Regimen Reference Order – H&N – cetuximab + fluorouracil + CARBOplatin

ARIA: H&N – [cetuximab + fluorouracil + CARBO]

Planned Course: Every 21 days for 6 cycles
Indication for Use: Squamous Cell Cancer of Head and Neck; Advanced/Recurrent

CVAD: Required (Ambulatory Pump)

Proceed with treatment if:
Day 1 ONLY
ANC equal to or greater than 1.5 x 10^9/L AND Platelets equal to or greater than 100 x 10^9/L
- **Contact Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – H&N – cetuximab + fluorouracil + CARBOplatin

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
Day 1		
dexamethasone	12 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 non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume on label* **Nursing Alert:* *IV tubing is primed with cetuximab* **Nursing Alert:* *CARBOplatin infusion starts after observation period is complete*
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
CARBOplatin	AUC 5 mg/mL.min	IV in D5W 250 mL over 30 minutes

	maximum dose 750 mg (see table below)	
fluorouracil	4000 mg/m^2	IV in D5W continuously over 96 hours by ambulatory infusion device
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 non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume on label* **Nursing Alert:* *IV tubing is primed with cetuximab*
Day 15		
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-medication(s) 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 non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume on label* **Nursing Alert:* *IV tubing is primed with cetuximab*
Cycles 2 to 6		
Day 1		
cetirizine	10 mg	Orally 30 minutes prior to cetuximab
dexamethasone	12 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medication(s) 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 non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume on label* **Nursing Alert:* *IV tubing is primed with cetuximab*
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
CARBOplatin	AUC 5 mg/mL.min	IV in D5W 250 mL over 30 minutes

	maximum dose 750 mg (see table below)	
fluorouracil	4000 mg/m^2	IV in D5W continuously over 96 hours by ambulatory infusion device
Days 8 and 15		
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-medication(s) 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 non-DEHP bags and non-DEHP administration sets with 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 H&N DSG – 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 Doses

- Clinical assessment of cetuximab-related skin toxicity

All Cycles

Day 1

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

Days 8 and 15

- No blood work required

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 (before the start of chemotherapy for Dose 1)

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 after cetuximab administration. Patient can be discharged from treatment room if stable whether they had a reaction or not
- For patients who have had a previous reaction to cetuximab, observe patient for one hour after cetuximab infusion. Full vital signs after one-hour observation

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
aprepitant	80 mg	Orally once daily on Days 2 and 3
dexamethasone	8 mg	Orally once daily on Days 2 and 3
metoclopramide	10 – 20 mg	Orally every 4 hours as needed for nausea and vomiting
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:		
doxycycline	100 mg	Orally twice daily as directed by clinic
hydrocortisone cream	1%	Apply topically daily at bedtime to face, hands, feet, neck, back and chest as directed by clinic

DISCHARGE INSTRUCTIONS

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Warn patients of the possibility of a late onset reaction to cetuximab as reactions may occur several hours after infusion or with subsequent infusions
- Instruct patient to continue taking anti-emetic(s) at home and use Recommended Support Medications
- 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

ADDITIONAL INFORMATION

- cetuximab causes dermatological and nail changes
- cetuximab can cause hypomagnesemia
- cetuximab can cause interstitial lung disease, pneumonitis and exacerbation of pre-existing fibrotic lung disease
- Administration site restrictions are in place for cetuximab. Dose 1 of cetuximab should only be administered at CCMB MacCharles or Tache in Winnipeg
- CARBOplatin dose considerations:
    - CCMB Head and Neck DSG uses **actual body weight** to calculate GFR
    - CCMB Head and Neck DSG uses a maximum CARBOplatin dose of 750 mg for this regimen
    - If calculated CARBOplatin dose differs **more than 10%** from prescribed CARBOplatin dose, contact the prescriber

CARBOplatin Dosing Calculations per CCMB Head & Neck DSG

Calculation of CARBOplatin dose: (max. 750 mg)

Dose (mg) = target AUC (GFR + 25)

$$\text{GFR} = \frac{\text{N} \times (140 - \text{age in years}) \times \text{Actual Body Weight (kg)}}{\text{serum creatinine in umol/L}} = \_\_\_ \text{ mL/min}$$

N = 1.23 in males
N = 1.04 in females

$$\frac{\text{AUC (mg/mL.min)}}{5} \times \frac{\text{GFR + 25 (mL/min)}}{\_\_\_\_ + 25} = \text{Total Dose (mg)}$$

AUC= Area Under Curve

The estimated creatinine clearance is based on limited evidence. Sound clinical judgment and interpretation of the estimation are required, because the equation may not be appropriate for some patient populations (for example, acute renal failure).