Pegylated Liposomal Doxorubicin (CAELYX) ® 28 days

INDICATIONS FOR USE:

INDICATION	ICD10	Protocol Code
Monotherapy for patients with metastatic breast cancer.	C50	00205a
Treatment of advanced ovarian cancer in women who have failed a first-line platinum-based chemotherapy regimen	C56	00205b

ELIGIBILTY:

- Indications as above
- ECOG status 3 or better
- Adequate haematologic, liver and cardiac function

EXCLUSIONS:

- Hypersensitivity to liposomal pegylated doxorubicin or to any of the excipients.
- Pre-existing cardiac myopathy or congestive heart failure.
- Hepatic dysfunction (see Dose Modifications below).

TESTS:

Baseline tests: FBC, U&Es, LFTs, ECG, MUGA or ECHO (to determine LVEF)

Regular tests:
FBC U&Es, LFTs, ECG, *MUGA or ECHO (to determine LVEF) prior to each cycle
*See Adverse Effects/Regimen specific complications for guidelines regarding cardiotoxicity.

Disease monitoring/assessment: Disease monitoring/assessment should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

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

Treatment is administered once every 4 weeks for a maximum of 6 cycles or until disease progression or unacceptable toxicity occurs.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Pegylated Liposomal Doxorubicin (Caelyx)	50mg/m^2	IV infusion	*250ml glucose 5% at rate of 1mg/min for first cycle (see note)	Repeat every 28 days

*For doses ≥ 90mg, use 500mL infusion bag
Do not use with in-line filters

NOTE: If no infusion reaction observed subsequent infusions may be administered over 60min.
For patients who experience an infusion reaction, the method of infusion should be modified as follows:5 % of the total dose should be infused slowly 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.

DOSE MODIFICATIONS:

Any dose modification should be discussed with a Consultant

Haematological Toxicity: (NCI-CTC).

GRADE	ANC (x10^9/L)	PLATELETS	MODIFICATION
1	1.5 – 1.9	75-150	Resume treatment with no dose reduction
2	1.0-< 1.5	50 -< 75	Wait until ANC ≥ 1.5 and platelets ≥ 75; redose with no dose reduction
3	0.5 -< 1.0	25 -< 50	Wait until ANC ≥ 1.5 and platelets ≥ 75; redose with no dose reduction
4	< 0.5	<25	Wait until ANC ≥ 1.5 and platelets ≥ 75; decrease dose by 25% or continue full dose with growth factor support.

Hepatic impairment:

Bilirubin µm/L	MODIFICATION
20.5 – 51.3	Decrease dose by 25%
> 51.3	Decrease dose by 50%

If the patient tolerates the first dose without an increase in serum bilirubin or liver enzymes, the dose for cycle 2 can be increased to the next dose level, i.e., if reduced by 25 % for the first dose, increase to full dose for cycle 2; if reduced by 50 % for the first dose, increase to 75 % of full dose for cycle 2. The dosage can be increased to full dose for subsequent cycles if tolerated. Pegylated liposomal doxorubucin can be administered to patients with liver metastases with concurrent elevation of bilirubin and liver enzymes up to 4 x the upper limit of the normal range.

Palmar-Plantar Erythrodysesthesia (PPE) and Stomatitis:

Week after prior pegylated liposomal doxorubicin dose			
Toxicity Grade At Current Assessment	**Week 4**	**Week 5**	**Week 6**
Grade 1	**Redose unless** patient has experienced a previous Grade 3 or 4 reaction, in which case wait an additional week	**Redose unless** patient has experienced a previous Grade 3 or 4 skin toxicity, in which case wait an additional week	PPE: Decrease dose by 25 %; return to 4 week interval Stomatitis: May withdraw patient per consultant's assessment
Grade 2	Wait an additional week	Wait an additional week	PPE: Decrease dose by 25 %; return to 4 week interval Stomatitis: May withdraw patient per consultant's assessment
Grade 3	**Wait an additional week**	**Wait an additional week**	**Withdraw patient**
Grade 4	**Wait an additional week**	**Wait an additional week**	**Withdraw patient**

SUPPORTIVE CARE

EMETOGENIC POTENTIAL: Moderate. Refer to local policy

PREMEDICATIONS:

None usually required.

TAKE HOME MEDICATIONS:
Refer to local PPE protocol.

OTHER SUPPORTIVE CARE:
Other strategies to prevent and treat PPE, which may be initiated for 4 to 7 days after treatment with pegylated liposomal doxorubicin include keeping hands and feet cool, by exposing them to cool water (soaks, baths, or swimming), avoiding excessive heat/hot water and keeping them unrestricted (no socks, gloves, or shoes that are tight fitting). 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.

- **Cardiotoxicity**: Frequent ECG monitoring is recommended. Reduction of the QRS complex suggests cardiac toxicity.
  LVEF monitoring using ECHO or MUGA should be applied during treatment. The evaluation of LVEF is considered to be mandatory before each additional administration of pegylated liposomal doxorubicin that exceeds a lifetime cumulative anthracycline dose of 450 mg/m^2. Cardiac toxicity also may occur at cumulative anthracycline doses lower than 450 mg/m^2 in patients with prior mediastinal irradiation or in those receiving concurrent cyclophosphamide therapy.
- **Acute Infusion Reaction:** Usually seen during the first infusion
- **Palmar-plantar erythrodysesthesia syndrome (PPE):** Monitor patient for presence of PPE. If present, patient may require an interruption in treatment (see dose modifications).
- **Extravasation:** Pegylated liposomal doxorubicin is considered an irritant**. (Refer to local guidelines)**

DRUG INTERACTIONS:
- No formal medicinal product interaction studies have been carried out.
- Exercise caution in the concomitant use of pegylated liposomal doxorubicin with products known to interact with standard doxorubicin hydrochloride.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Doxorubicin - L01DB01

REIMBURSEMENT CATEGORY:

Pegylated liposomal doxorubicin (CAELYX®) is funded through local hospital budgets (February 2014).

PRESCRIPTIVE AUTHORITY:

Medical Oncologist

REFERENCES:

1. Alberts DS, et al. Efficacy and safety of liposomal anthracyclines in phase I/II clinical trials. Semin Oncol 2004;32(Suppl 13):53-90.
2. O'Brien, M. E., N. Wigler, M. Inbar, et al. Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCl (CAELYX/Doxil) versus conventional doxorubicin for first-line treatment of metastatic breast cancer. Ann.Oncol. 2004;15(3):440-449
3. Gordon, A. N., J. T. Fleagle, 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.
4. Rose, P. G. Pegylated liposomal doxorubicin: optimizing the dosing schedule in ovarian cancer. Oncologist. 2005;10(3):205-214.
5. Kim, R. J., G. Peterson, B. Kulp, et al. .Skin toxicity associated with pegylated liposomal doxorubicin (40 mg/m2) in the treatment of gynecologic cancers." Gynecol.Oncol. 2005 97(2):374-378.
6. Gordon, A. N., M. Tonda, S. Sun, et al. Long-term survival advantage for women treated with pegylated liposomal doxorubicin compared with topotecan in a phase 3 randomized study of recurrent and refractory epithelial ovarian cancer. Gynecol Oncol 2004; 95(1):1-8.
7. Caelyx ®Summary of product characteristics. Accessed June 2016. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR__Product_Information/human/000089/WC500020180.pdf

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

Version control

Version	Date	Amendment	Approved By
1	10/2/2014		Dr Maccon Keane
2	29/7/2014	Treatment dose update	Dr Maccon Keane
3	15/06/2016	Inserted Disease monitoring statement and clarified frequency of regular testing	Dr Maccon Keane