Nivolumab 360mg and Chemotherapy

Please note the information contained in this regimen relates to nivolumab only.

Please refer to the appropriate regimen for details of the chemotherapy regimen being administered in combination with nivolumab.

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Nivolumab in combination with platinum-based chemotherapy for the neoadjuvant treatment of resectable non-small cell lung cancer at high risk of recurrence in adult patients whose tumours have PD-L1 expression ≥ 1%	C34	00849a	Nivolumab: ODMS 01/05/24 Chemotherapy: N/A

* This is for post 2012 indications only

NOTE: This regimen is also available in NCIS in combination with the following SACT regimens:

- **NCCP Regimen 00304 CARBOplatin (AUC6) and PACLitaxel 200mg/m^2 Therapy (00849.1)**
- **NCCP Regimen 00310 Gemcitabine (1000mg/m^2) and CARBOplatin (AUC5) Therapy-21 day (00849.2)**
- **NCCP Regimen 00281 Gemcitabine (1250mg/m^2) and CISplatin 75mg/m^2 Therapy (00849.3)**
- **NCCP Regimen 00318 PEMEtrexed and CARBOplatin Therapy (00849.4)**
- **NCCP Regimen 00317 PEMEtrexed and CISplatin Therapy (00849.5)**

These combinations are not available as unique National SACT regimens but have been built in NCIS to facilitate therapy planning.

Please refer to the relevant SACT treatment table below.

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Nivolumab is administered on Day 1 of a 21 day cycle in combination with chemotherapy as per relevant chemotherapy regimen above and corresponding treatment table below.

Treatment with nivolumab and chemotherapy is continued for a maximum of 3 cycles, or less if disease progression or unacceptable toxicity develops.

Patients should be monitored continuously (at least up to 5 months after the last dose) as an adverse reaction with nivolumab may occur at any time during or after discontinuation of therapy.

Facilities to treat anaphylaxis MUST be present when the systemic anti-cancer therapy (SACT) is administered.

Table 1: Treatment schedule for Nivolumab 360mg, CARBOplatin (AUC6) and PACLitaxel 200mg/m^2 Therapy (00849.1)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Nivolumab	360mg	IV infusion[a]	Infuse over 30 minutes through a sterile, non-pyrogenic, low protein binding in-line filter with a pore size of 0.2-1.2 µm[b]	Every 21 days **for 3 cycles**
2	1	PACLitaxel[c, d]	200mg/m^2	IV infusion	500mL 0.9% NaCl over 3 hours	Every 21 days **for 3 cycles**
3	1	CARBOplatin	AUC 6	IV infusion	500mL glucose 5% over 30 minutes	Every 21 days **for 3 cycles**
[a] Nivolumab must not be administered as an intravenous push or bolus injection.						
[b] Nivolumab can be infused directly as a 10mg/mL solution or can be diluted to as low as 1mg/mL with sodium chloride 9mg/mL (0.9%) solution for injection or glucose 50mg/mL (5%) solution for injection.						
[c] PACLitaxel must be supplied in non-PVC containers and administered using non-PVC giving sets and through an in-line 0.22 µm filter with a microporous membrane.						
[d] PACLitaxel should be diluted to a concentration of 0.3-1.2mg/mL.						

- Relevant information about the above chemotherapy is available in NCCP Regimen 00304 CARBOplatin (AUC6) and PACLitaxel 200mg/m^2 Therapy.

Table 2: Treatment schedule for Nivolumab 360mg, Gemcitabine (1000mg/m^2) and CARBOplatin (AUC5) Therapy (00849.2)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Nivolumab	360mg	IV infusion[a]	Infuse over 30 minutes through a sterile, non-pyrogenic, low protein binding in-line filter with a pore size of 0.2-1.2 µm[b]	Every 21 days **for 3 cycles**
2	1 and 8	Gemcitabine	1000mg/m^2	IV infusion	250mL NaCl 0.9% over 30 minutes	Every 21 days **for 3 cycles**
3	1	CARBOplatin	AUC5	IV infusion	500mL glucose 5% over 30 minutes	Every 21 days **for 3 cycles**
[a] Nivolumab must not be administered as an intravenous push or bolus injection.						
[b] Nivolumab can be infused directly as a 10mg/mL solution or can be diluted to as low as 1mg/mL with sodium chloride 9mg/mL (0.9%) solution for injection or glucose 50mg/mL (5%) solution for injection.						

