certified with REVLIMID REMS® can prescribe and dispense the product to patients who are enrolled and meet all the conditions of the REVLIMID REMS® program.
- Female patients of reproductive potential must use at least one highly effective method of contraception and at least one additional method, concurrently, every time they have sex with a male.
- If pregnancy does occur, REVLIMID must be immediately discontinued. Any suspected embryo-fetal exposure to REVLIMID must be reported immediately to the FDA via the MedWatch number at 1-800-FDA-1088 and also to the Celgene Customer Care Center at 1-888-423-5436. The patient should be referred to an OB/GYN experienced in reproductive toxicity.
- Male patients must be instructed to use a latex or synthetic condom every time they have sexual intercourse with a female of reproductive potential.
- Instruct patients to return unused REVLIMID capsules to Celgene, their REVLIMID prescriber, or their REVLIMID dispensing pharmacy for disposal.

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Selected Safety Information

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 REVLIMID REMS® program.

Information about the REVLIMID REMS® program is available at www.celgeneriskmanagement.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 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 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.

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
REVLIMID® (lenalidomide) in combination with dexamethasone is indicated for the treatment of patients with multiple myeloma

Start with REVLIMID plus dex for patients with ndMM and rrMM¹

The recommended starting dose of REVLIMID for MM combination therapy is 25 mg orally once daily on Days 1-21 of repeated 28-day cycles

- For patients who are auto-HSCT eligible, hematopoietic stem cell mobilization should occur within 4 cycles of receiving a REVLIMID-containing therapy
- In the ndMM trial, REVLIMID was given with oral dex on Days 1, 8, 15, and 22. The dose for dex was 40 mg for patients ≤75 years or 20 mg for patients >75
- In the rrMM trials, REVLIMID was given with 40 mg oral dex daily 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 to 4

REVLIMID should be continued until disease progression or unacceptable toxicity

ndMM, newly diagnosed multiple myeloma; rrMM, relapsed refractory multiple myeloma.

SELECTED SAFETY INFORMATION: 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

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Dose modifications may help patients with MM stay on REVLIMID until progression\(^1\)

Dose modification guidelines are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia or other Grade 3 or 4 toxicity judged to be related to REVLIMID

<table>
<thead>
<tr>
<th>Neutropenia</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>If ANC falls to (&lt;1000/mcL)</td>
<td>Interrupt treatment, follow CBC weekly</td>
</tr>
<tr>
<td>When ANC returns to (\geq1000/mcL)</td>
<td>If neutropenia is the only toxicity, resume at 25 mg daily or initial starting dose. If other toxicity, resume at next lower dose*</td>
</tr>
<tr>
<td>For each subsequent drop in ANC to (&lt;1000/mcL)</td>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>When ANC returns to (\geq1000/mcL)</td>
<td>Resume REVLIMID at next lower dose*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thrombocytopenia</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>If platelets fall to (&lt;30,000/mcL)</td>
<td>Interrupt treatment, follow CBC weekly</td>
</tr>
<tr>
<td>When platelets return to (\geq30,000/mcL)</td>
<td>Resume REVLIMID at next lower dose*</td>
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<td>For each subsequent drop in platelets to (&lt;30,000/mcL)</td>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>When platelets return to (\geq30,000/mcL)</td>
<td>Resume REVLIMID at next lower dose*</td>
</tr>
</tbody>
</table>

*Do not dose below 2.5 mg daily for Days 1 to 21 of 28-day cycles. CBC, complete blood count.

SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity: See Boxed WARNINGS
- Females of Reproductive Potential: See Boxed WARNINGS
- Males: 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
- Blood Donation: 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

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
REVLIMID® (lenalidomide) is indicated as maintenance therapy in patients with MM following auto-HSCT

REVLIMID maintenance therapy without dexamethasone offers the convenience of once-daily oral dosing

REVLIMID maintenance therapy should be initiated at hematologic recovery

- Patients were randomized to REVLIMID or placebo within 90-100 days post-transplant and 90-180 days post-transplant in Studies 1 and 2, respectively
- Hematologic recovery was defined as ANC ≥1000/mcL and/or platelet counts ≥75,000/mcL

The recommended starting dose of REVLIMID maintenance therapy is 10 mg continuously on Days 1-28 of repeated 28-day cycles

- If tolerated, dose can be increased to 15 mg after 3 cycles

REVLIMID should be continued until disease progression or unacceptable toxicity

SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS

REVLIMID REMS® Program: See Boxed WARNINGS: Prescribers and pharmacies must be certified with the REVLIMID 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

