PEMBROLIZUMAB

1. For the treatment of adults with advanced (unresectable or metastatic) melanoma - NICE 2015

2. For 1st line use in adults with metastatic NSCLC whose tumours express PD-L1 ≥ 50%, and are EGFR -ve and ALK -ve

3. An option for previously treated PD-L1+ve (≥1%) NSCLC which has progressed after treatment with at least two cycles of platinum-containing doublet chemotherapy for stage IIIB/IV disease *and* a targeted treatment if they have an EGFR or ALK-+ve tumour – NICE 2017
Blueteq registration and approval is required before treatment for NSCLC may start

4. Compassionate use programme for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy, ***or*** who are not eligible for cisplatin-containing chemotherapy

Drug/Dosage:

Melanoma, or previously treated NSCLC:
Pembrolizumab 2mg/kg IV Day 1

1st line NSCLC, or urothelial carcinoma:
Pembrolizumab 200 mg fixed dose IV Day 1

Administration:

Doses > 100mg in 100ml 0.9% sodium chloride over 30 minutes
Doses ≤ 100mg in 50ml 0.9% sodium chloride over 30 minutes
Administer via a 0.2 – 5.0 micron in-line filter (the polyethylene-lined giving sets used for paclitaxel are appropriate, with a 0.22 micron filter)

Infusion-related reaction	Management
Mild, Grade 1 (i.e. infusion interruption not indicated)	Increase the frequency of monitoring until the patient is stable.
Moderate (Grade 2)	Stop the infusion and manage symptomatically. For patients whose symptoms resolve within one hour of stopping the infusion, the infusion may be re-started at 50% of the original infusion rate. For other patients, do not complete the infusion. Give any further doses with close monitoring. Premedication with paracetamol and chlorphenamine should be considered with all further doses.
Severe (Grade 3 or 4)	Pembrolizumab must be permanently discontinued.

Frequency:

Melanoma: every 3 weeks until disease progression, unacceptable toxicity, or physician discretion (e.g. sustained complete response)
NSCLC or urothelial carcinoma: every 3 weeks for a maximum of 2 years, or until disease progression, or unacceptable toxicity.

Review for toxicities before each dose is due.
In addition, it is very important that the patient is educated to immediately report any key signs or symptoms to the treating oncology team (see Comments)

Main Toxicities:

immune-related toxicities (colitis, pneumonitis, hepatitis, etc)
the most common symptoms reported by patients are fatigue, nausea, cough, diarrhoea, rash, pruritis, arthralgia

Reason for Update: details for toxicity management removed; comp use for bladder cancer added; blood test cut-offs added	Approved by Consultant: Dr M Ajaz
Version: 6	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 5	Date: 11.10.17
Prepared by: S Taylor	Checked by: C Tucker

Anti- emetics:	mildly emetogenic	
Extravasation:	non-vesicant	
Regular Investigations:	FBC	before each dose
	U&Es	before each dose
	LFTs	before each dose, and as indicated
	Random blood glucose	before each dose
	LDH	before each dose (melanoma only)
	Thyroid function*	every 3 - 6 weeks, according to clinician preference
	Random cortisol	every 3 - 6 weeks, according to clinician preference

**to avoid treatment delays, use previous results for prescribing purposes, if previous result was within normal limits and no current concerns*

Comments:

Each patient must be provided with a Keytruda™ Patient Alert Card before they start treatment.

Patients may be given a supply of loperamide, along with counselling to contact the oncology team in the event of any diarrhoea.

Patients must be advised to contact the oncology team or the 24 hour hot-line immediately they experience any side effect, as some side effects worsen rapidly. Prompt management of side effects can ensure that the patient continues with treatment.

Dose Delays and Toxicity Management:

Dose reductions for toxicity management are not recommended.

With regards to blood tests, proceed with next cycle of immunotherapy if:
Platelets ≥ 75 x 10^9/l and Neutrophils ≥ 1.0 x 10^9/l
and
AST/ALT ≤ 3 x ULN
and
Serum creatinine ≤ 1.5 x baseline
and
TSH / free T_4 within range, or no change from baseline

For detailed guidelines for the management of immune-related adverse events, refer to the Alliance "Guidelines for Management of Immunotherapy-Related Adverse Events" document.

Pembrolizumab may be restarted within 12 weeks after last dose, if an adverse reaction remains at Grade ≤ 1 and corticosteroid dose has been reduced to ≤ 10 mg prednisone or equivalent per day.

Renal Impairment:

No dose adjustment is needed for patients with mild or moderate renal impairment. Pembrolizumab has not been studied in patients with severe renal impairment.

Hepatic Impairment:

No dose adjustment is needed for patients with mild hepatic impairment. Pembrolizumab has not been studied in patients with moderate or severe hepatic impairment.

References:

Ribas, A et al; Lancet 2015; 16 (8): 908 – 918 (melanoma)
Robert, C et al ; NEJM 2015 ; 372 :2521 – 2532 (melanoma)
Herbst, R et al ; Lancet 2016 ; 387 (10027) : 1540 – 1550 (NSCLC)
Reck, M et al ; NEJM 2016 ; 375: 1823 – 1833 (NSCLC)

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