Indication	**NSCLC** For untreated* PD-L1 positive metastatic stage IIIB or IV non-small-cell lung (squamous or non-squamous**), in patients with a performance status (PS) of 0 or 1 and potentially fit for platinum-based chemotherapy, with no active brain metastases or leptomeningeal metastases. The patient must not have received prior treatment with an anti-PD-1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody unless received as part of the pembrolizumab EAMS programme for this indication and meeting all other criteria listed. *Completion of treatment with chemotherapy and/or RT as part of neoadj/adj therapy is allowed as long as therapy was completed at least 6 months prior to the diagnosis of metastatic disease. **NB The patient either does not have an adenocarcinoma/non-squamous histology OR does have an adenocarcinoma/non-squamous histology but does not have an EGFR, ROS1 or ALK-positive tumour. The treatment of PD-L1-positive stage IIIb or IV NSCLC (squamous or non-squamous) after progression 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-positive tumour. NB: Patient must be PS 0-1with no active brain metastases or leptomeningeal metastases. The patient must not have had prior treatment with docetaxel for non-small cell lung cancer and must not have received prior treatment with an anti-PD-1, anti-PDL2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody. **Urothelial Cancer** For locally advanced or metastatic transitional cell urothelial cancer previously treated with platinum-based chemotherapy. Pembrolizumab as first line treatment of locally advanced or metastatic urothelial cancer in patients who are ineligible for cisplatin-based chemotherapy and whose tumours express PD L1 with a combined positive score (CPS) ≥ 10. **Hodgkins lymphoma** Relapsed or refractory classical Hodgkins lymphoma in patients who are stem cell transplant-ineligible and have failed brentuximab vedotin. **Melanoma** The treatment of Stage III adjuvant melanoma with lymph node involvement in adults who have had complete resection. Advanced (unresectable or metastatic) melanoma that has not previously been treated with ipilimumab or after the disease has progressed with ipilumumab and, for BRAF V600 mutation-positive disease, a BRAF or MEK inhibitor. **Head and Neck** For previously untreated metastatic or unresectable recurrent PD-L1 positive head and neck squamous cell carcinoma
Treatment Intent	Palliative / adjuvant (melanoma only)
Frequency and number of cycles	There are 2 alternative dosing schedules for pembrolizumab, **200mg IV** every **3 weeks** or **400mg IV** every **6 weeks**.

	Adjuvant melanoma: **Every 3 weeks:** Treatment with pembrolizumab will be continued for a maximum of 12 months (or a maximum of 18 cycles as given 3-weekly) from the start of treatment in the absence of disease recurrence, unacceptable toxicity or withdrawal of patient consent. **Every 6 weeks** Treatment with pembrolizumab will be continued for a maximum of 12 months (or a maximum of 9 cycles as given 6-weekly) from the start of treatment in the absence of disease recurrence, unacceptable toxicity or withdrawal of patient consent. **Advanced melanoma:** Until disease progression, unacceptable toxicity, or physician discretion (e.g. sustained complete response) or patient choice. Pembrolizumab may be discontinued after a minimum of 2 years on treatment, and then re-started at disease progression. **NSCLC, Urothelial Cancer, Hodgkin's Lymphoma and Head & Neck:** The patient will receive a maximum treatment duration of 2 years of uninterrupted treatment or 35 administrations of pembrolizumab every 3 weeks (or 17 administrations every 6 weeks), whichever is later. **NB** Atypical responses (i.e. an initial transient increase in tumour size or small new lesions within the first few months followed by tumour shrinkage) have been observed. It is recommended to continue treatment for clinically stable patients with initial evidence of disease progression until further disease progression is confirmed. A formal medical review as to whether treatment with pembrolizumab should continue or not should be scheduled in line with commissioning criteria. This would usually be before the 3rd cycle when given every 3 weeks, or before the 2nd cycle when given every 6 weeks.
Monitoring Parameters pre-treatment	• Monitor FBC, U&Es, LFTs, LDH, Ca++ and glucose at each cycle. In addition, for 6 weekly pembrolizumab, monitor FBC, U&Es, LFTs, LDH, Ca++ and glucose 3 weeks after first dose at nurse review. • If PLT <75 or neuts <1.0 d/w consultant. • Thyroid function and 9am cortisol level must be assessed at baseline then every 6 weeks. • Confirm the patient has no symptomatically active brain metastases or leptomeningeal metastases. • **Hepatic impairment:** No dose adjustment for mild hepatic impairment. Moderate or severe hepatic impairment d/w consultant. • **Renal impairment:** No specific dose adjustment is necessary in patients with mild to moderate renal impairment. Severe renal impairment d/w consultant, Pembrolizumab has not been studied in patients with CrCl < 30ml/min. • The use of systemic corticosteroids or immunosuppressants before starting pembrolizumab should be avoided. Systemic corticosteroids or other immunosuppressants can be used after starting pembrolizumab to treat immune-related adverse reactions. • **Dose reductions:** dose reductions are not recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability. • Immune-related adverse reactions may appear during or after treatment. The most common immune-related reactions are: pneumonitis, colitis, nephritis, hepatitis, symptomatic hypophysitis, hyperthyroidism, hypothyroidism and type 1 diabetes. The following additional, immune related adverse reactions have been reported in patients

