Cemiplimab Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement Status*
As monotherapy for the treatment of adult patients with recurrent or metastatic cervical cancer and disease progression on or after platinum-based chemotherapy	C53	00812a	N/A
As monotherapy is indicated for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma (mCSCC or laCSCC) who are not candidates for curative surgery or curative radiation	C44	00812b	ODMS 1/10/2024

* This is for post 2012 indications only.

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Cemiplimab is administered on day 1 of a 21 day cycle and continued until disease progression or unacceptable toxicity occurs.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Cemiplimab	350mg	IV infusion	[a]50mL NaCl 0.9% over 30 minutes	Every 21 days
Cemiplimab should be administered through an intravenous line containing a sterile, non-pyrogenic, low-protein binding, in-line or add-on filter (0.2 micron to 5 micron pore size). Other medicinal products should not be co-administered through the same infusion line.					
[a] Cemiplimab is diluted to a final concentration ranging from 1mg/mL to 20mg/mL					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate renal, hepatic and haematological function
- **Cutaneous squamous cell carcinoma indication:**
  - At least 1 measurable lesion

CAUTIONS:

- **Cutaneous squamous cell carcinoma indication:**
  - Patients who have received solid organ transplant

EXCLUSIONS:

- Hypersensitivity to cemiplimab or any of the excipients
- Immunosuppressive doses of systemic corticosteroids or other immunosuppressive medication(s) (defined as >10mg predniSOLONE/daily (or steroid equivalent, excluding inhaled or topical steroids)
- Any active clinically significant infection requiring therapy
- Active CNS metastases
- Information regarding prior therapy with an anti PD-1 or anti PD-L1 antibody is available here
- Pregnancy/breastfeeding

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Blood glucose
- Thyroid function tests
- Virology Screen: Hepatitis B (HBsAg, HBcoreAb) and Hepatitis C

Regular tests:

- FBC, renal and liver profile prior to each cycle
- Blood glucose prior to each cycle
- TSH every 3 to 6 weeks

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- No dose reductions are recommended.
- Dosing delay or discontinuation may be required based on individual safety and tolerability.
- Recommended modifications to manage adverse reactions are provided in Table 1.

Renal and Hepatic Impairment:

Table 1: Dose modification in renal and hepatic impairment

Renal Impairment	Hepatic Impairment	
Renal impairment: no need for dose adjustment is expected Haemodialysis: no need for dose adjustment is expected	**Mild**	No dose adjustment is needed
	Moderate/Severe	No need for dose adjustment is expected

Management of adverse events:

Table 2: Dose Modification for Adverse Events

Adverse reactions	Severity[b]	Dose modification	Additional intervention
Immune-mediated reactions			
Pneumonitis	Grade 2	Withhold treatment	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper
		Resume treatment if pneumonitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day predniSOLONE or equivalent	
	Grade 3 or 4 or recurrent grade 2	Permanently discontinue	Initial dose of 2 to 4 mg/kg/day predniSOLONE or equivalent followed by a taper
Colitis	Grade 2 or 3	Withhold treatment	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper
		Resume treatment if colitis or diarrhoea improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day predniSOLONE or equivalent	
	Grade 4 or recurrent Grade 3	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day predniSOLONE 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 treatment	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper
		Resume treatment if hepatitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day predniSOLONE 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 predniSOLONE or equivalent followed by a taper
Hypothyroidism	Grade 3 or 4	Withhold treatment	Initiate thyroid hormone replacement as clinically indicated
		Resume treatment when hypothyroidism returns to Grade 0 to 1 or is otherwise clinically stable	
Hyperthyroidism	Grade 3 or 4	Withhold treatment	Initiate symptomatic management
		Resume treatment when hyperthyroidism returns to Grade 0 to 1 or is otherwise clinically stable	

