Indication	For patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not candidates for curative surgery or curative radiation and have not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 21 days. A formal medical review as to whether treatment with cemiplimab should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment. Treatment to continue for a maximum duration 2 years (35 cycles) or until disease progression, unacceptable toxicity or patient's choice to stop treatment.
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, and LFTs at each cycle. • Thyroid function must be assessed at baseline then at least every 6 weeks. • 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 24hours of the last steroid dose. • Random blood glucose before each cycle. • The use of systemic corticosteroids or immunosuppressants before starting cemiplimab should be avoided. However, systemic corticosteroids or other immunosuppressants can be used to treat immune-related adverse reactions after starting treatment. • **Renal impairment:** No dose adjustment recommended. There are limited data for CrCL<30ml/min. • **Hepatic Impairment:** (prior to treatment, for immune related hepatitis see below) No dose adjustment in mild impairment. Insufficient data in moderate to severe impairment. • **Dose Reductions:** Dose reductions are not recommended. Dosing delay or discontinuation may be required based on individual safety and tolerability. • **Infusion-related reactions:** In the event of any grade 1 or 2 infusion related reaction interrupt or slow the rate of infusion and manage symptomatically (including with corticosteroids); premedication with antipyretic, corticosteroids and antihistamines should be considered for subsequent infusions. For any grade 3 or 4 infusion related reaction permanently discontinue cemiplimab. • **Immune related reactions:** ○ Immune-related reactions can involve any organ system, including, but not limited to meningitis, paraneoplastic encephalomyelitis, arthritis, Guillain-Barre syndrome, encephalitis, chronic inflammatory demyelinating polyradiculoneuropathy, central nervous system inflammation, autoimmune myocarditis, and immune thrombocytopenic purpura, myalgia, Sjogren's syndrome, vasculitis, myasthenia gravis. Also see table below for management of selected immune related adverse reactions. ○ Patients should be monitored for evidence of severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). ○ If corticosteroids are used to treat an immune related reaction they should be tapered over at least 1 month. Treatment should not be resumed while the patient is receiving immunosuppressive doses of corticosteroids (>10mg/day of prednisolone or equivalent) or other immunosuppressive therapy. Prophylactic antibiotics should be used to prevent opportunistic infections in patients receiving immunosuppressive therapy.

	○ For guidance on managing immune related reactions see table 1 below and guidelines available on KMCC website : https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/immunotherapy/ • Cemiplimab should be used with caution in immunosuppressed patients. • **Drug Interactions:** No drug to drug studies have been performed, monitor poly pharmacy patients closely. • The patient should be provided with the **Libtayo®** Patient Alert card, this should be carried during and until at least 5 months after the last dose of treatment and 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.
References	SPC accessed on line 11.10.2023

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1 SPC recommended treatment modifications for immune related reactions

Adverse reaction	Severity	Dose modification	Additional intervention
Pneumonitis	Grade 2	Withhold cemiplimab	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume cemiplimab if pneumonitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 3 or 4 or recurrent Grade 2	Permanently discontinue	Initial dose of 2 to 4 mg/kg/day prednisone or equivalent followed by a taper
Colitis	Grade 2 or 3	Withhold cemiplimab	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume cemiplimab if colitis or diarrhoea improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 4 or recurrent Grade 3	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Hepatitis	Grade 2 with AST or ALT >3 and ≤5×ULN or total bilirubin >1.5 and ≤3×ULN	Withhold cemiplimab	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume cemiplimab if hepatitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent or returns to baseline AST or ALT after completion of corticosteroid taper	
	Grade ≥3 with AST or ALT >5×ULN or total bilirubin >3×ULN	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Hypothyroidism	Grade 3 or 4	Withhold cemiplimab	Initiate thyroid hormone replacement as clinically indicated
		Resume cemiplimab when hypothyroidism returns to Grade 0 to 1 or is otherwise clinically stable	
Hyperthyroidism	Grade 3 or 4	Withhold cemiplimab	Initiate symptomatic management
		Resume cemiplimab when hyperthyroidism returns to Grade 0 to 1 or is otherwise clinically stable	
Thyroiditis	Grade 3 or 4	Withhold cemiplimab	Initiate symptomatic management
		Resume cemiplimab when thyroiditis returns to Grade 0 to 1 or is otherwise clinically stable	
Hypophysitis	Grade 2 to 4	Withhold cemiplimab	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated
		Resume cemiplimab if hypophysitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent or is otherwise clinically stable	
Adrenal insufficiency	Grade 2 to 4	Withhold cemiplimab	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper and hormone replacement as clinically indicated
		Resume cemiplimab if adrenal insufficiency improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent or is otherwise clinically stable	
Type 1 diabetes mellitus	Grade 3 or 4 (hyperglycaemia)	Withhold cemiplimab	Initiate treatment with anti-hyperglycaemics as clinically indicated
		Resume cemiplimab when diabetes mellitus returns to Grade 0 to 1 or is otherwise clinically stable	
Skin adverse reactions	Grade 2 lasting longer than 1 week, Grade 3 or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	Withhold cemiplimab	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume cemiplimab if skin reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 4 or confirmed SJS or TEN	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper

Immune-related skin reaction or other immune-related adverse reactions in patients with prior treatment with idelalisib	Grade 2	Withhold cemiplimab	Initiate management immediately, including initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume cemiplimab if skin reaction or other immune-related adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 3 or 4 (excluding endocrinopathies) or recurrent Grade 2	Permanently discontinue	Initiate management immediately, including initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Nephritis With renal disfunction	Grade 2 creatinine increased	Withhold cemiplimab	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume cemiplimab if nephritis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	Grade 3 or 4 creatinine increased	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
Other immune-related adverse reactions (including but not limited to paraneoplastic encephalomyelitis, meningitis, myositis, solid organ transplant rejection, graft-vs-host disease, Guillain-Barre syndrome, central nervous system inflammation, chronic inflammatory demyelinating polyradiculoneuropathy, encephalitis, myasthenia gravis, neuropathy peripheral, myocarditis, pericarditis, immune thrombocytopenia, vasculitis, arthralgia, arthritis, muscular weakness, myalgia, polymyalgia rheumatica, Sjogren's syndrome, pruritis, keratitis, immune-mediated gastritis, stomatitis and haemophagocytic lymphohistiocytosis)	Grade 2 or 3 based on type of reaction	Withhold cemiplimab	Initiate symptomatic management including initial dose of 1 to 2 mg/kg/day prednisone or equivalent followed by a taper
		Resume cemiplimab if other immune-related adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day prednisone or equivalent	
	– Grade 3 based on type of reaction or grade 4 adverse reaction (excluding endocrinopathies) – Grade 3 or 4 neurologic toxicity – Grade 3 or 4 myocarditis or pericarditis – Confirmed haemophagocytic lymphohistiocytosis – Recurrent severe Grade 3 immune-mediated adverse reaction – Persistent Grade 2 or 3 immune-mediated adverse reactions lasting 12 weeks or longer (excluding endocrinopathies) – Inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day prednisone or equivalent as clinically indicated followed by a taper
Infusion-related reaction	Grade 1 or 2	Interrupt or slow rate of infusion	Initiate symptomatic management
	Grade 3 or 4	Permanently discontinue	

Repeat every 21 days:

Day	Drug	Dose	Route	Infusion Duration	Administration
1	Metoclopramide	20mg	PO		stat
	CEMIPLIMAB	**350mg**	IV	30 mins	In 50ml Sodium chloride 0.9% via in-line 0.22 microns filter.