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/) (NIV24)

1. Nivolumab plus ipilimumab for previously untreated patients with microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) metastatic or locally advanced and inoperable colorectal cancer, have wild type or mutant RAS and BRAF status. Has no symptomatic brain or leptomeningeal metastases. PS 0 or 1. (TA1065)

REGIMEN IV

Cycles 1 to 4

Day 1	**NIVOLUMAB**	240mg	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 up to 2 calendar years from day 1 cycle 1

28 day regimen SC

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

The first dose should be administered 3 weeks after last dose of nivolumab ipilimumab combination.

28 day regimen IV

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

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 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 IV monotherapy maintenance every 28 days (or 14 days) up to maximum 2 calendar years from the 1st combination dose (ie day 1 cycle 1 of combination).

ANTI-EMETICS

None required

CONCURRENT MEDICATION REQUIRED

None required.
The use of systemic corticosteroids and other immunosuppressants at baseline, before starting nivolumab and ipilimumab, should be avoided because of their potential interference with the pharmacodynamic activity. However, systemic corticosteroids and other immunosuppressants can be used after starting nivolumab and ipilimumab to treat immune-related adverse reactions

EXTRAVASATION AND TYPE OF LINE / FILTERS

Ipilimumab - neutral
Nivolumab - neutral

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. CDF list