DOXOrubicin 75mg/m^2 Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of locally advanced unresectable or metastatic soft tissue sarcoma	C49	00500a	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.

DOXOrubicin is administered once every 21 days for 3-6 cycles or until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	[a]DOXOrubicin	[b]75mg/m^2	IV bolus		Every 21 days for 6 cycles
[a]Lifetime cumulative dose of DOXOrubicin is 450mg/m^2 **In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors outlined below[i] and to the age of the patient**					
[b]Consider dose reduction to 60mg/m^2 in patients >70 years					

ELIGIBILITY:

- Indication as above
- ECOG 0-2
- Adequate hepatic, renal, and bone marrow function

EXCLUSIONS:

- Hypersensitivity to DOXOrubicin or any of the excipients
- Congestive heart failure (LVEF < 50%) or other significant heart disease
- Pregnancy
- Lactation

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Cardiac function using MUGA or ECHO (LVEF ≥ 50% to administer DOXOrubicin) if >65 years or if clinically indicated (e.g. smoking history, hypertension)

Regular tests:

- FBC, renal and liver profile prior to each cycle
- Cardiac function as clinically indicated

Disease monitoring:

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

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

Table 1: Dose reduction levels for DOXOrubicin

Starting Dose	**75mg/m^2**
Level -1	60mg/m^2
Level -2	50mg/m^2
Level-3	Discontinue

Haematological:

Table 2: Dose modification of DOXOrubicin in haematological toxicity

ANC (x10^9/L)		**Platelets (x10^9/L)**	**Dose**
≥1	and	≥100	100%
<1	or	<100	Delay one week or until recovery. If > 2 week delay consider dose reduction by 1 dose level
Febrile neutropenia 1 st occurrence 2nd occurrence			 Consider addition of G-CSF to subsequent cycles Reduce dose by one dose level

Renal and Hepatic Impairment:

Table 3: Dose modification of DOXOrubicin in renal and hepatic impairment

Renal Impairment	**Hepatic Impairment**	
No dose reduction required. Clinical decision in severe impairment	**Total Bilirubin (micromol/L)**	**Dose**
	20-50	50%
	51-85	25%
	>85	Omit
	AST 2-3 ULN give 75% of dose	
	AST >3 ULN give 50% of dose	

Management of adverse events:

Table 4: Dose Modification of DOXOrubicin for Adverse Events

Adverse reactions	Recommended dose modification
Cardiotoxicity:	Treatment should be discontinued if absolute LVEF <45% or >20% reduction in baseline LVEF
Other grade 3-4 toxicities	Hold chemotherapy until toxicity improves to grade ≤1. Consider dose reduction by 1 dose level.

SUPPORTIVE CARE:

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

PREMEDICATIONS: None usually required

OTHER SUPPORTIVE CARE:

No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Cardiotoxicity**: DOXOrubicin is cardiotoxic and must be used with caution, if at all, in patients with severe hypertension or cardiac dysfunction
- **Extravasation:** DOXOrubicin causes pain and tissue necrosis if extravasated (**Refer to local policy**).

DRUG INTERACTIONS:

- DOXOrubicin cardiotoxicity is enhanced by previous or concurrent use of other anthracyclines, or other potentially cardiotoxic drugs (e.g. 5-Fluorouracil, cyclophosphamide or PACLitaxel) or with products affecting cardiac function (e.g. calcium antagonists).
- Current drug interaction databases should be consulted for more information.

ATC CODE:

DOXOrubicin L01DB01

REFERENCES:

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2. University College London. GeDDiS: A prospective randomised controlled phase III trial of gemcitabine and docetaxel compared with doxorubicin as first line treatment in previously untreated advanced

unresectable or metastatic soft tissue sarcomas [Internet]. Available from: https://www.ctc.ucl.ac.uk/TrialDocuments/Uploaded/GeDDiS%20Protocol%20v8.0%2022Mar2016_06062017_0.pdf
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4. Dosage Adjustment for Cytotoxics in Hepatic Impairment. North London Cancer Network. Available at http://londoncancer.org/media/65594/hepatic- impairment-dosage-adjustment-for-cytotoxics.pdf
5. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V2 2019. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
6. DOXOrubicin 2mg/ml Concentrate for Solution for Injection. Summary of Product Characteristics. Accessed July 2020 / Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2315-083-001_26022020112618.pdf

Version	Date	Amendment	Approved By
1	13/08/2018		Dr Michael McCarthy
2	30/07/2020	Updated eligibility criteria Updated exclusion criteria	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] Cardiotoxicity is a risk associated with anthracycline therapy that may be manifested by early (acute) or late (delayed) effects.
Risk factors for developing anthracycline-induced cardiotoxicity include:
• high cumulative dose, previous therapy with other anthracyclines or anthracenediones
• prior or concomitant radiotherapy to the mediastinal/pericardial area
• pre-existing heart disease
• concomitant use of other potentially cardiotoxic drugs
In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors above and to the age of the patient