# Pomalidomide Accord

Hard Capsules

**Prescribing Information**

**Pomalidomide 1mg, 2mg, 3mg, 4mg hard capsules**

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

**Presentation:** Each capsule contains either 1mg, 2mg, 3mg, 4mg of pomalidomide.

**Indications:** In combination with bortezomib and dexamethasone in the treatment of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide. In combination with dexamethasone 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 thesupervision of physicians experienced in the management of multiple myeloma. Dosing is continued or modified based upon clinical and laboratory findings. *Posology: Pomalidomide in combination with bortezomib and dexamethasone:* Recommended starting dose of pomalidomide is 4mg taken orally once daily on Days 1 to 14 of repeated 21- day cycles. For recommended dose of bortezomib and dexamethasone refer to SmPC. Treatment with pomalidomide combined with bortezomib and dexamethasone should be given until disease progression or until unacceptable toxicity occurs. *Pomalidomide dose modification or interruption:* To initiate a new cycle of pomalidomide, the neutrophil count must be $\geq 1 \times 10^9$/l and the platelet count must be $\geq 50 \times 10^9$/l. For instructions on dose interruptions or reductions for pomalidomide related adverse reactions as well as dose levels, refer to SmPC. If adverse reactions occur after dose reductions to 1mg, then the treatment should be discontinued. *Strong CYP1A2 inhibitors:* If strong inhibitors of CYP1A2 (e.g. ciprofloxacin, enoxacin and fluvoxamine) are co-administered with pomalidomide, the dose of pomalidomide should be reduced by 50%. *Bortezomib dose modification or interruption:* For instructions on dose interruptions or reductions for bortezomib related adverse reactions, refer to bortezomib SmPC. *Dexamethasone dose modification or interruption:* For instructions on dose interruptions or reductions for low-dose dexamethasone related adverse reactions refer to SmPC. However, dose interruption or resumption decisions are at the physician's discretion per SmPC. Discontinue dexamethasone if the patient is unable to tolerate 8 mg if $\leq 75$ years old or 4 mg if $> 75$ years old. In case of permanent discontinuation of any component of the treatment regimen, continuation of the remaining medicinal products is at the physician's discretion. *Pomalidomide in combination with dexamethasone:* Recommended starting dose of pomalidomide is 4mg taken orally once daily on Days 1 to 21 of each 28-day cycle. Recommended dose of dexamethasone is 40 mg taken orally once daily on Days 1, 8, 15 and 22 of each 28-day cycle. Treatment with pomalidomide combined with dexamethasone should be given until disease progression or until unacceptable toxicity occurs. *Pomalidomide dose modification or interruption:* Refer to SmPC for instructions for dose interruptions or reductions for pomalidomide related adverse reactions. *Special populations: Elderly:* No dose adjustment required for pomalidomide. *Pomalidomide in combination with bortezomib and dexamethasone for patients >75:* Starting dose of dexamethasone is: For cycles 1 to 8: 10 mg once daily on Days 1, 2, 4, 5, 8, 9, 11 and 12 of each 21-day cycle; For Cycles 9 and onwards: 10 mg once daily on Days 1, 2, 8 and 9 of each 21-day cycle. *Pomalidomide in combination with dexamethasone for patients >75:* Starting dose of dexamethasone is 20 mg once daily on days 1, 8, 15 and 22 of each 28-day cycle. *Hepatic impairment:* No adjustment to starting dose is required for patients with hepatic impairment as defined by the Child-Pugh criteria. However, patients with hepatic impairment should be carefully monitored for adverse reactions and dose reduction or interruption of pomalidomide should be used as needed. *Renal impairment:* No dose adjustment required. On haemodialysis days, patients should take their pomalidomide dose following haemodialysis. *Paediatric population:* No relevant use in children aged 0-17 years for the indication of multiple myeloma. *Method of administration:* Taken orally at the same time each day. Capsules should not be opened, broken or chewed and should be swallowed whole, preferably with water, with or without food. If the patient forgets to take a dose on one day, then the patient should take the normal prescribed dose as scheduled on the next day. Patients should not adjust the dose to make up for a missing dose on previous days. Recommended to press only on one end of the capsule to remove it from the blister thereby reducing the risk of capsule deformation or breakage.

