

# Regimen Reference Order

## ESOPH – pembrolizumab + CISplatin + fluorouracil

ARIA: ESOPH - [pembro + CISplatin + 5FU]  
ESOPH - [pembro q21d (maintenance)]  
ESOPH - [pembro q42d (maintenance)]

**Planned Course:** pembrolizumab + CISplatin + fluorouracil every 21 days for 6 cycles, followed by maintenance pembrolizumab:  
pembrolizumab every 21 days up to 29 cycles or until disease progression or unacceptable toxicity (maximum 2 years of therapy total)  
**OR**  
pembrolizumab every 42 days up to 15 cycles or until disease progression or unacceptable toxicity (maximum 2 years of therapy total)

**Indication for Use:** Esophageal Cancer/Gastroesophageal Junction Tumor; Metastatic

**Drug Alert:** Immune Checkpoint Inhibitor (pembrolizumab)

**CVAD:** Required (Ambulatory Pump)

**Proceed with treatment if:**

**Cycles 1 to 6**

- *ANC equal to or greater than  $1.5 \times 10^9/L$  AND Platelets equal to or greater than  $100 \times 10^9/L$*
- *AST/ALT equal to or less than 3 times the upper limit of normal*
- *Total bilirubin equal to or less than 1.5 times the upper limit of normal*
- *Creatinine clearance is greater than 45 mL/minute*

**pembrolizumab Maintenance**

- *ANC equal to or greater than  $1.5 \times 10^9/L$  AND Platelets equal to or greater than  $50 \times 10^9/L$*
- *AST/ALT equal to or less than 3 times the upper limit of normal*
- *Total bilirubin equal to or less than 1.5 times the upper limit of normal*
- *Creatinine clearance is equal to or greater than 30 mL/minute*

❖ **Contact Physician if parameters are not met**

### SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements		
Drug	Dose	CCMB Administration Guideline
Not Applicable		

### Treatment Regimen – ESOPH – pembrolizumab + CISplatin + fluorouracil

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
<b>Cycles 1 to 6 – pembrolizumab + CISplatin + fluorouracil</b>		
pembrolizumab	2 mg/kg	IV in normal saline 50 mL over 30 minutes <i>Use 0.2 or 0.22 micron filter</i>
magnesium sulfate	2 g	IV in normal saline 1000 mL over 2 hours (Pre hydration)
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
OLANzapine	2.5 mg	Orally 30 minutes pre-chemotherapy
CISplatin	80 mg/m <sup>2</sup>	IV in normal saline 500 mL over 1 hour <b>*Alert:</b> CISplatin infusion must be complete prior to mannitol administration
mannitol	12.5 g	IV in normal saline 1000 mL over 2 hours (Post hydration)
fluorouracil	4000 mg/m <sup>2</sup>	IV in D5W continuously over 96 hours by ambulatory infusion device

**pembrolizumab Maintenance starts three weeks after Cycle 6, Day 1**

**pembrolizumab Maintenance (Cycles 1 to 29 OR Cycles 1 to 15)**

pembrolizumab	2 mg/kg (every 21 days) <b>OR</b>	IV in normal saline 50 mL over 30 minutes <i>Use 0.2 or 0.22 micron filter</i>
	4 mg/kg (every 42 days)	IV in normal saline 100 mL over 30 minutes <i>Use 0.2 or 0.22 micron filter</i>

**Maximum pembrolizumab dose is 200 mg (every 21 days) or 400 mg (every 42 days)**

All doses will be automatically rounded that fall within CCMB Approved Dose Bands. See Dose Banding document for more information

**In the event of an infusion-related hypersensitivity reaction, refer to the ‘Hypersensitivity Reaction Standing Order’**

## REQUIRED MONITORING

### All Cycles

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin, glucose and TSH as per Physician Orders
- Medical oncologist or designate (i.e. family practitioner in oncology) must assess patient for immune-mediated adverse reactions prior to each cycle
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O<sub>2</sub> saturation) at baseline and as clinically indicated
- No observation period is required after pembrolizumab administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

### Cycles 1 to 6 Only

- Baseline blood pressure prior to magnesium infusion and repeat 15 minutes after start of magnesium infusion

### Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
<b>pembrolizumab + CISplatin + fluorouracil (Cycles 1 to 6)</b>		
aprepitant	80 mg	Orally once daily on Days 2 and 3
dexamethasone	8 mg	Orally once daily on Days 2, 3 and 4
OLANzapine	2.5 mg	Orally the evening of Day 1 then twice daily on Days 2, 3 and 4. Also use OLANzapine 2.5 to 5 mg AS NEEDED for breakthrough nausea and vomiting (including Days 1 to 4) up to a maximum of 10 mg per day. Contact clinic if nausea/vomiting is not adequately controlled
<b>pembrolizumab Maintenance</b>		
None required		

## DISCHARGE INSTRUCTIONS

### All Cycles

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Confirm that patient has received the CCMB Immune Checkpoint Inhibitor Medical Alert wallet card
- Reinforce to patient the immune-mediated adverse reactions and importance of reporting immediately
  - For severe symptoms, the patient should be instructed to go to the nearest emergency room. Oncologist on call should be contacted

### Cycles 1 to 6

- Instruct patient to continue taking anti-emetic(s) at home
- Ensure patient has received a home chemotherapy spill kit and instructions for use
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

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**ADDITIONAL INFORMATION**

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- pembrolizumab is an Immune Checkpoint Inhibitor. Consult with oncologist for immune-mediated adverse reactions; corticosteroids are often indicated
- CISplatin is ototoxic and nephrotoxic
- CISplatin can cause hypomagnesemia
- **Note:** Upon completion of 6 cycles of **ESOPH - [pembro + CISplatin + 5FU]**, patients should be started on maintenance treatment with **ESOPH - [pembro q21d (maintenance)]** or **ESOPH - [pembro q42d (maintenance)]**
  - **ESOPH - [pembro q21d (maintenance)]** or **ESOPH - [pembro q42d (maintenance)]** regimen starts three weeks after Cycle 6, Day 1 of **ESOPH - [pembro + CISplatin + 5FU]**