IPILIMUMAB NIVOLUMAB (Yervoy and Opdivo)

INDICATION (ICD10) C18, C20, C64

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (NIV9) (NIV10)

1. Nivolumab in combination with ipilimumab for the 1st line treatment of intermediate or poor risk unresectable locally advanced or metastatic treatment naïve **renal** cell adenocarcinoma with a clear cell component or is a papillary RCC. No symptomatic brain metastases or leptomeningeal metastases currently requiring steroids for symptom control. Karnofsy PS ≥70%. (TA581/TA780)
2. Nivolumab plus ipilimumab for patients with microsatellite instability high (MSI-H) or mismatch repair deficiency (dMMR) metastatic **colorectal** cancer after prior fluoropyrimidine-based chemotherapy for metastatic disease. No previous pembrolizumab. No symptomatic brain or leptomeningeal metastases. PS 0 or 1. (TA716)

REGIMEN

Cycles 1 to 4 IV

Day 1	**NIVOLUMAB**	3mg/kg	IV infusion	#ml sodium chloride 0.9% over 30 minutes
	IPILIMUMAB	1mg/kg	IV infusion	#ml sodium chloride 0.9% over 30 minutes

Cycle 5 onwards SC

28 day regimen SC

Day 1	**NIVOLUMAB**	1200mg	SC	over 3 to 5 minutes

The first dose should be administered 6 weeks after last dose of nivolumab ipilimumab combination.

Cycle 5 onwards IV

28 day regimen IV

Day 1	**NIVOLUMAB**	480mg	IV infusion	#ml sodium chloride 0.9% over 30 minutes

Renal - the first dose should be administered 6 weeks after last dose of nivolumab ipilimumab combination.
Colorectal - the first dose should be administered 3 weeks after last dose of nivolumab ipilimumab combination

diluent and diluent volume for dose prescribed as per national standardised product specification

Can be given 2 weekly SC or IV if necessary (see SPC for details including 2 weekly dose)

CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for 4 doses.
A formal medical review as to whether treatment with nivolumab and ipilimumab should continue will occur at least by the end of the 2nd 3-weekly cycle of treatment.
Nivolumab monotherapy maintenance every 28 days (or 14 days) until disease progression.

ANTI-EMETICS

None required

CONCURRENT MEDICATION REQUIRED

None required

ADMINISTRATION

Nivolumab	SC administer in the abdomen or thigh over 3 to 5 minutes. Alternate injection sites.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Ipilimumab - neutral
Nivolumab IV - neutral

IV use low protein binding 0.2 to 5micron in-line or add-on filter.
Peripheral or central line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs Neutrophils ≥1.5x10^9/L Platelets ≥100x10^9/L	baseline and every cycle
Thyroid function	baseline and every cycle
Random glucose	baseline and every cycle
Random cortisol	baseline and every cycle
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Ipilimumab	Immune related toxicities - pneumonitis, colitis or hepatitis etc
Nivolumab	Immune related toxicities - pneumonitis, colitis or hepatitis etc

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Ipilimumab	Corticosteroids Anticoagulants
Nivolumab	-

DOSE MODIFICATIONS

Non-haematological

Ipilimumab Nivolumab
Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline

Hepatic impairment

Ipilimumab
ALT/AST ≥5xULN or bilirubin >3xULN at baseline, use ipilimumab only with caution.

Nivolumab
Data from patients with moderate or severe hepatic impairment are too limited to draw conclusions. Nivolumab should be administered with caution in patients with moderate or severe hepatic impairment, i.e. bilirubin >1.5xULN and any AST.

Renal impairment

Ipilimumab
Data from patients with severe renal impairment (CrCl <30ml/min) are too limited to draw conclusions.

Nivolumab
Data from patients with severe renal impairment (CrCl <30ml/min) are too limited to draw conclusions.

REFERENCES

1. Motzer, R et al; NEJM 2018; 378 (14): 1277-1290

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed consent	x				
Clinical assessment	x		x		Every 12 weeks or as clinically indicated
SACT assessment (PS and toxicities)	x	x	x	x	Every cycle
Immunotherapy bloods FBC, U&E/renal profile, magnesium, LFTs (AST, ALT and bilirubin), TFTs, cortisol, blood glucose, LDH, CRP	x	x	x	x	Every cycle
Lipid profile (cholesterol)	x				At baseline then if clinically indicated
Fatigue profile eg B12, folate, iron profile, vitamin D, zinc, testosterone (men only), ESR	x				At baseline then if clinically indicated