OPDIVO®

(nivolumab)
Concentrate for solution for infusion

Risk Minimisation Information for Healthcare Professionals
Guide for Prescribing

OPDIVO® is indicated for the treatment of different types of tumours, as monotherapy or in combination with ipilimumab.
For a complete list of the current authorized indications and the type of patients in which you should use nivolumab with caution please refer to the nivolumab Summary of Product Characteristics (SmPC).

▼This medicinal product is subject to additional monitoring This will allow quick identification of new safety information..
Healthcare professionals are asked to report any suspected adverse reactions via Medicines Authority. ADR report forms can be downloaded from www.medicinsauthority.gov.mt/adrportal and sent to postlicensing.medicinesauthority@gov.mt or sent to Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN 3000, Malta
Adverse reactions should also be reported to Bristol-Myers Squibb Medical Information at www.ema.europa.eu or call medical information at 00 356 2397 6 505

Bristol-Myers Squibb

This Guide

- Is provided for healthcare professionals (HCPs) who are involved in the treatment of patients on nivolumab, with or without other medicinal products.
- Is essential to ensure the safe and effective use of nivolumab and appropriate management of some related adverse reactions.
- Is to be read before prescribing and administering nivolumab.
- Introduces the Patient Alert Card. It is important to review the Patient Alert Card with patients before each treatment cycle and at any patient's visit, in order to reinforce their understanding of side effects and the need to contact a HCP if they develop side effects.

Treating doctors should also advise their patients to keep the Patient Alert Card with them at all times and show it to any healthcare professional who may treat them. You can obtain Patient Alert Card at www.ema.europa.eu or call medical information at 00 356 2397 6 505

What is Nivolumab?[1]

Nivolumab is a human immunoglobulin G4 (IgG4) monoclonal antibody (HuMAb) which binds to the programmed death-1 (PD-1) receptor and blocks its interaction with PD-L1 and PD-L2. The PD-1 receptor is a negative regulator of T-cell activity that has been shown to be involved in the control of T-cell immune responses. Engagement of PD-1 with the ligands PD-L1 and PD-L2, which are expressed in antigen presenting cells and may be expressed by tumours or other cells in the tumour microenvironment, results in inhibition of T-cell proliferation and cytokine secretion. Nivolumab potentiates T-cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2 ligands.[1]

Combined nivolumab (anti-PD-1) and ipilimumab (anti-CTLA-4) mediated inhibition results in improved anti-tumour responses in selected approved indications as specified in the SmPC

Before prescribing nivolumab you should check:

- Liver function tests.
  Nivolumab must be administered with caution in patients with moderate hepatic impairment (total bilirubin > 1.5 × to 3 × the upper limit of normal [ULN] with any aspartate aminotransferase [AST] level) or severe (total bilirubin > 3 × ULN with any AST level)
- Signs and symptoms of electrolytic disturbances, dehydration, endocrinopathies, hyperglycaemia and changes to thyroid function
- If the patient is allergic to the active substance or to any of the excipients
- If the patient is taking other medicinal products known or suspected to have pharmacological interaction with nivolumab, in particular systemic corticosteroids and other immunosuppressants
- If the patient is driving or operating machinery
- If the patient is pregnant or planning to become pregnant or if the patient is breastfeeding
- If the patient belongs to any type of patient group in which caution is required, including when there is limitation or absence of data

Summary of Important Information

- Nivolumab, as monotherapy or in combination with ipilimumab, increases the risk of severe immune-related adverse reactions (irARs), which can include pneumonitis, colitis, hepatitis, nephritis and renal dysfunction, endocrinopathies, skin reactions, and other immune-related adverse reactions, as well as potential complications of allogeneic Haematopoietic Stem Cell Transplant (HSCT) in classical Hodgkin Lymphoma. These irARs can occur several months after the last dose of nivolumab.
- Early diagnosis and appropriate management of AEs are essential to minimise life-threatening complications.
- Suspected adverse reactions must be promptly evaluated to exclude infectious or other alternate aetiologies.
- Based on the severity of symptoms, the treatment should be withheld or discontinued and systemic high-dose corticosteroid therapy may be required. Upon improvement, treatment may be resumed after corticosteroid taper[1]; treatment must be permanently discontinued for any severe irAR that recurs and for any life-threatening irAR.[1]
- Patients and caregivers should be informed about the symptoms of irARs and the importance of reporting them immediately to the treating physician. A Patient Alert Card must be given to the patients at any visit, and may support the discussion about risks.
- Patients should be advised to carry the Patient Alert Card at all times and to show it to any HCP at all medical visits.

