Topotecan Monotherapy – Weekly[i]

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	00312a	Hospital
Treatment of patients with metastatic carcinoma of the fallopian tubes after failure of first-line or subsequent therapy	C57	00312b	Hospital
Treatment of patients with metastatic peritoneal carcinoma after failure of first-line or subsequent therapy	C48	00312c	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.

Topotecan is administered on days 1, 8 and 15 of a **28 day** cycle until disease progression or unacceptable toxicity develops.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1, 8 and 15	Topotecan	4mg/m^2	IV infusion	[a] 250ml 0.9% NaCl over 30 minutes	Every 28 days
[a] Topotecan should be diluted to a final concentration of between 25 and 50 microgram/ml.					

ELIGIBILITY:

- 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

**Selected patients with ECOG status 3 due to disease burden may be eligible at consultant discretion and with planned close monitoring for toxicity and clinical benefit and prophylactic GCSF support*

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 before 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 for cycles 2-6

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, consider dose reduction.
<0.5 for ≥ 7 days	and/or	< 25		Consider dose reduction.
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 25%
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. Sehouli, J., D. Stengel, P. Harter, et al. 2011. Topotecan Weekly Versus Conventional 5Day Schedule in Patients With Platinum Resistant Ovarian Cancer: a randomized multicenter phase II trial of the North Eastern German Society of Gynecological Oncology Ovarian Cancer Study Group. J Clin Oncol 2011;29(2):242-248.
2. HYCAMTIN Summary of Product Characteristics Accessed July 2020. Available at https://www.ema.europa.eu/en/documents/product-information/hycamtin-epar-product-information_en.pdf https://www.medicines.ie/medicines/hycamtin-1mg-and-4mg-solution-32399/smpc
3. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V2 2019. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

Version	Date	Amendment	Approved By
1	04/04/2016		Prof Maccon Keane
2	18/04/2018	Updated with new NCCP regimen template, standardization of treatment table and dosing in renal and hepatic impairment	Prof Maccon Keane
3	29/04/2020	Regimen review	Prof Maccon Keane
4	15/07/2020	Update dose modifications for haematological toxicity	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This regimen 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.