**Contraindications:** Pregnancy; Women of childbearing potential, unless all the conditions of the pregnancy prevention programme are met; Male patients unable to follow or comply with the required contraceptive measures; Hypersensitivity to the active substance or to any of the excipients.

**Warnings and Precautions:** *Teratogenicity:* Pomalidomide must not be taken during pregnancy, since a teratogenic effect is expected. Pomalidomide is structurally related to thalidomide. Thalidomide is a known human teratogen that causes severe life-threatening birth defects. The conditions of the Pregnancy Prevention Programme must be fulfilled for all patients unless there is reliable evidence that the patient does not have childbearing potential. *Criteria for women of non-childbearing potential:* A female patient or a female partner of a male patient is considered of non-childbearing potential if she meets at least one of the following criteria: Age $\geq 50$ years and naturally amenorrhoeic for $\geq 1$ year (amenorrhoea following cancer therapy or during breast-feeding does not rule out childbearing potential); Premature ovarian failure confirmed by a specialist gynaecologist; Previous bilateral salpingooophorectomy, or hysterectomy: XY genotype, Turner syndrome, uterine agenesis. *Counselling:* For women of childbearing potential, pomalidomide is contraindicated unless all of the following are met: She understands the expected teratogenic risk to the unborn child; She understands the need for effective contraception, without interruption, at least 4 weeks before starting treatment, throughout the entire duration of treatment, and at least 4 weeks after the end of treatment; Even if a woman of childbearing potential has amenorrhoea she must follow all the advice on effective contraception; She should be capable of complying with effective contraceptive measures; She is informed and understands the potential consequences of pregnancy and the need to rapidly consult if there is a risk of pregnancy; She understands the need to commence the treatment as soon as pomalidomide is dispensed following a negative pregnancy test; She understands the need and accepts to undergo pregnancy testing at least every 4 weeks except in case of confirmed tubal sterilisation; She acknowledges that she understands the hazards and necessary precautions associated with the use of pomalidomide. The prescriber must ensure that for women of childbearing potential: Patient complies with conditions of the Pregnancy Prevention Programme, including confirmation that she has an adequate level of understanding; Patient has acknowledged the aforementioned conditions. For male patients taking pomalidomide, pharmacokinetic data has demonstrated that pomalidomide is present in human semen during treatment. As a precaution, and taking into account special populations with potentially prolonged elimination time such as hepatic impairment, all male patients must meet the following conditions: He understands the expected teratogenic risk if engaged in sexual activity with a pregnant woman or a woman of childbearing potential; He understands the need for the use of a condom if engaged in sexual activity with a pregnant woman or a woman of childbearing potential not using effective contraception, throughout treatment duration, during dose interruption and for 7 days after dose interruptions and/or cessation of treatment. This includes vasectomised males who should wear a condom if engaged in sexual activity with a pregnant woman or a woman of childbearing potential as seminal fluid may still contain pomalidomide in the absence of spermatozoa; He

