

## Regimen Reference Order

### BRST – BrightNess PACLitaxel + CARBOplatin followed by AC (Dose Dense)

ARIA: BRST – [BrightNess - CARBO + PACLitaxel]

BRST – [BrightNess - dose dense AC]

Planned Course: PACLitaxel (weekly) + CARBOplatin every 21 days for 4 cycles,  
followed by AC every 14 days for 4 cycles

Indication for Use: Breast Cancer Neo-Adjuvant; “Triple negative”

CVAD: Preferred (VESICANT INVOLVED)

#### Proceed with treatment if:

##### **Cycles 1 to 4 (PACLitaxel + CARBOplatin):**

- ANC equal to or greater than  $1 \times 10^9/L$  AND Platelets equal to or greater than  $100 \times 10^9/L$
- Bilirubin less than 1.25 times upper limit of normal
- AST/ALT less than 10 times upper limit of normal

##### **Cycles 5 to 8 (AC [Dose Dense]):**

- ANC equal to or greater than  $1 \times 10^9/L$  AND Platelets equal to or greater than  $100 \times 10^9/L$
  - Creatinine clearance greater than 10 mL/minute
  - Bilirubin less than upper limit of normal
  - AST/ALT less than 2 times upper limit of normal
- ❖ Contact Physician if parameters not met

## SEQUENCE OF MEDICATION ADMINISTRATION

### Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
<b>Cycles 5 to 8 – AC (Dose Dense)</b>		
Instruct patient to start vigorous oral pre-hydration (600-900 mL) the morning of cyclophosphamide treatment (Self-administered at home)		

### Treatment Regimen

#### BRST – BrightNess PACLitaxel + CARBOplatin followed by AC (Dose Dense)

Establish primary solution 500 mL of: normal saline		
Drug	Dose	CCMB Administration Guideline
<b>Cycles 1 to 4 – PACLitaxel + CARBOplatin every 21 days</b>		
<b>Day 1</b>		
famotidine	40 mg	Orally 1 hour prior to PACLitaxel
aprepitant	125 mg	Orally 1 hour pre-chemotherapy

cetirizine	10 mg	Orally 1 hour prior to PACLitaxel
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes
<b>Wait 30 minutes after completion of IV pre-medications before starting PACLitaxel</b>		
PACLitaxel	80 mg/m <sup>2</sup>	IV in normal saline 250 mL over 1 hour <i>Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter</i>
CARBOplatin	AUC 6 mg/mL.min; maximum dose 900 mg (see table below)	IV in D5W 250 mL over 30 minutes
<b>Days 8 and 15</b>		
famotidine	40 mg	Orally 1 hour prior to PACLitaxel
cetirizine	10 mg	Orally 1 hour prior to PACLitaxel
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes
<b>Wait 30 minutes after completion of IV pre-medications before starting PACLitaxel</b>		
PACLitaxel	80 mg/m <sup>2</sup>	IV in normal saline 250 mL over 1 hour <i>Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter</i>
<b>Cycle 5 starts 1 week after Cycle 4, Day 15 (PACLitaxel + CARBOplatin)</b>		
<b>Cycles 5 to 8 – AC (Dose Dense) every 14 days</b>		
<b>Day 1</b>		
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
DOXOrubicin	60 mg/m <sup>2</sup>	IV Push over 10 to 15 minutes
cyclophosphamide	600 mg/m <sup>2</sup>	IV in normal saline 250 mL over 1 hour

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

## REQUIRED MONITORING

### Cycles 1 to 4 (PACLitaxel + CARBOplatin)

#### Day 1

- CBC, biochemistry and liver enzymes as per Physician Orders
- 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 required after PACLitaxel administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

#### Days 8 and 15

- CBC
- 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 required after PACLitaxel administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

### Cycles 5 to 8 (AC [Dose Dense])

- CBC, biochemistry and liver enzymes as per Physician Orders
- Cardiac monitoring:
  - Left Ventricular Ejection Fraction (LVEF) monitoring is recommended at baseline; only repeated as clinically indicated

## Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
<b>Cycles 1 to 4 – PACLitaxel + CARBOplatin</b>		
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
<b>Cycles 5 to 8 – AC (Dose Dense)</b>		
pegfilgrastim (brand name specific) (See Filgrastim Clinical Guide)	6 mg	Subcutaneous once on Day 2 <i>*Alert: pegfilgrastim to be given as a single dose once per chemotherapy cycle no sooner than 24 hours after chemotherapy</i>
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

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## DISCHARGE INSTRUCTIONS

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### Cycles 1 to 4 (PACLitaxel + CARBOplatin)

- 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
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

### Cycles 5 to 8 (AC [Dose Dense])

- Instruct patient to:
    - Continue taking anti-emetic(s) at home. Patients should be instructed not to use OLANzapine and metoclopramide concurrently due to drug interactions
    - Maintain oral intake of 2000 mL (8 glasses) of fluid daily at home
    - Empty bladder every 2 hours while awake and at bedtime for 24 hours after each dose of cyclophosphamide
    - Obtain immediate assistance as per your clinic's contact instructions if:
      - Symptoms of hemorrhagic cystitis (e.g. dysuria, hematuria)
      - Unable to drink recommended amount of fluid
  - 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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- PACLitaxel may cause progressive, irreversible neuropathy
- Cumulative DOXOrubicin dose should be calculated and should not exceed 360 mg/m<sup>2</sup>. If exceeding 360 mg/m<sup>2</sup>, consideration to adding dexrazoxane should be given if patient is benefiting from DOXOrubicin therapy
- **Note:** Upon completion of 4 cycles of BRST – [BrighTNess - CARBO + PACLitaxel], patients should be started on BRST – [BrighTNess - dose dense AC] to complete 8 cycles
  - BRST – [BrighTNess - dose dense AC] should begin 7 days after Cycle 4, Day 15 of BRST – [BrighTNess - CARBO + PACLitaxel]
- **Note:** At Cycle 4 of each regimen, an entry called "*Physician Reminder – BRIGHTNESS protocol timing 1 Units Insert Miscellaneous once*" will appear in the electronic drug order. No action is required. **This prompt is to remind the prescriber to order the next regimen as part of the BrighTNess protocol**
- CARBOplatin dose considerations:
  - CCMB Breast DSG uses **actual body weight** to calculate GFR
  - CCMB Breast DSG uses a maximum CARBOplatin dose of 900 mg for this regimen
  - If calculated CARBOplatin dose differs **more than 10%** from prescribed CARBOplatin dose, contact the prescriber

<b>CARBOplatin Dosing Calculations per CCMB Breast DSG</b>										
<i>Calculation of CARBOplatin dose: (max. 900 mg)</i>										
Dose (mg) = target AUC (GFR + 25)										
$\text{GFR} = \frac{N \times (140 - \text{age in years}) \times \text{Actual Body Weight (kg)}}{\text{serum creatinine in } \mu\text{mol/L}} = \text{___ mL/min}$										
N = 1.23 in males N = 1.04 in females										
<table border="1" style="margin: auto; border-collapse: collapse;"> <tr> <td style="padding: 5px;">AUC (mg/mL.min)</td> </tr> <tr> <td style="border-top: 1px solid black; text-align: center; padding: 5px;">6</td> </tr> </table>	AUC (mg/mL.min)	6	X	<table border="1" style="margin: auto; border-collapse: collapse;"> <tr> <td style="padding: 5px;">GFR + 25 (mL/min)</td> </tr> <tr> <td style="border-top: 1px solid black; text-align: center; padding: 5px;">___ + 25</td> </tr> </table>	GFR + 25 (mL/min)	___ + 25	=	<table border="1" style="margin: auto; border-collapse: collapse;"> <tr> <td style="padding: 5px;">Total Dose (mg)</td> </tr> <tr> <td style="border-top: 1px solid black; height: 20px;"></td> </tr> </table>	Total Dose (mg)	
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6										
GFR + 25 (mL/min)										
___ + 25										
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)*