Start with REVLIMID as a FOUNDATION in NDMM

Continue treatment until disease progression or unacceptable toxicity[1]

Revlimid® (lenalidomide) capsules
2.5 · 5 · 10 · 15 · 20 · 25 mg

Lenalidomide (REVLIMID)

- **The ONLY preferred National Comprehensive Cancer Network® (NCCN®) Category 1 doublet for NSCT NDMM patients (with low-dose dex)[2]***
- **The #1 prescribed therapy for NDMM[3]†**

Indications

REVLIMID® (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 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, REVLIMID REMS®.

Indication for REVLIMID + dexamethasone + daratumumab (DRd)

DRd is indicated for the treatment of adult patients with newly diagnosed MM who are ineligible for an autologous stem cell transplant.

Daratumumab is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

Information about DRd does not appear in the REVLIMID full Prescribing Information. Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

REVLIMID Selected Safety Information: Boxed WARNINGS

WARNING: EMBRYO-FETAL TOXICITY, HEMATOLOGIC TOXICITY, and VENOUS and ARTERIAL THROMBOEMBOLISM
See page 8 and full Prescribing Information for complete Boxed WARNINGS.

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.**

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.**

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.

*See full NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines®) for further detail about recommended therapies.
†Claims data 07/2017-06/2020. Source: IntrinsiQ Data © 2020, IntrinsiQ Specialty Solutions, Inc.

dex, dexamethasone; DRd, daratumumab + REVLIMID + dexamethasone; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; NSCT, non-stem cell transplant.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

Rd Continuous prolonged OS vs a non-REVLIMID triplet, MPT[1]

MEDIAN OS: 10.4-MONTH INCREASE VS MPT IN AN INTERIM ANALYSIS[1]

Median OS (secondary endpoint)

Rd Continuous
(n=535)

58.9
MONTHS OS
(95% CI 56.0, NE)

VS

MPT
(n=547)

48.5
MONTHS OS
(95% CI 44.2, 52.0)

(HR 0.75; 95% CI 0.62, 0.90)

- **OS was a prespecified secondary endpoint and the interim analysis did not show a statistically significant difference between these two arms**
- **The median follow-up time for all surviving patients in the interim OS analysis was 45.5 months (data cutoff: Mar 3, 2014). In that time, 78% of prespecified events required for the planned final OS analysis (697 death events) were reported**

Lenalidomide (REVLIMID) + low-dose dex: The ONLY preferred NCCN Category 1 doublet for NSCT NDMM patients[2]

REVLIMID Selected 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.

dex, dexamethasone; MPT, melphalan + prednisone + thalidomide; NCCN, National Comprehensive Cancer Network; NDMM, newly diagnosed multiple myeloma; NSCT, non-stem cell transplant; OS, overall survival; Rd, REVLIMID + dexamethasone.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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Rd Continuous extended PFS (primary endpoint)[1]

- Median PFS: 25.5 months (95% CI 20.7, 29.4) with Rd Continuous vs 21.2 months (95% CI 19.3, 23.2) with MPT (HR 0.72; 95% CI 0.61, 0.85; *P*<0.0001)

Trial design:

FIRST (Frontline Investigation of REVLIMID + dexamethasone versus Standard Thalidomide) trial was a randomized, multicenter, open-label, 3-arm study of 1623 newly diagnosed patients who did not receive a stem cell transplant. The primary endpoint was PFS and secondary endpoints included OS and response rates. The primary efficacy comparator was REVLIMID + low-dose dex (Rd Continuous; n=535) vs ≤12 42-day cycles of melphalan + prednisone + thalidomide (MPT; n=547). A secondary efficacy comparison was Rd Continuous vs ≤18 28-day cycles of Rd (Rd18; n=541).