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Dose modifications may help patients with MM stay on REVLIMID maintenance therapy until progression\textsuperscript{1}

Dose modification guidelines are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia or other Grade 3 or 4 toxicity judged to be related to REVLIMID

<table>
<thead>
<tr>
<th>Neutropenia</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>If ANC falls to &lt;500/mcL</td>
<td>Interrupt treatment, follow CBC weekly</td>
</tr>
<tr>
<td>When ANC returns to ≥500/mcL</td>
<td>Resume at next lower dose continuously for Days 1 to 28 of repeated 28-day cycle</td>
</tr>
<tr>
<td>If, at the 5 mg daily dose, there is a subsequent drop in ANC to &lt;500/mcL</td>
<td>Interrupt treatment*</td>
</tr>
<tr>
<td>When ANC returns to &gt;500/mcL</td>
<td>Resume at 5 mg daily for Days 1 to 21 of 28-day cycle*</td>
</tr>
</tbody>
</table>

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<tr>
<th>Thrombocytopenia</th>
<th>Dose Modification</th>
</tr>
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<tr>
<td>If platelets fall to &lt;30,000/mcL</td>
<td>Interrupt treatment, follow CBC weekly</td>
</tr>
<tr>
<td>When platelets return to ≥30,000/mcL</td>
<td>Resume REVLIMID at next lower dose, continuously for Days 1 to 28 of repeated 28-day cycle</td>
</tr>
<tr>
<td>If, at the 5 mg daily dose, there is a subsequent drop in platelets to &lt;30,000/mcL</td>
<td>Interrupt treatment*</td>
</tr>
<tr>
<td>When platelets return to ≥30,000/mcL</td>
<td>Resume at 5 mg daily for Days 1 to 21 of 28-day cycle*</td>
</tr>
</tbody>
</table>

*Do not dose below 5 mg daily for Days 1 to 21 of 28-day cycle.

**SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS**

**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. **MM:** Patients taking REVLIMID/dex or REVLIMID as maintenance therapy should have their complete blood counts (CBC) assessed every 7 days for the first 2 cycles, on days 1 and 15 of cycle 3, and every 28 days thereafter. **MDS:** 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 dose reduction. Please see the Black Box WARNINGS for further information. **MCL:** Patients taking REVLIMID for MCL should have their CBCs monitored weekly for the first cycle (28 days), every 2 weeks during cycles 2–4, and then monthly thereafter. Patients may require dose interruption and/or dose reduction.

Please see Important Safety Information on pages 15–19 and full Prescribing Information, including Boxed WARNINGS.
REVLOMID® (lenalidomide) is indicated for the treatment of patients with MCL whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

REVLOMID offers once-daily oral dosing for patients with relapsed or refractory MCL

The recommended starting dose for relapsed or refractory MCL is 25 mg orally once daily on Days 1-21 of repeated 28-day cycles.

REVLOMID should be continued until disease progression or unacceptable toxicity.

SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS

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 REVLOMID. 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 patient’s underlying risks. 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 REVLOMID 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 REVLOMID arm. REVLOMID is not indicated and not recommended for use in CLL outside of controlled clinical trials.

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

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Dose modification may help keep patients with relapsed or refractory MCL on therapy

Dose modification guidelines are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia or other Grade 3 or 4 toxicity judged to be related to REVLIMID

<table>
<thead>
<tr>
<th>MCL Dose Adjustments for Hematologic Toxicities¹</th>
<th>Neutropenia</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>If ANC falls to &lt;1000/mcL for at least 7 days, or falls to &lt;1000/mcL with an associated temperature ≥38.5°C, or falls to &lt;500/mcL</td>
<td>Interrupt and follow CBC weekly</td>
<td></td>
</tr>
<tr>
<td>When ANC returns to ≥1000/mcL</td>
<td>Resume at 5 mg less than the previous dose*</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thrombocytopenia</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>If platelets fall to &lt;50,000/mcL</td>
<td>Interrupt and follow CBC weekly</td>
</tr>
<tr>
<td>When platelets return to ≥50,000/mcL</td>
<td>Resume at 5 mg less than the previous dose*</td>
</tr>
</tbody>
</table>

*Do not dose below 5 mg daily for Days 1 to 21 of 28-day cycle.

For other 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

SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS

Increased Mortality with Pembrolizumab: In clinical trials in patients with multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma 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/dex. 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

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
REVLIMID® (lenalidomide) is indicated for the treatment of 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

REVLIMID offers once-daily oral dosing for patients with del 5Q MDS with or without other cytogenetic abnormalities

The recommended starting dose for patients with MDS is 10 mg orally once daily

Revised 28-Day Cycles

DAYS 1-28
10 mg/day

(Capsule shown is not actual size.)

