ESHAP Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of relapsed Non Hodgkins Lymphoma	C85	00838a	Hospital
Treatment of relapsed Hodgkins Lymphoma	C81	00838b	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.

Treatment with ESHAP can be repeated at 21 day intervals depending on myelosuppression for 2 cycles pre-transplant. Treatment may be continued for up to 6 cycles in patients not eligible for transplant.

Facilities to treat anaphylaxis MUST be present when systemic anti cancer therapy (SACT) is administered.

Day	Drug	Dose	Route and Method of Administration	Diluent & Rate
1-5	Methylprednisolone	500mg	IV infusion	100ml 0.9% NaCl over 30mins
1-4	Etoposide	40mg/m^2	IV infusion	500ml 0.9% NaCl over 1 hour
1-4	[1]CISplatin	25mg/m^2	IV infusion	1000ml 0.9% NaCl over 24 hours
5	Cytarabine	2000mg/m^2	IV infusion	1000mls 0.9% NaCl over 2 hours
From day 6 onwards	[2]G-CSF	5mcg/kg	SC (Round to nearest whole syringe)	Continued until ANC >1x10^{9}/L for 2 consecutive days

[1]Pre hydration therapy required for CISplatin
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:

1. Administer 10mmol magnesium sulphate ($MgSO_4$) ((+/-KCl 20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above

[2]G-CSF support is required with this regimen (**Refer to local policy or see Suggested support above**)

ELIGIBILITY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to CISplatin, etoposide, cytarabine or any of the excipients.
- Moderate/severe renal impairment (creatinine clearance < 60 mL/min)
- Significant hearing impairment/tinnitus

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist or Consultant Haematologist working in the area of haematological malignancies.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- LDH, Urate
- Audiology and creatinine clearance if clinically indicated
- Virology screen -Hepatitis B (HBsAg, HBcoreAb) & C, HIV.
  *See Adverse Effects/Regimen Specific Complications re Hepatitis B Reactivation

Regular tests:

- FBC, renal and liver profile
- LDH prior to each cycle
- Regular glucose monitoring while receiving steroid therapy-urinalysis 2-4 times/day
  If glucose detected in urinalysis, monitor blood glucose daily

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

Renal and Hepatic Impairment:

Table 1: Dose modifications based on renal and hepatic impairment

Drug	Renal impairment		Hepatic impairment			
CISplatin	**CrCl (ml/min)**	**Dose**	No dose modification required			
	>60	100%				
	45-60	75%				
	<45	consider carboplatin				
Etoposide	**Cr Cl (ml/min)**	**Dose**	**Total 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 response					
Cytarabine	**CrCl (ml/min)**	**Dose**	If bilirubin >34micromol/L, give 50% dose. Escalate doses in subsequent cycles in the absence of toxicity.			
	>60	100%				
	45-60	60%				
	30-45	50%				
	<30	Avoid				

SUPPORTIVE CARE:

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

PREMEDICATIONS:

- Hydration prior to CISplatin administration **(Refer to local policy or see recommendations above)**
- To prevent a chemical induced conjunctivitis developing with cytarabine, prednisolone eye drops (e.g. Pred Mild) 1-2 drops per eye 4 hourly during waking hours prior to cytarabine and continued 5 days post treatment should be considered.

OTHER SUPPORTIVE CARE:

- Tumour lysis syndrome prophylaxis **(Refer to local policy)**
- Proton pump Inhibitor**(Refer to local policy)**
- PJP prophylaxis **(Refer to local policy)**
- Anti-viral prophylaxis **(Refer to local policy)**
- Anti-fungal prophylaxis **(Refer to local policy)**

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

- **Myelosuppression:** Cytarabine is a potent bone marrow suppressant. Patients receiving this drug must be under close medical supervision and,should have leucocyte and platelet counts performed daily
- **Renal toxicity:** Renal toxicity is common with CISplatin. Encourage oral hydration.
- **Ototoxicity and sensory neural damage** should be assessed by history prior to each cycle of CISplatin
- **Neurotoxicity:** This may occur in patients treated with high dose cytarabine. Assess cerebellar function prior to each cytarabine dose. The risk of neurotoxicity is enhanced in the presence of renal impairment. Ensure that dose of cytarabine is adjusted in renal impairment (Ref Table 1).
- **Cytarabine syndrome:** Treatment with cytarabine may cause a 'Cytarabine Syndrome' characterised by flu-like symptoms, skin rash and occasionally chest pain.
- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy. **(Refer to local infectious disease policy**). These patients should be considered for assessment by hepatology.

DRUG INTERACTIONS:

- Avoid concurrent use of CISplatin with nephrotoxic drugs (e.g. aminoglycosides, NSAIDS) due to additive nephrotoxicity. If necessary monitor renal function closely.
- Current drug interaction databases should be consulted for more information.

REFERENCES:

1. Velasquez WS. et al. ESHAP- An effective chemotherapy regimen in Refractory and Relapsing Lymphoma: A 4-year Follow up Study. J Clin Oncol 1994;12, (6):1169-1176.
2. Aparicio J, Segura A. et al. ESHAP is an active regimen for relapsing Hodgkin's disease. Ann Oncol. 1999;10(5):593.
3. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network.
4. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009;North London Cancer Network.
5. Cisplatin 1mg/ml Concentrate for Solution for Infusion. Summary of Product Characteristics Accessed May 2020. Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2315-081-001_13022020153905.pdf
6. Etoposide Summary of Product Characteristics Accessed May 2020. Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-036-001_29072019103821.pdf
7. Cytarabine 100mg/ml Solution for Injection or Infusion. Accessed May 2020 Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2315-082-001_18102019163721.pdfhttp://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1390-091-001_09122014091042.pdf

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Comments and feedback welcome at oncologydrugs@cancercontrol.ie.