Patients <65 years of age were not a candidate for stem cell transplant if the patient refused or did not have access to stem cell transplant. Patients were stratified by age, stage, and country. Rd Continuous and Rd18 were dosed as REVLIMID 25 mg once daily on Days 1-21 of 28-day cycles with dex 40 mg on Days 1, 8, 15, and 22. Patients >75 years old received dex 20 mg on Days 1, 8, 15, and 22. Initial dose and regimens for Rd Continuous and Rd18 were adjusted by age and renal function, and all patients received prophylactic anticoagulation, with the most commonly used being aspirin.

OS was defined as the time from randomization to death from any cause. NE included patients with no response assessment and those whose only assessment was “response not evaluable.”

PFS was defined as the time from randomization to the first documentation of disease progression as determined by Independent Response Adjudication Committee (IRAC), based on International Myeloma Working Group (IMWG) criteria, or death due to any cause, whichever occurred first during the study until the end of the PFS follow-up phase. The data cutoff was May 24, 2013.

REVLIMID Selected Safety Information (continued)

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.

dex, dexamethasone; MPT, melphalan + prednisone + thalidomide; NE, not evaluable; OS, overall survival; PFS, progression-free survival; Rd, REVLIMID + dexamethasone.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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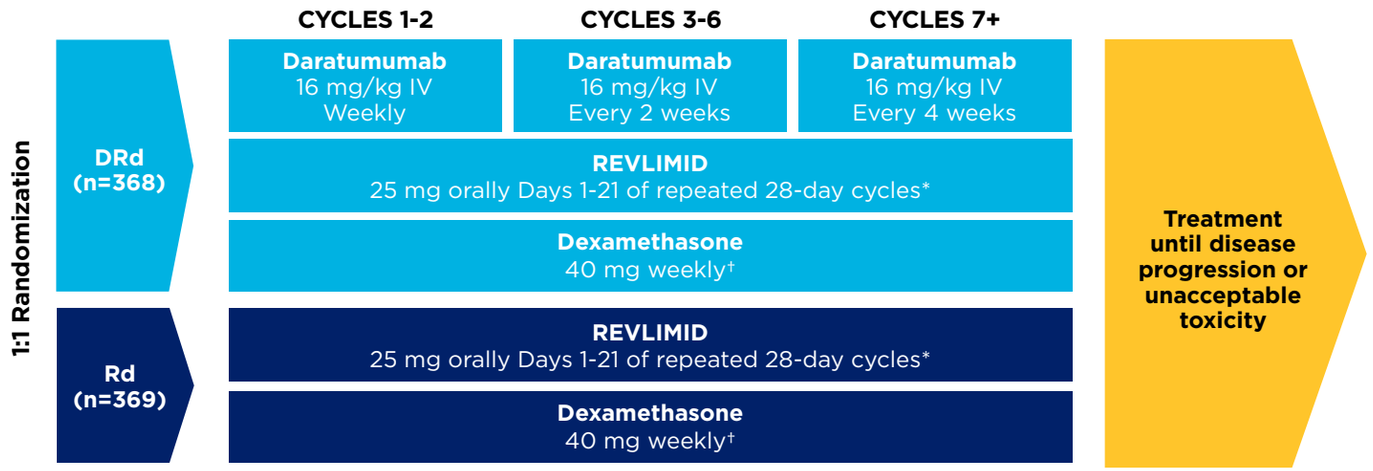
DRd: An FDA-approved triplet with REVLIMID for NSCT NDMM patients[4,5]

MAIA STUDY DESIGN (N=737)



MAIA was a Phase 3, open-label, randomized, multicenter trial of DRd (n=368) vs Rd (n=369) in adult patients with NDMM who were ineligible for an auto-SCT. Patients were stratified by ISS stage, region, and age (<75 vs ≥75 years). The primary endpoint was PFS according to IMWG criteria. Secondary endpoints included ORR (PR, VGPR, CR, sCR), MRD, and safety, among others. The original protocol provided for Rd dosing in the DRd arm for a maximum of 2 years. Dex was continued as a premedication for dara administration even after Rd treatment was discontinued.