Early Diagnosis and Appropriate Management

- Prompt recognition of adverse events and appropriate treatment are essential to minimise life-threatening complications. Systemic high-dose corticosteroids with or without additional immunosuppressive therapy may be required for the management of severe irARs.[1]
- Please refer to the nivolumab SmPC (and ipilimumab SmPC if you are using a combination therapy) for guidelines on treatment.
- Report any suspected adverse reaction to the National Health Authority in accordance with the national reporting system
- Patients should be monitored continuously (at least up to 5 months after the last dose) as an adverse reaction with nivolumab or nivolumab in combination with ipilimumab may occur at any time during or after discontinuation of therapy.[1]
- If immunosuppression with corticosteroids is used to treat an adverse reaction, a taper of at least one month duration should be initiated upon improvement[1], as rapid tapering may lead to worsening or recurrence of the adverse reaction.[1]
- Nivolumab or nivolumab in combination with ipilimumab should not be resumed while the patient is receiving immunosuppressive doses of corticosteroids or other immunosuppressive therapy.[1]
- When nivolumab is administered in combination with ipilimumab, if either agent is withheld, the other agent should also be withheld. If dosing is resumed after a delay, either the combination treatment or nivolumab monotherapy could be resumed based on the evaluation of the individual patient. [1]
- In addition to when reported in the following tables for treatment modifications, the treatment with nivolumab or nivolumab in combination with ipilimumab must be permanently discontinued for[1]:
  - Any severe (Grade 3) irAR that recurs (withhold treatment if it is the first occurrence)
  - Any life threatening (Grade 4) irAR
  - Any grade 2 or 3 irAR that persists despite treatment modifications
  - Grade 3 myocarditis
  - Inability to reduce corticosteroid dose to 10 mg prednisone (8 mg methylprednisolone) or equivalent per day