- Relevant information about the above chemotherapy is available in NCCP Regimen 00310 Gemcitabine (1000mg/m^2) and CARBOplatin (AUC5) Therapy.

Table 3: Treatment schedule for Nivolumab 360mg, Gemcitabine 1250mg/m^2 and CISplatin 75mg/m^2 Therapy (00849.3)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Nivolumab	360mg	IV infusion[a]	Infuse over 30 minutes through a sterile, non-pyrogenic, low protein binding in-line filter with a pore size of 0.2-1.2 µm[b]	Every 21 days **for 3 cycles**
2	1 and 8	Gemcitabine	1250mg/m^2	IV infusion	250mL NaCl 0.9% over 30 minutes	Every 21 days **for 3 cycles**
3	1	CISplatin[c]	75mg/m^2	IV infusion	1000mL NaCl 0.9% over 60 minutes	Every 21 days **for 3 cycles**

[a] Nivolumab must not be administered as an intravenous push or bolus injection.

[b] Nivolumab can be infused directly as a 10mg/mL solution or can be diluted to as low as 1mg/mL with sodium chloride 9mg/mL (0.9%) solution for injection or glucose 50mg/mL (5%) solution for injection.

[c] **Pre and post hydration therapy required for CISplatin**

See local hospital policy recommendations.

Suggested prehydration for CISplatin therapy:

- Administer 1000mL NaCl 0.9% over 60 minutes.
- Administer CISplatin as described above.

Post hydration:

- Administer 10mmol magnesium sulphate (MgSO4) and 20mmol potassium chloride (KCl) in 1000mL 0.9% NaCl over 2 hours (Refer to relevant local hospital policy for advice on administration of electrolyte infusions).
- Mannitol 10% may be used as per local policy to induce diuresis, although there is no conclusive evidence that this is required. The routine use of furosemide to increase urine flow is not recommended unless there is evidence of fluid overload.

- Relevant information about the above chemotherapy is available in NCCP Regimen 00281 Gemcitabine 1250mg/m^2 and CISplatin 75mg/m^2 Therapy.

Table 4: Treatment schedule for Nivolumab 360mg, PEMEtrexed and CARBOplatin Therapy (00849.4)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Nivolumab	360mg	IV infusion[a]	Infuse over 30 minutes through a sterile, non-pyrogenic, low protein binding in-line filter with a pore size of 0.2-1.2 µm[b]	Every 21 days **for 3 cycles**
2	1	PEMEtrexed[c]	500mg/m^2	IV infusion	100mL 0.9% NaCl over 10 minutes	Every 21 days **for 3 cycles**
3	1	CARBOplatin	AUC 5	IV infusion	500mL glucose 5% over 30 minutes	Every 21 days **for 3 cycles**
		Folic Acid or multivitamin containing 350-1000 micrograms folic acid	350-1000 micrograms[d]	PO		

[a] Nivolumab must not be administered as an intravenous push or bolus injection.

[b] Nivolumab can be infused directly as a 10mg/mL solution or can be diluted to as low as 1mg/mL with sodium chloride 9mg/mL (0.9%) solution for injection or glucose 50mg/mL (5%) solution for injection.

[c] PEMEtrexed is physically incompatible with diluents containing calcium, including lactated Ringer's injection and Ringer's injection.

[d] At least five doses of folic acid must be taken during the seven days preceding the first dose of PEMEtrexed, and dosing must continue during the full course of therapy and for 21 days after the last dose of PEMEtrexed.
See Premedications for further treatment required.

- Relevant information about the above chemotherapy is available in NCCP Regimen 00318 PEMEtrexed and CARBOplatin Therapy.

