Topotecan Oral Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of adult patients with relapsed small cell lung cancer (SCLC) for whom re-treatment with the first –line regimen is not considered appropriate	C34	00587a	CDS

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 orally 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	Cycle
1, 2, 3, 4 and 5	Topotecan[1,2,3]	2.3 mg/m^2	PO	Every 21 days for 6 cycles
[1]Topotecan is available as 0.25mg and 1mg hard capsules				
[2]Store capsules in a refrigerator (2°C - 8°C). Do not freeze.				
[3]Take capsules with or without food. The capsules must be swallowed whole, and must not be chewed, crushed or divided.				

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate organ function; Haemoglobin ≥ 9.0 g/dL, ANC > 1.5 x10^9 cells/L, platelets 100 x10^9/L

EXCLUSIONS:

- Hypersensitivity to topotecan or any of its excipients
- Breast-feeding
- Gastrointestinal conditions or drugs affecting gastrointestinal absorption

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile

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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: Recommended dose modification of topotecan in haematological toxicity (subsequent cycles)

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Haemoglobin level		WBC ($x10^9$/L)	Dose
≥ 1	and	≥ 100	≥ 9 g/dL (after transfusion if necessary	and	≥3.0	100% Dose
<1	and/ Or	<100		And/ Or	<3.0	Delay therapy for one week. Upon recovery within normal parameters proceed to 100% dose
<0.5 for ≥ 7 days	and/ Or	< 25				Reduce dose by 0.4mg/m²/day to 1.9 mg/m2/day (or subsequently down to 1.5mg/m2/day if necessary).
Febrile neutropenia						
Neutropenia with infection						

Renal and Hepatic Impairment

Table 2: Recommended dose modification of topotecan in renal and hepatic impairment

Renal Impairment		Hepatic Impairment
Cr Cl (ml/min)	**Dose**	Insufficient data available to make a recommendation
≥50	100% dose	
30-49	83% dose (1.9mg/m²/ day if reduced from full dose)*	
<30	Insufficient data available to make a recommendation	
* If well tolerated, the dose may be increased to 2.3 mg/m²/day in subsequent cycles		

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Management of adverse events:

Table 3: Recommended dose Modification of Topotecan for Adverse Events

Adverse reactions	Recommended dose modification
Grade ≥3 diarrhoea	Decrease dose by 0.4mg/m²/ day for subsequent courses Patients with Grade 2 diarrhoea may need to follow the same dose modification guidelines.
Interstitial lung disease (ILD)	Discontinue

SUPPORTIVE CARE:

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

PREMEDICATIONS: None

OTHER SUPPORTIVE CARE:

- Anti-diarrhoeal treatment (**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.

- **Neutropenia**; Fever or other evidence of infection must be assessed promptly and treated aggressively.
- **Diarrhoea**: Proactive management of diarrhoea with anti-diarrhoeal agents is important. Severe cases of diarrhoea may require administration of oral or intravenous electrolytes and fluids, and interruption of topotecan therapy.
- **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 fatal. 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:

- Current drug interaction databases should be consulted for more information

ATC CODE: L01XX17

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REFERENCES:

1. O'Brien, M et al. Phase III Trial Comparing Supportive Care Alone With Supportive Care With Oral Topotecan in Patients With Relapsed Small-Cell Lung Cancer. J Clin Oncol 2006. 34 (5441-5447).
2. Von Pawel, J et al. Phase II comparator study of oral versus intravenous topotecan in patients with chemosensitive small-cell lung cancer. J Clin Oncol. 2001;19(6):1743.
3. Eckardt JR et al. Phase III study of oral compared with intravenous topotecan as second-line therapy in small-cell lung cancer. J Clin Oncol. 2007;25(15):2086.
4. Hycamtin® Summary of Product characteristics. Accessed Dec 2020. Available at https://www.ema.europa.eu/en/documents/product-information/hycamtin-epar-product-information_en.pdf
5. 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

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1	06/12/2019		Prof Maccon Keane
2	06/01/2021	Reviewed	Prof. Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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