

# Regimen Reference Order – ESOPH – pembrolizumab + FOLFOX-6

ARIA: ESOPH - [pembrolizumab + FOLFOX-6]

ESOPH - [pembro q21d (maintenance)]

ESOPH - [pembro q42d (maintenance)]

**Planned Course:** FOLFOX every 14 days for 9 cycles with pembrolizumab every 42 days, 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)

*See Appendix (page 5) for regimen Dosing Schema*

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

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

**CVAD:** Required (Ambulatory Pump)

**Proceed with treatment if:**

**FOLFOX**

- *ANC equal to or greater than  $1.5 \times 10^9/L$  AND Platelets equal to or greater than  $100 \times 10^9/L$*
  - *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 not met*

## SEQUENCE OF MEDICATION ADMINISTRATION

### Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

### Treatment Regimen – ESOPH – pembrolizumab + FOLFOX-6

Establish primary solution 500 mL of: D5W

Drug	Dose	CCMB Administration Guideline
<b>Cycles 1, 4 and 7 – pembrolizumab + FOLFOX</b>		
pembrolizumab	4 mg/kg	IV in normal saline 100 mL over 30 minutes <i>Use 0.2 or 0.22 micron filter</i>
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
oxaliplatin	85 mg/m <sup>2</sup>	IV in D5W 500 mL over 2 hours <i>*Nursing Alert: oxaliplatin and leucovorin may be infused over the same 2-hour period using a Y-site connector</i>
leucovorin	400 mg/m <sup>2</sup>	IV in D5W 500 mL over 2 hours
fluorouracil	400 mg/m <sup>2</sup>	IV Push over 5 minutes
fluorouracil	2400 mg/m <sup>2</sup>	IV in D5W continuously over 46 hours by ambulatory infusion device

#### Cycles 2, 3, 5, 6, 8 and 9 – FOLFOX

ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
oxaliplatin	85 mg/m <sup>2</sup>	IV in D5W 500 mL over 2 hours <i>*Nursing Alert: oxaliplatin and leucovorin may be infused over the same 2-hour period using a Y-site connector</i>
leucovorin	400 mg/m <sup>2</sup>	IV in D5W 500 mL over 2 hours
fluorouracil	400 mg/m <sup>2</sup>	IV Push over 5 minutes
fluorouracil	2400 mg/m <sup>2</sup>	IV in D5W continuously over 46 hours by ambulatory infusion device

**pembrolizumab Maintenance starts two weeks after Cycle 9, 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)	

**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 and glucose as per Physician Orders
- TSH once monthly 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 dose of pembrolizumab
- 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

### Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
<b>pembrolizumab + FOLFOX-6 (Cycles 1 to 9)</b>		
dexamethasone	8 mg	Orally once daily on Days 2 and 3
prochlorperazine	10 mg	Orally every 6 hours as needed for nausea and vomiting
<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 9

- 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
- Numerous dosing variations exist for FOLFOX and depend on the primary cancer diagnosis
- oxaliplatin causes cold intolerance and laryngopharyngeal dysesthesia
  - no ice chips or cold drinks
- oxaliplatin may cause progressive, irreversible neuropathy
  - dose modification may be required
- **Note:** upon completion of 9 cycles of **ESOPH - [pembrolizumab + FOLFOX-6]**, 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 two weeks after Cycle 9, Day 1 of **ESOPH - [pembrolizumab + FOLFOX-6]**

### Appendix Dosing Schema

**ESOPH - [pembrolizumab + FOLFOX-6] – Cycles 1 to 9 (14-day cycle)**

		Cycle 1			Cycle 2			Cycle 3			Cycle 4			Cycle 5			Cycle 6			
		Day	1	8	Day	1	8	Day	1	8	Day	1	8	Day	1	8	Day	1	8	
	pembrolizumab																			
	FOLFOX																			

  

		Cycle 7			Cycle 8			Cycle 9		
		Day	1	8	Day	1	8	Day	1	8
	pembrolizumab									
	FOLFOX									

**Starting 14 days after Cycle 9, Day 1 of ESOPH - [pembrolizumab + FOLFOX-6]:**

**ESOPH - [pembro q21d (maintenance)]**

		Cycles 1 to 29 (21-day cycle)			
		Day	1	8	15
	pembrolizumab				

OR

**ESOPH - [pembro q42d (maintenance)]**

		Cycles 1 to 15 (42-day cycle)						
		Day	1	8	15	22	29	36
	pembrolizumab							

Key:



Indicates that *pembrolizumab* will be administered on this day



Indicates that *chemotherapy* will be administered on this day