PEGYLATED LIPOSOMAL DOXORUBICIN

INDICATION (ICD10) C41, C49, C56

1. Second-line (or subsequent treatment of women with partially platinum-sensitive, platinum resistant or platinum refractory advanced ovarian cancer, and for women who are allergic to platinum based compounds.
2. Endometrial recurrence or metastatic 1st line if unable to have taxanes.
3. Fibromatosis (local funding).
4. *Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)* (PDL1)
   The treatment of sarcomas in patients with cardiac impairment requiring an anthracycline, 1st or 2nd line indication (unlicensed).

REGIMEN

Day 1 PEGYLATED LIPOSOMAL DOXORUBICIN 40mg/m^2 in #ml glucose 5% IV infusion

diluent volume for dose prescribed as per national standardised product specification

The first infusion to be given at a maximum rate of 1mg/minute.
If well tolerated subsequent infusions may be given over 60 minutes.
In those patients who experience an infusion reaction 5% of the total volume 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.

CYCLE FREQUENCY AND NUMBER OF CYCLES

Ovarian, endometrial - every 28 days for up to 6-8 cycles
Sarcoma - every 28 days for up to 6 cycles

ANTI-EMETICS

Low emetic risk day 1

CONCURRENT MEDICATION REQUIRED

Liposomal doxorubicin	Benzdyamine mouthwash, saltwater mouthwash

EXTRAVASATION AND TYPE OF LINE / FILTERS

Liposomal doxorubicin - exfoliant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.0
Platelets x 10^9/L ≥100 (also see haematological dose modifications)
ECG (possible ECHO) required if patient has preexisting cardiac disease
CA125 baseline and day 1 every cycle (ovarian)
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Liposomal doxorubicin	Avoid where hypersensitivity to the active substance, peanut or soya. Cardiotoxicity – monitor cardiac function. Liposomal doxorubicin may be stopped in future cycles if signs of cardiotoxicity eg cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. GI disturbances, mucositis, stomatitis. Paraesthesia. Infusion related reactions – allergic or anaphylactic like reactions discontinue infusion, treat, once fully recovered restart at reduced infusion rate. Palmar-plantar erythema - treat with steroids prednisolone 30mg od or dexamethasone 8mg od. Consider pyridoxine.

DOSE MODIFICATIONS

Liposomal doxorubicin maximum lifetime dose
= 400mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation)
= 450-550mg/m^2 (with normal cardiac function)

Haematological

Grade 1 ANC 1.5-1.9x10^9/l Platelets 75-150x10^9/l	Resume treatment with no dose reduction.
Grade 2 ANC 1.0-1.5x10^9/l Platelets 50-75x10^9/l	Wait until ANC ≥1.5 and platelets ≥75 redose with no dose reduction.
Grade 3 ANC 0.5-1.0x10^9/l Platelets 25-50x10^9/l	Wait until ANC ≥1.5 and platelets ≥75 redose with no dose reduction.
Grade 4 ANC <0.5x10^9/l Platelets <25x10^9/l	Wait until ANC ≥1.5 and platelets ≥75 give 75% dose or continue with GCSF.

For AIDS-KS patients haematological toxicity may require dose reduction or suspension or delay of therapy. Temporarily suspend treatment in patients when the ANC count is <1x10^9/l and/or the platelet count is <50x10^9/l. G-CSF may be given as concomitant therapy to support the blood count when the ANC count is <1x10^9/l in subsequent cycles.

Non-haematological

Palmar-plantar erythrodysethesia – week after prior pegylated liposomal doxorubicin dose

Current assessment	Week 4	Week 5	Week 6
Grade 1 (not interfering with daily activities)	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	Give 75% dose return to 4 week interval
Grade 2 (interfere with, but not preclude normal physical activities. Blisters <2cm diameter)	Wait an additional week	Wait an additional week	Give 75% dose return to 4 week interval
Grade 3 (interfere with walking or normal daily activities. Can't wear regular clothes)	Wait an additional week	Wait an additional week	Withdraw patient
Grade 4 (diffuse or local infections, bedridden or hospitalised)	Wait an additional week	Wait an additional week	Withdraw patient

Stomatitis week after prior pegylated liposomal doxorubicin dose

Current assessment	Week 4	Week 5	Week 6
Grade 1 (painless ulcers, erythema, mild soreness)	Redose unless patient has experienced a previous grade 3 or 4 stomatitis toxicity, in which case wait an additional week	Redose unless patient has experienced a previous grade 3 or 4 stomatitis toxicity, in which case wait an additional week	Give 75% dose return to 4 week interval or withdraw patient per physician's assessment
Grade 2 (painful erythema, oedema, ulcers, but can eat)	Wait an additional week	Wait an additional week	Give 75% dose return to 4 week interval or withdraw patient per physician's assessment
Grade 3 (painful erythema, oedema, ulcers, but can't eat)	Wait an additional week	Wait an additional week	Withdraw patient
Grade 4 (requires parenteral or enteral support)	Wait an additional week	Wait an additional week	Withdraw patient

Hepatic impairment

Bilirubin 20-50micromol/L	give 75% dose
Bilirubin >51micromol/L	give 50% dose

Patients with impaired hepatic function should be reduced based as follows:
at initiation of therapy, if the bilirubin 1.2-3.0mg/dl, the first dose is reduced to 75%,
bilirubin >3.0mg/dl, the first dose is reduced to 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 to 75% for the first dose, increase to full dose for cycle 2; if reduced to 50% for the first dose, increase to 75% of full dose for cycle 2.
Dosage can be increased to full dose for subsequent cycles if tolerated.
It can be administered to patients with liver metastases with concurrent elevation of bilirubin and liver enzymes up to 4xULN.
Prior to administration, evaluate hepatic function using conventional clinical laboratory tests such as ALT/AST, alkaline phosphatase, and bilirubin.

REFERENCES

1. SPC January 2024