E Carbo F – Epirubicin, Carboplatin and 5-fluorouracil

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
Weekly	**5-Fluorouracil**	**200 mg/m^2/day**	Continuous IV Infusion	Variable depending on rate

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

***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

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.

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	CTC grade	Adjustment
≥ 2.0	0	Full dose
1.5 – 1.9	1	Full dose
1.0 – 1.4	2	Continue 5FU and delay Carboplatin and Epirubicin until recovery. Restart Carboplatin and Epirubicin at full dose unless delay
0.5 – 0.9	3	Stop 5FU infusion, and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 25% dose reduction

< 0.5	4	Stop 5FU and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 50% dose reduction

Thrombocytopenia

Platelets	CTC Grade	Adjustment
100	0	Full dose
75 -99	1	Continue 5FU full dose and delay Carboplatin and Epirubicin until recovery. Restart Carboplatin and Epirubicin at full dose unless delay >1 week
50 - 74	2	Stop 5FU and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 25% reduction and full dose 5FU
25 - 49	3	Stop 5FU and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 50% reduction and full dose 5FU
< 25	4	Stop 5FU and delay Carboplatin and Epirubicin until recovery. Omit Epirubicin from subsequent cycles

Non- Haematological toxicity: 5FU

	Grade I	Grade II	Grade III	Grade IV
Stomatitis	Consider mouthwashes such as *Difflam*® (benzydamine 0.15%)	Stop chemo, restart at 150mg/m^2/day on recovery	Stop chemo until recovered. Restart at 100mg/m^2/day.	Stop chemo until recovered. Restart at 50mg/m^2/day.
PPE (hand-foot syndrome)	Commence emollient as per local formulary	Stop chemo, until recovered. Restart at 150mg/m^2/day	Stop chemo until recovered. Restart at 100mg/m^2/day.	Stop chemo until recovered. Restart at 50mg/m^2/day.
Diarrhoea	Loperamide 4mg initially, then 2mg after each motion	Stop chemo, until recovered. Restart at 150mg/m^2/day	Stop chemo until recovered. Restart at 100mg/m^2/day.	Stop chemo until recovered. Restart at 50mg/m^2/day.

Any patient with > grade I toxicity should be prescribed the therapeutic option for grade I toxicity in addition to 5FU dose modification.

Renal dysfunction:

- 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 carboplatin may be required, discuss with Oncologist
- If the GFR is 30ml/min or less DO NOT GIVE and consult with prescriber before proceeding

Hepatic dysfunction: Epirubicin

- If bilirubin <24 µmol/l then epirubicin should be omitted
- IF ALT >= 5ULN or ALP >= 5ULN, DO NOT GIVE and consult with prescriber before proceeding

- **Infection Epirubicin**
- 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. Highley MS, Parnis FX, Trotter GA et al. (1994) Combination chemotherapy with epirubicin, cisplatin and 5-fluorouracil for the palliation of advanced gastric and oesophageal adenocarcinoma. Br J Surgery. **81**: 1763-5
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 Epirubicin amended	
	1.3	Protocol reviewed critical tests added, , Antiemetic advice updated	