Topotecan – IV (gynae)

Indication

Palliative therapy for relapsed ovarian, fallopian tube or primary peritoneal cancer.

Second line treatment of partially platinum sensitive, platinum resistant or platinum refractory advanced ovarian cancer or in patients who are allergic to platinum based compounds and for whom Caelyx® and paclitaxel are not considered appropriate.

(NICE TA91)

ICD-10 codes

Codes prefixed with C48, 56 and 57.

Regimen details

Day	Drug	Dose	Route
1 - 5	Topotecan	1.5mg/m^2*	IV infusion

* This dose and schedule may be too toxic for some patients, especially those heavily pre-treated with platinum based therapy. In such patients consider a reduced starting dose of 1.0-1.25mg/m^2.

Alternatively patients may be prescribed the modified weekly regimen as per the table below. This regimen has been shown to be equivalent, less toxic and more convenient than the 5 day schedule. Note: this dosing is unlicensed.

Day	Drug	Dose	Route
1, 8, 15	Topotecan	3.5mg/m^2	IV infusion

Cycle frequency

21 days (or 28 days for the modified weekly regimen)

Number of cycles

6 cycles

Administration

Topotecan is administered in 50-100mL* sodium chloride 0.9% or glucose 5% over 30 minutes.

*the final concentration should be between 25-50 micrograms/mL.

Pre-medication

Nil

Emetogenicity

This regimen has a moderate - low emetogenic potential

Additional supportive medication

Loperamide. Patients should be advised of the risk and management of topotecan induced diarrhoea, including recognition of symptoms, use of loperamide and prophylactic antibiotics, fluid intake and the need for

hospitalisation. Supplies of antibiotics (ciprofloxacin 250-500mg BD) should be given in addition to loperamide and the patient should be advised if diarrhoea persists beyond 24 hours of loperamide treatment to commence the antibiotics.

Extravasation

Topotecan is an exfoliant (Group 4)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
CA125	28 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

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)	≥ 40mL/min
Bilirubin	< 10 x ULN

Dose modifications

- **Haematological toxicity**

If neutrophils < 1.5 x 10^9/L and/or platelets < 100 x 10^9/L delay treatment for 1 week or until count recovery.

If any of the following are experienced, future doses should be reduced:

- Neutrophils < 0.5 x 10^9/L for 7 days or more or severe neutropenia with fever
- Treatment delay due to neutropenia
- Platelets < 25 x 10^9/L at any point during treatment

In the case of febrile neutropenia consider prophylactic antibiotics for all further cycles.

- **Renal impairment**

CrCl (mL/min)	**Topotecan dose**
≥ 40	100%
20-39	50%
< 20	Contraindicated

- **Hepatic impairment**

There is a lack of information available for dosing in hepatic impairment, however topotecan is not recommended in severe hepatic impairment with bilirubin > 10 x ULN.

- **Other toxicities**

For all other grade 3 toxicities (except alopecia and nausea/vomiting) delay treatment until resolved to ≤ grade 1 and resume with dose reduction of 0.25mg/day. If further toxicity occurs or grade 4 toxicity withhold treatment or consider an additional dose reduction (discuss with consultant).

If delays of > 3 weeks or > 2 dose reductions, discontinue treatment.

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

- **Serious side effects**

Myelosuppression
Interstitial lung disease
Paraesthesia

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Constipation, diarrhoea*
Fatigue
Abdominal pain

* this can be severe, ensure patients are counselled on management of diarrhoea (see supportive medication)

- **Other side effects**

Alopecia
Headache
Rash
Stomatitis

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

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.
Clozapine: increased risk of agranulocytosis; avoid concomitant use.
Digoxin tablets: reduced absorption (give digoxin as liquid form).
P-glycoprotein inhibitors: (cyclosporin, ketoconazole, ritonavir, saquinavir) increase exposure of topotecan.
Phenytoin: may increase topotecan clearance

Additional comments

Nil

References

- National Institute for Clinical Excellence. Technology Appraisal Guidance 91. Accessed 14 August 2014 via www.nice.org.uk
- Summary of Product Characteristics Topotecan (GlaxoSmithKlein) accessed 14 August 2014 via www.medicines.org.uk
- Rowinsky EK. Weekly Topotecan: An Alternative to Topotecan's Standard Daily x 5 Schedule? The Oncologist, 2002 7(4): 324-330.
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.

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