Prescribing Information: IMNOVID® ▼ (pomalidomide) 1mg, 2mg, 3mg, 4mg hard capsules

Refer to the Summary of Product Characteristics (SmPC) before prescribing

Presentation: Hard capsules containing pomalidomide 1mg, 2mg, 3mg or 4mg

Indications: IMNOVID® in combination with bortezomib and dexamethasone is indicated in the treatment of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide.

IMNOVID® in combination with dexamethasone is indicated in the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.

Dosage and administration: Treatment must be initiated and monitored under the supervision of physicians experienced in the management of multiple myeloma. *Pomalidomide in combination with bortezomib and dexamethasone:* The recommended starting dose of pomalidomide is 4 mg orally once daily on Days 1 to 14 of repeated 21-day cycles. The recommended starting dose of bortezomib is 1.3 mg/m^2 intravenous or subcutaneous once daily on Days 1, 4, 8 and 11 (*cycle 1-8*) and Days 1 and 8 (*cycle 9 onwards*). The recommended dose of dexamethasone is 20 mg orally once daily on Days 1, 2, 4, 5, 8, 9, 11 and 12 (*cycle 1-8*) and Days 1, 2, 8 and 9 (*cycle 9 onwards*). See the SmPC for dosing recommendations and for dose modifications for treatment-related adverse reactions. Treatment with pomalidomide combined with bortezomib and dexamethasone should be given until disease progression or until unacceptable toxicity occurs.

Pomalidomide in combination with dexamethasone: The recommended starting dose of pomalidomide is 4mg orally once daily on Days 1 to 21 of each 28-day cycle. The recommended dose of dexamethasone is 40mg orally once daily on Days 1, 8, 15 and 22 of each 28-day cycle. See the SmPC for dosing recommendations and for dose modifications for treatment-related adverse reactions. Treatment with pomalidomide combined with dexamethasone should be given until disease progression or until unacceptable toxicity occurs. **Special populations:** *Paediatric population*: There is no relevant use of pomalidomide in children aged 0-17 years for the indication of multiple myeloma. *Elderly:* No dose adjustment is required for pomalidomide. *Pomalidomide in combination with bortezomib and dexamethasone:* For patients >75 years of age, the starting dose of dexamethasone is 10 mg once daily, on days 1, 2, 4, 5, 8, 9, 11 and 12 of each 21-day cycle (*cycles 1-8*) and 10 mg once daily, on days 1, 2, 8 and 9 of each 21-day cycle (*cycles 9 onwards*). *Pomalidomide in combination with dexamethasone:* For patients >75 years of age, the starting dose of dexamethasone is 20mg once daily on Days 1, 8, 15 and 22 of each 28-day treatment cycle. *Hepatic impairment:* Hepatic impairment has a modest effect on the pharmacokinetics of pomalidomide. No adjustment of the starting dose of pomalidomide is required for patients with hepatic impairment as defined by the Child-Pugh criteria. Carefully monitor for adverse reactions and dose reduction or interruption of pomalidomide should be used as needed. *Renal impairment*: No dose adjustment of pomalidomide is required for patients with renal impairment. On haemodialysis days, patients should take pomalidomide following haemodialysis.

Contraindications: Pregnancy. Women of childbearing potential, unless all the conditions for the Pregnancy Prevention Programme (PPP) have been met. Male patients unable to follow or comply with the required contraceptive measures. Hypersensitivity to active substance or excipients.

