**E Carbo F – Epirubicin, Carboplatin and 5-fluorouracil**

**DRUG ADMINISTRATION SCHEDULE**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Glucose 5%</td>
<td>500ml</td>
<td>Infusion</td>
<td>Fast Running / Line Flush</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>8mg</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ondansetron</td>
<td>8mg</td>
<td>Oral /Slow bolus/15 min infusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epirubicin</td>
<td>50 mg/m²</td>
<td>IV Bolus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Carboplatin</td>
<td>AUC 3 to 5*</td>
<td>IV Infusion</td>
<td>500/250ml 5% Glucose over 30 to 60 Minutes</td>
</tr>
<tr>
<td>Weekly</td>
<td>5-Fluorouracil</td>
<td>200 mg/m²/day</td>
<td>Continuous IV Infusion</td>
<td>Variable depending on rate</td>
</tr>
</tbody>
</table>

*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/m².
- 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**

<table>
<thead>
<tr>
<th>ANC</th>
<th>CTC grade</th>
<th>Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2.0</td>
<td>0</td>
<td>Full dose</td>
</tr>
<tr>
<td>1.5 – 1.9</td>
<td>1</td>
<td>Full dose</td>
</tr>
<tr>
<td>1.0 – 1.4</td>
<td>2</td>
<td>Continue 5FU and delay Carboplatin and Epirubicin until recovery. Restart Carboplatin and Epirubicin at full dose unless delay</td>
</tr>
<tr>
<td>0.5 – 0.9</td>
<td>3</td>
<td>Stop 5FU infusion, and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 25% dose reduction</td>
</tr>
</tbody>
</table>
### E Carbo F – Epirubicin, Carboplatin and 5-fluourouracil

<table>
<thead>
<tr>
<th>Platelets</th>
<th>CTC Grade</th>
<th>Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5</td>
<td>4</td>
<td>Stop 5FU and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 50% dose reduction</td>
</tr>
</tbody>
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#### Thrombocytopenia

<table>
<thead>
<tr>
<th>Platelets</th>
<th>CTC Grade</th>
<th>Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>0</td>
<td>Full dose</td>
</tr>
<tr>
<td>75 - 99</td>
<td>1</td>
<td>Continue 5FU full dose and delay Carboplatin and Epirubicin until recovery. Restart Carboplatin and Epirubicin at full dose unless delay &gt;1 week</td>
</tr>
<tr>
<td>50 - 74</td>
<td>2</td>
<td>Stop 5FU and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 25% reduction and full dose 5FU</td>
</tr>
<tr>
<td>25 - 49</td>
<td>3</td>
<td>Stop 5FU and delay Carboplatin and Epirubicin until recovery. Restart Epirubicin with 50% reduction and full dose 5FU</td>
</tr>
<tr>
<td>&lt; 25</td>
<td>4</td>
<td>Stop 5FU and delay Carboplatin and Epirubicin until recovery. Omit Epirubicin from subsequent cycles</td>
</tr>
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#### Non-Haematological toxicity: 5FU

<table>
<thead>
<tr>
<th>Stomatitis</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider mouthwashes such as Difflam® (benzydamine 0.15%)</td>
<td>Stop chemo, restart at 150mg/m²/day on recovery</td>
<td>Stop chemo until recovered. Restart at 100mg/m²/day.</td>
<td>Stop chemo until recovered. Restart at 50mg/m²/day.</td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>PPE (hand-foot syndrome)</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commence emollient as per local formulary</td>
<td>Stop chemo, until recovered. Restart at 150mg/m²/day</td>
<td>Stop chemo until recovered. Restart at 100mg/m²/day.</td>
<td>Stop chemo until recovered. Restart at 50mg/m²/day.</td>
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<table>
<thead>
<tr>
<th>Diarrhoea</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loperamide 4mg initially, then 2mg after each motion</td>
<td>Stop chemo, until recovered. Restart at 150mg/m²/day</td>
<td>Stop chemo until recovered. Restart at 100mg/m²/day.</td>
<td>Stop chemo until recovered. Restart at 50mg/m²/day.</td>
<td></td>
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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.
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- 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:

Document Control

<table>
<thead>
<tr>
<th>Document Title:</th>
<th>ECarboF CNTW protocol CRP09 UGI005</th>
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<tr>
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<tr>
<td>Current Version:</td>
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<tr>
<td>Reviewer(s):</td>
<td>Chris Beck – Chemo Pharmacist NCA</td>
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<tr>
<td>Date Approved:</td>
<td>09.03.2018</td>
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<tr>
<td>Approved by:</td>
<td>Steve Williamson Consultant Pharmacist Northern Cancer Alliance</td>
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<tr>
<td>Due for Review:</td>
<td>09.03.2021</td>
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<tr>
<td>Summary of Changes:</td>
<td>1.1 Reformatted from old NCN/CCA versions</td>
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<tr>
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<td>1.2 Protocol reviewed. Typing errors corrected. Cumulative dose Epirubicin amended</td>
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<tr>
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<td>1.3 Protocol reviewed critical tests added, Antiemetic advice updated</td>
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