Opdualag ® ▼ (nivolumab / relatlimab) PRESCRIBING INFORMATION
United Kingdom

Consult Summary of Product Characteristics (SmPC) before prescribing.

▼ **This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.**

PRESENTATION:

- Each mL of concentrate for solution for infusion contains 12 mg of nivolumab and 4 mg of relatlimab
- One vial of 20 mL contains 240 mg of nivolumab and 80 mg of relatlimab

INDICATION (SmPC section 4.1):

- The first line treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents ≥ 12 years of age.

DOSAGE AND ADMINISTRATION (SmPC section 4.2):

- **DOSAGE**
- 480 mg nivolumab and 160 mg relatlimab every 4 weeks administered as an intravenous infusion over 30 minutes. This dose is established for adolescent patients ≥ 12 years of age, weighing at least 30 kg.
- Treatment should be continued as long as clinical benefit is observed or until treatment is no longer tolerated by the patient.
- Dose escalation or reduction is not recommended. For details on dosing delay and discontinuation, refer to SmPC section 4.2.
- **ADMINISTRATION**
- for intravenous (I.V.) use only. It is to be administered as an I.V. infusion over a period of 30 minutes. Must not be administered as an I.V. push or bolus injection.
- Instructions on dilution and handling, refer to SmPC sections 4.2 and 6.6.

CONTRAINDICATIONS (SmPC section 4.3):

Hypersensitivity to the active substances or to any of the excipients listed in SmPC section 6.1.

WARNINGS AND PRECAUTIONS (SmPC section 4.4, 4.5):

Immune related adverse reactions can occur with Opdualag. Immune related adverse reactions affecting more than one body system can occur simultaneously. Patients should be monitored continuously (at least up to 5 months after the last dose) as an adverse reaction may occur at any time during or after discontinuation of therapy. Based on the severity of the adverse reaction, Opdualag should be withheld and corticosteroids administered. Non corticosteroid immunosuppressive therapy should be added if there is worsening or no improvement despite corticosteroid use. Opdualag should not be resumed while the patient is receiving immunosuppressive doses of corticosteroids or other immunosuppressive therapy. Prophylactic antibiotics may be used to prevent opportunistic infections in patients receiving immunosuppressive therapy. Opdualag must be permanently discontinued for any severe immune related adverse reaction that recurs and for any life threatening immune related adverse reaction. *Immune-related pneumonitis*, colitis*, hepatitis*, nephritis*, renal dysfunction*, endocrinopathies, hyperglycaemia*:* Monitor patients for signs and symptoms. Cytomegalovirus (CMV) infection*/reactivation has been reported in patients with corticosteroid-refractory immune-related colitis*. Transaminase* and total bilirubin elevations* are signs and symptoms of hepatitis*. Severe endocrinopathies, including adrenal insufficiency* (including secondary adrenocortical insufficiency*), have been observed with nivolumab in combination with relatlimab. Patients should be monitored for clinical signs and symptoms of endocrinopathies, and for hyperglycaemia and changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation). Patients may present with fatigue, headache, mental status changes*, abdominal pain, unusual bowel habits*, and hypotension*, or nonspecific symptoms which may resemble other causes such as brain metastasis or underlying disease. Cases of diabetic ketoacidosis* have been observed with nivolumab monotherapy and could potentially occur with nivolumab in combination with relatlimab. Please refer to the SmPC for further management guidance including discontinuation of treatment. *Thyroid dysfunction:* Symptomatic hypothyroidism* and symptomatic hyperthyroidism*, please refer to the SmPC for further management guidance including discontinuation of treatment. *Adrenal insufficiency*:* Monitor patients for signs and symptoms. Please refer to the SmPC for further management guidance including discontinuation of treatment. *Hypophysitis*:* Monitor patients for signs and symptoms. Corticosteroids at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents should also be considered if acute inflammation of the pituitary gland* is suspected. Please refer to the SmPC for further management guidance including discontinuation of treatment. *Diabetes mellitus*:* Monitor patients for signs and symptoms. Please refer to the SmPC for further management guidance including discontinuation of treatment. *Immune related skin adverse reactions:* Severe rash*, Stevens-Johnson Syndrome (SJS)* or toxic epidermal necrolysis (TEN)* has been observed. Monitor patients for signs and symptoms. Please refer to the SmPC for further management guidance including discontinuation of treatment. *Immune related myocarditis*:* Severe immune related myocarditis* has been observed. Patients with cardiac or cardio pulmonary symptoms should be assessed for potential myocarditis*. Monitor patients for signs and symptoms. Please refer to the SmPC for further management guidance including discontinuation of treatment. *Other immune related adverse reactions:* uveitis*, pancreatitis*, Guillain Barré syndrome*, myositis*/rhabdomyolysis, encephalitis*, haemolytic anaemia*, Vogt Koyanagi Harada syndrome (VKH), demyelination*, autoimmune neuropathy (including facial and abducens nerve paresis)*, myasthenia gravis*, myasthenic syndrome*, aseptic meningitis*, gastritis, sarcoidosis*, duodenitis*, hypoparathyroidism*, and cystitis noninfective*. Monitor patients for signs and symptoms. Please refer to the SmPC for further management guidance including discontinuation of treatment. *Other important warnings and precautions, including class effects:* An increased risk of rejection in solid organ transplant recipients* has been reported in the post marketing setting in patients treated with PD 1 inhibitors. The benefit of treatment with nivolumab in combination with relatlimab versus the risk of possible organ rejection should be considered in these patients. Haemophagocytic lymphohistiocytosis (HLH)* has been observed. Monitor patients for signs and symptoms. If HLH is confirmed, administration of nivolumab in combination with relatlimab should be discontinued and treatment for HLH initiated. Please refer to the SmPC for further management guidance including discontinuation of treatment. In patients treated with nivolumab before or after allogeneic Haematopoietic Stem Cell Transplantation (HSCT), rapid onset and severe graft versus host disease (GVHD)*, some with fatal outcome, have been reported. *Infusion reactions:* Severe infusion reactions have

