OPDIVO® (NIVOLUMAB) PRESCRIBING INFORMATION

This prescribing information contains information on the use of OPDIVO monotherapy, and contains information on the use of YERVOY (ipilimumab) in combination with Opdivo, as relevant in combination therapy. Consult Summary of Product Characteristics (SmPC) before prescribing. If prescribing OPDIVO in combination with YERVOY, please also consult the YERVOY SmPC.

PRESENTATION: Opdivo 10 mg/mL concentrate for solution for infusion. Each mL of concentrate contains 10 mg of Opdivo.

INDICATION: For use in adults only:

As monotherapy:
- Advanced (unresectable or metastatic) melanoma. Relative to nivolumab monotherapy, an increase in progression free survival (PFS) and overall survival (OS) for the combination of Opdivo with Yervoy is established only in patients with low tumour PD-L1 expression.
- Adjunctive treatment with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.
- Locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy.
- Advanced renal cell carcinoma (RCC) after prior therapy.
- Relapsed or refractory classical Hodgkin lymphoma (cHL) after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin.
- Recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) in patients progressing on or after platinum-based therapy.
- Unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) after prior fluoropyrimidine- and platinum-based combination chemotherapy.

In combination with YERVOY:
- First-line treatment for intermediate/poor-risk advanced RCC and advanced (unresectable or metastatic) melanoma.

In combination with YERVOY and chemotherapy:
- First-line treatment of metastatic NSCLC whose tumours have no sensitising EGFR mutation or ALK translocation.

DOSAGE: Opdivo as monotherapy: 240 mg every 2 weeks over 30 minutes intravenously (IV). For melanoma (advanced and adjuvant treatment) and RCC only, Opdivo can also be administered at 480 mg every 4 weeks over 60 minutes IV. Opdivo in combination with Yervoy:
- Induction phase for advanced melanoma: 1 mg/kg Opdivo IV over 30 minutes + 3 mg/kg Yervoy IV over 90 minutes every 3 weeks for the first 4 doses. Induction phase for RCC: 3 mg/kg Opdivo IV over 30 minutes + 1 mg/kg Yervoy IV over 30 minutes every 3 weeks for the first 4 doses. Maintenance phase for both advanced melanoma and RCC: Opdivo monotherapy IV at either 240 mg every 2 weeks (3 weeks after last dose of induction phase) or 480 mg every 4 weeks (6 weeks after last dose of induction phase). Refer to section 4.2 of SmPC for full details.
- Opdivo in combination with ipilimumab and chemotherapy: Non-small cell lung cancer: 360 mg Opdivo administered intravenously over 30 minutes every 3 weeks in combination with 1 mg/kg ipilimumab administered intravenously over 30 minutes every 6 weeks, and platinum-based chemotherapy administered every 3 weeks. After completion of 2 cycles of chemotherapy, treatment is continued with 360 mg nivolumab administered intravenously every 3 weeks in combination with 1 mg/kg ipilimumab every 6 weeks. Treatment is recommended until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression. Refer to section 4.2 of SmPC for full details. Administration: Refer to SmPC section 4.2.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients listed in SmPC.

WARNING AND PRECAUTIONS: Immune-related adverse reactions have occurred at higher frequencies with Opdivo in combination with Yervoy than with Opdivo monotherapy. Most adverse reactions improve or resolve with appropriate management, including corticosteroids and treatment modification. Cardiac and pulmonary adverse events including pulmonary embolism have also been reported with combination therapy. Monitor patients for cardiac and pulmonary adverse reactions, plus clinical signs, symptoms, and laboratory abnormalities indicative of electrolyte disturbances and dehydration before and during treatment. Discontinue Opdivo in combination with Yervoy for life threatening or recurrent severe cardiac and pulmonary adverse reactions. Monitor patients continuously (at least every 5 days) for life threatening immune-related adverse reaction with Opdivo or Opdivo in combination with Yervoy may occur at any time during or after discontinuation of therapy. Immune-related pneumonitis, colitis, hepatitis, nephritis, renal dysfunction, endocrinopathies; Monitor patients for signs and symptoms. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-related colitis. Please refer to SmPC for further management guidance including discontinuation of treatment. Immune-related skin adverse reactions: Monitor patients for rash, including Stevens-Johnson Syndrome (SJS) or toxic epidermal necrolysis (TEN). Use caution when considering Opdivo in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer agents. Other immune-related adverse reactions (reported in less than 1% of patients in clinical trials): Opdivo as monotherapy or in combination with Yervoy may cause extracutaneous immune-related adverse reactions such as autoimmune neuropathy (including facial and abducens nerve paresis), Guillain-Barré syndrome, myasthenia gravis, myasthenic syndrome, aseptic meningitis, encephalitis, gastritis, sarcoidosis, duodenitis, myositis, myocarditis and rhabdomyolysis. Cases of Vogt-Koyanagi Harada syndrome have been reported post-marketing. If a patient develops signs and symptoms of myotoxicity (myositis, myasthenia, and rhabdomyolysis), close monitoring should be implemented, and the patient referred to a specialist for assessment and treatment without delay. Based on the severity of myotoxicity, Opdivo or Opdivo in combination with Yervoy should be withheld or discontinued and appropriate treatment instituted. Sudden organ transplant rejection has been reported in the post-marketing setting in patients treated with PD-1 inhibitors. Treatment with Opdivo may increase the risk of rejection in solid organ transplant recipients. The benefit of treatment with Opdivo versus the risk of possible organ rejection should be considered in these patients. Haemophagocytic lymphohistiocytosis (HLH) has been observed with Opdivo as monotherapy and Opdivo in combination with Yervoy. Caution should be taken when Opdivo is administered as monotherapy or in combination with Yervoy. If HLH is confirmed, treatment with Opdivo or Opdivo in combination with Yervoy should be discontinued and treatment for HLH initiated. Infusion reactions: Severe infusion reactions have been reported. Disease-specific precautions: In the absence of data in some population subgroups nivolumab or nivolumab combinations should be used with caution after careful consideration of the potential benefit-risk on an individual basis. Physicians should consider the delayed onset of nivolumab effect before initiating treatment in some tumour types. Please refer to SmPC section 4.4, ‘Disease-specific precautions’ for more details. Patients on controlled sodium diet: Please refer to SmPC. Refer to SmPC section 4.4 for further information and for specific management guidelines for immune-related adverse reactions. 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. PREGNANCY AND LACTATION: Opdivo is not recommended during pregnancy 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 of Opdivo. It is unknown whether Opdivo is secreted in human milk. UNDESIRABLE EFFECTS: Opdivo monotherapy: Very Common (≥ 1/10): nausea, rash, pruritus, fatigue, increased AST*/ ALT* / ALP/ lipase/ amylase/ creatinine, hypocalcaemia, hyperglycaemia*, hypoglycaemia, lymphopaenia, leucopenia, thrombocytopenia, anaemia, hypercalcaemia, hyperkalaemia, hypokalaemia, hypomagnesaemia, hyponatraemia. Common (≥ 1/10 to < 1/10): upper respiratory tract infection, infusion-related reaction*,