REVLIMID should be continued or modified based upon clinical and laboratory findings

SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS

Severe Cutaneous Reactions Including Hypersensitivity Reactions:
Angioedema and severe cutaneous reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. DRESS may present with a cutaneous reaction (such as rash, or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis. These events can be fatal. Patients with a prior history of Grade 4 rash associated with thalidomide treatment should not receive REVLIMID. REVLIMID interruption or discontinuation should be considered for Grade 2-3 skin rash. REVLIMID must be discontinued for angioedema, Grade 4 rash, exfoliative or bullous rash, or if SJS, TEN, or DRESS is suspected and should not be resumed following discontinuation for these reactions

Tumor Lysis Syndrome (TLS): Fatal instances of TLS have been reported during treatment with lenalidomide. The patients at risk of TLS are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Optimizing REVLIMID dosing may give patients the opportunity to stay on treatment

Cytopenias are associated with REVLIMID in MDS and should be monitored closely. Dose adjustments are expected in the initial cycles of therapy and may help manage cytopenias. Dose modification guidelines are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia.

<table>
<thead>
<tr>
<th>MDS Dose Adjustments for Hematologic Toxicities1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia Dose Modification</td>
</tr>
<tr>
<td>Baseline ANC $\geq$1000/mcL</td>
</tr>
<tr>
<td>If ANC falls to &lt;750/mcL</td>
</tr>
<tr>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>When ANC returns to $\geq$1000/mcL</td>
</tr>
<tr>
<td>Resume REVLIMID at 5 mg daily</td>
</tr>
<tr>
<td>Baseline ANC &lt;1000/mcL</td>
</tr>
<tr>
<td>If ANC falls to &lt;500/mcL</td>
</tr>
<tr>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>When ANC returns to $\geq$500/mcL</td>
</tr>
<tr>
<td>Resume REVLIMID at 5 mg daily</td>
</tr>
<tr>
<td>If neutropenia develops WITHIN 4 weeks of starting at 10 mg daily</td>
</tr>
<tr>
<td>If ANC falls to &lt;500/mcL for $\geq$7 days or &lt;500/mcL associated with fever ($\geq$38.5°C)</td>
</tr>
<tr>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>When ANC returns to $\geq$500/mcL</td>
</tr>
<tr>
<td>Resume REVLIMID at 5 mg daily</td>
</tr>
<tr>
<td>If neutropenia develops AFTER 4 weeks of starting at 10 mg daily</td>
</tr>
<tr>
<td>If ANC falls to &lt;500/mcL for $\geq$7 days or &lt;500/mcL associated with fever ($\geq$38.5°C)</td>
</tr>
<tr>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>When ANC returns to $\geq$500/mcL</td>
</tr>
<tr>
<td>Resume REVLIMID at 5 mg daily</td>
</tr>
<tr>
<td>If neutropenia develops at 5 mg daily</td>
</tr>
<tr>
<td>If ANC falls to &lt;500/mcL for $\geq$7 days or &lt;500/mcL associated with fever ($\geq$38.5°C)</td>
</tr>
<tr>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>When ANC returns to $\geq$500/mcL</td>
</tr>
<tr>
<td>Resume REVLIMID at 2.5 mg daily</td>
</tr>
</tbody>
</table>

SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS

Tumor Flare Reaction (TFR): TFR has occurred during investigational use of lenalidomide for CLL and lymphoma. Monitoring and evaluation for TFR is recommended in patients with MCL. 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 $\leq$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.

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Optimizing REVLIMID dosing may give patients the opportunity to stay on treatment (continued)

Cytopenias are associated with REVLIMID in MDS and should be monitored closely. Dose adjustments are expected in the initial cycles of therapy and may help manage cytopenias. Dose modification guidelines are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia.

