CISPLATIN & ETOPOSIDE

First-line use in small cell lung cancer, for patients being treated radically, or with good PS
For use in small cell cancer of the cervix, and other tumours with small cell histology where there is insufficient data to support the use of carboplatin.
For use in large cell neuroendocrine cancers
Merkel cell carcinoma, in patients suitable for cisplatin chemotherapy

Drug / Dosage:	Cisplatin	75mg/m^2	IV	Day 1
	Etoposide	100mg/m^2	IV	Day 1
	Etoposide	200mg/m^2	po	once daily on Day 2 and Day 3

Administration: Etoposide IV diluted in 500 - 1000ml 0.9% sodium chloride and infused over a minimum of 1 hour

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 3 hours
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgSO_4$ IV over 2 hours
500ml 0.9% sodium chloride IV **or** 500ml – 1 litre water orally over 1 hour

Oral etoposide is available as 50mg and 100mg soft capsules.
Each dose should be swallowed whole on an empty stomach or an hour before food.

Radiotherapy: For SCLC patients with limited stage disease, concurrent radiotherapy may be administered with one of the cycles as follows:
40Gy in 15 fractions (2.67 Gy/#) over 3 weeks, on weekdays only.
This is usually initiated on Day 1 of the 2nd or 3rd cycle of chemotherapy.
Radiotherapy is to be given **after** chemotherapy on Day 1 of the cycle.

Frequency: 3 weekly cycle for 6 cycles

Main Toxicities: myelosuppression; nephrotoxicity; neuropathy / ototoxicity; alopecia; ovarian failure / infertility

Anti-emetics: highly emetogenic, including aprepitant

Extravasation: non-vesicants

Regular Investigations:	FBC	Day 1
	LFTs	Day 1
	U&Es	Day 1
	Mg^{2+} and Ca^{2+}	Day 1
	EDTA	prior to 1st cycle
	CT scan	after 2nd cycle

Comments: For patients on Cycle 1 whose EDTA is not yet available, Cockcroft & Gault formula may be used to calculate creatinine clearance. 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.

Reason for Update: SCLC, large cell and merkel cell indications added; aprepitant included; b.d .etoposide oral changed to o.d.; WBC cut-off removed	Approved by Consultant: Dr A Mehta
Version: 4	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 3	Date: 20.4.17
Prepared by: S Taylor	Checked by: C Tucker

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

Ensure that patient is reviewed for side effects indicative of neurotoxicity or ototoxicity.

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 +/- 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.

Dose Modifications

Haematological Toxicity:

Neutrophils < 1.5 x 10^9/l
or
Platelets < 100 x 10^9/l

Delay for 1 week. Repeat FBC and, if within normal parameters, resume treatment.

If significant myelosuppression, consider reduction of oral etoposide dose to 100mg/m^2 once daily on Day 2 and Day 3. The use of prophylactic G-CSF should be discussed with the consultant.

Renal Impairment:

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

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100%
45 – 59	Give 75%
< 45	CI (consider carboplatin)

CrCl (ml/min)	Etoposide Dose
> 50	Give 100%
15 – 50	Give 75%
< 15	Give 50%

Hepatic Impairment:

Creatinine clearance is the strongest predictor of etoposide clearance. There is conflicting information about dose reduction with hepatic impairment. Use the table below but, if in doubt, discuss with Consultant.

Bilirubin (μmol/l)		AST (units/l)	Etoposide Dose
26 – 51	**or**	60 - 180	Give 50% dose
> 51	**or**	> 180	Clinical decision