Pegylated liposomal doxorubicin hydrochloride - Caelyx® (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.

(NICE TA91)

ICD-10 codes

Codes prefixed with C48, 56 and 57.

Regimen details

Day	Drug	Dose	Route
1	Caelyx®	40-50mg/m^2*	IV infusion

* The licensed dose is 50mg/m^2, however this is not tolerated by many patients so it may be appropriate to commence at a lower dose of 40mg/m^2.

Cycle frequency

28 days

Number of cycles

6 cycles

Administration

Caelyx® is administered in 250mL glucose 5%. For the first dose Caelyx® should be given over 60 minutes or at a rate of 1mg/minute (whichever is longer). If well tolerated subsequent infusions can be administered over 60 minutes. Infusions of Caelyx® **must not** be filtered.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of Caelyx®. Facilities for the treatment of hypotension and bronchospasm **must** be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of the infusion and appropriate therapy initiated.

Pre-medication

Nil

Emetogenicity

This regimen has a moderate - low emetogenic potential

Additional supportive medication

Mouthwashes as per local policy.
Loperamide if required.

Extravasation

Caelyx® 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

ECHO if history of cardiac dysfunction.

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	> 1.0 x 10^9/L
Platelets	> 100 x 10^9/L
Bilirubin	< ULN

Dose modifications

- **Haematological toxicity**

If neutrophils < 1.0 x 10^9/L and/or platelets < 100 x 10^9/L delay treatment for 1 week or until count recovery.

In the case of febrile neutropenia reduce Caelyx® to 75% for all future cycles.

- **Renal impairment**

No dose modifications are required for renal impairment.

- **Hepatic impairment**

Bilirubin (x ULN)	**Caelyx® dose**
≤ 1.0	100%*
1.0-2.5	75%*
2.5-3.5	50%*
> 3.5	Avoid

*If the first dose is tolerated without an increase in bilirubin or LFTs the second dose can be increased to the next dose increment (i.e. 50% to 75% and 75% to 100%) and then titrated back to full dose on subsequent cycles if tolerated.

- **Other toxicities**

Cutaneous toxicity (stomatitis or palmar plantar erythema – PPE) – treat symptomatically until toxicity resolved then dose as per table below.

Toxicity grade	**Toxicity resolved day 28** (day next cycle due)	**Toxicity resolved day 35** (1 week delay)	**Toxicity not resolved by day 42** (2 weeks delay)
Grade 1	Continue 100% dose	Continue 75% dose	Discontinue
Grade 2	Continue 75% dose	Continue 75% dose	Discontinue
Grade 3 or 4	Discontinue		

To minimise the risk of PPE for the first week after Caelyx® infusion:

- Keep hands and feet as cool as possible.
- Avoid tight-fitting gloves, sock, footwear and high-heeled shoes.
- Avoid exposing the skin to very hot water.
- Avoid vigorous rubbing of skin-pat skin dry after washing.
- Avoid use of topical anaesthetics as these can worsen skin reactions.

For all other grade 3 toxicities (except alopecia) delay treatment until resolved to ≤ grade 1 and resume with Caelyx® 75%. 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
Infertility
Peripheral neuropathy
Thromboembolism
Optic neuritis
Convulsions

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Alopecia
Constipation, diarrhoea
Stomatitis and mucositis
Fatigue
Allergic reactions
Palmar plantar erythema (PPE)

- **Other side effects**

Discoloured urine

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.

Additional comments

Consider previous anthracyclines exposure. Doxorubicin has a lifetime maximum cumulative dose of 450mg/m^2.

References

- National Institute for Clinical Excellence. Technology Appraisal Guidance 91. Accessed 14 August 2014 via www.nice.org.uk
- Rose PG. Pegylated liposomal doxorubicin: optimizing the dosing schedule in ovarain cancer. The Oncologist. 2004;10 (3):205–14.
- Summary of Product Characteristics Caelyx (Janssen-Cilag) accessed 14 August 2014 via www.medicines.org.uk
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.

Written/reviewed by: Dr R Bowen (Consultant Oncologist, Royal United Hospital, Bath), Dr A Walther (Consultant Oncologist, UHBristol NHS Trust)

Checked by: Sarah Murdoch (Senior Oncology Pharmacist, SW Strategic Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Strategic Clinical Network)

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