Nivolumab 480mg, CISplatin 80mg/m^2 and 5-Fluorouracil Infusional Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Nivolumab in combination with fluoropyrimidine and platinum-based combination chemotherapy for the first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) with tumour cell programmed death ligand 1 (PD-L1) expression ≥1%.	C15	00832a	Nivolumab: ODMS 1st July 2023 CISplatin: Hospital 5-Fluorouracil: Hospital

Note: As the platinum and fluoropyrimidine based chemotherapy is not defined in the EMA licensed indication other evidence based platinum and fluoropyrimidine regimens may be used in combination with nivolumab. Prior therapy with an anti – PD-1 or anti-PD-L1 antibody is an exclusion criteria.

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; treatment with nivolumab is administered until disease progression, unacceptable toxicity or up to 24 months in patients without disease progression.

CISplatin is administered on Day 1 and 5-Fluorouracil 800 mg/m^2 per day is given by continuous intravenous (IV) infusion on Days 1–5 of each cycle, as detailed in Table 1. Alternatively, 5-Fluorouracil may be administered at a dose of 1000 mg/m^2 per day given by continuous IV infusion on Days 1–4 of each cycle as detailed in Table 2 below.

Treatment with CISplatin and 5-Fluorouracil is administered until disease progression or unacceptable toxicity.

Each cycle is 28 days.

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 480mg, CISplatin 80mg/m^2 and 5-Fluorouracil 800mg/m^2/day Days 1-5

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Nivolumab	480mg	IV infusion[1]	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^2	Every 28 days **for up to 24 months**
2	1	CISplatin	80mg/m^2	IV infusion	1000ml NaCl 0.9% over 1 hour[3,4]	Every 28 days
3	1-5	5-Fluorouracil[5]	800mg/m^2/day (total dose = 4000mg/m^2 over 120 hours)	Continuous IV infusion over 5 days	Infusor pump	Every 28 days

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

[2] 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.

[3] **Pre and post hydration therapy required for CISplatin**
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:
- Administer 10mmol magnesium sulphate (MgSO4) ((+/-KCl 10-20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above.
Post hydration: Administer 1000 ml 0.9% NaCl over 60mins.

[4] Mannitol 10% may be used to 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.

[5] See dose modifications section for patients with identified partial dihydropyrimidine dehydrogenase (DPD) deficiency.

Table 2: Alternate Treatment schedule for Nivolumab, CISplatin 80mg/m^2 and 5-Fluorouracil 1000mg/m^2/day Days 1-4

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Nivolumab	480mg	IV infusion[1]	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^2	Every 28 days **for up to 24 months**
2	1	CISplatin	80mg/m^2	IV infusion	1000ml NaCl 0.9% over 1 hour[3,4]	Every 28 days
3	1-4	5-Fluorouracil[5]	1000mg/m^2/day (total dose = 4000mg/m^2 over 96 hours)	Continuous IV infusion over 4 days	Infusor pump	Every 28 days

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

[2] 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.

[3] **Pre and post hydration therapy required for CISplatin**
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:
- Administer 10mmol magnesium sulphate (MgSO4) ((+/-KCl 10-20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above.
Post hydration: Administer 1000 ml 0.9% NaCl over 60mins.

[4] Mannitol 10% may be used to 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.

[5] See dose modifications section for patients with identified partial dihydropyrimidine dehydrogenase (DPD) deficiency.

ELIGIBILITY:

- Indication as above
- Aged ≥18 years
- ECOG 0-2
- PD-L1 expression ≥1% as demonstrated by a validated test method
- Adequate haematological, hepatic and renal function

CAUTION:

Use with caution in:

- Patients with clinically significant autoimmune disease

EXCLUSIONS:

- Hypersensitivity to nivolumab, CISplatin, 5-Fluorouracil or any of the excipients
- Previous treatment with an anti-PD1/PD-L1 monoclonal antibody
- 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
- Symptomatic CNS metastases
- Any active clinically significant infection requiring therapy
- Pregnancy / breastfeeding
- Moderate/severe renal impairment (CrCl < 60 mL/min)
- Significant hearing impairment / tinnitus
- Pre-existing neuropathies ≥ grade 2
- Known complete dihydropyrimidine dehydrogenase (DPD) deficiency where used in combination with 5-Fluorouracil

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 with the DAKO autostainer using the 28-8 Pharm DX antibody on the request of a Consultant Medical Oncologist where there is an intention to treat with nivolumab in line with this licensed indication

- Audiology and creatinine clearance if clinically indicated
- DPD testing prior to first treatment with 5-Fluorouracil - using phenotype and/or genotype testing unless patient has been previously tested

Regular tests:

- FBC, renal and liver profile prior to each cycle
- Glucose prior to each cycle
- TFTs every 4 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 3 below

CISplatin and 5-Fluorouracil:

- Consider a reduced starting dose of 5-Fluorouracil in patients with identified partial DPD deficiency
    - Initial dose reduction may impact the efficacy of treatment
    - In the absence of serious toxicity, subsequent doses may be increased with careful monitoring
- Dose reductions to manage chemotherapy-induced adverse reactions are permitted for CISplatin and 5-Fluorouracil and are outlined in Table 4, 5 and 6 below

Table 3: 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 Grade 3 or 4 myocarditis	Withhold dose(s) until symptoms resolve and management with corticosteroids is complete 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).

