Chemotherapy Protocol

GYNAECOLOGICAL CANCER

LIPOSOMAL DOXORUBICIN (Caelyx)

Please note this protocol is based on information for the use of the Caelyx brand of liposomal doxorubicin. Brands may not be interchangeable.

Regimen

- Ovary – Liposomal Doxorubicin (Caelyx)

Indication

- Second line or subsequent treatment of partially platinum-sensitive, platinum-resistant or platinum-refractory ovarian cancer, or for women who are allergic to platinum-based compounds.
- WHO performance status 0,1, 2
- Palliative intent

Toxicity

Drug	Adverse Effect
Liposomal Doxorubicin	Palmar plantar erythrodysthesia (hand and foot syndrome), rash, GI disturbances, cardiotoxicity, asthenia, paresthesia

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

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day 1 of each cycle
- CA125 prior to day 1 of each cycle
- Ensure adequate cardiac function before starting therapy. Baseline ECG and LVEF should be measured in patients with a history of cardiac problems or in the elderly. Discontinue liposomal doxorubicin if cardiac failure develops

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.
Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Prior to cycle 1 the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $100x10^9$/L

Day 1

Neutrophils ($x10^9$/L)	Dose Modifications (liposomal doxorubicin)
1 or greater	100%
0.5 - 1	Delay until recovery to $1x10^9$/L or greater then continue at full dose
less than 0.5	Delay until recovery to $1x10^9$/L or greater then continue at 75% of the original dose
Platelets ($x10^9$/L)	**Dose Modifications**
75 or greater	100%
25 - 74	Delay until recovery to $75x10^9$/L or greater then continue at full dose
less than 25	Delay until recovery to $75x10^9$/L or greater then continue at 75% of the original dose

Hepatic Impairment

Doses recommended below are for initial dosing. If the first dose of liposomal doxorubicin is well tolerated with minimal toxicity and no increase in bilirubin or liver enzymes the dose may be increased from 75% to 100% and from 50% to 75% at the next cycle (and from 75% to 100% on subsequent cycles where appropriate.)

Drug	Bilirubin (µmol/L)	Dose (% of original dose)
Liposomal Doxorubicin	less than 20	100%
	21-51	75%
	51 or greater	50%

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Liposomal Doxorubicin	30 or greater	No dose modification needed
	less than 30	Clinical decision

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose should then be reduced to 75% of the original dose or discontinued as appropriate.

Palmer-Plantar Erythrodesia / Stomatitis			
NCI-CTC Toxicity Grade	Number of Weeks after the Dose of Liposomal Doxorubicin		
	4	5	6
1	Re-dose unless patient has experienced a previous grade 3 or 4 skin toxicity, in which case wait an additional week	Re-dose unless patient has experienced a previous grade 3 or 4 skin toxicity, in which case wait an additional week	Decrease dose by 25 % and return to 4 week interval or stop treatment
2	Wait an additional week	Wait an additional week	Decrease dose by 25 % and return to 4 week interval or stop treatment
3	Wait an additional week	Wait an additional week	Stop treatment
4	Wait an additional week	Wait an additional week	Stop treatment

Regimen

28 day cycle for 6 cycles

Drug	Dose	Days	Administration
Liposomal Doxorubicin	40mg/m^2	1	Intravenous infusion in 500ml glucose 5%. The first infusion to be given at a maximum rate of 1mg/minute. If well tolerated subsequent infusions may be given over 60 minutes

Dose Information

- The licensed dose for this indication is 50mg/m^2. However, many patients do not tolerate this dose. Clinicians may choose to commence treatment at 40mg/m^2 and escalated on subsequent cycles where appropriate.

- Liposomal Doxorubicin will be dose banded according to the CSCCN agreed bands

- The maximum lifetime cumulative dose of doxorubicin is 450mg/m². However prior radiotherapy to mediastinal/pericardial area should receive a lifetime cumulative doxorubicin dose of no more than 400mg/m². Also consider previous anthracycline exposure.

Administration Information

Extravasation

- Liposomal Doxorubicin – exfoliant

Other

- The first infusion of liposomal doxorubicin is to be given at a maximum rate of 1mg/minute. If this is well tolerated subsequent infusions may be given over 60 minutes. The default time on Aria is 120 minutes.

- If the patient experiences early symptoms or signs of infusion reaction immediately discontinue the infusion and administer appropriate treatment with chlorpheniramine and hydrocortisone. Once the patient has fully re-covered the infusion may be restarted slowly by infusing 5% of the total dose over the first 15 minutes. If tolerated without reaction, the infusion rate may then be doubled for the next 15 minutes. If tolerated, the infusion may then be completed over the next hour for a total infusion time of 90 minutes.

- Liposomal doxorubicin is incompatible with sodium chloride 0.9%. Always use a glucose 5% flush.

- Do not use in-line filters during the administration of liposomal doxorubicin.

- Doses of liposomal doxorubicin less than 90mg may be diluted in 250ml of glucose 5%. Doses of 90mg and above should be diluted in 500ml of glucose 5%.

Additional Therapy

- Antiemetics

  15 – 30 minutes prior to chemotherapy

  - dexamethasone 8mg oral or intravenous
  - metoclopramide 10mg oral or intravenous

  As take home medication

  - dexamethasone 4mg oral once a day for 3 days
  - metoclopramide 10mg oral three times a day for 3 days then as required

- Mouthwashes for the treatment and prevention of mucositis or stomatitis as per local policy.

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

- For patients experiencing infusion reactions with this regimen consider administering premedication with all subsequent cycles:

  - chlorphenamine 10mg intravenous
  - dexamethasone 20mg intravenous (remove anti-emetic dose)
  - ranitidine 50mg intravenous

Coding (OPCS 4.6)

- Procurement – X71.4

- Delivery – X72.3

References
1. Gordon A, Fleagle J Guthrie D et al. Recurrent epithelial ovarian carcinoma: a randomized phase III study of pegylated liposomal doxorubicin versus topotecan. J Clin Oncol 2001; 19(14): 3312-3322.
2. NICE Guidance TA91 - Ovarian cancer (advanced) - paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan (review). May 2005.
3. Summary of product characteristics. Caelyx 2mg/ml concentrate for solution for infusion. Janssen-Cilag Ltd. Nov 2011

REGIMEN SUMMARY

Liposomal Doxorubicin (Caelyx)

Day 1

1. Dexamethasone 8mg oral or intravenous

2. Metoclopramide 10mg oral or intravenous

3. Liposomal Doxorubicin 40mg/m^2 intravenous infusion in 500ml glucose 5% over 120 minutes.

Take Home Medicines

4. Dexamethasone 4mg oral once a day for 3 days starting the day after chemotherapy

5. Metoclopramide 10mg oral three times a day for 3 days then 10mg three times a day when required for nausea.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	April 2014	Bolus removed from intravenous bolus throughout text Metoclopramide dose changed to 10mg from 10-20mg OPCS codes updated Disclaimer updated	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	May 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Clare Green Consultant Medical Oncologist Dr Cheng Yeoh Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.