Immune Related Adverse Reactions and Treatment Modifications

Immune related adverse reaction	Severity	Recommended treatment (nivolumab or nivolumab + ipilimumab) modification
Pneumonitis (radiographic changes like focal ground glass opacities or patchy filtrates, dyspnoea, hypoxia)	Grade 2 pneumonitis	Withhold treatment. Initiate corticosteroids at a dose of 1 mg/kg/day methylprednisolone equivalents. Upon improvement, treatment may be resumed after corticosteroid taper. If worsening or no improvement occurs despite initiation of corticosteroids, corticosteroid dose should be increased to 2 to 4 mg/kg/day methylprednisolone equivalents and treatment must be permanently discontinued.
	Grade 3 or 4 pneumonitis	Permanently discontinue treatment. Initiate corticosteroids at a dose of 2 to 4 mg/kg/day methylprednisolone equivalents.
Colitis (diarrhoea, abdominal pain, mucus or blood in stool)	Grade 2 diarrhoea or colitis	Withhold treatment. If persistent, manage with corticosteroids at a dose of 0.5 to 1 mg/kg/day methylprednisolone equivalents. Upon improvement, treatment may be resumed after corticosteroid taper, if needed. If worsening or no improvement occurs despite initiation of corticosteroids, corticosteroid dose should be increased to 1 to 2 mg/kg/day methylprednisolone equivalents and treatment must be permanently discontinued.
	Grade 3 diarrhoea or colitis (nivolumab monotherapy only)	Withhold treatment. Initiate corticosteroids at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents. Upon improvement, nivolumab monotherapy may be resumed after corticosteroid taper. If worsening or no improvement occurs despite initiation of corticosteroids, nivolumab monotherapy must be permanently discontinued.
	Grade 3 (combination therapy only) or Grade 4 (monotherapy and combination) diarrhoea or colitis	Permanently discontinue treatment. Initiate corticosteroids at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents.
Hepatitis (transaminase or total bilirubin elevations)	Grade 2 elevation in transaminase or total bilirubin	Withhold treatment. Persistent elevations in laboratory values should be managed with corticosteroids at a dose of 0.5 to 1 mg/kg/day methylprednisolone equivalents. Upon improvement, treatment may be resumed after corticosteroid taper, if needed. If worsening or no improvement occurs despite initiation of corticosteroids, corticosteroid dose should be increased to 1 to 2 mg/kg/day methylprednisolone equivalents and treatment must be permanently discontinued.
	Grade 3 or 4 elevations in transaminase or total bilirubin	Permanently discontinue treatment. Initiate corticosteroids at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents.
Skin (rash, pruritus, Stevens-Johnson syndrome [SJS], toxic epidermal necrolysis [TEN])	Grade 3 rash	Withhold treatment until symptoms resolve. Severe rash should be managed with high-dose corticosteroid at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents
	Grade 4 rash	Permanently discontinue treatment. Severe rash should be managed with high-dose corticosteroid at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents.
	SJS or TEN	If suspected SJS or TEN, withhold treatment and refer the patient to a specialised unit for assessment and treatment. If the patient has confirmed SJS or TEN then permanently discontinue treatment.

Grade definition according to NCI CTCAE v. 4

	Grade1	Grade2	Grade3	Grade4	Grade5
Pneumonitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; medical intervention indicated; limiting instrumental Activity Daily Living (ADL)	Severe symptoms; limiting self-care ADL; oxygen indicated	Life-threatening respiratory compromise; urgent intervention indicated (e.g., tracheotomy or intubation)	Death
Colitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Abdominal pain; mucus or blood in stool	Severe abdominal pain; change in bowel habits; medical intervention indicated; peritoneal signs	Life-threatening consequences; urgent intervention indicated	Death
Hepatobiliary disorders	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated	Death
ALT/AST increase	>ULN - 3.0 x ULN	>3.0 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN	
Bilirubin increase	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN	>10.0 x ULN	
Allergic reaction	Transient flushing or rash, drug fever <38°C (<100.4°F); intervention not indicated	Intervention or infusion interruption indicated; responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS, narcotics); prophylactic medications indicated for ≤24 hours	Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae (e.g., renal impairment, pulmonary infiltrates)	Life-threatening consequences; urgent intervention indicated	Death
Rash acneiform	Papules and/or pustules covering <10% BSA, which may or may not be associated with symptoms of pruritus or tenderness	Papules and/or pustules covering 10 - 30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL	Papules and/or pustules covering >30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; limiting self-care ADL; associated with local superinfection with oral antibiotics indicated	Papules and/or pustules covering any % BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection with IV antibiotics indicated; life-threatening consequences	Death
Toxic Epidermal Necrolysis				Skin sloughing covering ≥30% Body Surface Area (BSA) with associated symptoms (e.g., erythema, purpura, or epidermal detachment)	Death