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understands that if his female partner becomes pregnant whilst he is taking pomalidomide or 7 days after he has stopped taking pomalidomide, he should inform his treating physician immediately and that it is recommended to refer the female partner to a physician specialised or experienced in teratology for evaluation and advice. *Contraception:* Women of childbearing potential must use 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 even in case of dose interruption unless the patient commits to absolute and continuous abstinence confirmed on a monthly basis. If not established on effective contraception, the patient must be referred to an appropriately trained health care professional for contraceptive advice in order that contraception can be initiated. Examples of suitable methods of contraception: Implant; Levonorgestrel-releasing intrauterine system; Medroxyprogesterone acetate depot; Tubal sterilisation; Sexual intercourse with a vasectomised male partner only; vasectomy must be confirmed by two negative semen analyses; Ovulation inhibitory progesterone-only pills (i.e. desogestrel). Because of the increased risk of venous thromboembolism in patients with multiple myeloma taking pomalidomide and dexamethasone, combined oral contraceptive pills are not recommended. If a patient is using combined oral contraception the patient should switch to one of the effective methods listed above. The risk of venous thromboembolism continues for 4-6 weeks after discontinuing combined oral contraception. Efficacy of contraceptive steroids may be reduced during cotreatment with dexamethasone. Implants and levonorgestrel-releasing intrauterine systems are associated with an increased risk of infection at the time of insertion and irregular vaginal bleeding. Prophylactic antibiotics should be considered particularly in patients with neutropenia. Insertion of copper-releasing intrauterine devices is not recommended due to the potential risks of infection at the time of insertion and menstrual blood loss which may compromise patients with severe neutropenia or severe thrombocytopenia. *Pregnancy testing:* Medically supervised pregnancy tests with a minimum sensitivity of 25 mIU/mL must be performed for women of childbearing potential as outlined below. This requirement includes women of childbearing potential who practice absolute and continuous abstinence. Ideally, pregnancy testing, issuing a prescription and dispensing should occur on the same day. Dispensing of pomalidomide to women of childbearing potential should occur within 7 days of the prescription. *Prior to starting treatment:* Medically supervised pregnancy test should be performed during the consultation, when pomalidomide is prescribed, or in the 3 days prior to the visit to the prescriber once the patient had been using effective contraception for at least 4 weeks. The test should ensure the patient is not pregnant when she starts treatment. *Follow-up and end of treatment:* Medically supervised pregnancy test should be repeated at least every 4 weeks, including at least 4 weeks after the end of treatment, except in the case of confirmed tubal sterilisation. Pregnancy tests should be performed on the day of the prescribing visit or in the 3 days prior to the visit to the prescriber. *Additional precautions:* Instruct patients never to give this medicinal product to another person and to return any unused capsules to their pharmacist at the end of treatment. Patients should not donate blood, semen or sperm during treatment (including during dose interruptions) and for at least 7 days following discontinuation of pomalidomide. 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. *Educational materials, prescribing and dispensing restrictions:* In order to assist patients in avoiding foetal exposure to pomalidomide, the Marketing Authorisation Holder will provide educational material to healthcare professionals to reinforce the warnings about the expected teratogenicity of pomalidomide, to provide advice on contraception before treatment is started, and guidance on the need for pregnancy testing. The prescriber must inform the patient about the expected teratogenic risk and the strict pregnancy prevention measures as specified in the Pregnancy Prevention Programme and provide patients with appropriate patient educational brochure, patient card and/or equivalent tool as agreed with each National Competent Authority. In collaboration with each National Competent Authority, a controlled access programme has been implemented which includes the use of a patient card and/or equivalent tool for prescribing and /or dispensing controls, and the collection of information relating to the indication in order to monitor the off-label use within the national territory. 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 haematological adverse reaction in patients with relapsed/refractory multiple myeloma, followed by anaemia and thrombocytopenia. Monitor patients for haematological adverse reactions, especially neutropenia. Patients should be advised to report febrile episodes promptly. Observe patients for signs of bleeding including epistaxes, especially with use of concomitant medicinal products 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. Patients may require use of blood product support and /or growth factors. *Thromboembolic events:* Patients receiving pomalidomide either in combination with bortezomib and dexamethasone or in combination with dexamethasone have developed venous thromboembolic events (predominantly deep vein thrombosis and pulmonary embolism) and arterial thrombotic events (myocardial infarction and cerebrovascular accident). Patients with known risk factors for thromboembolism – including prior thrombosis – should be closely monitored. Action should be taken to try to minimise all modifiable risk factors (e.g. smoking, hypertension, and hyperlipidaemia). Patients and physicians are advised to be observant for the signs and symptoms of thromboembolism. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, arm or leg swelling. Anti-coagulation therapy (unless contraindicated) is recommended, (such as acetylsalicylic acid, warfarin, heparin or clopidogrel), especially in patients with additional thrombotic risk factors. A decision to take prophylactic measures should be made after a careful assessment of the individual patient's underlying risk factors. Use of erythropoietic agents carries a risk of thrombotic events including thromboembolism. Therefore, erythropoietic agents, as well as other agents that may increase the risk of thromboembolic events, should be used with caution. *Thyroid disorders:* Hypothyroidism has 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:* Appropriate caution should be exercised when considering the treatment of patients with patients with ongoing ≥ Grade 2 peripheral neuropathy. *Significant cardiac dysfunction:* Cardiac events, including congestive cardiac failure, pulmonary oedema and atrial fibrillation, have been reported, mainly in patients with pre-existing cardiac disease or cardiac risk factors. Appropriate caution should be exercised when considering the treatment of such patients with pomalidomide, including periodic monitoring for signs or symptoms of cardiac events. *Tumour lysis syndrome:* Patients at greatest risk are those with high tumour burden prior to treatment. These patients should be monitored closely and appropriate precautions taken. *Second primary malignancies:* Second primary malignancies, such as non-melanoma skin cancer, have been reported in patients receiving pomalidomide. 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:* Angioedema, anaphylactic reaction and severe dermatologic reactions including SJS, TEN and DRESS have been reported. Advise patients of the signs and symptoms of these reactions and to seek medical attention immediately if they develop these symptoms. Discontinue pomalidomide if exfoliative or bullous rash, or if SJS, TEN or DRESS is suspected, and do not resume following discontinuation for these reactions. Patients with aprior history of serious allergic reactions associated with thalidomide or lenalidomide may be at higher risk of hypersensitivity reactions and should not receive pomalidomide. Pomalidomide interruption or discontinuation should be considered for Grade 2-3 skin rash. Discontinue pomalidomide permanently for angioedema and anaphylactic reaction. *Dizziness*

