Carboplatin and Etoposide (Sarcoma)

Indication
Relapsed or refractory Ewing sarcoma

ICD-10 codes
Codes pre-fixed with C49

Regimen details

Day	Drug	Dose	Route
1	Carboplatin	AUC5*	IV infusion
1	Etoposide	120mg/m²	IV infusion
2 and 3	Etoposide	120mg/m² ***OR***	IV infusion
		240mg/m²	PO

* Carboplatin dose calculated using the Calvert equation: **Carboplatin dose (mg) = AUC (CrCl +25)**
The creatinine clearance (CrCl) is calculated using the Cockcroft and Gault equation, however for patients where the creatinine level may not truly reflect renal function (e.g. in extremes of BSA or debilitated patients) an EDTA should be performed.
CrCl should be capped at 125mL/min

Cycle frequency
21 days

Number of cycles
4 - 6 cycles (usually 4)

Administration
Day 1
Carboplatin is administered in 500mL 5% glucose over 30 minutes.

Etoposide is administered in 1000mL sodium chloride 0.9% and infused over a minimum of 1 hour.

Days 2 and 3
IV etoposide is administered in 1000mL sodium chloride 0.9% and infused over a minimum of 1 hour.

Oral etoposide is available as 50mg and 100mg capsules. The dose should be rounded to nearest 50mg and swallowed whole on an empty stomach or an hour before food. In the event that the patient cannot swallow capsules, etoposide injection can be taken orally (diluted with orange juice immediately prior to administration) at a dose of 70% of the usual oral capsule dose on days 2 and 3. (This is an unlicensed use based on medical information from Bristol- Myers Squibb).
Note: oral absorption of etoposide is variable.

Pre-medication
Antiemetics as per local guidelines.

Emetogenicity
This regimen has moderate emetic potential.

Additional supportive medication

Proton pump inhibitor if required
Mouthwashes as per local policy
Loperamide if required
Consider GCSF for patients with extensive disease, poor performance status or age >70 years.

Extravasation

Carboplatin and etoposide are irritant (Group 3)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	7 days
U+E (including creatinine)	7 days
LFTs	7 days
Albumin	7 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days
Albumin	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥1.5 x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine Clearance (CrCl)	≥ 50mL/min
Bilirubin	≤2.5 x ULN
ALT/AST	≤3 x ULN
Albumin	≥30g/L (see hepatic impairment section below)
Sodium	≥125 x 10^9/L (if < 125 – discuss with consultant)

Dose modifications

Consider GCSF and/or etoposide dose reduction (see below) for patients with poor performance status.

- **Haematological toxicity**

Defer therapy for 1 week if neutrophils < 1.5 x 10^9/L or platelets < 100 x 10^9/L. If repeat FBC within range continue without dose modification. If febrile neutropenia occurs or treatment is delayed due to neutropenia, add GCSF if this is not already prescribed.
If neutropenia despite GCSF, platelets <50 x 10^9/L at any point in the cycle or if treatment delayed > 1 week due to platelets, reduce oral etoposide dose to 100mg/m^2 on days 2 and 3.
If further haematological toxicity despite the above measures, consider a further reduction to the etoposide dose or reduction of carboplatin dose to AUC4.

- **Renal impairment**

CrCl (mL/min)	**Etoposide dose**
>50	100%
20-50	75%
<20	Discontinue

Carboplatin is contraindicated if CrCl <20mL/min.
If the calculated creatinine clearance falls by >10% from previous cycle, recalculate dose of carboplatin. If the calculated creatinine clearance appears to improve the dose **should not** be increased unless a clear cause of renal function improvement is documented (e.g. treatment of urinary tract obstruction).

- **Hepatic impairment**

Etoposide: if bilirubin <2.5 x ULN with normal albumin and renal function, no dose reduction indicated. If bilirubin >2.5 x ULN **or** albumin < 30g/L, consider dose reduction to 50% dose and increase if tolerated.

Carboplatin: No dose modification required

- **Other toxicities**

Any Grade 3-4 toxicity (except mucositis and alopecia) – delay until ≤ grade 1 toxicity and reduce doses of carboplatin and etoposide to 75%.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Neuropathy
Hypersensitivity reactions
Nephrotoxicity

- **Frequently occurring side effects**

Myelosuppression
Alopecia
Nausea and vomiting
Electrolyte disturbances

- **Other side effects**

Rash
Flu like illness
Abnormal LFTs

Significant drug interactions – for full details consult product literature/ reference texts

Phenylbutazone, sodium salicylate and salicylic acid: can affect protein binding of etoposide.
Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.
Carboplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
Clozapine: increased risk of agranulocytosis, avoid concomitant use
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Phenytoin: carboplatin reduces absorption and efficacy of phenytoin

Additional comments

For patients with limited stage disease and good performance status, concomitant radiotherapy may be administered to start with cycle 2.

References

- Summary of Product Characteristics Carboplatin (Hospira) accessed 26 June 2025 via www.medicines.org.uk
- Summary of Product Characteristics Etoposide (Bristol Myers Squibb) accessed 26 June 2025 via www.medicines.org.uk
- Krens S D, Lassche, Jansman GFGA, et al**.** Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20:e201-08. Supplementary appendix
- rEEcur trial. An international randomised controlled trial of chemotherapy for the treatment of recurrent and primary refractory Ewing sarcoma. Trial protocol available via https://www.birmingham.ac.uk/research/crctu/trials/reecur/index.aspx
- Van Maldegem, AM et al. Etoposide and carbo or cisplatin combination therapy in refractory or relapsed Ewings sarcoma: A large retrospective study Pediatric Blood Cancer 2015 62(1):40-4

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