Regimen Reference Order – GAST – cetuximab + encorafenib

ARIA: GAST – [cetuximab + encorafenib]

Planned Course: cetuximab weekly AND encorafenib daily until disease progression or unacceptable toxicity (1 cycle = 28 days)

Indication for Use: Colorectal Cancer Metastatic, BRAF V600E Mutation Positive

CVAD: At Provider's Discretion

Proceed with treatment if:

encorafenib

Days 1 and 15 of every cycle

- *ANC equal to or greater than 1.5 x 10^9/L AND Platelets equal to or greater than 100 x 10^9/L*
- *AST/ALT less than 3 times the upper limit of normal*
- *Total bilirubin less than 2 times the upper limit of normal*

cetuximab

- *On Day 1, proceed with cetuximab only when encorafenib starts*
- *On subsequent treatment days, proceed with cetuximab regardless of CBC*
  - ❖ **Contact Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – GAST – cetuximab + encorafenib

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
encorafenib	300 mg	Orally once daily on **Days 1 to 28** Take with or without food. Swallow whole **(Self-administered at home)** ** Alert: encorafenib dose may be adjusted pending evaluation of Day 15 blood work*
Day 1		
dexamethasone	8 mg	IV in normal saline 50 mL over 15 minutes
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medications before starting cetuximab		

cetuximab	400 mg/m^2 Loading Dose	IV over 2 hours (administered undiluted) Doses greater than 1200 mg must be administered over 2.5 hours *Use 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume on label* **Nursing Alert:* *IV tubing is primed with cetuximab*
Day 8		
dexamethasone	8 mg	IV in normal saline 50 mL over 15 minutes
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medications before starting cetuximab		
cetuximab	250 mg/m^2	IV over 1 hour (administered undiluted) Doses greater than 600 mg must be infused over 2 hours *Use 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume on label* **Nursing Alert:* *IV tubing is primed with cetuximab*
Days 15 and 22		
cetirizine	10 mg	Orally 30 minutes prior to cetuximab
dexamethasone	8 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medications before starting cetuximab		
cetuximab	250 mg/m^2	IV over 1 hour (administered undiluted) Doses greater than 600 mg must be infused over 2 hours *Use 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume on label* **Nursing Alert:* *IV tubing is primed with cetuximab*
Cycle 2 and Onwards		
encorafenib	300 mg	Orally once daily on **Days 1 to 28** Take with or without food. Swallow whole **(Self-administered at home)** **Alert:* *encorafenib dose may be adjusted pending evaluation of Day 15 blood work*
Days 1, 8, 15 and 22		
cetirizine	10 mg	Orally 30 minutes prior to cetuximab
dexamethasone	8 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medications before starting cetuximab		
cetuximab	250 mg/m^2	IV over 1 hour (administered undiluted) Doses greater than 600 mg must be infused over 2 hours *Use 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume on label* **Nursing Alert:* *IV tubing is primed with cetuximab*

All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See GAST DSG – Dose Banding document for more information

encorafenib (Braftovi®) available dosage strength: 75 mg capsule
Classification: Cytotoxic, Hazardous

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

REQUIRED MONITORING

Baseline

- EKG at baseline and as clinically indicated

All Cycles

Days 1 and 15

- CBC, serum creatinine, urea, electrolytes including magnesium and calcium, liver enzymes, glucose and albumin as per Physician Orders

Days 8 and 22

- No blood work required

All Doses (cetuximab)

- Clinical assessment for cetuximab-related skin toxicity

Doses 1 and 2 (cetuximab)

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline, after one hour observation and as clinically indicated
- Observe patient for 1 hour after cetuximab infusion. Full vital signs prior to discharge

Dose 3 and Onwards (cetuximab)

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- For patients with no prior reactions to cetuximab, no observation period is required. Patient can be discharged from treatment room if stable
- For patients who have had a previous reaction to cetuximab, observe patient for one hour after cetuximab infusion. Full vital signs prior to discharge

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
Sunscreen	Minimum SPF 15 (PABA free, zinc oxide or titanium dioxide preferred)	Apply topically a broad-spectrum sunscreen liberally 30 minutes before going outdoors. Reapply every 2 hours and after swimming
Moisturizing lotion	Fragrance-free	Apply topically to face, hands, feet, neck, back and chest daily in the morning on rising and ***as needed***
In the event of a cetuximab-induced skin rash:		
hydrocortisone cream	1%	Apply topically daily at bedtime to face, hands, feet, neck, back and chest as directed by clinic
doxycycline	100 mg	Orally twice daily as directed by clinic

DISCHARGE INSTRUCTIONS

- Warn patients of the possibility of a late onset reaction to cetuximab as reactions may occur several hours after infusion or with subsequent infusions
- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Instruct patient to report rash to clinic
- Instruct patient to use recommended support medications
- encorafenib has potential for significant drug-drug interactions. Patients should notify clinic prior to starting any new medication
- Avoid grapefruit and grapefruit juice
- Reinforce applicable safe handling precautions of medications, blood and body fluids while on encorafenib

ADDITIONAL INFORMATION

- cetuximab AND encorafenib can cause hypomagnesemia
- cetuximab can cause interstitial lung disease, pneumonitis and exacerbation of pre-existing fibrotic lung disease
- cetuximab can cause nail changes
- cetuximab AND encorafenib can cause dermatological changes including rash and hand and foot syndrome
- encorafenib has been associated with ocular toxicity
- Administration site restrictions are in place for cetuximab. Dose 1 of cetuximab should only be administered at CCMB MacCharles or Tache in Winnipeg