	receiving pembrolizumab: uveitis, arthritis, myositis, pancreatitis, severe skin reactions, myasthenic syndrome, encephalitis, Guillian-Barre syndrome, optic neuritis, rhabdomyolysis, sarcoidosis, myocarditis, haemolytic anaemia and partial seizures arising in a patient with inflammatory foci in brain parenchyma.
	• See guidelines for management of immune-related adverse reactions following immunotherapy: http://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/
	• Cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), some with fatal outcome, have been reported. For signs or symptoms of SJS or TEN, pembrolizumab should be withheld and the patient should be referred to a specialised unit for assessment and treatment. If SJS or TEN is confirmed, pembrolizumab should be permanently discontinued.
	• Pembrolizumab may have a minor influence on the ability to drive and use machines. Fatigue has been reported following administration of pembrolizumab.
	• Each patient should be given a copy of the Keytruda ® patient alert card at each cycle.
	• Patients must be advised to contact the oncology team or the 24 hour hot-line immediately if they experience any side effect, as some side effects worsen rapidly. Prompt management of side effects can ensure that the patient continues with treatment.
	
	• Severe infusion-related reactions have been reported in patients receiving pembrolizumab.
	  ○ For severe infusion reactions (grade 3-4), infusion should be stopped and pembrolizumab permanently discontinued.
	  ○ Patients with mild or moderate infusion reaction may continue to receive pembrolizumab with close monitoring; premedication with antipyretic and antihistamine may be considered.
	• *Pembrolizumab may be restarted within 12 weeks beyond the expected cycle length if an adverse reaction remains at Grade ≤ 1 and corticosteroid dose has been reduced to ≤ 10 mg prednisone or equivalent per day.

References	North London cancer network protocol "PEMBROLIZUMAB" v9, SPC accessed online 05/04/19 KMCC protocol MULTI-003 v5 SPC accessed online 01.12.20 blueteq form accessed online 01.12.20

NB For funding information, refer to the CDF and NICE Drugs funding spread sheet

Repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	Pembrolizumab	**200mg**	IV	30min	In 100ml Sodium Chloride 0.9% via in-line low- protein binding 0.22 microns filter. Flush the line with sodium chloride 0.9% for injection at the end of the infusion
TTO	Drug	Dose	Route	Directions	
	Metoclopramide	10mg	PO	Up to TDS PRN (max. 30mg per day including 20mg pre-chemo dose) Do not take for more than 5 days continuously.	
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if specified.	

Repeat every 42 days (alternative dosing schedule):

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	Pembrolizumab	**400mg**	IV	30min	In 100ml Sodium Chloride 0.9% via in-line low- protein binding 0.22 microns filter. Flush the line with sodium chloride 0.9% for injection at the end of the infusion
TTO	Drug	Dose	Route		Directions
	Metoclopramide	10mg	PO	Up to TDS PRN (max. 30mg per day including 20mg pre-chemo dose) Do not take for more than 5 days continuously.	
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if specified.	