Pegylated Liposomal DOXOrubicin 50mg/m^2 28 days

Please note that the Myocet® product, which contains non-pegylated liposomal DOXOrubicin should not be used when treating patients with this regimen.

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Monotherapy for patients with metastatic breast cancer.	C50	00205a	Hospital
Treatment of advanced ovarian cancer in women who have failed a first-line platinum-based chemotherapy regimen	C56	00205b	Hospital
Metastatic soft tissue sarcoma	C49	00205c	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.

Treatment is administered once every 4 weeks for a maximum of 6 cycles or until disease progression or unacceptable toxicity occurs.
Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

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

[a]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.

ELIGIBILITY:

- Indications as above
- Adequate haematologic, liver and cardiac function

Breast cancer, ovarian cancer:

- ECOG 0-3

Sarcoma:

- ECOG 0-2

EXCLUSIONS:

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

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- ECG
- MUGA or ECHO (to determine LVEF)

Regular tests:

- FBC, renal and liver profile prior to each cycle
- ECG
- *MUGA or ECHO (to determine LVEF as clinically indicated)
  *See Adverse Effects/Regimen specific complications for guidelines regarding cardiotoxicity

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:

Table 1: Dose modification of pegylated liposomal DOXOrubicin in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
1.5-1.9	and	≥75	**100%**
1-<1.5	or	50-74	Wait until ANC ≥ 1.5 and platelets ≥ 75; redose with no dose reduction
0.5-<1	or	<50	Wait until ANC ≥ 1.5 and platelets ≥ 75; redose with no dose reduction
<0.5	or	<25	Wait until ANC ≥ 1.5 and platelets ≥ 75; decrease dose by 25% or continue full dose with growth factor support.

Renal and Hepatic Impairment:

Table 2: Dose modification of pegylated liposomal DOXOrubicin in renal and hepatic impairment

Renal Impairment	Hepatic Impairment	
No dose reduction necessary	**Bilirubin (micromol/L)**	**Dose**
	20-51	**75%**
	>51	**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.		

Management of adverse events:

Table 3: Dose Modification of pegylated liposomal DOXOrubicin 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 skin toxicity, 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 and stomatitis: Decrease dose by 25 %; OR Stomatitis: Consider discontinuation - clinician decision
Grade 2	Wait an additional week	Wait an additional week	PPE and stomatitis: Decrease dose by 25 %; OR Stomatitis: Consider discontinuation - clinician decision
Grade 3	Wait an additional week	Wait an additional week	Discontinue
Grade 4	Wait an additional week	Wait an additional week	Discontinue

SUPPORTIVE CARE:

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

PREMEDICATIONS: None usually required

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. 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.
- **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.

REFERENCES:

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Version	Date	Amendment	Approved By
1	10/02/2014		
2	29/07/2014	Treatment dose update	Prof Maccon Keane
3	15/06/2016	Inserted Disease monitoring statement and clarified frequency of regular testing	Prof Maccon Keane
4	20/06/2018	Updated with new NCCP template, updated title	Prof Maccon Keane
5	10/06/2020	Reviewed.	Prof Maccon Keane
6	25/05/2022	New indication added	Dr Mark Doherty
7	28/07/2023	Removed reference to brand name	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.