℞ Only

Prescription only medicine

WARNING : Not to be used by pregnant women or women capable of becoming pregnant as as single dose of Lenalidomide taken by pregnant women or capable of becoming pregnant can cause severe birth defects or death to an inbom baby.

Lenalidomide Capsules

Evermide 5mg

Each hard gelatin capsule contains:
Lenalidomide 5 mg
Excipients qs
Approved colours used in empty capsule shell.

Evermide 10mg

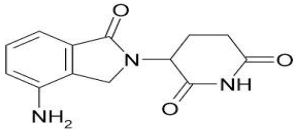
Each hard gelatin capsule contains:
Lenalidomide 10 mg
Excipients qs
Approved colours used in empty capsule shell.

Evermide 25mg

Each hard gelatin capsule contains:
Lenalidomide 25 mg
Excipients qs
Approved colours used in empty capsule shell.

DESCRIPTION

Lenalidomide , a thalidomide analogue, is an immunomodulatory agent with antiangiogenic and antineoplastic properties. The chemical name is 3-(4-amino-1-oxo 1,3-dihydro-2H-isoindol-2-yl) piperidine-2,6-dione and it has the following chemical structure:



The empirical formula for lenalidomide is C13H13N3O3, and the gram molecular weight is 259.3.
Lenalidomide is an off-white to pale-yellow solid powder. It is soluble in organic solvent/water mixtures, and buffered aqueous solvents. Lenalidomide is more soluble in organic solvents and low pH solutions. Solubility was significantly lower in less acidic buffers, ranging from about 0.4 to 0.5 mg/ml. Lenalidomide has an asymmetric carbon atom and can exist as the optically active forms S(-) and R(+), and is produced as a racemic mixture with a net optical rotation of zero.
Lenalidomide is available in 5 mg, 10 mg,and 25 mg capsules for oral administration.

INDICATIONS AND USAGE

Multiple Myeloma
Lenalidomide in combination with dexamethasone is indicated for the treatment of patients with multiple myeloma (MM) who have received at least one prior therapy.
Myelodysplastic Syndromes
Lenalidomide 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.
Mantle Cell Lymphoma
Lenalidomide 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

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity
Lenalidomide is a thalidomide analogue and is contraindicated for use during pregnancy. Thalidomide is a known human teratogen that causes life-threatening human birth defects or embryo-fetal death An embryo-fetal development study in monkeys indicates that lenalidomide produced malformations in the offspring of female monkeys who received the drug during pregnancy, similar to birth defects observed in humans following exposure to thalidomide during pregnancy.
Lenalidomide Females of Reproductive Potential Females of reproductive potential must avoid pregnancy for at least 4 weeks before beginning Lenalidomide therapy, during therapy, during dose interruptions and for at least 4 weeks after completing therapy.
Females must commit either to abstain continuously from heterosexual sexual intercourse or to use two methods of reliable birth control, beginning 4 weeks prior to initiating treatment with Lenalidomide , during therapy, during dose interruptions and continuing for 4 weeks following discontinuation of Lenalidomide therapy.

Two negative pregnancy tests must be obtained prior to initiating therapy. The first test should be performed within 10-14 days and the second test within 24 hours prior to prescribing Lenalidomide therapy and then weekly during the first month, then monthly thereafter in women with regular menstrual cycles or every 2 weeks in women with irregular menstrual cycles.

Lenalidomide is present in the semen of patients receiving the drug. Therefore, males must always use a latex or synthetic condom during any sexual contact with females of reproductive potential while taking Lenalidomide and for up to 28 days after discontinuing Lenalidomide , even if they have undergone a successful vasectomy. Male patients taking Lenalidomide must not donate sperm
Blood Donation
Patients must not donate blood during treatment with Lenalidomide and for 1 month following discontinuation of the drug because the blood might be given to a pregnant female patient whose fetus must not be exposed to Lenalidomide .

DRUG INTERACTIONS

Results from human in vitro studies show that Lenalidomide is neither metabolized by nor inhibits or induces the cytochrome P450 pathway suggesting that lenalidomide is not likely to cause or be subject to P450-based metabolic drug interactions.
In vitro studies demonstrated that Lenalidomide is not a substrate of human breast cancer resistance protein (BCRP), multidrug resistance protein (MRP) transporters MRP1, MRP2, or MRP3, organic anion transporters (OAT) OAT1 and OAT3, organic anion transporting polypeptide 1B1 (OATP1B1 or OATP2), organic cation transporters (OCT) OCT1 and OCT2, multidrug and toxin extrusion protein (MATE) MATE1, and organic cation transporters novel (OCTN) OCTN1 and OCTN2.
In vitro, lenalidomide is a substrate, but is not an inhibitor of P-glycoprotein (P-gp).