Immune Related Adverse Reactions and Treatment Modifications

Immune related adverse reaction	Severity	Recommended treatment (nivolumab or nivolumab + ipilimumab) modification
Nephritis and Renal Dysfunction (increase of serum creatinine)	Grade 2 or 3 serum creatinine elevation	Withhold treatment. Initiate corticosteroids at a dose of 0.5 to 1 mg/kg/day methylprednisolone equivalents. Upon improvement, treatment may be resumed after corticosteroid taper. If worsening or no improvement occurs despite initiation of corticosteroids, corticosteroid dose should be increased to 1 to 2 mg/kg/day methylprednisolone equivalents, and treatment must be permanently discontinued.
	Grade 4 serum creatinine elevation	Permanently discontinue treatment. Initiate corticosteroids at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents.
Endocrinopathies (hypothyroidism, hyperthyroidism, adrenal insufficiency, hypophysitis, diabetes, diabetic ketoacidosis)	Symptomatic, hypothyroidism	Treatment should be withheld or permanently discontinued for life threatening situations. Initiate thyroid hormone replacement as needed. Monitoring of thyroid function should continue to ensure appropriate hormone replacement is utilised.
	Symptomatic, hyperthyroidism	Treatment should be withheld or permanently discontinued for life threatening situations. Initiate antithyroid medication as needed. Consider initiating corticosteroids at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents if acute inflammation of the thyroid is suspected. Upon improvement, treatment may be resumed after corticosteroid taper, if needed.
	Symptomatic, adrenal insufficiency	Treatment should be withheld for Grade 2 adrenal insufficiency. Treatment must be permanently discontinued for Grade 3 and 4 adrenal insufficiency. Physiologic corticosteroid replacement should be initiated as needed. Monitoring of adrenal function and hormone levels should continue to ensure appropriate corticosteroid replacement is utilised.
	Symptomatic hypophysitis	Treatment should be withheld for Grade 2 or 3 hypophysitis. Initiate hormone replacement as needed. Consider initiating corticosteroids at a dose of 1 to 2 mg/kg/day methylprednisolone equivalents if acute inflammation of the pituitary gland is suspected. Upon improvement, treatment may be resumed after corticosteroid taper, if needed. Treatment must be permanently discontinued for Grade 4 hypophysitis. Monitoring of pituitary function and hormone levels should continue to ensure appropriate hormone replacement is utilised.
	Symptomatic diabetes	Treatment should be withheld for symptomatic diabetes. Treatment must be permanently discontinued for life threatening diabetes. Initiate insulin replacement as needed. Monitoring of blood sugar should continue to ensure appropriate insulin replacement is utilised.

Other Reactions

Infusion reactions	Mild or moderate infusion reaction	Closely monitor administration of nivolumab or nivolumab in combination with ipilimumab and use premedication according to local treatment guidelines for prophylaxis of infusion reactions.
	Severe or life-threatening infusion reaction	Nivolumab or nivolumab in combination with ipilimumab infusion must be discontinued and appropriate medical therapy administered.

Grade definition according to NCI CTCAE v. 4					
	Grade1	Grade2	Grade3	Grade4	Grade5
Creatinine increased	>1 - 1.5 x baseline; >ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 baseline; >3.0 - 6.0 x ULN	>6.0 x ULN	
Renal and urinary disorders	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Moderate, local or noninvasive intervention indicated; limiting instrumental ADL	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated	Death
Hyperthyroidism	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; thyroid suppression therapy indicated; limiting instrumental ADL	Severe symptoms; limiting self-care ADL; hospitalization indicated	Life-threatening consequences; urgent intervention indicated	Death
Hypothyroidism	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; thyroid replacement indicated; limiting instrumental ADL	Severe symptoms; limiting self-care ADL; hospitalization indicated	Life-threatening consequences; urgent intervention indicated	Death
Hypophysitis (endocrine disorders general)	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated	Death
Adrenal insufficiency	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Moderate symptoms; medical intervention indicated	Severe symptoms; hospitalization indicated	Life-threatening consequences; urgent intervention indicated	Death
Diabetes mellitus (hyperglycaemia)	Fasting glucose value >ULN - 160 mg/dL; Fasting glucose value >ULN - 8.9 mmol/L	Fasting glucose value >160 - 250 mg/dL; Fasting glucose value >8.9 - 13.9 mmol/L	>250 - 500 mg/dL; >13.9 - 27.8 mmol/L; hospitalization indicated	>500 mg/dL; >27.8 mmol/L; life-threatening consequences	Death
Acidosis	pH <normal, but ≥7.3		pH <7.3	Life-threatening consequences	Death