Special warnings and precautions: *Pregnancy warning:* Pomalidomide must not be taken during pregnancy, since a teratogenic effect is expected. The conditions of the PPP must be fulfilled for all patients unless there is reliable evidence that the patient does not have childbearing potential. Refer to section 4.4 of SmPC for a full list of the criteria for women of non-childbearing potential. Women of childbearing potential must understand the expected teratogenic risk to the unborn child, the need for at least one effective method of contraception for at least 4 weeks before therapy, during therapy, and until at least 4 weeks after pomalidomide therapy; and accept to undergo medically supervised pregnancy testing at least every 4 weeks except in case of confirmed tubal sterilisation. Male patients taking pomalidomide must understand the expected teratogenic risk if engaged in sexual activity with a pregnant woman or a woman of childbearing potential and the need for the use of a condom throughout treatment, during dose interruption and for 7 days after dose interruptions and/or cessation of treatment. Vasectomised males should wear a condom if engaged in sexual activity with a pregnant woman or woman of childbearing potential. See section 4.4 of the SmPC for examples of suitable methods of contraception. Patients should not donate blood, semen or sperm during treatment (including during dose interruptions) and for 7 days following discontinuation of pomalidomide. Prescriptions for women of childbearing potential can be for a maximum duration of treatment of 4 weeks according to the approved indications dosing regimens, and prescriptions for all other patients can be for a maximum duration of 12 weeks. *Haematological events:* Neutropenia was the most frequently reported Grade 3 or 4 haematologic adverse reaction followed by anaemia and thrombocytopenia. Patients should be monitored for haematologic adverse reactions, especially neutropenia and advised to promptly report febrile episodes. Physicians should observe for signs of bleeding including epistaxis, especially with use of concomitant medication known to increase the risk of bleeding. Complete blood counts should be monitored at baseline, weekly for the first 8 weeks and monthly thereafter. A dose modification may be required (see section 4.2 of the SmPC). Patients may require use of blood product support and/or growth factors. *Thromboembolic events:* Venous thromboembolic events (predominantly deep vein thrombosis and pulmonary embolism) and arterial thrombotic events have been reported, therefore patients with known risk factors for thromboembolism – including prior thrombosis – should be closely monitored. Anti-coagulation therapy (unless contraindicated) is recommended, especially in patients with additional thrombotic risk factors. Erythropoietic agents, as well as other agents that may increase the risk of thromboembolic events, should be used with caution. *Thyroid disorders:* Cases of hypothyroidism have been reported. Optimal control of co-morbid conditions influencing thyroid function is recommended before start of treatment. Baseline and ongoing monitoring of thyroid function is recommended. *Peripheral neuropathy:* Caution should be exercised when treating patients with ongoing ≥ Grade 2 peripheral neuropathy. *Significant cardiac dysfunction:* Caution should be exercised when considering patients with significant cardiac dysfunction (patients with congestive heart failure [NY Heart Association Class III or IV]; myocardial infarction up to 12 months before starting pomalidomide treatment; unstable or poorly controlled angina pectoris), as they were excluded from clinical studies with pomalidomide. Periodically monitor for signs or symptoms of cardiac events. *Tumour lysis syndrome:* Patients with high tumour burden should be monitored closely and appropriate precautions taken. *Second primary malignancies:* Physicians should carefully evaluate patients before and during treatment using standard cancer screening for occurrence of second primary malignancies and institute treatment as indicated. *Allergic reactions and severe skin reactions*: Reports include angioedema, anaphylactic reaction and severe dermatologic reactions including Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Advise patients of signs and symptoms and need to seek medical attention immediately if these develop. Discontinue permanently for exfoliative or bullous rash, SJS, TEN, DRESS, angioedema or anaphylactic reaction. Patients with prior history of serious allergic reactions with thalidomide or lenalidomide should not receive pomalidomide. Consider pomalidomide interruption or discontinuation for Grade 2-3 skin rash. *Dizziness and confusion:* Patients must avoid situations where dizziness or confusion may be a problem and not to take other medications that may cause dizziness or confusion without adequate medical advice. *Interstitial lung disease (ILD):* Assess patients with acute onset or unexplained worsening of pulmonary symptoms to exclude ILD. Interrupt treatment pending investigation of ILD symptoms. Initiate appropriate ILD treatment as required and only resume pomalidomide after thorough risk-benefit evaluation. *Hepatic disorders:* Regularly monitor liver function for the first 6 months of treatment and as clinically indicated thereafter. *Infections:* Reactivation of hepatitis B has been reported rarely in patients receiving pomalidomide in combination with dexamethasone who have previously been infected with the hepatitis B virus (HBV). Some of these cases have progressed to acute hepatic failure, resulting in discontinuation of pomalidomide. Establish Hepatitis B virus status before initiating treatment with pomalidomide. For patients who test positive for HBV infection, consultation with a physician with expertise in the treatment of hepatitis B is recommended. Caution should be exercised when pomalidomide in combination with dexamethasone is used in patients previously infected with HBV, including patients who are anti-HBc positive but HBsAg negative. These patients should be closely monitored for signs and symptoms of active HBV infection throughout therapy. Progressive multifocal leukoencephalopathy* (PML): Cases of PML, including fatal cases, have been reported several months to years after treatment initiation. Monitor patients at regular intervals and consider PML in the differential diagnosis in patients with new or worsening neurological, cognitive or behavioural symptoms. The evaluation for PML should be based on neurological examination, magnetic resonance imaging of the brain, and cerebrospinal fluid analysis for JC virus (JCV) DNA by polymerase chain reaction (PCR) or a brain biopsy with testing for JCV. A negative JCV PCR does not exclude PML. Suspend treatment if PML is suspected and permanently discontinue treatment if PML is confirmed. *Handling:* Healthcare professionals and caregivers should wear disposable gloves when handling the blister or capsule. Women who are pregnant or suspect they may be pregnant should not handle the blister or capsule. *Sodium content:* Each capsule contains less than 1 mmol sodium (23 mg), i.e. essentially 'sodium-free'.

