ECarboX – Epirubicin, Carboplatin and Capecitabine

NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Drug	Daily Dose	Route	Diluent & Rate
Day 1	Glucose 5%	500ml	Infusion	Fast Running / Line Flush
	Dexamethasone	8mg	Oral	
	Ondansetron	8mg	Oral /Slow bolus/15 min infusion	
	Epirubicin	**50 mg/m^2**	IV Bolus	
	Carboplatin	**AUC 3 to 5***	IV Infusion	500/250ml 5% Glucose over 30 to 60 Minutes
1 to 21	**Capecitabine**	**625mg/m^2 TWICE Daily**	Oral	N/A

*Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.

DOSE FORM
Capecitabine is supplied as 150mg and 500mg tablets.

***CARBOPLATIN DOSAGE**
Dose (mg) = AUC x (GFR + 25) standard dose is AUC=5 but this can be reduced depending on patients performance status

Where the GFR is the non-corrected EDTA clearance.
If estimated GFR is undertaken the Wright formula should be used with AUC 5. Avoid use of Cockcroft & Gault formulae as it is less accurate.

CYCLE LENGTH AND NUMBER OF DAYS
21 DAYS usually for 6-8 cycles

APPROVED INDICATIONS
Upper GI cancers including metastatic oesophago-gastric cancers

ELIGIBILITY CRITERIA
ECOG performance status 0-1, Karnofsky performance status >70% Adequate hepatic, renal, marrow and cardiac function

EXCLUSION CRITERIA
Inability to swallow Capecitabine tablets

PREMEDICATION
As above

RECOMMENDED TAKE HOME MEDICATION
Ondansetron 8mg twice daily for 2 to 3 days
Dexamethasone 4mg twice daily for 1 to 3 days
Metoclopramide 10 mg three times daily as required
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED
FBC, U&Es and LFTs. Check renal function before commencing platinum.
Use EDTA or Wright formulae to calculate GFR

Prior to each cycle
FBC, U&Es, LFTs as required; GFR doubled checked using Wright formulae

ASSESSMENT OF RESPONSE
Metastatic: Tumour size and patient symptomatic response

REVIEW BY CLINICIAN
To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW
On cycles where not seen by clinician.

ADMINISTRATION NOTES

- Carboplatin is frequently substituted for cisplatin in chemotherapy protocols due to greater tolerability. However, in certain tumour groups, including oesophageal carcinoma, evidence from early trials suggested carboplatin is less active.
- Evidence from a published case series (Price et al 2002) suggests that the substitution of carboplatin 'does not appear to be deleterious in the palliative treatment of advanced oesophageal carcinoma.'
- ECarboF and ECarboX may be used instead of ECF and ECX respectively however it must be noted there is more evidence of benefit for the EOX combination.
- Patient needs Glomerular Filtration Rate (GFR) prior to commencement of treatment for calculation of Carboplatin dosage. Subsequent measurement of GFR only needed if serum creatinine changes by >20% from initial measurement.

Counselling Points for Oral Capecitabine
How to take: Take tablets 12 hours apart, within 30 minutes after the end of meal (i.e. breakfast & evening meal.) Swallow whole with water

Side effects Common side effects to discuss with patient include; diarrhoea, nausea & vomiting, stomatitis (mouth ulcers), hand-foot syndrome (painful red swelling in hands and feet), fever or infection. If patients notice any of these advise them to stop taking treatment, contact doctor/chemotherapy day unit who will take steps to manage side effects and advise on continuing treatment.

Missed dose: If remember half an hour after they should have taken their tablets, then take the missed dose, otherwise only take the regular dose at next scheduled time. Do not double-up doses to make up for the missed doses or take extra doses at the end of the treatment cycle.

Post dose vomiting: In the case of vomiting within a few hours after drug intake, never repeat the administration of the dose.

Storage/ Disposal Tablets should be stored in cool dry place less than 30°C. Unused medicines must be returned to hospital pharmacy for disposal

Diarrhoea is common and may require intervention with fluids and electrolytes if severe. If diarrhoea is a problem, give loperamide 2 to 4 mg four times daily as required or codeine phosphate 30mg four times daily and stop taking Capecitabine if diarrhoea moderate/severe.