The MAIA trial protocol was amended to continue REVLIMID in the DRd arm until disease progression or unacceptable toxicity[4,6]

Dose adjustments due to toxicity for REVLIMID and dexamethasone were applied according to the REVLIMID Prescribing Information.

Information about DRd does not appear in the REVLIMID full Prescribing Information. Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

*The starting dose of REVLIMID was adjusted for patients with renal impairment.
†Or reduced dose of 20 mg/week for patients >75 years or BMI <18.5. On daratumumab infusion days, the dexamethasone dose was given as a pre-infusion medication.

PFS was defined as the time from randomization to either disease progression or death.

REVLIMID Selected Safety Information (continued)

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 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.

auto-SCT, autologous stem cell transplantation; BMI, body mass index; CR, complete response; dara, daratumumab; dex, dexamethasone; DRd, daratumumab + REVLIMID + dexamethasone; IMWG, International Myeloma Working Group; ISS, International Staging System; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NSCT, non-stem cell transplant; ORR, overall response rate; PFS, progression-free survival; PR, partial response; Rd, REVLIMID + dexamethasone; sCR, stringent complete response; VGPR, very good partial response.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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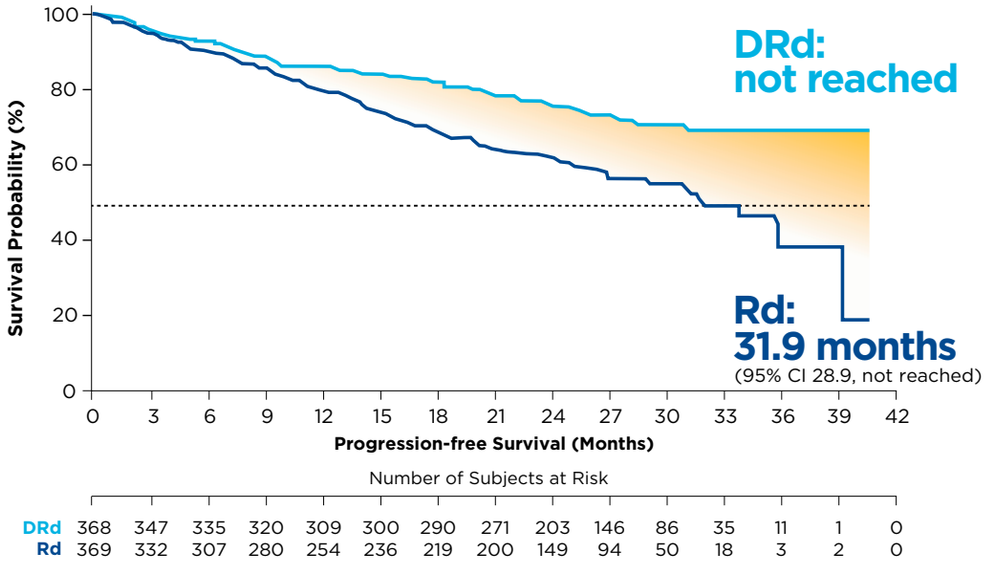
44% reduction in the risk of disease progression or death with DRd[4,5]

MEDIAN PFS (PRIMARY ENDPOINT)



HR 0.56 (95% CI 0.43, 0.73; *P*<0.0001)

DRd (n=368)
Rd (n=369)

DRd and Rd were continued until disease progression or unacceptable toxicity[4]

Daratumumab Selected Safety Information

WARNINGS AND PRECAUTIONS FOR DARATUMUMAB

- **Infusion-related Reactions:** Interrupt daratumumab infusion for infusion-related reactions of any severity. Permanently discontinue the infusion in case of anaphylactic reactions or life-threatening infusion reactions and institute appropriate emergency care.
- **Interference With Cross-Matching and Red Blood Cell Antibody Screening:** Type and screen patients prior to starting treatment. Inform blood banks that a patient has received daratumumab.
- **Neutropenia:** Monitor complete blood cell counts periodically during treatment. Monitor patients with neutropenia for signs of infection. Consider withholding daratumumab until recovery of neutrophils.
- **Thrombocytopenia:** Monitor complete blood cell counts periodically during treatment. Consider withholding daratumumab until recovery of platelets.
- **Interference With Determination of Complete Response:** Daratumumab can interfere with the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.
- **Embryo-Fetal Toxicity:** Can cause fetal harm. Advise pregnant women of the potential risk to a fetus and advise females of reproductive potential to use effective contraception.

