PEMBROLIZUMAB (Keytruda) CISPLATIN (40) with concurrent RT (neoadjuvant then adjuvant)

INDICATION (ICD10) C76

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (PEMB34)

1. Pembrolizumab for SACT treatment naïve resectable, locally advanced, non-metastatic head and neck squamous cell carcinoma of the oral cavity, larynx, hypopharynx, or oropharynx.in adults (HPV-positive oropharyngeal stage III (T4, N0-2, M0) or HPV-negative oropharyngeal, larynx, hypopharynx, or oral cavity stage III or IVA) whose tumours express PD-L1 with a combined positive score of 1 or more. PS 0 or 1.

REGIMEN SC (pembrolizumab before chemotherapy)

Cycle 1 (neoadjuvant)

Day 1	PEMBROLIZUMAB	790mg subcutaneous* (4.8ml) over 2 minutes

Cycle 2 with RT (adjuvant)

Day 1	PEMBROLIZUMAB	790mg subcutaneous* (4.8ml) over 2 minutes
Days 1, 8, 15, 22, 29 and 36 Prehydration		
	CISPLATIN 40mg/m^{2*} in 1000ml sodium chloride 0.9% IV infusion over 60 minutes	
	Post hydration	

Cycles 3 to 9

Day 1	PEMBROLIZUMAB	790mg subcutaneous* (4.8ml) over 2 minutes

*Into the thigh or abdomen, avoiding the 5cm area around the navel

REGIMEN IV (pembrolizumab before chemotherapy)

Cycle 1 (neoadjuvant)

Days 1 and 22	PEMBROLIZUMAB	200mg in 100ml sodium chloride IV infusion over 30 minutes

Cycle 2 with RT (adjuvant)

Day 1	PEMBROLIZUMAB	400mg in 100ml sodium chloride IV infusion over 30 minutes
Days 1, 8, 15, 22, 29 and 36 Prehydration		
	CISPLATIN 40mg/m^{2*} in 1000ml sodium chloride 0.9% IV infusion over 60 minutes	
	Post hydration	

Cycles 3 to 9

Day 1	PEMBROLIZUMAB	400mg in 100ml sodium chloride IV infusion over 30 minutes

*Head and neck patients cap dose at BSA 2.0 (maximum 80mg)

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 42 days for 9 cycles

ADMINISTRATION

Pembrolizumab SC - withdraw the required volume using a transfer needle (18-21G recommended). To avoid needle clogging, change the needle to a 25-30G, 13 mm hypodermic injection needle immediately prior to SC injection.

ANTI-EMETICS

Moderate emetic risk days 1, 8, 15, 22, 29 and 35 cycle 2

CONCURRENT MEDICATION REQUIRED

Cisplatin	Ensure adequate pre and post hydration. If urine output is <100ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.
Pembrolizumab	None required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin – exfoliant
Pembrolizumab IV – neutral

Cisplatin - filter not required
Pembrolizumab IV – use low protein binding 0.2 to 5micron in-line or add-on filter

Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E, Mg^{++} and LFTs every week
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Ideally EDTA GFR should be used
Creatinine clearance (GFR) calculated, at the Consultant's discretion
Serum creatinine
Thyroid function* baseline, then every cycle
Random cortisol baseline, then every cycle (or as specified in Trust guideline)
Random glucose every cycle
Hba1c baseline
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
Pembrolizumab	Immune related toxicities - pneumonitis, colitis or hepatitis etc Pembrolizumab SC skin reactions at site of administration route

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.
Pembrolizumab	-

DOSE MODIFICATIONS

Non-haematological

Cisplatin
If patient complains of tinnitus, tingling of fingers and/or toes, discuss with SpR or Consultant before administration.

Pembrolizumab
Immune-related adverse reactions - refer to TV immune-oncology agent immune related adverse event clinical guideline.
If the drug-related toxicity does not resolve to grade 0-1 within 12 weeks after onset of toxicity, discontinuation is recommended.

Hepatic impairment
Cisplatin
No dose adjustment is needed

Pembrolizumab
No dose adjustment is needed

Renal impairment
Cisplatin

CrCl >60ml/min	give 100% dose
CrCl 50-59ml/min	give 75% dose
CrCl 40-49ml/min	give 50% dose (curative intent) not recommended (palliative intent)
CrCl <40ml/min	not recommended

Pembrolizumab
No dose adjustment is needed

REFERENCES
1. Uppaluri et al; KEYNOTE-689 Investigators. Neoadjuvant and Adjuvant Pembrolizumab in Locally Advanced Head and Neck Cancer. N Engl J Med. 2025 Jul 3;393(1):37-50