Two Day Etoposide CISplatin (EP) Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Emergency treatment of women with Gestational Trophoblastic Neoplasia (GTN) who are acutely unwell from liver or CNS disease and particularly those at risk of respiratory failure.	D39	00267a	Hospital

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Emergency treatment:
Patients who are acutely unwell from liver or CNS disease and particularly those with large lung metastases who are at risk of respiratory failure should be admitted and emergency chemotherapy started as soon as possible. Patients are treated with etoposide and CISplatin for two consecutive days. This can be repeated weekly for 1-3 weeks and then altered to EMA/CO (NCCP Regimen 00248) or EMA/EP (NCCP Regimen 00264) as clinically indicated.

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate
1	1, 2	Etoposide[a]	100mg/m^2	IV	1000ml 0.9% NaCl over 60 mins
2	1, 2	CISplatin[b]	20mg/m^2	IV	1000ml 0.9% NaCl over 2 hours

[a]Hypotension following rapid IV administration has been reported.
Longer infusion times may be required based on the patient's tolerance

[b]**Pre hydration therapy required for CISplatin**
See local hospital policy recommendations.
Suggested pre hydration for CISplatin therapy:
1. Administer 10mmol magnesium sulphate ($MgSO_4$) (+/-KCl 10-20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above.

ELIGIBILITY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to etoposide, CISplatin or any of the excipients
- CISplatin
  - Pre-existing neuropathies ≥ grade 2
  - Creatinine clearance < 60 mL/min
  - Significant hearing impairment/tinnitus
- Severe hepatic impairment (etoposide)

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Serum human chorionic gonadotropin (hCG) using a validated test method
- Audiology and creatinine clearance if clinically indicated

Regular tests:

- FBC, renal and liver profile
- 24hr creatinine clearance prior to cycle 3
- Serum hCG (using a validated test method) should be done on day one of each cycle or more frequently if required.
    - After remission is achieved, serum hCG (using a validated test method) should be measured fortnightly for six months after consolidation therapy then monthly for a further six months and then every two months for two years.

Disease monitoring:
Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- In general treatment may proceed if neutrophils ≥ 1 x10^9/L and platelets > 75 x10^9/L.
- The use of G-CSF support may be considered.

Renal and Hepatic Impairment:

Table 1: Dose modifications in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment			
Etoposide	**CrCl (ml/min)**	**Dose**	**Bilirubin (micromol/L)**		**AST**	**Dose**
	>50	100%	26-51	or	60-180	50%
	15-50	75%	>51	or	>180	Clinical decision
	<15	50%				
	Subsequent doses should be based on clinical responses					
CISplatin	**CrCl (ml/min)**	**Dose**	No dose reduction necessary			
	>60	100%				
	45-59	75%				
	<45	Consider CARBOplatin				

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:
Etoposide: Low **(Refer to local policy).**
CISplatin: High **(Refer to local policy).**

PREMEDICATIONS:
Hydration prior to CISplatin administration **(Reference local policy or see recommendations above).**

OTHER SUPPORTIVE CARE: G-CSF may be used to mitigate the risk of haematological toxicities.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

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

- **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated appropriately. G-CSF will likely be needed to maintain white blood cell count.
- **Hypersensitivity**: Hypersensitivity reactions have been reported with etoposide and CISplatin. Monitor infusion of etoposide for the first 15 minutes for signs of hypotension.
- **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. If oral hydration is not possible (e.g. excessive nausea), IV hydration is indicated. Avoid nephrotoxic drugs such as aminoglycoside antibiotics where possible. Where treatment with nephrotoxic drugs must be used, monitor renal function.
- **Ototoxicity and sensory neural damage** should be assessed by history prior to each cycle of CISplatin.

DRUG INTERACTIONS:

- CISplatin may potentiate the nephrotoxic and ototoxic effects of loop diuretics and aminoglycosides so concurrent use should be avoided.
- Concomitant CISplatin therapy is associated with reduced total body clearance of etoposide.
- CYP3A4 inducers may increase the clearance of etoposide.
- CYP3A4 and p-gp inhibitors may decrease the clearance of etoposide.
- Current drug interaction databases should be consulted for more information.

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Version	Date	Amendment	Approved By
1	1/02/2016		Prof Maccon Keane
2	22/02/2018	Clarified dosing in renal and hepatic impairment. Applied new NCCP regimen template	Prof Maccon Keane
3	21/08/2019	Standardisation of administration fluid volume of CISplatin	Prof Maccon Keane
4	22/10/2021	Reviewed. Updated Indication and Treatment section. Amended CISplatin prehydration (KCl). Updated Exclusions and Baseline tests. Updated hCG testing (baseline and regular tests). Updated emetogenic potential. Updated adverse effects and drug interactions.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.