DRd, daratumumab + REVLIMID + dexamethasone; PFS, progression-free survival; Rd, REVLIMID + dexamethasone.

Information about DRd does not appear in the REVLIMID full Prescribing Information. Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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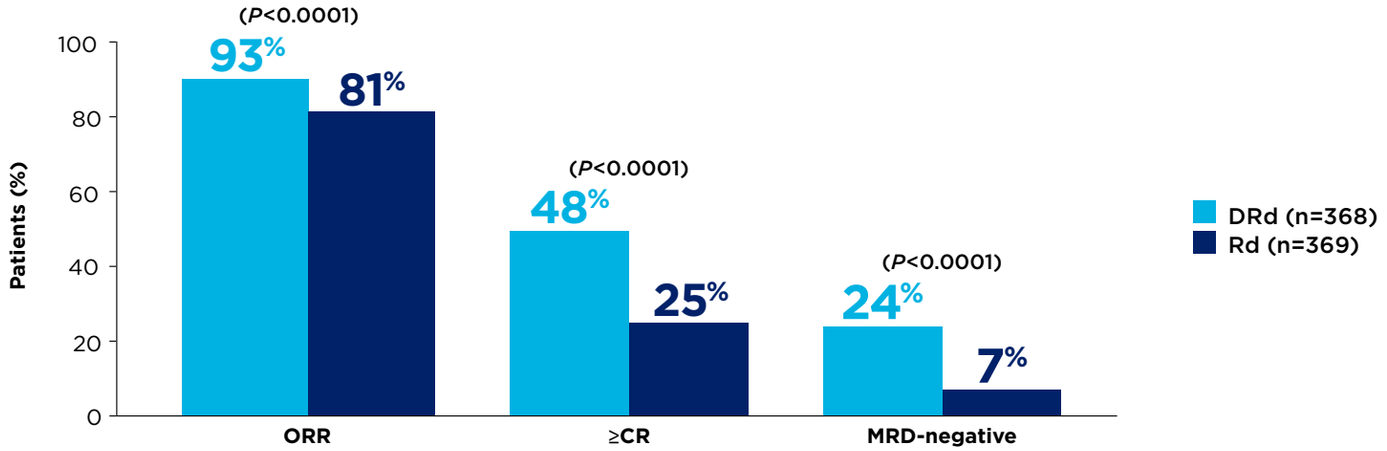
48% of patients achieved ≥CR with DRd[4]

RESPONSE AND MRD-NEGATIVE RATES



- ≥CR = CR + sCR
- DRd ORR = sCR (30.4%) + CR (17.1%) + VGPR (31.8%) + PR (13.6%)
- Rd ORR = sCR (12.5%) + CR (12.5%) + VGPR (28.2%) + PR (28.2%)
- MRD was measured by next-generation sequencing (NGS) to 10^{-5}

Information about DRd does not appear in the REVLIMID full Prescribing Information. Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

DRd and Rd were continued until disease progression or unacceptable toxicity[4]

REVLIMID Selected Safety Information (continued)

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.

