Regimen Reference Order – GYNE – PORTEC

ARIA: GYNE - [PORTEC (Phase 1)]
GYNE - [PORTEC (Phase 2)]

Planned Course: **CISplatin every 21 days for 2 doses (with concurrent radiation) followed by PACLitaxel and CARBOplatin every 21 days for 4 cycles**

Indication for Use: **Endometrioid Endometrial Cancer; Stage III**

CVAD: At Provider's Discretion

Proceed with treatment if:

CISplatin:

- ***ANC equal to or greater than 1.5 x 10^9/L AND Platelets equal to or greater than 100 x 10^9/L***
- ***Creatinine clearance equal to or greater than 50 mL/minute***

PACLitaxel and CARBOplatin:

- ***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 – GYNE – PORTEC

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Phase 1 – CISplatin (Cycles 1 and 2)		
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	50 mg/m^2	IV in normal saline 500 mL over 1 hour **Alert: CISplatin infusion must be complete prior to mannitol administration*
mannitol	12.5 g	IV in normal saline 1000 mL over 2 hours (Post hydration)

Phase 2 starts 3 weeks after completion of radiotherapy		
Phase 2 – PACLitaxel and CARBOplatin (Cycles 3 to 6)		
cetirizine	20 mg	Orally 1 hour prior to PACLitaxel
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to PACLitaxel **Nursing Alert: PACLitaxel starts **1 hour after completion** of dexamethasone infusion*
Wait 1 hour after completion of IV pre-medication(s) before starting PACLitaxel		
PACLitaxel	175 mg/m^2	IV in normal saline 500 mL over 3 hours, following the administration rates below: • Administer at 100 mL/hour for 15 minutes, then • Administer remaining volume over 2 hours and 45 minutes *Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Nursing Alert: Gently invert bag 8 to 10 times immediately prior to administration of PACLitaxel to evenly distribute the drug*
CARBOplatin	AUC 5 to 6 mg/mL.min; maximum dose up to 900 mg (see table below)	IV in D5W 250 mL over 30 minutes
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

CISplatin (Phase 1)

All Cycles

- CBC, serum creatinine, urea, electrolytes, liver enzymes and albumin as per Physician Orders
- Baseline blood pressure prior to magnesium infusion and repeat 15 minutes after start of magnesium infusion

PACLitaxel and CARBOplatin (Phase 2)

All Cycles

- CBC, serum creatinine, urea, electrolytes, liver enzymes and albumin as per Physician Orders
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- No observation period is required after PACLitaxel 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
Phase 1 – CISplatin (Cycles 1 and 2)		
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
Phase 2 – PACLitaxel + CARBOplatin (Cycles 3 to 6)		
filgrastim (brand name specific) *(See Filgrastim Clinical Guide)*	5 mcg/kg (rounded to nearest 300 mcg or 480 mcg)	Subcutaneous once daily for 5 days to start on Day 3
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

DISCHARGE INSTRUCTIONS

All Phases

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Instruct patient to continue taking anti-emetic(s) at home. Patients should be instructed to not use OLANZapine and metoclopramide concurrently due to drug interactions
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

PACLitaxel + CARBOplatin (Phase 2)

- Ensure patient receives filgrastim supply if patient is self-administering at home

ADDITIONAL INFORMATION

- CISplatin and radiation should begin within 8 weeks from surgery
- Since CISplatin is given concurrently with radiation, site restrictions are in place for Phase 1
- CISplatin is ototoxic and nephrotoxic
- CISplatin can cause hypomagnesemia
- PACLitaxel may cause progressive, irreversible neuropathy
- CARBOplatin dose considerations:
  - CARBOplatin dose in the PORTEC trial was AUC 5 to 6
    - The ARIA regimen for PORTEC is built with an AUC of 5
    - At the discretion of the Gyne-oncologist, CARBOplatin dose may be increased to AUC 6
    - CCMB Gynecological DSG uses a maximum CARBOplatin dose of 900 mg for this regimen
  - CCMB Gynecological DSG uses **actual body weight** to calculate GFR
  - If calculated CARBOplatin dose differs **more than 10%** from prescribed CARBOplatin dose, contact the prescriber

CARBOplatin Dosing Calculations per CCMB Gynecological DSG

Calculation of CARBOplatin dose: (maximum 900 mg)

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

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

N = 1.04 in females

$$\frac{\text{AUC (mg/mL.min)}}{5 \text{ to } 6} \times \frac{\text{GFR + 25 (mL/min)}}{\_\_\_\_ + 25} = \text{Total Dose (mg)}$$

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 above may not be appropriate for some patient populations (for example, acute renal failure).