Immune-Related Adverse Reactions

In the pooled dataset of **nivolumab 3 mg/kg as monotherapy** across tumour types the most frequent adverse reactions (≥ 10%) were fatigue, rash, pruritus, diarrhoea, and nausea. The majority of adverse reactions were mild to moderate (Grade 1 or 2).[1]

In the pooled dataset of **nivolumab in combination with ipilimumab** in clinical trials **where studied**, the most frequent adverse reactions (≥ 10%) were rash, fatigue, diarrhoea, pruritus, nausea, pyrexia, decreased appetite, hypothyroidism, vomiting, colitis, abdominal pain, arthralgia, and headache. The majority of adverse reactions were mild to moderate (Grade 1 or 2). [1]

Other Immune-Related Adverse Reactions

The following irARs were reported in less than 1% of patients treated with nivolumab monotherapy in clinical trials across doses and tumour types:[1]

- Pancreatitis
- Uveitis
- Demyelination
- Autoimmune neuropathy (including facial and abducens nerve paresis)
- Guillain-Barré syndrome
- Hypopituitarism
- Myasthenic syndrome

Rare cases of myotoxicity (myositis, myocarditis, and rhabdomyolysis), some with fatal outcome, have been reported with nivolumab or nivolumab in combination with ipilimumab. If a patient develops signs and symptoms of myotoxicity, close monitoring should be implemented, and the patient referred to a specialist for assessment and treatment without delay. Based on the severity of myotoxicity, nivolumab or nivolumab in combination with ipilimumab should be withheld or discontinued and appropriate treatment instituted.

Across clinical trials of nivolumab in combination with ipilimumab, the following additional clinically significant, irARs were reported in less than 1% of patients:

- Gastritis
- Sarcoidosis
- Duodenitis.

Potential Risk of Complication of Allogeneic Hematopoietic Stem Cell Transplant in classical Hodgkin Lymphoma

Preliminary results from the follow up of patients undergoing allogeneic Hematopoietic Stem Cell Transplant (HSCT) after previous exposure to nivolumab showed a higher than expected number of cases of acute graft-versus-host-disease (aGVHD) and transplant related mortality (TRM). Until further data become available, careful consideration to the potential benefits of allogeneic HSCT and the possible increased risk of transplant related complications should be made case by case.

Educational material for the Patient

It is important that you distribute the Patient Alert Card to any patient receiving nivolumab or nivolumab in combination with ipilimumab for the first time and at each visit. You can use the Patient Alert Card to discuss treatment and the related risks.

This educational material is designed to help the patients to understand their treatment and how to act should they experience adverse reactions. You should complete your contact details in the Patient Alert Card and advise the patient to carry it at all times.

OPDIVO® (nivolumab)
Patient Alert Card

▼ Nivolumab is subject to additional monitoring to quickly identify new safety information. You can help by reporting any side effects that you may get to your Doctor

OPDIVO® (nivolumab)
This card contains important information.
Always carry this card with you and show it if you need to consult another doctor (for example, if you are travelling).

Tell your doctor right away if you have any of these symptoms or any other symptoms

LUNGS[1]
breathing difficulties, cough

BOWEL and STOMACH[1]
diarrhoea (watery, loose, or soft stools), blood or mucous in your stools, dark-coloured stools, pain or tenderness in your stomach or abdominal area

LIVER[1]
eye or skin yellowing (jaundice), pain on the right side of your stomach area, tiredness

KIDNEYS[1]
decreased amount of urine

DIABETES/DIABETIC KETOACIDOSIS[1]
thirst, increased appetite with loss of weight, tiredness, weakness, drowsiness, depression, irritability, feeling unwell, increased amount of urine

SKIN[1]
severe skin reactions, like skin rash with or without itching, blisters and/or peeling of the skin (possibly fatal), ulcers, dry skin, skin nodules

HORMONE-PRODUCING GLANDS[1]
headaches, blurry or double vision, fatigue, tiredness, weight changes, behavioural changes (eg. less sex drive, irritability or forgetfulness)