been reported in clinical studies (see SmPC section 4.8). *Patients excluded from pivotal advanced melanoma clinical study:* Patients with active autoimmune disease, uveal melanoma, active or untreated brain, or leptomeningeal metastases, and those with a history of myocarditis*, elevated troponin levels > 2 times upper limit of normal, medical conditions requiring systemic treatment with moderate or high dose corticosteroids or immunosuppressive medicinal products, ECOG performance status score ≥ 2. In the absence of data, Opdualag should be used with caution in these populations. *Traceability:* In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.
*asterisk denotes serious adverse drug reactions, including those that are potentially fatal or life-threatening

PREGNANCY AND LACTATION (SmPC section 4.6)

Not recommended during pregnancy and in women of child-bearing potential not using effective contraception unless clinical benefit outweighs potential risk. Effective contraception should be used for at least 5 months following the last dose. It is unknown whether nivolumab and/or relatlimab is secreted in human milk or effects male and female fertility.

UNDESIRABLE EFFECTS (SmPC section 4.8):

Refer to SmPC for full details on adverse reactions. *Very Common (≥ 1/10):* Urinary tract infection*, anaemia*, lymphopaenia*, neutropaenia*, hypothyroidism*, headache*, dyspnoea*, diarrhoea*, abdominal pain*, rash*, vitiligo*, pruritus*, fatigue*, increased AST* / ALT* / creatinine* / alkaline phosphatase*, hyponatraemia*, hyperkalaemia*, hypocalcaemia*, hypomagnesaemia*, hypercalcaemia*, hypokalaemia*, leucopaenia, decreased appetite, cough, vomiting, nausea, constipation, musculoskeletal pain, arthralgia, pyrexia. *Common (≥ 1/100 to < 1/10):* adrenal insufficiency*, hypophysitis*, hyperthyroidism*, diabetes mellitus*, uveitis*, myocarditis*, pneumonitis*, colitis*, pancreatitis*, hepatitis*, increased bilirubin*, hypermagnesaemia*, infusion-related reaction*, back pain*, pneumonia*, upper respiratory tract infection, thrombocytopaenia, eosinophilia, thyroiditis, hypoglycaemia, weight decreased, hyperuricaemia, hypoalbuminaemia, dehydration, confusional state, peripheral neuropathy, dizziness, dysgeusia, visual impairment, dry eye, increased lacrimation, phlebitis, nasal congestion, gastritis, dysphagia, stomatitis, dry mouth, alopecia, lichenoid keratosis, photosensitivity reaction, dry skin, arthritis, muscle spasms, muscular weakness, renal failure, proteinuria, oedema, influenza-like illness, chills, hypernatraemia, troponin / gamma-glutamyl transferase / blood lactate dehydrogenase / lipase / amylase increased, . *Uncommon (≥ 1/1,000 to < 1/100):* Haemolytic anaemia*, hypopituitarism*, encephalitis*, Guillain-Barré syndrome*, Vogt-Koyanagi-Harada disease*, myositis*, nephritis*. *Unknown:* Interstitial lung disease*, lung infiltration*, frequent bowel movement*, renal dysfunction*.
*asterisk denotes serious adverse drug reactions, including those that are potentially fatal or life-threatening

LEGAL CATEGORY:

Prescription Only Medicine

MARKETING AUTHORISATION NUMBER and BASIC NHS PRICE (SmPC section 8):

20 mL vial (PLGB 15105/0192): £6134.75

MARKETING AUTHORISATION HOLDER (SmPC section 7)

Bristol Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, D15 T867, Ireland

FOR FURTHER INFORMATION CONTACT:

medical.information@bms.com or 0800 731 1736.

DATE OF PREPARATION: December 2024

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval code: 1425-GB-2400095

Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store; Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736.