

## EC DOCETAXEL TRASTUZUMAB (Herceptin subcutaneous)

### INDICATION (ICD10) C50

1. Neoadjuvant breast cancer and adjuvant HER 2+ve node positive good performance status <= 65 years breast cancer. Consider use in >65 years only if extremely good performance status.

### REGIMEN

#### Cycles 1 to 3

Day 1 EPIRUBICIN 100mg/m<sup>2</sup> IV bolus  
CYCLOPHOSPHAMIDE 500mg/m<sup>2</sup> IV bolus

#### Cycles 4 to 6

Day 1 Premedication: Dexamethasone 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days  
DOCETAXEL 100mg/m<sup>2</sup> in 250ml\* sodium chloride 0.9% infusion over 1 hour  
\*\*TRASTUZUMAB 600mg SC over 5 minutes  
\* doses 200mg to 360mg in 500ml sodium chloride 0.9%

#### Cycles 7 to 21

Day 1 \*\*TRASTUZUMAB 600mg SC over 5 minutes

\*\*For patients unable to receive SC trastuzumab see the trastuzumab monotherapy regimen for IV trastuzumab doses, observation times etc.

Trastuzumab - observation time post injection 30 minutes after the first injection and for 15 minutes after subsequent injections.

### CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days for 6 cycles

Trastuzumab monotherapy every 21 days from cycle 7 up to cycle 21

### ANTI-EMETICS

High risk day 1 cycles 1 to 3

Low risk day 1 cycles 4 to 6

Minimal risk day 1 cycles 7 to 21

### CONCURRENT MEDICATION REQUIRED

Docetaxel	Ensure premedication given before docetaxel. This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. Loperamide prn every docetaxel cycle
Trastuzumab	Infusion related chills and/or fevers – treat with paracetamol and chlorphenamine.
GCSF	GCSF for 7 days starting at least 24 hours after chemotherapy

### EXTRAVASATION AND TYPE OF LINE / FILTERS

Cyclophosphamide – neutral

Docetaxel – exfoliant

Epirubicin – vesicant

Filter not required

Central (or peripheral) line

## INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs every cycle

Neutrophils x 10<sup>9</sup>/L ≥1.0 (0.8-1.0 on the day of chemo go ahead with GCSF support as per local policy).

Platelets x 10<sup>9</sup>/L ≥100

ECHO baseline monitor cardiac function according to network guidelines

Baseline weight and every cycle

## MAIN TOXICITIES AND ADVERSE REACTIONS

Cyclophosphamide	may irritate bladder, drink copious volumes of water.
Epirubicin	Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Docetaxel	Cutaneous reactions, peripheral neuropathy or fluid retention, hypersensitivity reactions
Trastuzumab	Cardiotoxicity - monitor cardiac function. Trastuzumab infusion related chills and/or fevers are commonly observed during the first infusion (but infrequently with subsequent infusions). Other symptoms may include nausea, hypertension, vomiting, pain, rigors, headache, cough, dizziness, rash, and asthenia. Some adverse reactions to trastuzumab infusion including dyspnoea, hypotension, wheezing, bronchospasm, supraventricular tachyarrhythmia, reduced oxygen saturation and respiratory distress can be serious and potentially fatal. If symptoms of back ache, nausea or vomiting, do a set of obs. Give hydrocortisone 100mg IV, chlorphenamine 10mg IV.

## INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Cyclophosphamide	Cytochrome P450 enzyme inducers (e.g. rifampicin, carbamazepine, phenytoin, St Johns Wort, corticosteroids): may increase active cyclophosphamide metabolites. Allopurinol, Cimetidine and protease inhibitors: may increase active metabolites. Aprepitant, Ciprofloxacin, Fluconazole, Itraconazole: may reduce activation of cyclophosphamide and alter the effectiveness of treatment. Grapefruit juice: decreased or delayed activation of cyclophosphamide. Patients should be advised to avoid grapefruit juice for 48 hours before and on day of cyclophosphamide dose.
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## DOSE MODIFICATIONS

Epirubicin maximum lifetime dose

= 650mg/m<sup>2</sup> (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

= 1000mg/m<sup>2</sup> (with normal cardiac function)

## Haematological

Previous neutropenic sepsis, Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant

### Non-haematological

#### Docetaxel

Discuss dose reductions if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

#### Trastuzumab

No dose reduction or cessation of Trastuzumab is required if patient has acute reversible neutropenia.

### Hepatic impairment:

#### Docetaxel

ALT and/or AST >1.5xULN and ALP >2.5xULN	recommended SPC dose for 100mg/m <sup>2</sup> is give 75mg/m <sup>2</sup>
Bilirubin >ULN and ALT and AST >3.5xULN with ALP >6xULN	should not be used unless strictly indicated.

#### Epirubicin

Bilirubin 24-51micromol/L	give 50% dose
Bilirubin 52-85micromol/L or AST >4xULN	give 25% dose
Bilirubin >86micromol/L or Child Pugh C	not recommended

### Renal impairment

#### Cyclophosphamide

CrCl 10-29ml/min	Consider giving 75% dose
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### REFERENCES

1. Effects of Chemotherapy and hormonal therapy for early breast cancer on recurrence and 15 year survival: an overview of the randomised trials. EBCTG. Lancet 2005; 365: 1687–1717
2. Martin, M et al; NEJM (2005); 352 (22): 2302–2313
3. Roche, H et al; JCO (2006); 24 (36) (PACS 01 trial)
4. Del Maestro, L et al; Lancet 2015; 385: 1863 – 1872 (no benefit for 5FU)