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*and confusion:* Patients must avoid situations where dizziness or confusion may be a problem and not to take other medicinal products that may cause dizziness or confusion without first seeking medical advice. I*nterstitial lung disease (ILD) and related events, including cases of pneumonitis:* Careful assessment of patients with an acute onset or unexplained worsening of pulmonary symptoms should be performed to exclude ILD. Pomalidomide should be interrupted pending investigation of these symptoms and if ILD is confirmed, appropriate treatment should be initiated. Only resume pomalidomide after a thorough evaluation of the benefits and the risks. *Hepatic disorders:* Markedly elevated levels of alanine aminotransferase and bilirubin have been observed. There have also been cases of hepatitis that resulted in discontinuation of pomalidomide. Regular monitoring of liver function is recommended 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. Hepatitis B virus status should be established before initiating treatment. 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 progressive multifocal leukoencephalopathy, including fatal cases, have been reported with pomalidomide. PML was reported several months to several years after starting the treatment. Cases have generally been reported in patients taking concomitant dexamethasone or prior treatment with other immunosuppressive chemotherapy. Monitor patients at regular intervals and consider PML in the differential diagnosis in patients with new or worsening neurological symptoms, cognitive or behavioural signs or symptoms. Patients should also be advised to inform their partner or caregivers about their treatment, since they may notice symptoms that the patient is not aware of. 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. Additional follow-up and evaluation may be warranted if no alternative diagnosis can be established. If PML is suspected, further dosing must be suspended until PML has been excluded. If PML is confirmed, pomalidomide must be permanently discontinued. *Sodium content:* This medicinal product contains less than 1 mmol sodium (23mg) per capsule, i.e. essentially 'sodium-free'.

