ECF

For locally advanced (inoperable) or metastatic oesophageal or gastric cancer;
peri-operative use in oesophageal or gastric cancer; adenocarcinoma of unknown primary

Drugs/Dosage:	Epirubicin	50mg/m^2	IV	D1
	Cisplatin	60mg/m^2	IV	D1
	5-Fluorouracil	200mg/m^2/24hrs	IV continuous	D1 – D21

Administration: Epirubicin via fast running infusion of 0.9% Sodium Chloride
5FU continuous IV via central venous catheter & ambulatory infusion device

Cisplatin: 1 litre 0.9% Sodium Chloride + 20mmol KCl + 10mmol $MgSO_4$ IV over 2 hours
Mannitol 20% 100ml IV over 15 minutes
Cisplatin in 1 litre 0.9% Sodium Chloride IV over 2 hours
1 litre 0.9% Sodium Chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hrs
500ml 0.9% Sodium Chloride IV **or** 500ml - 1 litre water orally over 1 hour

Frequency: 3 weekly cycle
Advanced / metastatic use: up to 6 cycles. All patients for full clinical review after 3 cycles – for locally advanced cases with no other assessable disease, a restaging OGD to assess mucosal response is required after Cycle 3.
Perioperative use: 3 cycles before surgery, plus a further 3 cycles post surgery

Main Toxicities: myelosuppression; alopecia; diarrhoea; mucositis; nephrotoxicity; neuropathy / ototoxicity; palmar-plantar erythema (PPE); cardiomyopathy; coronary artery spasm (see Comments); ovarian failure/infertility

Anti-emetics: highly emetogenic

Extravasation: Epirubicin is a vesicant

Regular Investigations:	FBC	D1
	LFTs & U&Es	D1
	Mg^{2+} and Ca^{2+}	D1
	EDTA	Prior to 1st cycle
	MUGA scan	see Comments
	Restaging	after Cycle 3 as indicated (see Frequency)

Comments: Maximum cumulative dose Epirubicin = 950mg/m^2
A baseline MUGA scan should be performed where the patient is considered at risk of having significantly impaired cardiac contractility. If ejection fraction is less than 50%, an alternative regimen should be given. MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment.

For patients on Cycle 1 whose EDTA is not yet available, Cockcroft & Gault may be used to predict GFR. Cisplatin dose should be adjusted if necessary once EDTA available. EDTA should only be repeated if the result is borderline at the start of treatment or if there is a 30% change in serum creatinine.

Check electrolytes – additional supplementation of magnesium, calcium or potassium may be required.

Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hr must be maintained throughout treatment, and cisplatin infusion should not be commenced unless this urine output is achieved. If the urine output is inadequate, the patient should be assessed and

urine output increased by administering 500ml Sodium Chloride 0.9% IV +/- furosemide 20 - 40mg. Furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload. The patient should be asked to drink 2 litres of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Coronary artery spasm is a recognised complication of 5FU although the evidence base regarding aetiology, management and prognosis is not particularly strong. Coronary artery spasm is more common in patients receiving continuous infusions of 5FU, and is usually reversible on discontinuing the infusion. Should a patient receiving 5FU present with chest pains, stop the 5FU. Standard investigation and treatment of angina may be required. If re-challenge is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the 5FU should be withdrawn permanently (COIN Guidelines Oct 2000). Refer to Consultant to discuss.

Dose Modifications

Haematological Toxicity:

WBC < 3.0 x 10^9/l or Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l	Delay epirubicin and cisplatin for 1 week. Continue with 5FU only if neutrophils ≥ 1.0 x 10^9/l and platelets ≥ 75 x 10^9/l. After one week repeat FBC and, if normal, resume treatment at full dose. If there is a 2 week delay, give all drugs at 75% dose. If > 2 week delay, give all drugs at 50% dose.

Renal Impairment: NB Cisplatin is both eliminated primarily (>90%) in the urine and is itself nephrotoxic

GFR (ml/min)	Cisplatin Dose
> 60	100%
50 – 60	75%
40 – 50	50%
< 40	CI (consider ECarboF)

Hepatic Impairment:

Bilirubin (µmol/l)	Epirubicin Dose
24 - 51	Give 50% dose
52 - 85	Give 25% dose
> 85	Omit

Moderate hepatic impairment	Reduce initial 5FU dose by 1/3
Severe hepatic impairment	Reduce initial 5FU dose by 1/2

Increase dose if no toxicity. If in doubt, check with relevant consultant.

5FU-Related Non-Haematological Toxicities:

This includes diarrhoea, mucositis and palmar/plantar erythema.
Patients with any grade PPE should receive Pyridoxine 50mg po tds throughout remainder of treatment. Standard anti-diarrhoeal drugs and mouthwashes should be used for symptomatic control.
For Grade 2 and above toxicities, PVI 5FU should be discontinued until healing has occurred, and then recommenced with dose reduction according to toxicity grading:
Patient experienced Grade 2 toxicity: Reduce 5FU dose by 50mg/m^2
Patient experienced Grade 3 toxicity: Reduce 5FU dose by 100mg/m^2
Patient experienced Grade 4 toxicity: Reduce 5FU dose by 150mg/m^2, **only after discussion with Consultant**
Once dose reduction has been made, all subsequent treatment should remain at reduced dose.

Neuropathy: If patient develops Grade 2 neuropathy or ototoxicity, change from cisplatin to carboplatin. Discuss with consultant.

References: Bamias, A et al; Cancer 1996; 77 (10): 1978-1985
Cunningham, D et al; NEJM 2006; 355: 11-20 (peri-operative use of ECF)