Table 5: Treatment schedule for Nivolumab 360mg, PEMEtrexed and CISplatin Therapy (00849.5)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Nivolumab	360mg	IV infusion[a]	Infuse over 30 minutes through a sterile, non-pyrogenic, low protein binding in-line filter with a pore size of 0.2-1.2 µm[b]	Every 21 days **for 3 cycles**
2	1	PEMEtrexed[c]	500mg/m^2	IV infusion	100mL 0.9% NaCl over 10 minutes	Every 21 days **for 3 cycles**
3	1	CISplatin[d]	75mg/m^2	IV infusion	1000mL 0.9% NaCl over 60 minutes to start 30 minutes after completion of PEMEtrexed	Every 21 days **for 3 cycles**
		Folic Acid or multivitamin containing 350-1000 micrograms folic acid	350-1000 micrograms[e]	PO		

[a] Nivolumab must not be administered as an intravenous push or bolus injection.

[b] Nivolumab can be infused directly as a 10mg/mL solution or can be diluted to as low as 1mg/mL with sodium chloride 9mg/mL (0.9%) solution for injection or glucose 50mg/mL (5%) solution for injection.

[c] PEMEtrexed is physically incompatible with diluents containing calcium, including lactated Ringer's injection and Ringer's injection.

[d] **Pre and post hydration therapy required for CISplatin**
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:
- Administer 1000mL NaCl 0.9% over 60 minutes.
- Administer CISplatin as described above.

Post hydration:
- Administer 10mmol magnesium sulphate (MgSO4) and 20mmol potassium chloride (KCl) in 1000 mL 0.9% NaCl over 2 hours (Refer to relevant local hospital policy for advice on administration of electrolyte infusions).
- Mannitol 10% may be used as per local policy to induce diuresis, although there is no conclusive evidence that this is required. The routine use of furosemide to increase urine flow is not recommended unless there is evidence of fluid overload.

[e] At least five doses of folic acid must be taken during the seven days preceding the first dose of PEMEtrexed, and dosing must continue during the full course of therapy and for 21 days after the last dose of PEMEtrexed.
See Premedications for further treatment required.

- Relevant information about the above chemotherapy is available in NCCP Regimen 00317 PEMEtrexed and CISplatin Therapy.

ELIGIBILITY:

- Indications as above
- Adults aged ≥ 18 years
- Newly diagnosed stage II-IIIA disease according to the 7th edition AJCC/UICC TNM staging criteria
- ECOG status 0-1
- Confirmation of PD-L1 expression on ≥1% of tumour cells as demonstrated by a validated test method on the biopsy or cytology sample of NCSLC, of predominantly non-squamous type as determined by hospital laboratory validated processes.
- Nivolumab is not recommended during pregnancy and in women of childbearing potential not using effective contraception unless prescribing consultant deems clinical benefit outweighs the potential risk. Effective contraception should be used for at least 5 months following the last dose of nivolumab
- Adequate haematological, hepatic and renal function
- Please refer to relevant chemotherapy regimen for additional eligibility criteria

CAUTION:

Use with caution in:

- Patients with clinically significant autoimmune disease

EXCLUSIONS:

- Hypersensitivity to nivolumab or to any of the excipients
- Symptomatic CNS metastases
- Any medical condition that requires immunosuppressive doses of systemic corticosteroids or other immunosuppressive medication(s) (defined as >10mg prednisolone/daily (or steroid equivalent, excluding inhaled or topical steroids)
- Symptomatic interstitial lung disease
- Any active clinically significant infection requiring therapy
- Known EGFR mutations or ALK translocations
- Information regarding prior therapy with an anti PD-1 or anti PD-L1 antibody is available here
- Additional exclusions maybe required depending on the choice of chemotherapy chosen by the treating consultant
- Pregnancy or breast feeding
- Please refer to relevant chemotherapy regimen for additional exclusion criteria

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Glucose
- Thyroid Function Tests (TFTs)
- Virology: All patients should be tested for both HBsAg and HBcoreAb as per local policy and Hepatitis C (HCV RNA)
- PD-L1 testing on the Ventana platform using the SP263 antibody on the biopsy or cytology sample of NCSLC
- EGFR and ALK testing using validated test methods. This may be carried out in parallel or sequential to PD-L1 testing in order to facilitate timely test turnaround times