EXTRAVASATION *See NCA/ Local Policy*
Epirubicin is a vesicant drug. If extravasation occurs there is high risk of tissue damage

TOXICITIES

- Risk of hypersensitivity and anaphylaxis, particularly on first and second cycle, start within a few minutes of administration
- Palmar/Plantar Erythrodysesthesia - Can be severe, patients must be forewarned
- Nausea and vomiting
- Cardiotoxicity. Maximum cumulative dose of epirubicin 900 mg/m^2.
- Hypotension and bradycardia
- Myelosuppression, particularly, thrombocytopenia, anaemia & neutropenia
- Nephrotoxicity
- Alopecia
- Peripheral neuropathy
- Otological impairment, especially at 8000 Hz
- Myalgia
- Back pain on administration
- Diarrhoea
- Stomatitis
- Hyperpigmentation
- Red urine for up to 24 hours with epirubicin

DOSE MODIFICATION / TREATMENT DELAYS

Haematological toxicity:

ANC	PLT	Adjustment
≥ 1.5	≥ 100	Full dose
1.0 – 1.5	75 – 100	Delay Carboplatin and Epirubicin until recovery. If patient well capecitabine can continue. Restart Carboplatin, Epirubicin at full dose unless delay > 1 week
0.5 – 1.0	50 – 75	Interrupt Capecitabine, delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 25% dose reduction
< 0.5	< 25	Interrupt Capecitabine and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 50% dose reduction

Non-Haematological Toxicity for Oral Capecitabine

Any patient with CTC toxicity should be prescribed the therapeutic option for grade 1 toxicity in addition to dose modification.

Table of dose adjustments according to Common Toxicity Criteria (CTC)

	Grade 2	Grade 3	Grade 4
1st appearance	Interrupt until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible	Interrupt until resolved to grade 0/1, then continue at 75% of original dose with prophylaxis where possible	**Discontinue treatment**
2nd appearance	Interrupt until resolved to grade 0/1, then continue at 75% of original dose	Interrupt until resolved to grade0/1, then continue at 50% of original dose	
3rd appearance	Interrupt until resolved to grade 0/1, then continue at 50% of original dose	**Discontinue treatment**	
4th appearance	**Discontinue treatment**		

Table of hand/ foot toxicity grading for capecitabine only

Grade	Clinical	Functional
1	Numbness, dysesthesia/paraesthesia,	Discomfort but no interruption of normal activities
2	Painful erythema with swelling	Discomfort which affects activities of daily living
3	Moist desquamation, ulceration, blistering, severe pain	Severe discomfort, unable to work or perform activities of daily living

Table of Diarrhoea toxicity grading for capecitabine only

CTC Grade	Toxicity	% Capecitabine
1	Diarrhoea (watery stool 2-3 times/day)	Hold until recovery, then resume at 100% dose for remainder of course
2	Diarrhoea (watery stool 4-6 times/day)	Hold until recovery, then resume at 75% dose for remainder of course
3/4	Diarrhoea (watery stool >7 times/day	Following grade 3 or 4 diarrhoea, subsequent doses of capecitabine should be decreased or treatment discontinued permanently (grade 4).

Renal dysfunction:

Capecitabine

- Capecitabine is renally excreted; therefore, patients with moderate renal impairment (CrCl < 50ml/min) require a 25% dose reduction.
- Contra-indicated in severe renal failure (CrCl < 30ml/min) (Wright equation or measured GFR)

Carboplatin

- Serum creatinine should be checked before each cycle of treatment. If there is a >20% increase compared to the baseline, then the EDTA must be repeated.
- If Wright formulae calculated clearance alters by > 20%, an EDTA clearance should be repeated and dose modification of the chemotherapy may be required, discuss with Oncologist
- If the GFR is 30 ml/min or less DO NOT GIVE and consult with prescriber before proceeding

Hepatic dysfunction:

- If bilirubin > 30µmol/L, then epirubicin should be omitted.
- No studies have been performed to examine safety of capecitabine in severe hepatic dysfunction.
- IF ALT >= 5ULN or ALP >= 5ULN, DO NOT GIVE and and consult with prescriber before proceeding

Infection

- Grade III infection associated with neutropenia requires a dose reduction of epirubicin by 25%
- Grade IV infection associated with neutropenia requires a dose reduction of epirubicin by 50%

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

REFERENCES:

1. Cunningham D et al. Capecitabine and Oxaliplatin for Advanced Esophagogastric Cancer. NEJM 2008 358;1:36-46.
2. Tim Price, Mark Hill, Andrew Norman, Kate Sumpter, David Cunningham (2002) The Royal Marsden Experience of the Use of Carboplatin in Oesophageal Carcinoma Gastrointestinal Oncology, Volume 4, Number 1 / 2002 p 23 – 26

Document Control

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Summary of Changes	1.1	Reformatted from old NCN/CCA versions	
	1.2	Protocol reviewed. Typing errors corrected. Cumulative dose of Epirubicin amended.	
	1.3	Protocol reviewed and reissued, Antiemetic advice updated	
	1.4	Updated with Chemocare parameters, updated capecitabine advice.	