Pegylated liposomal doxorubicin hydrochloride - Caelyx® (sarcoma)

Indication
First or second line treatment of sarcoma in patients with cardiac impairment requiring an anthracycline.

(NHS England Routinely Commissioned)

ICD-10 codes
Codes prefixed with C49.

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 250-500mL 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 low emetogenic potential

Additional supportive medication
Mouthwashes as per local policy.
Emollients as per local policy.
Loperamide if required.

Extravasation

Caelyx® is an irritant (Group 3)

Investigations - pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Echocardiogram	Baseline

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days
Echocardiogram	After 3 cycles or as clinically indicated

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

If an adverse event occurs Caelyx® should be dose reduced as per the following table:

Dose level	**Caelyx® dose**
Full dose	50mg/m^2
First dose reduction	40mg/m^2
Second dose reduction	30mg/m^2
Third dose reduction	25mg/m^2

- ### 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 or if nadir neutrophils <0.5 x 10^9/L or platelets < 25 x 10^9/L reduce Caelyx® by one dose level for all future cycles.

- ### Renal impairment

No dose modifications are required for renal impairment.

- ### Hepatic impairment

Bilirubin (x ULN)	**Caelyx® dose* (if starting dose 40mg/m2)**	**Caelyx® dose* (if starting dose 50mg/m2)**
≤ 1.0	40mg/m2	50mg/m2
1.0-2.5	30mg/m2	40mg/m2
2.5-4	25mg/m2	25mg/m2
> 4	Avoid	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 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	Maintain dose	Reduce by one dose level	Discontinue
Grade 2	Reduce by one dose level	Reduce by one dose level	Discontinue
Grade 3 or 4	Discontinue	Discontinue	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® reduced by one dose level. 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)
Decreased appetite

- **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 or DOAC during treatment.

Additional comments

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

References

- Summary of Product Characteristics Caelyx (Janssen-Cilag) accessed 06 January 2022 via www.medicines.org.uk
- Judson, I. *et al.* Randomised phase II trial of pegylated liposomal doxorubicin (DOXIL/CAELYX) versus doxorubicin in the treatment of advanced or metastatic soft tissue sarcoma: a study by the EORTC soft tissue and bone sarcoma group. Eur J Cancer 2001:37(7):870-877.
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.

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Date: January 2022