Regular tests:

- FBC, renal and liver profile prior to each cycle
- Glucose prior to each cycle
- TFTs every 3-6 weeks

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Nivolumab:

- Dose escalation or reduction is not recommended. Any dose modification should be discussed with a Consultant
- Management of immune-related adverse reactions may require withholding of a dose or permanent discontinuation of nivolumab therapy and institution of systemic high-dose corticosteroid
- If immunosuppression with corticosteroids is used to treat an adverse reaction, a taper of at least 1 month duration should be initiated upon improvement. Rapid tapering may lead to worsening or recurrence of the adverse reaction. Non-corticosteroid immunosuppressive therapy should be added if there is worsening or no improvement despite corticosteroid use. Nivolumab should not be resumed while the patient is receiving immunosuppressive doses of corticosteroids or other immunosuppressive therapy
- Guidelines for withholding of doses or permanent discontinuation are described in Table 6 below

Table 6: Recommended Treatment Modifications for Nivolumab

Immune-related adverse reaction	Severity	Treatment Modification
Immune-related pneumonitis	Grade 2 pneumonitis	Withhold dose(s) until symptoms resolve, radiographic abnormalities improve, and management with corticosteroids is complete
	Grade 3 or 4 pneumonitis	Permanently discontinue treatment
Immune-related colitis	Grade 2 diarrhoea or colitis	Withhold dose(s) until symptoms resolve and management with corticosteroids, if needed, is complete
	Grade 3 diarrhoea or colitis	Withhold dose(s) until symptoms resolve and management with corticosteroids is complete
	Grade 4 diarrhoea or colitis	Permanently discontinue treatment
Immune-related hepatitis	Grade 2 elevation in aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin	Withhold dose(s) until laboratory values return to baseline and management with corticosteroids, if needed, is complete
	Grade 3 or 4 elevation in AST, ALT, or total bilirubin	Permanently discontinue treatment
Immune-related nephritis and renal dysfunction	Grade 2 or 3 creatinine elevation	Withhold dose(s) until creatinine returns to baseline and management with corticosteroids is complete
	Grade 4 creatinine elevation	Permanently discontinue treatment
Immune-related endocrinopathies	Symptomatic Grade 2 or 3 hypothyroidism, hyperthyroidism, hypophysitis, Grade 2 adrenal insufficiency Grade 3 diabetes	Withhold dose(s) until symptoms resolve and management with corticosteroids (if needed for symptoms of acute inflammation) is complete. Treatment should be continued in the presence of hormone replacement therapy as long as no symptoms are present
	Grade 4 hypothyroidism Grade 4 hyperthyroidism Grade 4 hypophysitis Grade 3 or 4 adrenal insufficiency Grade 4 diabetes	Permanently discontinue treatment
Immune-related skin adverse reactions	Grade 3 rash	Withhold dose(s) until symptoms resolve and management with corticosteroids is complete
	Grade 4 rash	Permanently discontinue treatment
	Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	Permanently discontinue treatment
Immune-related Myocarditis	Grade 2 myocarditis	Withhold dose(s) until symptoms resolve and management with corticosteroids is complete
	Grade 3 or 4 myocarditis	Permanently discontinue treatment

Other immune-related adverse reactions	Grade 3 (first occurrence) Grade 4 or recurrent Grade 3 ; persistent Grade 2 or 3 despite treatment modification ; inability to reduce corticosteroid dose to 10mg prednisone or equivalent per day	Withhold dose(s) Permanently discontinue treatment

Toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 (NCI-CTCAE v4).

Renal and Hepatic Impairment:

Table 7: Recommended dose modifications for in renal and hepatic impairment

Drug	Renal Impairment	Hepatic Impairment	
Nivolumab[a]	No dose adjustment is needed Haemodialysis: no need for dose adjustment is expected.	**Mild/moderate**	No dose adjustment is needed.
		Severe	No need for dose adjustment is expected.
[a]Dose modifications from Giraud et al.			

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

Nivolumab: Minimal **(Refer to local policy)**

PREMEDICATIONS:

Nivolumab: Not usually required.

