

## Chemotherapy Protocol

### GASTROINTESTINAL (UPPER) CANCER

#### CISPLATIN, EPIRUBICIN and FLUOROURACIL

#### (ECF)

#### Regimen

- Gastrointestinal Cancer (upper) – Cisplatin-Epirubicin-Fluorouracil (ECF)

#### Indication

- First line therapy of advanced / metastatic eosophagogastric cancer
- Neoadjuvant therapy of potentially operable eosophagogastric cancer
- WHO performance status 0, 1, 2

#### Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Epirubicin	Cardiac failure, urinary discolouration
Fluorouracil	Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

#### Monitoring

#### *Regimen*

- Ensure adequate cardiac function before starting therapy. Baseline LVEF should be measured, particularly in patients with a history of cardiac problems or in the elderly.
- FBC, LFT's and U&E's prior to each cycle
- Patients with complete or partial dihydropyrimidine dehydrogenase (DPD) deficiency are at increased risk of severe and fatal toxicity during treatment with fluorouracil. All patients should be tested for DPD deficiency before initiation (cycle 1) to minimise the risk of these reactions

#### Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule

for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

### Haematological

Prior to prescribing the first cycle following criteria must be met.

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

Consider blood transfusion or the prescription of an erythropoietin produce according to NICE TA 323 if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Neutrophils ( $\times 10^9/L$ )	Adjustment
1 or above	Full dose
0.5-0.9	Stop the fluorouracil and delay until recovery. Delay the cisplatin and epirubicin until recovery. Re-start the cisplatin at the last dose and reduce the epirubicin to $37.5\text{mg}/\text{m}^2$
less than 0.5	Stop the fluorouracil and delay the cisplatin and epirubicin until recovery. Restart the cisplatin at the last dose and reduce the epirubicin to $25\text{mg}/\text{m}^2$ .

Platelets ( $\times 10^9/L$ )	Adjustment
100	Full dose
75-99	Continue fluorouracil at the full dose and delay the cisplatin and epirubicin until the counts have recovered. Restart the cisplatin and epirubicin at the full dose unless the delay was greater than seven days.
50-74	Stop the fluorouracil and delay the cisplatin and epirubicin until recovery. Restart the cisplatin at the last dose and the epirubicin at $37.5\text{mg}/\text{m}^2$
25-49	Stop the fluorouracil and delay the cisplatin and epirubicin until recovery. Restart the cisplatin at the last dose and the epirubicin at $25\text{mg}/\text{m}^2$
less than 25	Stop all three agents until counts have recovered. Omit the epirubicin from subsequent cycles.

Dose reductions should apply to all future cycles.

### Hepatic Impairment

Drug	Dose (% of original dose)
Cisplatin	No dose reduction necessary
Epirubicin	If the bilirubin concentration is between 24-51umol/L reduce the dose by 50%. If the bilirubin concentration is more than 51 then administer 25% of the dose
Fluorouracil	In moderate hepatic impairment reduce the initial dose by 33%. In severe hepatic impairment reduce the initial dose by 50%. The dose may be increased as tolerated.  Fluorouracil is contra-indicated when the bilirubin is more than 85 or the AST/ALT are more than 180units

### Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	more than 60	100
	45-59	75
	less than 45	Consider alternative
Epirubicin	Reduce doses in cases of severe impairment	
Fluorouracil	Consider dose adjustment in severe renal impairment	

### Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes. Dose limiting toxicities include diarrhoea, abdominal pain, emesis, stomatitis and palmar-plantar erythrodysesthesia among others.

#### Cisplatin

Neurotoxicity occurring at a NCI-CTC grade 2 or above or a new functional deterioration in hearing and / or tinnitus should be approached by substituting the cisplatin for carboplatin AUC5.

