Indication	**NSCLC:** **1st line of treatment of locally advanced or metastatic disease (no treatment for early stage disease within 6 months).** First line treatment* of IIIB, IIIC or metastatic non-small cell lung cancer which expresses PD-L1 with a tumour proportion score of at least 50% and is EGFR and ALK negative. *NB: Chemotherapy and/or radiotherapy or checkpoint inhibitor immunotherapy may have been given as neoadjuvant/adjuvant/maintenance therapy as long as treatment was completed at least 6 months prior to the diagnosis of recurrent or metastatic disease. **IIB, IIIC or metastatic disease that is either previously treated or has progressed within 6 months of treatment for early stage disease.** The treatment of PD-L1-positive stage IIIB, IIIC or IV NSCLC (squamous or non-squamous) after either • Progression with at least two cycles of platinum-containing doublet chemotherapy for stage IIIB/IIIC/IV disease and a targeted treatment if they have an EGFR or ALK-positive or ROS1 or MET exon 14 or KRAS G12C or RET or BRAF V600 tumour. or • progression within 6 months of completing platinum-based adjuvant, neo-adjuvant or chemoradiation and targeted treatment if they have an EGFR, ALK-positive, ROS1, MET exon 14, KRAS G12C, RET or BRAF V600 tumour. **Hodgkins lymphoma** Relapsed or refractory classical Hodgkins lymphoma in patients who: A) are stem cell transplant-ineligible and have failed at least two lines of chemo and also brentuximab vedotin or B) have been treated with stem cell transplantation but have not previously received brentuximab. Or C) have received 2 prior lines of cytotoxic chemotherapy but have **NOT** been previously treated with stem cell transplantation or brentuximab vedotin. NB the patient must have not received prior treatment with any antibody which targets PD-1 or PD-L1 or PD-L2 or CD137 or OX40 or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4). **Melanoma** The treatment of Stage III adjuvant melanoma with lymph node involvement in adults who have had complete resection. Or Adjuvant treatment of newly diagnosed and completely resected stage IIB or stage IIC malignant melanoma. Adjuvant treatment must commence no more than 3 months since the date of resection. Advanced (unresectable or metastatic) melanoma that has not previously been treated with ipilimumab or after the disease has progressed with ipilimumab 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.

	Colorectal For the 1st line treatment of patients with metastatic colorectal cancer exhibiting microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR). For previously treated unresectable or metastatic colorectal cancer exhibiting MSI-H or dMMR in patients unsuitable for nivolumab plus ipilimumab therapy. **Renal cell carcinoma** For the adjuvant treatment of renal cell carcinoma at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions. Treatment must commence no more than 12 weeks since the date of nephrectomy or metastasectomy. ***NB** the 6-weekly schedule of administration of pembrolizumab should be used unless there are clear clinical reasons for preferring the 3-weekly schedule. **Gynae** For the treatment of advanced or recurrent or metastatic endometrial carcinoma exhibiting MSI-H or dMMR, in patients who have progressive disease during or following prior platinum-containing therapy given in any setting for advanced or recurrent or metastatic disease and who are not candidates for potentially curative surgery or radiotherapy or chemoradiotherapy. **UGI** For previously treated unresectable or metastatic gastric, small intestinal or biliary tract cancer exhibiting MSI-H or dMMR.
Treatment Intent	Palliative / adjuvant (melanoma and RCC only) Disease modification (Hodgkins lymphoma 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 and RCC*:** **Every 3 weeks:** Treatment with pembrolizumab will be continued for a maximum of 12 months (or a maximum of 17 cycles when 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, Colorectal, Gynae, UGI, 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.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • 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 must be assessed at baseline then every 6-8 weeks or as clinically indicated. • Cortisol monitoring should be undertaken in line with ESMO immunotherapy toxicity guidance available on KMCC website (see link below). Cortisol level should not be taken within 24 hours of the last steroid dose. • Confirm the patient has no symptomatically active brain metastases or leptomeningeal metastases. • **Hepatic impairment:** Prior to treatment: No dose adjustment is needed for patients with for mild or moderate hepatic impairment. Pembrolizumab has not been studied in patients with severe hepatic impairment (bilirubin > 1.5 x ULN, ALT, AST > 2.5 x ULN in the absence of liver metastases at baseline). During treatment: For immune related hepatitis see immune related toxicity guidance below. • **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: https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/immunotherapy/

	• 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. • **Infusion related reactions:** Severe infusion-related reactions have been reported in patients receiving pembrolizumab. o For severe infusion reactions (grade 3-4), infusion should be stopped and pembrolizumab permanently discontinued. o 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	KMCC protocol MULTI-003 V10 SPC accessed online 31.10.2023

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	30 min	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	
Day 1	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.	

Repeat every 42 days (alternative dosing schedule):

Day	Drug	Dose	Route	Infusion Duration	Administration

1	Metoclopramide	20mg	PO		stat
	PEMBROLIZUMAB	**400mg**	IV	30 min	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
Day 1	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.	