Thyroiditis	Grade 3 to 4	Withhold treatment	Initiate symptomatic management
		Resume treatment when thyroiditis returns to Grade 0 to 1 or is otherwise clinically stable	
Hypophysitis	Grade 2 to 4	Withhold treatment	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper and hormone replacement as clinically indicated
		Resume treatment if hypophysitis improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day predniSOLONE or equivalent or is otherwise clinically stable	
Adrenal insufficiency	Grade 2 to 4	Withhold treatment	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper and hormone replacement as clinically indicated
		Resume treatment if adrenal insufficiency improves and remains at Grade 0 to 1 after corticosteroid taper to ≤10 mg/day predniSOLONE or equivalent or is otherwise clinically stable	
Type 1 diabetes mellitus	Grade 3 or 4 (hyperglycaemia)	Withhold treatment	Initiate treatment with anti-hyperglycaemics as clinically indicated
		Resume treatment 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 treatment	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper
		Resume treatment if skin reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day predniSOLONE or equivalent	
	Grade 4 or confirmed SJS or TEN	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper
Immune-mediated skin reaction or other immune-mediated adverse reactions in patients with prior treatment with idelalisib	Grade 2	Withhold treatment	Initiate management immediately, including initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper
		Resume treatment if skin reaction or other immune-mediated adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day predniSOLONE 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 predniSOLONE or equivalent followed by a taper
Nephritis with renal dysfunction	Grade 2 creatinine increased	Withhold treatment	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent followed by a taper

		Resume treatment 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 predniSOLONE or equivalent followed by a taper
Other immune-mediated adverse reactions	Grade 2 or 3 based on type of reaction	Withhold treatment	Initiate symptomatic management including initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent as clinically indicated followed by a taper
		Resume treatment if other immune-mediated adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to ≤ 10 mg/day predniSOLONE or equivalent	
	-Grade 3 based on type of reaction or Grade 4(excluding endocrinopathies) –Grade 3 or 4 neurologic toxicity –Grade 3 or 4 myocarditis or pericarditis --Confirmed haemophagocytic lymphohistiocytosis –Recurrent 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 predniSOLONE or equivalent per day within 12 weeks	Permanently discontinue	Initial dose of 1 to 2 mg/kg/day predniSOLONE or equivalent as clinically indicated followed by a taper
Infusion-related reactions			
Infusion-related reaction	Grade 1 or 2	Interrupt or slow rate of infusion	Initiate symptomatic management

	Grade 3 or 4	Permanently discontinue	
[b]Toxicity should be graded with the current version of National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE).			

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting linked here

Cemiplimab: Minimal **(Refer to local policy)**

For information:
Within NCIS regimens, anti-emetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - link here
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - link here

PREMEDICATIONS: No specific recommendations

OTHER SUPPORTIVE CARE:

- Women of childbearing potential should use effective contraception during treatment with cemiplimab and for at least 4 months after the last dose of cemiplimab.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.
- **This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.**

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

COMPANY SUPPORT RESOURCES/Useful Links:

Please note that this is for information only and does not constitute endorsement by the NCCP

Patient Alert Card: https://www.hpra.ie/img/uploaded/swedocuments/9f2169f9-19c8-4af9-b585-ce43a9b917ec.pdf

Patient Guide: https://www.hpra.ie/img/uploaded/swedocuments/cbf7d99a-7ff6-4eee-9b72-261ded2a7870.pdf

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3. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
5. Cemiplimab (Libtayo®) Summary of Product Characteristics. Last updated: 12/01/2024. Accessed May 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/libtayo-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	10/03/2023		Prof Maccon Keane
2	17/07/2024	Reviewed. Eligibility and Exclusions updated, Cautions section added. Renal and hepatic dose modifications updated to recommendations by Giraud et al 2023. Updated Table 2 (other immune-mediated adverse reactions). Updated Emetogenic Potential, Adverse Effects and Drug Interactions sections to align with NCCP standardisation.	Prof Maccon Keane
3	21/08/2024	Updated exclusion criteria	Prof Maccon Keane
3a	1/10/2024	Updated reimbursement status for indication 812b	NCCP

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.