

CARBOplatin (AUC7) and Etoposide- Autologous Conditioning Germ Cell Tumour Regimen

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Indicator
Treatment of metastatic relapsed/refractory germ cell tumours	C62	00453a	

If a reimbursement indicator (e.g. ODMS, CDS¹) is not defined, the drug and its detailed indication have not been assessed through the formal HSE reimbursement process.

TREATMENT:

CARBOplatin and etoposide are administered for 3 consecutive days (days -5,-4 and -3) and stem cell transfusion is carried out on Day 0 according to treatment table below.

A second cycle may be given on recovery (minimum interval between cycles is 28 days), unless there was a grade 4 non-haematologic toxicity or no response to first cycle

A minimum of 1 million CD34+ cells per kilogram of body weight is required for each cycle of high-dose chemotherapy

Consideration should be given to the administration of a maintenance oral dose of 50mg/m² of etoposide for 21 consecutive days every 4 weeks for three cycles in patients who have a complete or partial remission after two cycles of high-dose CARBOplatin and etoposide chemotherapy and who have normal serum levels of human chorionic gonadotropin (hCG) and alpha-fetoprotein.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Admin Order	Day	Drug	Dose	Route	Diluent & Rate
1	-5, -4, -3	CARBOplatin	AUC 7	IV Infusion	500ml 5% glucose over 60mins
2	-5, -4, -3	Etoposide	^a 750mg/m ²	IV Infusion	*0.9% NaCl over 2 hours
	0	Stem cell infusion			
	Start day +1	G-CSF (Round to nearest whole syringe)	5mcg/kg	sc	Continue until ANC > 1 x 10 ⁹ /L for two consecutive days
Consideration should be given to stability of etoposide when determining volume of fluid required for reconstitution (Refer to local policy)					
Maintain strict fluid balance during therapy, by (1) monitoring fluid balance and (2) daily weights. If fluid balance becomes positive by >1000mls or weight increases by >1 Kg, the patient should be reviewed and consideration given to diuresing with furosemide					

The dose in mg of CARBOplatin to be administered is calculated as follows:

$$(\text{mg}) = \text{target AUC (mg/ml x min)} \times (\text{GFR ml/min} + 25)$$

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Reference NCCP Protocol 00261 CARBOplatin Monotherapy for information on calculation of CARBOplatin dose.

ELIGIBILITY:

- Indication as above

EXCLUSIONS:

- Hypersensitivity to etoposide, ^bCARBOplatin or any of the excipients.
- Severe liver impairment (etoposide)
- Pregnancy
- Breast Feeding

^bIf it is felt that the patient may have a major clinical benefit from CARBOplatin, it may in exceptional circumstances be feasible to rechallenge a patient with a prior mild hypersensitivity reaction e.g using a desensitisation protocol, but only with immunology advice, premedication as advised, and a desensitisation protocol under carefully controlled conditions with resuscitation facilities available and medical and/or ITU/ HDU supervision (1).

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- LDH, Urate
- Creatinine Clearance
- Pulmonary function tests
- Echocardiogram
- Audiology if clinically indicated
- Virology screen -Hepatitis B (HBsAg, HBcoreAb), Hepatitis C, HIV I and II, CMV and HSV.

*Hepatitis B reactivation: See Adverse events/ Regimen specific complications

Regular tests:

- FBC, renal and liver profile required daily during therapy

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

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Renal and Hepatic Impairment:

Table 1: Dose modification in renal and hepatic impairment

Drug	Renal impairment		Hepatic Impairment			
Etoposide	Cr Cl (ml/min)	Dose	Bilirubin (micromol/L)		AST (Units/L)	Dose Etoposide
	>50	100%				
	15-50	75%	>51	or	>180	Clinical decision
	Subsequent dosing should be based on patient tolerance and clinical effect. Data are not available in patients with CrCl < 15ml/min and further dose reductions should be considered in these patients.					
CARBOplatin	GFR (ml/min)	Dose	No dose reduction necessary			
	<60	Greater risk of developing myelosuppression				
	<20	Contra-indicated				

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: High (Refer to local policy)

PREMEDICATIONS:

- Prior to stem cell infusion administer premedications as per local policy.

OTHER SUPPORTIVE CARE:

- Anti-viral prophylaxis (Refer to local policy)
- Anti-fungal prophylaxis (Refer to local policy)
- Mouthcare (Refer to local policy)
- Proton Pump Inhibitor (Refer to local policy)
- PJP prophylaxis (Refer to local policy) *Do not give Co-trimoxazole until engraftment achieved and continue until day 100 or CD4 count> 200/microlitre.*
- All patients must receive irradiated cellular blood components starting one week prior to conditioning and until 12 months after stem cell infusion to prevent transfusion associated graft versus host disease.

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. Avoid aminoglycoside antibiotics.
- Neurotoxicity and ototoxicity:** Neurological evaluation and an assessment of hearing should be performed in patients receiving high dose CARBOplatin. Neurotoxicity, such as parasthesia, decreased deep tendon reflexes, and ototoxicity are more likely seen in patients previously treated with cisplatin, other platinum

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treatments and other ototoxic agents. Frequency of neurologic toxicity is also increased in patients older than 65 years.

- **Hepatitis B Reactivation:** All patients receiving stem cell transplantation should be tested for both HBsAg and HBcoreAb as per local policy. If either Hepatitis B test is positive, patients should be treated with lamivudine 100 mg/day orally during transplantation and for six months afterwards and should be monitored with at least monthly liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis

DRUG INTERACTIONS:

- Avoid concurrent use of CARBOplatin with nephrotoxic drugs (e.g. aminoglycosides, NSAIDS) due to additive nephrotoxicity. If necessary monitor renal function closely.
- Avoid concurrent use of CARBOplatin with ototoxic drugs (e.g. aminoglycosides, NSAIDS). When necessary perform regular audiometric testing.
- Current drug interaction databases should be consulted for more information e.g interaction potential with CYP3A4 inhibitors/ inducers.

ATC CODE:

CARBOplatin L01XA02
Etoposide L01CB01

REFERENCES:

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2. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network. Available at <http://londoncancer.org/media/65600/renal-impairment-dosage-adjustment-for-cytotoxics.pdf>
3. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009;North London Cancer Network. Available at <http://londoncancer.org/media/65594/hepatic-impairment-dosage-adjustment-for-cytotoxics.pdf>
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5. Etoposide 20 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics. Accessed Sept 2017 Available at http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1809-020-001_07102015115038.pdf

Version	Date	Amendment	Approved By
1	18/12/2017		Prof Maccon Keane
2			

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Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

¹ ODMS – Oncology Drug Management System

CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes

Further details on the Cancer Drug Management Programme is available at;

<http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/>

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