**Serious adverse reaction*

Interactions: Pomalidomide is not anticipated to cause clinically relevant pharmacokinetic drug-drug interactions due to P450 isoenzyme inhibition or induction or transporter inhibition when pomalidomide is co-administered with substrates of these enzymes or transporters. Pomalidomide is partly metabolised by CYP1A2 and CYP3A4/5 and a substrate for P-glycoprotein - refer to SmPC for further information. If strong inhibitors of CYP1A2 (e.g. ciprofloxacin, enoxacin and fluvoxamine) are co-administered with pomalidomide, reduce the dose of pomalidomide by 50%. The effect of dexamethasone on warfarin is unknown. Close monitoring of warfarin concentration is advised. For information on other medicinal products given in combination with pomalidomide, refer to the respective current SmPC.

Fertility, Pregnancy and Lactation: *Pregnancy:* A teratogenic effect of pomalidomide in humans is expected**.** *Breast-feeding:* Unknown whether pomalidomide is excreted in human milk. Pomalidomide was detected in milk of lactating rats following administration to the mother. Due to potential for adverse reactions in breast-fed infants, a decision must be made whether to discontinue breast-feeding or to discontinue the medicinal product, considering the benefit of breast feeding for the child and the benefit of the therapy for the woman. *Fertility:* Pomalidomide was found to impact negatively on fertility.

Side effects: *Very common (≥ 1/10) and common (≥ 1/100 to < 1/10) Adverse Reactions in patients treated with pomalidomide in combination with bortezomib and dexamethasone in multiple myeloma clinical trials:* Abdominal distension, Abdominal pain, Abdominal pain upper, Acute kidney injury*, Alanine aminotransferase increased*, Anaemia*, Atrial fibrillation*, Back pain, Basal cell carcinoma*, Bone pain, Bronchiolitis*, Bronchitis, Cataract*, Chronic kidney injury*, Clostridium difficile colitis*, Constipation, Cough, Deep vein thrombosis*, Depression, Diarrhoea, Dizziness*, Dry mouth, Dysgeusia, Dyspnoea*, Fall, Fatigue, Febrile neutropenia*, Hypercalcaemia, Hyperglycaemia, Hyperkalaemia*, Hypertension, Hypocalcaemia, Hypokalaemia, Hypomagnesaemia, Hypophosphataemia, Hypotension, Influenza, Insomnia, Leucopenia*, Lower respiratory tract infection*, Lung infection, Lymphopenia, Muscle spasms, Muscular weakness, Nausea, Neutropenia*, Non-cardiac chest pain*, Oedema, Oedema peripheral*, Paraesthesia, Peripheral sensorimotor neuropathy*, Peripheral sensory neuropathy*, Pneumonia*, Pulmonary embolism*, Pyrexia, Rash*, Respiratory tract infection*, Sepsis*, Septic shock*, Stomatitis, Syncope*, Thrombocytopenia*, Tremor, Upper respiratory tract infection, Urinary retention*, Urinary tract infection, Viral upper respiratory tract infection, Vomiting, Weight decreased.