**Fertility, Pregnancy & Lactation:** W*omen of childbearing potential/Contraception in males and females:* Effective method of contraception should be used. If pregnancy occurs, treatment must be stopped and the patient referred to a physician specialised or experienced in teratology for evaluation and advice. If pregnancy occurs in a partner of a male patient taking pomalidomide, it is recommended to refer the female partner to a physician specialised or experienced in teratology for evaluation and advice. Pomalidomide is present in human semen. All male patients taking pomalidomide should use condoms throughout treatment duration, during dose interruption and for 7 days after cessation of treatment if their partner is pregnant or of childbearing potential and has no contraception. *Pregnancy:* A teratogenic effect of pomalidomide in humans is expected. Pomalidomide is contraindicated during pregnancy and in women of childbearing potential, except when all the conditions for pregnancy prevention have been met. *Breast-feeding:* It is unknown whether pomalidomide is excreted in human milk. Because of the potential for adverse reactions in breastfed infants, a decision must be made whether to discontinue breast-feeding or to discontinue the medicinal product, taking into account the benefit of breast-feeding for the child and the benefit of the therapy for the woman.

**Adverse Events include:**

*Adverse events which could be considered serious:* Pneumonia (bacterial, viral and fungal infections, including opportunistic infections), bronchitis, upper respiratory tract infection, viral upper respiratory tract infection, sepsis, septic shock, neutropenic sepsis, *Clostridium difficile* colitis, respiratory tract infection, lower respiratory tract infection, influenza, bronchiolitis, urinary tract infection, herpes zoster, hepatitis B reactivation, basal cell carcinoma, basal cell carcinoma of the skin, squamous cell carcinoma of the skin, neutropenia, thrombocytopenia, leucopenia, anaemia, febrile neutropenia, pancytopenia, angioedema, anaphylactic reaction, solid organ transplant rejection, hypothyroidism, hypokalaemia, hyperkalaemia, tumour lysis syndrome, depression, peripheral sensory neuropathy, syncope, peripheral sensorimotor neuropathy, depressed level of consciousness, intracranial haemorrhage, cerebrovascular accident, cataract, atrial fibrillation, cardiac failure, myocardial infarction, deep vein thrombosis, hypertension, dyspnoea, pulmonary embolism, interstitial lung disease, gastrointestinal haemorrhage, hyperbilirubinaemia, hepatitis, Drug Reaction with Eosinophilia and Systemic Symptoms, Toxic Epidermal Necrolysis, Stevens-Johnson Syndrome, acute kidney injury, urinary retention, renal failure, pyrexia.

*Other Very Common adverse events:* Hyperglycaemia, decreased appetite, insomnia, dizziness, tremor, cough, diarrhoea, vomiting, nausea, constipation, abdominal pain, rash, muscular weakness, back pain, bone pain, muscle spasms, fatigue, oedema peripheral.

*Other Common adverse events:* Bronchopneumonia, lung infection, nasopharyngitis, lymphopenia, urticaria, hypomagnesaemia, hypocalcaemia, hypophosphataemia, hypercalcaemia, hyponatraemia, hyperuricaemia, confusional state, paraesthesia, dysgeusia, vertigo, hypotension, epistaxis, abdominal pain upper, stomatitis, dry mouth, abdominal distension, pruritus, chronic kidney injury, pelvic pain, non-cardiac chest pain, alanine aminotransferase increased, weight decreased, neutrophil count decreased, white blood cell count decreased, platelet count decreased, blood uric acid increased, oedema, fall.

See SmPC for details of other adverse events.

**Presentation and Price:** 1mg x 21 £8,884, 2mg x 21 £8,884, 3mg x 21 £8,884, 4mg x 21 £8,884

**Legal Category:** POM

**Further information is available from:** Accord Healthcare Limited, Sage House, 319 Pinner Road, North Harrow, Middlesex, HA1 4HF, United Kingdom

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard

Adverse events should also be reported to Accord-UK LTD on 01271 385257 or email medinfo@accord-healthcare.com.