Digoxin

When digoxin was co-administered with multiple doses of Lenalidomide (10 mg/day) the digoxin Cmax and AUC0-∞ were increased by 14%. Periodic monitoring of digoxin plasma levels, in accordance with clinical judgment and based on standard clinical practice in patients receiving this medication, is recommended during administration of Lenalidomide .

Warfarin

Co-administration of multiple dose Lenalidomide (10 mg) with single dose warfarin (25 mg) had no effect on the pharmacokinetics of total lenalidomide or R- and S-warfarin. Expected changes in laboratory assessments of PT and INR were observed after warfarin administration, but these changes were not affected by concomitant Lenalidomide administration. It is not known whether there is an interaction between dexamethasone and warfarin. Close monitoring of PT and INR is recommended in multiple myeloma patients taking concomitant warfarin.Concomitant Therapies That May Increase the Risk of Thrombosis
Erythropoietic agents, or other agents that may increase the risk of thrombosis, such as estrogen containing therapies, should be used with caution in multiple myeloma patients receiving lenalidomide with dexamethasone
The following adverse reactions are described in detail in other labeling sections:

Neutropenia and thrombocytopenia
Deep vein thrombosis and pulmonary embolism
Allergic Reactions
Tumor lysis syndrome
Tumor flare reactions]
Hepatotoxicity
Second Primary Malignancies [
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
Clinical Trials Experience in Multiple Myeloma
Data were evaluated from 703 patients in two studies who received at least one dose of Lenalidomide /dexamethasone (353 patients) or placebo/dexamethasone (350 patients).
In the Lenalidomide /dexamethasone treatment group, 269 patients (76%) underwent at least one dose interruption with or without a dose reduction of Lenalidomide compared to 199 patients (57%) in the placebo/dexamethasone treatment group. Of these patients who had one dose interruption with or without a dose reduction, 50% in the Lenalidomide /dexamethasone treatment group underwent at least one additional dose interruption with or without a dose reduction compared to 21% in the placebo/dexamethasone treatment group. Most adverse events and Grade 3/4 adverse events were more frequent in patients who received the combination of Lenalidomide /dexamethasone compared to placebo/dexamethasone.
There is no specific experience in the management of lenalidomide overdose in patients; although in dose-ranging studies, some patients were exposed to up to 150 mg and in single-dose studies, some patients were exposed to up to 400 mg.In studies, the dose-limiting toxicity was essentially hematological. In the event of overdose, supportive care is advised.

DOSAGE AND ADMINISTRATION

Lenalidomide should be taken orally at about the same time each day, either with or without food. Lenalidomide capsules should be swallowed whole with water. The capsules should not be opened, broken, or chewed.
Multiple Myeloma
The recommended starting dose of Lenalidomide is 25 mg once daily on Days 1-21 of repeated 28-day cycles. The recommended dose of dexamethasone is 40 mg once daily on Days 1-4, 9-12, and 17-20 of each 28-day cycle for the first 4 cycles of therapy and then 40 mg once daily orally on Days 1-4 every 28 days. Treatment is continued or modified based upon clinical and laboratory findings.
Dose Adjustments for Hematologic Toxicities During Multiple Myeloma Treatment
Dose modification guidelines, as summarized below, are recommended to manage Grade 3 or