MUSCLES (including heart)[1]
signs and symptoms of myositis (inflammation of the muscles), myocarditis (inflammation of the heart muscle), and rhabdomyolysis (breakdown of skeletal muscle), which may include muscle pain, stiffness, weakness, chest pain, irregular heartbeat, palpitations, confusion, decreased amount of urine, dark urine, or severe fatigue

OTHER[1]
eye pain or redness, blurry vision, or other vision problems; upper abdominal pain (inflammation of the pancreas), decreased appetite, nausea or vomiting; indigestion or heartburn; tingling or numbness in arms and legs or difficulty walking; fever, swollen lymph nodes

IMPORTANT

- Early management of side effects reduces the likelihood that treatment with nivolumab or nivolumab in combination with ipilimumab will need to be temporarily or permanently stopped, allowing patients to get the maximum benefit from treatment.
- Symptoms that may appear mild can quickly worsen if left untreated.[1]
- Don't try to treat these symptoms yourself.
- Report any of these symptoms or any other symptoms to your doctor right away.
- Signs and symptoms may be delayed and may occur weeks to months after your last injection.[1]

- Carry this Patient Alert Card, show it to any doctor you might interact with, and say that you are being treated with nivolumab or nivolumab in combination with ipilimumab.

TELL YOUR DOCTOR IMMEDIATELY IF YOU:

- know you are allergic to nivolumab or any other medicine or medicine ingredients,
- have an autoimmune disease,
- have melanoma of the eye,
- have experienced side effects with another drug, such as ipilimumab,
- have been told cancer has spread to your brain,
- have taken medicine to suppress your immune system,
- have history of inflammation of lungs,
- are pregnant or planning to become pregnant, or are breastfeeding,
- are taking or have taken any other medicines,
- are on a low salt diet.

More information on OPDIVO® Package Leaflet or call Medical Information at 00 356 2397 6505

My Doctor's contact information
Name of Doctor
Office Phone
After-hours Phone

My contact information
My Name and Phone Number
Emergency Contact (in case of emergency)

IMPORTANT Information For Healthcare Providers

- This patient is treated with **nivolumab or nivolumab in combination with ipilimumab.**
- Immune-related adverse reactions (irARs), may appear at any time during the treatment or months after its discontinuation.
- Early diagnosis and appropriate management are essential to minimise life-threatening complications. Nivolumab specific management guidelines for irARs are available.
- If you are a doctor who is not a specialist in oncology, please contact an oncologist

Please consult OPDIVO® Summary of Product Characteristics or call Medical Information at 00 356 2397 6505 for more information.

1. OPDIVO® Package leaflet.

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Checklist for patient's visit (first or following)

FIRST VISIT

- Discuss the treatment with the patient, fill in the Patient Alert Card and inform the patient to carry it at all times
- Inform the patient not to treat their own symptoms and to seek immediate medical attention should any adverse reaction occur or worsen
- Inform the patient that they may experience growth of existing tumours or develop new tumours, and that it does not mean that the treatment is ineffective
- Make the appropriate check (see page 2 of this guide and the SmPC)
- Check for signs and symptoms of conditions that are in the *Warnings and Precautions* or *Contraindications* sections of the SmPC

ANY FOLLOWING VISIT

- Make the appropriate check (see page 2 of this guide and the SmPC)
- Remind the patient not to treat their own symptoms
- Remind the patient to contact you immediately should they experience an adverse reaction, even if mild
- Remind the patient that early diagnosis and appropriate management are essential to minimise the severity of adverse reactions and their associated complications

All healthcare professionals are asked to report any suspected adverse reactions via the national reporting system via Medicines Authority. ADR report forms can be downloaded from www.medicinsauthority.gov.mt/adrportal and sent to postlicensing.medicinesauthority@gov.mt or sent to Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN 3000, Malta

If you require any further information regarding the use of nivolumab, please contact Bristol-Myers Squibb Medical Information department at www.ema.europa.eu or call medical information at 00 356 2397 6 505

References:

1. Opdivo. Summary of Product Characteristics.

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