OTHER SUPPORTIVE CARE:

Nivolumab: No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Nivolumab:

- **Cardiac adverse events and pulmonary embolism**: Patients should be monitored for cardiac and pulmonary adverse reactions continuously, as well as for clinical signs, symptoms, and laboratory abnormalities indicative of electrolyte disturbances and dehydration prior to and periodically during treatment.

- **Immune related adverse reactions:**

Adverse reaction	Withhold/ discontinue	Recommended action -1st occurrence
Immune-related pneumonitis Patients should be monitored for signs and symptoms of pneumonitis such as radiographic changes (e.g., focal ground glass opacities, patchy filtrates), dyspnoea, and hypoxia. Infectious and disease-related aetiologies should be ruled out.		
Grade 2 (symptomatic)	Withhold	Initiate corticosteroids at a dose of 1mg/kg/day methylprednisolone (/equivalents) Upon improvement, nivolumab may be resumed after corticosteroid taper
If worsening or no improvement occurs despite initiation of corticosteroids	Permanently discontinue	Increase corticosteroid dose to 2 to 4mg/kg/day methylprednisolone (/equivalents)
Grade 3 or 4	Permanently discontinue	Initiate corticosteroids at a dose of 2 to4mg/kg/day methylprednisolone (/equivalents)
Immune-related colitis Patients should be monitored for diarrhoea and additional symptoms of colitis, such as abdominal pain and mucus or blood in stool. Infectious and disease-related aetiologies should be ruled out. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-related colitis. Consider if patient has persistent colitis despite appropriate colitis therapy		
Grade 2 diarrhoea or colitis	Withhold	Initiate corticosteroids at a dose of 0.5 to 1mg/kg/day methylprednisolone (/equivalents) Upon improvement, nivolumab may be resumed after corticosteroid taper
If worsening or no improvement occurs despite initiation of corticosteroids	Permanently discontinue	Increase corticosteroid dose to 1 to 2mg/kg/day methylprednisolone (/equivalents)
Grade 3 diarrhoea or colitis	Withhold	Initiate corticosteroids at a dose of 1 to 2mg/kg/day methylprednisolone (/equivalents) Upon improvement, nivolumab may be resumed after corticosteroid taper
If worsening or no improvement occurs despite initiation of corticosteroids	Permanently discontinue	
Grade 4 diarrhoea or colitis	Permanently discontinue	Initiate corticosteroids at a dose of 1 to 2mg/kg/day methylprednisolone (/equivalents)
Immune-related hepatitis Patients should be monitored for signs and symptoms of hepatitis such as transaminase and total bilirubin elevations. Infectious and disease-related aetiologies should be ruled out.		
Grade 2 transaminase or total bilirubin elevation	Withhold	Persistent elevations in these laboratory values should be managed with corticosteroids at a dose of 0.5 to 1mg/kg/day methylprednisolone equivalents. Upon improvement, nivolumab may be resumed after corticosteroid taper