Thrombocytopenia in MMPlatelet counts
Thrombocytopenia in MM
When Platelets Recommended Course
Fall to <30,000/mcL Interrupt Lenalidomide treatment, follow CBC weekly
Return to ≥30,000/mcL Restart Lenalidomide at 15 mg daily
For each subsequent drop <30,000/mcL Interrupt Lenalidomide treatment
Return to ≥30,000/mcL Resume Lenalidomide at 5 mg less than the previous dose. Do not dose below 5 mg daily
Absolute Neutrophil counts (ANC)
Neutropenia in MM
When Neutrophils Recommended Course
Fall to <1000/mcL Interrupt Lenalidomide treatment, add G-CSF, follow CBC weekly
Return to ≥1,000/mcL and neutropenia is the only toxicity Resume Lenalidomide at 25 mg daily
Return to ≥1,000/mcL and if other toxicity Resume Lenalidomide at 15 mg daily
For each subsequent drop <1,000/mcL Interrupt Lenalidomide treatment
Return to ≥1,000/mcL Resume Lenalidomide at 5 mg less than the previous dose. Do not dose below 5 mg daily
Other Grade 3 / 4 Toxicities in MM
For other Grade 3/4 toxicities judged to be related to Lenalidomide , hold treatment and restart at the physician's discretion at next
lower dose level when toxicity has resolved to ≤ Grade 2.
Starting Dose Adjustment for Renal Impairment in MM:
See Section 2.4.Myelodysplastic Syndromes
The recommended starting dose of Lenalidomide is 10 mg daily. Treatment is continued or modified based upon clinical and laboratory findings.
Dose Adjustments for Hematologic Toxicities During MDS Treatment
Patients who are dosed initially at 10 mg and who experience thrombocytopenia should have their dosage adjusted as follows:
Platelet counts
If thrombocytopenia develops WITHIN 4 weeks of starting treatment at 10 mg daily in MDS
If baseline ≥100,000/mcL
When Platelets Recommended Course
Fall to <50,000/mcL Interrupt Lenalidomide treatment
Return to ≥50,000/mcL Resume Lenalidomide at 5 mg daily
If baseline <100,000/mcL
When Platelets Recommended Course
Fall to 50% of the baseline value Interrupt Lenalidomide treatment
If baseline ≥60,000/mcL and
returns to ≥50,000/mcL Resume Lenalidomide at 5 mg daily
If baseline <60,000/mcL and
returns to ≥30,000/mcL Resume Lenalidomide at 5 mg daily
If thrombocytopenia develops AFTER 4 weeks of starting treatment at 10 mg daily in MDS
When Platelets Recommended Course
<30,000/mcL or <50,000/mcL
with platelet transfusions Interrupt Lenalidomide treatment
Return to ≥30,000/mcL
(without hemostatic failure) Resume Lenalidomide at 5 mg daily
Patients who experience thrombocytopenia at 5 mg daily should have their dosage adjusted as follows:
If thrombocytopenia develops during treatment at 5 mg daily in MDS
When Platelets Recommended Course
<30,000/mcL or <50,000/mcL
with platelet transfusions Interrupt Lenalidomide treatment
Return to ≥30,000/mcL
(without hemostatic failure) Resume Lenalidomide at 2.5 mg daily
Patients who are dosed initially at 10 mg and experience neutropenia should have their dosage adjusted as follows:
Absolute Neutrophil counts (ANC)
If neutropenia develops WITHIN 4 weeks of starting treatment at 10 mg daily in MDS
If baseline ANC ≥1,000/mcL
When Neutrophils Recommended Course
Fall to <750/mcL Interrupt Lenalidomide treatment
Return to ≥1,000/mcL Resume Lenalidomide at 5 mg daily
If baseline ANC <1,000/mcL
When Neutrophils Recommended Course
Fall to <500/mcL Interrupt Lenalidomide treatment
Return to ≥500/mcL Resume Lenalidomide at 5 mg daily
If neutropenia develops AFTER 4 weeks of starting treatment at 10 mg daily in MDS
When Neutrophils Recommended Course
<500/mcL for ≥7 days or <500/mcL
associated with fever (≥38.5°C) Interrupt Lenalidomide treatment
Return to ≥500/mcL Resume Lenalidomide at 5 mg daily
Patients who experience neutropenia at 5 mg daily should have their dosage adjusted as follows:

If neutropenia develops during treatment at 5 mg daily in MDS
When Neutrophils Recommended Course
<500/mcL for ≥7 days or <500/mcL
associated with fever (≥38.5°C) Interrupt Lenalidomide treatment
Return to ≥500/mcL Resume Lenalidomide at 2.5 mg daily
Other Grade 3 / 4 Toxicities in MDS
For other Grade 3/4 toxicities judged to be related to Lenalidomide , hold treatment and restart at the physician's discretion at next lower dose level when toxicity has resolved to ≤ Grade 2.
Starting Dose Adjustment for Renal Impairment in MDS:
Mantle Cell Lymphoma
The recommended starting dose of Lenalidomide is 25 mg/day orally on Days 1-21 of repeated 28-day cycles for relapsed or refractory mantle cell lymphoma. Treatment should be continued until disease progression or unacceptable toxicity.
Treatment is continued, modified or discontinued based upon clinical and laboratory findings.
Dose Adjustments for Hematologic Toxicities During MCL Treatment
Dose modification guidelines as summarized below are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia or other Grade 3 or 4 toxicities considered to be related to Lenalidomide .
Platelet counts
Thrombocytopenia during treatment in MCL
When Platelets Recommended Course
Fall to <50,000/mcL Interrupt Lenalidomide treatment and follow CBC weekly

Return to ≥50,000/mcL Resume Lenalidomide at 5 mg less than the previous dose. Do not dose below 5 mg daily

Absolute Neutrophil counts (ANC)
Neutropenia during treatment in MCL
When Neutrophils Recommended Course
Fall to <1000/mcL for at least 7 days
OR
Falls to < 1,000/mcL with an associated temperature ≥38.5°C
OR
Falls to < 500 /mcL Interrupt Lenalidomide treatment and follow CBC weekly

Return to ≥1,000/mcL Resume Lenalidomide at 5 mg less than the previous dose. Do not dose below 5 mg daily

Storage : Store below 30ºC. Protect from light & moisture.

Presentation:
10 Capsules in a HDPE bottle.

Manufactured by:
BETA DRUGS LTD.
Kharuni-Lodhimajra Road Vil. Nandpur,Baddi,
Distt Solan, Himachal Pradesh-173205

Marketed by:
NEOVA BIOGENE PRIVATE LIMITED.
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