Haematological:

Table 4: Dose modification of CISplatin and 5-Fluorouracil for Haematological Toxicity

ANC (x 10^9/L		Platelets (x 10^9/L	Dose
≥ 1.5	and	≥ 100	100%
1 to < 1.5	or	75 to <100	**Delay**[a] then 100% for 1st event[b]
<1	or	<75	**Delay**[a] then 75%

[a]Delay until ANC ≥1.5 x 10^9/L and platelets ≥75 x 10^9/L.
[b]Consider dose reduction to 75% for subsequent events and/ or prolonged delays of more than 2 weeks.

Renal and Hepatic Impairment:

Table 5: Dose modification in renal and hepatic impairment

Drug	Renal impairment		Hepatic impairment	
Nivolumab	**Mild / Moderate**	No dose adjustment necessary	**Mild**	No dose adjustment necessary
	Severe	Has not been studied	**Moderate / Severe**	Has not been studied Nivolumab must be administered with caution in patients with: • moderate (total bilirubin >1.5x to 3x ULN and any AST) or • severe (total bilirubin >3 x ULN and any AST) hepatic impairment
CISplatin	CrCl (ml/min)	Dose	No dose reduction necessary	
	≥60	100%		
	45-59	75%		
	<45	Consider CARBOplatin		
5-Fluorouracil	Consider dose reduction in severe renal impairment only		**Bilirubin (micromol/L)**	**AST** / **Dose**
			<85	<180 / 100%
			>85 or >180	Contraindicated
			Clinical decision. Moderate hepatic impairment; reduce initial dose by 33%. Severe hepatic impairment, reduce initial dose by 50%. Increase dose if no toxicity.	

Management of adverse events:

Table 6: Dose modification schedule based on adverse events induced by CISplatin and 5-Fluorouracil

Adverse Event	Dose Modification
Stomatitis or Diarrhoea Grade 2 Grade ≥3	 Reduce dose of 5-Fluorouracil to 75% Discontinue or delay until toxicity resolved then resume at 50%.
Hand-foot syndrome Grade 2 Grade 3	 Reduce dose of 5-fluorouracil to 75% until resolved then consider increasing dose by 100% Delay until resolved then resume at 75%
Neurotoxicity Grade ≥ 2	 Omit CISplatin

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

Nivolumab: Minimal **(Refer to local policy)**
CISplatin: High **(Refer to local policy)**
5-fluorouracil: Low **(Refer to local policy)**

PREMEDICATIONS:

- Not usually required for nivolumab

OTHER SUPPORTIVE CARE:

- Hydration pre and post CISplatin administration (**Refer to local policy** or see recommendations above)
- Anti-diarrhoeal treatment **(Refer to local policy)**
- Mouth care **(Refer to local policy)**

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

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

- **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated appropriately.

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 to 4mg/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 and 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	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 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 immune-stimulatory 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

CISplatin

- **Renal toxicity**: Nephrotoxicity is common with CISplatin. Strongly encourage oral hydration. If oral hydration is not possible (e.g. excessive nausea), IV hydration is indicated. Avoid nephrotoxic drugs such as aminoglycoside antibiotics where possible. Where treatment with nephrotoxic drugs must be used, monitor renal function.
- **Ototoxicity and sensory neural damage**: These are associated with CISplatin therapy. They should be assessed by history prior to each cycle.

5-Fluorouracil

- **Myocardial ischaemia and angina:** Cardiotoxicity is a serious complication during treatment with 5-Fluorouracil. Patients, especially those with a prior history of cardiac disease or other risk factors, treated with 5-Fluorouracil, should be carefully monitored during therapy.
- **DPD deficiency:** DPD is an enzyme encoded by the DPYD gene which is responsible for the breakdown of fluoropyrimidines. Patients with DPD deficiency are therefore at increased risk of fluoropyrimidine-related toxicity, including for example stomatitis, diarrhoea, mucosal inflammation, neutropenia and neurotoxicity. Treatment with 5-Fluorouracil, capecitabine or tegafur-containing medicinal products is contraindicated in patients with known complete DPD deficiency. Consider a reduced starting dose in patients with identified partial DPD deficiency. Initial dose reduction may impact the efficacy of treatment.

In the absence of serious toxicity, subsequent doses may be increased with careful monitoring. Therapeutic drug monitoring (TDM) of 5-Fluorouracil may improve clinical outcomes in patients receiving continuous 5-Fluorouracil infusions.

- **Hand-foot syndrome (HFS): HFS,** also known as palmar-plantar erythrodysaesthesia (PPE), has been reported as an unusual complication of high dose bolus or protracted continuous therapy for 5-Fluorouracil.

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.
- Avoid concurrent use of CISplatin with nephrotoxic drugs (e.g. aminoglycosides, furosemide, NSAIDS) due to additive nephrotoxicity. If necessary, monitor renal function closely.
- Marked elevations of prothrombin time and INR have been reported in patients stabilized on warfarin therapy following initiation of 5-Fluorouracil regimes.
- Concurrent administration of 5-Fluorouracil and phenytoin may result in increased serum levels of phenytoin.
- Caution should be taken when using 5-Fluorouracil in conjunction with medications which may affect DPD activity.
- 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

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

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1	28/06/2023		Prof Maccon Keane
1a	08/01/2024	Formatting changes and grammatical corrections.	NCCP

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.