CR, complete response; DRd, daratumumab + REVLIMID + dexamethasone; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; Rd, REVLIMID + dexamethasone; sCR, stringent complete response; VGPR, very good partial response.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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Safety profile for DRd vs Rd[4]

MOST FREQUENTLY REPORTED ADVERSE REACTIONS (≥20%) OF ANY GRADE (%)

	DRd (n=364)	Rd (n=365)
Neutropenia	91	77
Leukopenia	90	82
Lymphopenia	84	75
Thrombocytopenia	67	58
Anemia	47	57
Infusion-related reactions[a]	41	0
Diarrhea	57	46
Constipation	41	36
Nausea	32	23
Peripheral edema	41	33
Fatigue	40	28

MOST FREQUENTLY REPORTED ADVERSE REACTIONS (≥20%) OF ANY GRADE (%)

	DRd (n=364)	Rd (n=365)
Asthenia	32	25
Pyrexia	23	18
Upper respiratory tract infection	52	36
Bronchitis	29	21
Pneumonia	26	14
Decreased appetite	22	15
Back pain	34	26
Muscle spasms	29	22
Peripheral sensory neuropathy	24	15
Dyspnea	32	20
Cough	30	18

[a]Infusion-related reactions determined by investigators.

- Grade 3 or 4 hematology laboratory abnormalities in the DRd arm compared to the Rd arm included: neutropenia (DRd 56% vs Rd 39%), lymphopenia (DRd 52% vs Rd 42%), leukopenia (DRd 35% vs Rd 24%), anemia (DRd 13% vs Rd 24%), and thrombocytopenia (DRd 9% vs Rd 11%)
- Serious adverse reactions with a 2% greater incidence in the DRd arm compared to the Rd arm were pneumonia (DRd 15% vs Rd 8%), bronchitis (DRd 4% vs Rd 2%), and dehydration (DRd 2% vs Rd <1%)

DRd, daratumumab + REVLIMID + dexamethasone; Rd, REVLIMID + dexamethasone.

Information about DRd does not appear in the REVLIMID full Prescribing Information. Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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Indications

REVLIMID® (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 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, REVLIMID REMS®.

Indication for REVLIMID + dexamethasone + daratumumab (DRd)

DRd is indicated for the treatment of adult patients with newly diagnosed MM who are ineligible for an autologous stem cell transplant.

Information about DRd does not appear in the REVLIMID full Prescribing Information. Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

Important 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.

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.

CONTRAINDICATIONS FOR DARATUMUMAB

Daratumumab is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

Please see additional Important Safety Information on pages 9-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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Important Safety Information (continued)

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. Patients may require a dose interruption and/or dose reduction. **MM:** Monitor complete blood counts 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.

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.

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.

Please see additional Important Safety Information on pages 8, 10, and 11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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Important Safety Information (continued)

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 has 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 (≥10 x 10^9/L).

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

WARNINGS AND PRECAUTIONS FOR DARATUMUMAB

- **Infusion-related Reactions:** Interrupt daratumumab infusion for infusion-related reactions of any severity. Permanently discontinue the infusion in case of anaphylactic reactions or life-threatening infusion reactions and institute appropriate emergency care.
- **Interference With Cross-Matching and Red Blood Cell Antibody Screening:** Type and screen patients prior to starting treatment. Inform blood banks that a patient has received daratumumab.
- **Neutropenia:** Monitor complete blood cell counts periodically during treatment. Monitor patients with neutropenia for signs of infection. Consider withholding daratumumab until recovery of neutrophils.
- **Thrombocytopenia:** Monitor complete blood cell counts periodically during treatment. Consider withholding daratumumab until recovery of platelets.
- **Interference With Determination of Complete Response:** Daratumumab can interfere with the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.
- **Embryo-Fetal Toxicity:** Can cause fetal harm. Advise pregnant women of the potential risk to a fetus and advise females of reproductive potential to use effective contraception.

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 (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%).

Information about DRd does not appear in the REVLIMID full Prescribing Information. Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

Please see additional Important Safety Information on pages 8, 9, and 11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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Important Safety Information (continued)

- **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%).