If worsening or no improvement occurs despite initiation of corticosteroids	Permanently discontinue	Increase corticosteroid dose to 1 to 2mg/kg/day methylprednisolone (/equivalents)
Grade 3 or 4 transaminase or total bilirubin elevation	Permanently discontinue	Initiate corticosteroids at a dose of 1 to 2mg/kg/day methylprednisolone (/equivalents)
Immune-related nephritis or renal dysfunction Patients should be monitored for signs and symptoms of nephritis and renal dysfunction. Most patients present with asymptomatic increases in serum creatinine. Disease-related aetiologies should be ruled out.		
Grade 2 or 3 serum creatinine elevation If worsening or no improvement occurs despite initiation of corticosteroids	Withhold Permanently discontinue	Initiate corticosteroids at a dose of 0.5 to 1mg/kg/day methylprednisolone (/equivalents) Upon improvement, nivolumab may be resumed after corticosteroid taper Increase corticosteroid dose to 1 to 2mg/kg/day methylprednisolone (/equivalents)
Grade 4 serum creatinine elevation	Permanently discontinue	Initiate corticosteroids at a dose of 1 to 2mg/kg/day methylprednisolone (/equivalents)
Immune-related endocrinopathies 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. Unless an alternate etiology has been identified, signs or symptoms of endocrinopathies should be considered immune-related		
Symptomatic hypothyroidism	Withhold	Thyroid hormone replacement should be initiated as needed
Symptomatic hyperthyroidism	Withhold	Antithyroid medication should be initiated as needed Corticosteroids at a dose of 1 to 2mg/kg/day methylprednisolone equivalents should also be considered if acute inflammation of the thyroid is suspected. Upon improvement, nivolumab may be resumed after corticosteroid taper, if needed. Monitoring of thyroid function should continue to ensure appropriate hormone replacement is utilised.
Life-threatening hyperthyroidism or hypothyroidism	Permanently discontinue	
Symptomatic Grade 2 adrenal insufficiency	Withhold	Physiologic corticosteroid replacement should be initiated as needed.
Severe (Grade 3) or life-threatening (Grade 4) adrenal insufficiency	Permanently discontinue	Monitoring of adrenal function and hormone levels should continue to ensure appropriate corticosteroid replacement is utilised.
Symptomatic Grade 2 or 3 hypophysitis	Withhold	Hormone replacement should be initiated as needed. Corticosteroids at a dose of 1 to 2mg/kg/day methylprednisolone (/ equivalents) should also be considered if acute inflammation of the pituitary gland is suspected. Upon improvement, nivolumab may be resumed after corticosteroid taper, if needed.
Life-threatening (Grade 4) hypophysitis	Permanently discontinue	Monitoring of pituitary function and hormone levels should continue to ensure appropriate hormone replacement is utilised

Symptomatic diabetes	Withhold	Insulin replacement should be initiated as needed. Monitoring of blood sugar should continue to ensure appropriate insulin replacement is utilised.
Life-threatening diabetes	Permanently discontinue	
Immune-related skin adverse reactions		
Grade 3 rash	Withhold	Severe rash should be managed with high-dose corticosteroid at a dose of 1 to 2mg/kg/day methylprednisolone equivalents. Rare cases of Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) some of them with fatal outcome have been observed. If symptoms or signs of SJS or TEN appear, nivolumab treatment should be discontinued and the patient referred to a specialised unit for assessment and treatment. If the patient has developed SJS or TEN with the use of nivolumab, permanent discontinuation of nivolumab is recommended. Caution should be used when considering the use of nivolumab in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immunestimulatory anticancer agents
Grade 4 rash	Permanently discontinue	
Other immune-related adverse reactions For suspected immune-related adverse reactions, adequate evaluation should be performed to confirm aetiology or exclude other causes. Based on the severity of the adverse reaction, nivolumab should be withheld and corticosteroids administered. Upon improvement, nivolumab may be resumed after corticosteroid taper. Nivolumab must be permanently discontinued for any severe immune-related adverse reaction that recurs and for any life-threatening immune-related adverse reaction.		
Infusion reactions		
Mild or moderate infusion reaction	Caution	May receive nivolumab with close monitoring and use of premedication according to local treatment guidelines for prophylaxis of infusion reactions
Severe or life-threatening infusion reaction	Discontinue infusion	Administer appropriate medical therapy

DRUG INTERACTIONS:

- No formal pharmacokinetic drug interaction studies have been conducted with nivolumab. Since nivolumab is cleared from the circulation through catabolism, no metabolic drug-drug interactions are expected.
- The use of systemic corticosteroids or immunosuppressants before starting nivolumab should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of nivolumab. However, systemic corticosteroids or other immunosuppressants can be used after starting nivolumab to treat immune-related adverse reactions.
- Current drug interaction databases should be consulted for more information.

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP

Patient Alert Card:
Nivolumab:
https://www.hpra.ie/img/uploaded/swedocuments/c02753be-51a5-44fd-8117-123823bdcff8.pdf

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5. Nivolumab (Opdivo®) SmPC. Last updated: 04/04/2024. Accessed: 18/04/2024 Available at: https://www.ema.europa.eu/en/documents/product-information/opdivo-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	27/04/2024		Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.