## Fluorouracil

	Grade 1	Grade 2	Grade 3	Grade 4
<b>Stomatitis</b>	Consider mouthwashes	Stop fluorouracil and restart with a 50mg/m <sup>2</sup> dose reduction	Stop fluorouracil until recovered and restart with a 100mg/m <sup>2</sup> dose reduction	Stop fluorouracil until recovered and restart with a 150mg/m <sup>2</sup> dose reduction
<b>Palmer-plantar</b>	Consider topical emollients	Stop fluorouracil and restart with a 50mg/m <sup>2</sup> dose reduction	Stop fluorouracil until recovered and restart with a 100mg/m <sup>2</sup> dose reduction	Stop fluorouracil until recovered and restart with a 150mg/m <sup>2</sup> dose reduction
<b>Diarrhoea</b>	Consider anti-diarrheal	Stop fluorouracil until recovered and restart with a 50mg/m <sup>2</sup> dose reduction	Stop fluorouracil until recovered and restart with a 100mg/m <sup>2</sup> dose reduction	Stop fluorouracil until recovered and restart with a 150mg/m <sup>2</sup> dose reduction

## [Regimen](#)

### 21 day cycle for 8 cycles

Drug	Dose	Days	Route
Cisplatin	60mg/m <sup>2</sup>	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin per minute (minimum 120 minutes)
Epirubicin	50mg/m <sup>2</sup>	1	Intravenous bolus over 10 minutes
Fluorouracil	1400mg/m <sup>2</sup> over 7 days	1, 8, 15	Continuous intravenous infusion

## [Dose Information](#)

- Cisplatin will be dose banded in accordance with the national dose bands (1mg/ml)
- Epirubicin will be dose banded in accordance with the national dose bands (2mg/ml PM)

- Fluorouracil will be dose banded in accordance with the national dose bands (50mg/ml)

### Administration Information

#### *Extravasation*

- Cisplatin - exfoliant
- Epirubicin – vesicant
- Fluorouracil – inflammitant

#### *Other*

- Central venous access and use of an ambulatory infusion pump is required.

### Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy

- dexamethasone 8mg oral or intravenous
- ondansetron 8mg oral or intravenous

As take home medication;

- dexamethasone 4mg twice a day for 3 days oral
- metoclopramide 10mg three times a day when required
- ondansetron 8mg twice a day for 3 days oral

- Cisplatin pre and post hydration as follows;

Pre

Furosemide 40mg oral or intravenous

1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Post

1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- Oral loperamide 4mg after the first loose stool then 2-4mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours).
- Mouthwashes as per national or local guidelines for the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H<sub>2</sub> antagonist may be considered in patients considered at high risk of GI ulceration or bleed

#### Additional Information

- The folinic acid may be replaced with calcium levofolinate 175mg intravenous infusion in 250ml glucose 5% over 120 minutes

#### References

1. Cunningham D, Starling N, Rao S et al. Capecitabine and Oxaliplatin for Advanced Esophagogastric Cancer. N Engl J Med 2008; 358 (1): 36-46.

## REGIMEN SUMMARY

### CISPLATIN-EPIRUBICIN-FLUOROURACIL (ECF)

#### Day One

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Furosemide 40mg oral or intravenous
4. Epirubicin 50mg/m<sup>2</sup> intravenous bolus over 10 minutes
5. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
6. Cisplatin 60mg/m<sup>2</sup> intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 120 minutes)
7. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes
8. Fluorouracil 1400mg/m<sup>2</sup> (total dose) continuous infusion in an ambulatory pump over 7 days

#### Day Eight

9. Fluorouracil 1400mg/m<sup>2</sup> (total dose) continuous infusion in an ambulatory pump over 7 days

#### Day Fifteen

10. Fluorouracil 1400mg/m<sup>2</sup> (total dose) continuous infusion in an ambulatory pump over 7 days

#### Take Home Medicines (Day One Only)

9. Dexamethasone 4mg twice a day oral for 3 days starting on day 2 of the cycle
10. Metoclopramide 10mg three times a day when required oral
11. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day 1 of the cycle

## DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Nov 2020	Updated monitoring with DPD testing Dose banding updated Coding removed	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	June 2015	None	Dr Deborah Wright Pharmacist	Dr T Iveson Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust  
 NHS Isle of Wight  
 Portsmouth Hospitals NHS Trust  
 Salisbury NHS Foundation Trust  
 University Hospital Southampton NHS Foundation Trust  
 Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.