### MDS Dose Adjustments for Hematologic Toxicities (continued)

<table>
<thead>
<tr>
<th>Thrombocytopenia</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Platelet Count ≥100,000/mcL</strong></td>
<td></td>
</tr>
<tr>
<td>If platelets fall to &lt;50,000/mcL</td>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>When platelets return to ≥50,000/mcL</td>
<td>Resume REVLIMID at 5 mg daily</td>
</tr>
<tr>
<td><strong>Baseline Platelet Count &lt;100,000/mcL</strong></td>
<td></td>
</tr>
<tr>
<td>If platelets fall to 50% of the baseline value</td>
<td>Interrupt treatment</td>
</tr>
<tr>
<td>If baseline ≥60,000/mcL and returns to ≥50,000/mcL</td>
<td>Resume REVLIMID at 5 mg daily</td>
</tr>
<tr>
<td>If baseline &lt;60,000/mcL and returns to ≥30,000/mcL</td>
<td>Resume REVLIMID at 5 mg daily</td>
</tr>
</tbody>
</table>

If thrombocytopenia develops AFTER 4 weeks of starting at 10 mg daily

| If platelets fall to <30,000/mcL, or <50,000/mcL with platelet transfusions | Interrupt treatment |
| When platelets return to ≥30,000/mcL (without hemostatic failure) | Resume REVLIMID at 5 mg daily |

If thrombocytopenia develops at 5 mg daily

| If platelets fall to <30,000/mcL, or <50,000/mcL with platelet transfusions | Interrupt treatment |
| When platelets return to ≥30,000/mcL (without hemostatic failure) | Resume REVLIMID at 2.5 mg daily |

For other 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

**SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS**

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

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
REVLIMID can be used in all levels of renal function for patients with MM, MDS, and MCL

Since REVLIMID is primarily excreted unchanged by the kidney, adjustments to the starting dose of REVLIMID are recommended to provide appropriate drug exposure in patients with renal impairment.

### REVLIMID Starting Dose by Renal Function for MM, MDS, and MCL

<table>
<thead>
<tr>
<th>Renal Function</th>
<th>MM Combination Therapy</th>
<th>MM Maintenance Therapy</th>
<th>MCL</th>
<th>MDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl 30-60 mL/min</td>
<td>10 mg once daily</td>
<td>5 mg once daily</td>
<td>10 mg once daily</td>
<td>5 mg once daily</td>
</tr>
<tr>
<td>CrCl &lt;30 mL/min (not requiring dialysis)</td>
<td>15 mg every other day</td>
<td>2.5 mg once daily</td>
<td>15 mg every other day</td>
<td>2.5 mg once daily</td>
</tr>
<tr>
<td>CrCl &lt;30 mL/min (requiring dialysis)*</td>
<td>5 mg once daily</td>
<td>2.5 mg once daily</td>
<td>5 mg once daily</td>
<td>2.5 mg once daily</td>
</tr>
</tbody>
</table>

*On dialysis days, administer the dose following dialysis.

Visit [REVLIMIDDosingCalendar.com](http://REVLIMIDDosingCalendar.com) for customizable, downloadable dosing calendars

### Important Dosing Information

- The capsules should not be opened, broken, or chewed
- Lenalidomide 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
- MM: 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
- MCL: Monitor CBCs weekly for the first cycle (28 days), every 2 weeks during cycles 2-4, then monthly thereafter
- MDS: Monitor CBCs weekly for the first 8 weeks, and at least 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 other Grade 3/4 toxicities judged to be related to lenalidomide 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 Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
CrCl is widely used to estimate glomerular filtration rate (GFR)³

- GFR is the best measure of renal function
- Serum creatinine (SCr) alone is not a sufficient measure of renal function because age, gender, race, and body size also impact GFR
- Direct measurement of GFR using a timed urine sample (e.g., 24-hour urine collection) is difficult and does not provide a better estimate of GFR vs calculating CrCl using SCr
- The National Kidney Foundation recognizes the Cockcroft-Gault equations (shown below) as appropriate methods for estimating GFR in adults

\[
\text{Cockcroft-Gault Equations}^4
\]

\[
\text{Male: } \text{CrCl} = \frac{(140 - \text{age in years}) \times \text{[weight in kg]}}{72 \times \text{SCr (mg/dL)}}
\]

\[
\text{Female: } \text{CrCl} = 0.85 \times \frac{(140 - \text{age in years}) \times \text{[weight in kg]}}{72 \times \text{SCr (mg/dL)}}
\]

³A correction for lean or ideal body weight should be considered in certain conditions (e.g., elderly, obese, fluid overload) when body weight may not be indicative of SCr levels.

SELECTED SAFETY INFORMATION: WARNINGS AND PRECAUTIONS

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 (≥10 x 10⁹/L)

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
REVlimID® (lenalidomide) in combination with dexamethasone (dex) is indicated for the treatment of patients with multiple myeloma (MM).

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

REVlimID® is 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.

REVlimID® 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 bortezomib.