ADVERSE REACTIONS FOR DRd

- The most frequent (≥20%) adverse reactions (DRd arm) were: diarrhea (57%), upper respiratory tract infection (52%), infusion reactions (41%), constipation (41%), peripheral edema (41%), fatigue (40%), back pain (34%), nausea (32%), asthenia (32%), dyspnea (32%), cough (30%), bronchitis (29%), muscle spasms (29%), pneumonia (26%), peripheral sensory neuropathy (24%), pyrexia (23%), decreased appetite (22%).
- Grade 3 or 4 hematology laboratory abnormalities (DRd arm) included: neutropenia (56%), lymphopenia (52%), leukopenia (35%), anemia (13%), thrombocytopenia (9%).

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

REFERENCES

1. REVLIMID [package insert]. Summit, NJ: Celgene Corp.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.4.2021. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed December 20, 2020. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.
3. Data on file. Bristol-Myers Squibb Co; 2020.
4. Daratumumab [package insert]. Horsham, PA: Janssen Biotech, Inc.
5. Facon T, Kumar S, Plesner T, et al. Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. *N Engl J Med*. 2019;380(22):2104-2115.
6. Clinicaltrials.gov. NCT02252172. https://clinicaltrials.gov/ct2/history/NCT02252172?A=4&B=51&C=merged#StudyPageTop. Accessed December 8, 2020.

Please see additional Important Safety Information on pages 8-10 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

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Start with REVLIMID as a FOUNDATION in newly diagnosed MM

REVLIMID is the most prescribed NDMM therapy[3]*

#1 PRESCRIBED

ONLY NCCN CATEGORY 1

Lenalidomide (REVLIMID) + low-dose dex is the ONLY preferred NCCN Category 1 doublet for NSCT NDMM patients[2]

Indications

REVLIMID® (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 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, REVLIMID REMS®.

DRd: An FDA-approved triplet with REVLIMID for NSCT NDMM[4]

44% reduction in the risk of disease progression or death with DRd[4]

- Median PFS (primary endpoint): not reached in DRd vs 31.9 months in Rd (95% CI 28.9, not reached) (HR 0.56; 95% CI 0.43, 0.73; *P*<0.0001)[4]

Daratumumab Selected Safety Information

Daratumumab is associated with the following Warnings and Precautions: Infusion-related Reactions, Interference With Serological Testing, Neutropenia, Thrombocytopenia, Interference With Determination of Complete Response, and Embryo-Fetal Toxicity.

Information about DRd does not appear in the REVLIMID full Prescribing Information. Please see the daratumumab full Prescribing Information and Important Safety Information at www.darzalex.com.

REVLIMID Selected Safety Information

- **REVLIMID has Boxed WARNINGS for EMBRYO-FETAL TOXICITY, a RESTRICTED DISTRIBUTION PROGRAM—the REVLIMID REMS®, HEMATOLOGIC TOXICITY, and VENOUS and ARTERIAL THROMBOEMBOLISM.**
- REVLIMID has contraindications for Pregnancy and Severe Hypersensitivity Reactions.
- Warnings and Precautions include Embryo-Fetal Toxicity, REVLIMID REMS® Program, Hematologic Toxicity, Venous and Arterial Thromboembolism, Increased Mortality in Patients With CLL, Second Primary Malignancies, Increased Mortality With Pembrolizumab, Hepatotoxicity, Severe Cutaneous Reactions, Tumor Lysis Syndrome, Tumor Flare Reaction, Impaired Stem Cell Mobilization, Thyroid Disorders, Early Mortality in Patients With MCL, and Hypersensitivity.

*Claims data 07/2017-06/2020. Source: IntrinsiQ Data © 2020, IntrinsiQ Specialty Solutions, Inc.

dex, dexamethasone; DRd, daratumumab + REVLIMID + dexamethasone; MM, multiple myeloma; NCCN, National Comprehensive Cancer Network; NDMM, newly diagnosed multiple myeloma; NSCT, non-stem cell transplant; PFS, progression-free survival; Rd, REVLIMID + dexamethasone.

Please see Important Safety Information on pages 8-11 and full Prescribing Information, including Boxed WARNINGS, for REVLIMID.

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