Topotecan Monotherapy – 5 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Status
Treatment of patients with metastatic carcinoma of the ovary after failure of first-line or subsequent therapy	C56	00311a	Hospital
Treatment of patients with relapsed small cell lung cancer (SCLC) for whom re-treatment with the first-line regimen is not considered appropriate	C34	00311b	Hospital
Treatment of patients with metastatic carcinoma of the fallopian tubes after failure of first-line or subsequent therapy[i]	C57	00311c	Hospital
Treatment of patients with metastatic peritoneal carcinoma after failure of first-line or subsequent therapy[i]	C48	00311d	Hospital

**If the reimbursement status is not defined[ii], the indication has yet to be assessed through the formal HSE reimbursement process.*

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.

Topotecan is administered on five consecutive days (days 1-5) of a 21 day cycle for 6 cycles or until disease progression or unacceptable toxicity develops.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
[a]1-5	Topotecan	1.5mg/m^2	IV infusion	[b]100ml 0.9% NaCl over 30 minutes	Every 21 days for 6 cycles
[a] May be reduced to Days 1-3 or Days 1-4 if signs of toxicity or in heavily pre-treated patients at the discretion of the prescribing consultant.					
[b] Topotecan should be diluted to a final concentration of between 25 and 50 microgram/ml.					

ELIGIBILTY:

- Indications as above
- Life expectancy > 3months
- ECOG status 0-2
- Adequate organ function; ANC > 1.5 x10^9 cells/L, platelets 100 x10^9/L

EXCLUSIONS:

- Hypersensitivity to topotecan or any of the excipients
- Breast Feeding

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile

Regular tests:

- FBC, renal and liver profile prior to each cycle

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.

Haematological:

G-CSF may be used to maintain neutrophil counts or dose reduction may be used as shown in table 1.

Table 1: Dose modification of topotecan in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Haemaglobin level	Dose
≥ 1	and	≥ 100	≥ 9 g/dl (after transfusion if necessary	100% Dose
0.5 to 0.99	and/or	<100	< 9g/dl	Delay treatment until recovery. Following recovery from neutropenia, reduce dose by 0.25 mg/m^2/day to 1.25 mg/m^2/day (or subsequently down to 1mg/m^2/day if necessary).
<0.5 for ≥ 7 days	and/or	< 25		Reduce dose by 0.25 mg/m^2/day to 1.25mg/m^2/day (or subsequently down to 1mg/m^2/day if necessary).
Febrile neutropenia				
Neutropenia with infection				

Renal and Hepatic Impairment:

Table 2: Dose modification of topotecan in renal and hepatic impairment

Renal Impairment		Hepatic Impairment	
CrCl (ml/min)	**Dose**	**Bilirubin (micromol/L)**	**Dose**
>40	100%	<170	100%
20-39	50%	>170	Clinical decision
<20	Contra-indicated		

Management of adverse events:

Table 3: Dose Modification of topotecan for Adverse Events

Adverse reactions	Recommended dose modification
Grade ≥ 3 (except nausea)	Decrease dose by 0.25mg/m^2/day
Interstitial lung disease	Discontinue

SUPPORTIVE CARE:

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

PREMEDICATIONS: None

OTHER SUPPORTIVE CARE:
No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

- **Neutropeni**a; Fever or other evidence of infection must be assessed promptly and treated aggressively.
- **Neutropenic enterocolitis:** Topotecan-induced neutropenia may lead to neutropenic enterocolitis. This should be considered in patients presenting with neutropenia, fever, and abdominal pain.
- **Interstitial lung disease:** Topotecan has been associated with reports of interstitial lung disease (ILD), some of which have been fata. Underlying risk factors include history of ILD, pulmonary fibrosis, lung cancer, thoracic exposure to radiation and use of pneumotoxic drugs and/or colony stimulating factors.
  Patients should be monitored for pulmonary symptoms indicative of ILD (e.g. cough, fever, dyspnoea and/or hypoxia), and topotecan should be discontinued if a new diagnosis of ILD is confirmed.

DRUG INTERACTIONS:

- Increased toxicity of topotecan possible with p glycoprotein inhibitors due to reduced clearance.
- Concurrent use of topotecan and platinums (e.g. CISplatin and CARBOplatin) may result in severe myelosuppression. Administration of platinums before topotecan resulted in worse thrombocytopenia and neutropenia than topotecan preceeding platinums.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Topotecan - L01XX17

REFERENCES:

1. Bokkel Huinink WT, et al. Topotecan versus paclitaxel for the treatment of recurrent epithelial ovarian cancer. J Clin Oncol 1997; 15:2183-2193.
2. von Pawel J., J. H. Schiller, F. A. Shepherd, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. J Clin Oncol.1999; 17(2):658-667
3. HYCAMTIN Summary of Product Characteristics Accessed April 2018. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000123/WC500051542.pdf

Version	Date	Amendment	Approved By
1	4/4/2016		Prof Maccon Keane
2	18/04/2018	Updated with new NCCP regimen template, standardisation of treatment table and clarification of regular testing and dosing in renal and hepatic impairment	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This indication is outside its licensed indication in Ireland. Patients should be informed of the unlicensed nature of this indication and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be aware of their responsibility in communicating any relevant information to the patient and also in ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy

[ii] 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/