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

### Important Safety Information

<table>
<thead>
<tr>
<th>WARNING: EMBRYO-FETAL TOXICITY, HEMATOLOGIC TOXICITY, and VENOUS and ARTERIAL THROMBOEMBOLISM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Embryo-Fetal Toxicity</strong></td>
</tr>
<tr>
<td>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 REVlimID REMS® program.</td>
</tr>
</tbody>
</table>

Information about the REVlimID REMS® program is available at [www.celgeneriskmanagement.com](http://www.celgeneriskmanagement.com) or by calling the manufacturer’s toll-free number 1-888-423-5436.

<table>
<thead>
<tr>
<th><strong>Hematologic Toxicity (Neutropenia and Thrombocytopenia)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>REVlimID can cause significant neutropenia and thrombocytopenia. Eighty percent of patients with del 5q MDS 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.</td>
</tr>
</tbody>
</table>

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<tr>
<th><strong>Venous and Arterial Thromboembolism</strong></th>
</tr>
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<tr>
<td>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 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.</td>
</tr>
</tbody>
</table>

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Important Safety Information (continued)

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
- Males: 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.
- Blood Donation: 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.

REVLIMID REMS® Program: See Boxed WARNINGS: Prescribers and pharmacies must be certified with the REVLIMID 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. MM: Patients taking REVLIMID/dex or REVLIMID as maintenance therapy should have their complete blood counts (CBC) assessed every 7 days for the first 2 cycles, on days 1 and 15 of cycle 3, and every 28 days thereafter. MDS: 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 dose reduction. Please see the Black Box WARNINGS for further information. MCL: Patients taking REVLIMID for MCL should have their CBCs monitored weekly for the first cycle (28 days), every 2 weeks during cycles 2-4, and then monthly thereafter. Patients may require dose interruption and/or dose reduction.

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 patient’s underlying risks. ESAs and estrogens may further increase the risk of thrombosis and their use should be based on a benefit-risk decision.

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Important Safety Information (continued)

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.

Second Primary Malignancies (SPM): In clinical trials in patients with MM receiving REVLIMID, an increase of hematologic plus solid tumor SPM, notably AML and MDS, have been 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 multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma 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/dex. 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 Including Hypersensitivity Reactions: Angioedema and severe cutaneous reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. DRESS may present with a cutaneous reaction (such as rash, or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis. These events can be fatal. Patients with a prior history of Grade 4 rash associated with thalidomide treatment should not receive REVLIMID. REVLIMID interruption or discontinuation should be considered for Grade 2-3 skin rash. REVLIMID must be discontinued for angioedema, Grade 4 rash, exfoliative or bullous rash, or if SJS, TEN, or DRESS is suspected and should not be resumed following discontinuation for these reactions.

Tumor Lysis Syndrome (TLS): Fatal instances of TLS have been reported during treatment with lenalidomide. The patients at risk of TLS are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

Tumor Flare Reaction (TFR): TFR has occurred during investigational use of lenalidomide for CLL and lymphoma. Monitoring and evaluation for TFR is recommended in patients with MCL. 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.

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Important Safety Information (continued)

Thyroid Disorders: Both hypothyroidism and hyperthyroidism have been reported. Measure thyroid function before start of 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 (≥10 x 10^9/L).

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.

• The most common adverse reactions reported in ≥20% (Arm Rd Continuous): diarrhea (46%), 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 (21%), muscle spasm (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 (5%, 47%), nasopharyngitis (2%, 35%), cough (10%, 27%), gastroenteritis (0%, 23%), diarrhea (55%, 39%), rash (32%, 8%), fatigue (23%, 11%), asthenia (0%, 30%), muscle spasm (0%, 33%), and pyrexia (8%, 21%).

• 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 (28% 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%).

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
Important Safety Information (continued)

- 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%), pruritus (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%)

DRUG INTERACTIONS

Periodic monitoring of digoxin plasma levels is recommended due to increased Cmax and AUC with concomitant REVLIMID therapy. Patients taking concomitant therapies such as erythropoietin stimulating agents or estrogen containing therapies may have an increased risk of thrombosis. It is not known whether there is an interaction between dex 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 Celgene Corporation 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 female patients not to breastfeed during treatment with REVLIMID

- PEDIATRIC USE: Safety and effectiveness have not been established in pediatric patients

- RENAL IMPAIRMENT: Adjust the starting dose of REVLIMID based on the creatinine clearance value and in patients on dialysis

Please see full Prescribing Information, including Boxed WARNINGS, at link below.

Please see Important Safety Information on pages 15-19 and full Prescribing Information, including Boxed WARNINGS.
References:


Please see Important Safety Information on pages 15-19 and full *Prescribing Information*, including Boxed WARNINGS.