**Serious adverse reactions*

Very common (≥ 1/10) and common (≥ 1/100 to < 1/10) Adverse Reactions in patients treated with pomalidomide in combination with dexamethasone in multiple myeloma clinical trials: Alanine aminotransferase increased*, Anaemia*, Bone pain, Bronchitis, Bronchopneumonia, Confusional state*, Constipation, Cough, Decreased appetite, Deep vein thrombosis*, Depressed level of consciousness*, Diarrhoea, Dizziness*, Dyspnoea*, Fatigue, Febrile neutropenia*, Gastrointestinal haemorrhage*, Herpes zoster, Hyperkalaemia*, Hyponatraemia, Leucopenia*, Muscle spasms, Nasopharyngitis, Nausea, Neutropenia*, Neutropenic sepsis*, Neutrophil count decreased, Oedema peripheral*, Pelvic pain, Peripheral sensory neuropathy*, Platelet count decreased, Pneumonia (bacterial, viral and fungal infections, including opportunistic infections)*, Pruritus, Pulmonary embolism*, Pyrexia, Rash*, Renal failure*, Respiratory tract infection*, Thrombocytopenia*, Tremor, Upper respiratory tract infection, Urinary retention*, Vertigo, Vomiting, White blood cell count decreased.

**Serious adverse reactions*

Other Serious Adverse Reactions in patients treated with pomalidomide in combination dexamethasone in multiple myeloma clinical trials: Basal cell carcinoma, Hyperbilirubinaemia, Squamous cell carcinoma of the skin.

Common (≥ 1/100 to < 1/10) Adverse Reactions in patients treated with pomalidomide reported in post-marketing use: Angioedema*, Atrial fibrillation*, Blood uric acid increased, Cardiac failure*, Epistaxis*, Hyperuricaemia, Interstitial lung disease*, Intracranial haemorrhage*, Myocardial infarction*, Pancytopenia*, Urticaria.

**Serious adverse reactions*

Other Serious Adverse Reactions in patients treated with pomalidomide in post-marketing use: Anaphylactic reaction, Cerebrovascular accident, DRESS, Hepatitis, Hepatitis B reactivation, Hypothyroidism, SJS, TEN, Teratogenicity, Tumour lysis syndrome.

Prescribers should consult the SmPC in relation to other adverse reactions.

NHS list price: 21 capsules x 1mg £8884, 21 capsules x 2mg £8884, 21 capsules x 3mg £8884, 21 capsules x 4mg £8884.

Legal category: POM

Marketing authorisation numbers: EU/1/13/850/001, EU/1/13/850/002, EU/1/13/850/003, and EU/1/13/850/004.

Marketing authorisation holder: Celgene Europe B.V., Winthontlaan 6 N, 3526 KV Utrecht, Netherlands.

For further information contact: Celgene Ltd, 1 Longwalk Road, Stockley Park, Uxbridge, UB11 1DB, United Kingdom. Tel: +44(0)208 831 8300.

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Adverse events should be reported. Reporting forms and information can be found at:
UK - MHRA under the Yellow Card Scheme website www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Ireland - Please report any suspected adverse reactions directly via the HPRA Pharmacovigilance website: www.hpra.ie.

Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (UK); 1 800 749 749 (Ireland).