DOXOrubicin (60mg/m^2) Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of unresectable or metastatic hepatocellular carcinoma not suitable for treatment with regional therapies	C22	00386a	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	DOXOrubicin[a]	60mg/m^2	IV bolus	Slow bolus with 0.9% NaCl	Every 21 days for 3-6 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.					

ELIGIBILTY:

- Indications as above
- ECOG 0-3
- Adequate hepatic, renal, and bone marrow function

EXCLUSIONS:

- Hypersensitivity to DOXOrubicin or any of the excipients
- Pregnancy
- Lactation

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, liver and renal 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, liver and renal profile prior to each cycle

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 DOXOrubicin in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Recommended Dose
>1	And	>100	100%
<1	Or	<100	Delay

Renal and Hepatic Impairment:

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

Renal Impairment	Hepatic Impairment	
No dose modification required	**Total Bilirubin (micromole/L)**	**Dose**
	20-50	50%
	51-85	25%
	>85	Omit
	If AST 2-3 x normal, give 75% dose. If AST >3x ULN, give 50% dose	

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:

1. Falkson G, Moertel CG, Lavin P, et al. Chemotherapy studies in primary liver cancer: a prospective randomized clinical trial. Cancer. 1978;42(5):2149.
2. Sciarrino E, Simonetti RG, Le Moli S, Pagliaro L et al Adriamycin treatment for hepatocellular carcinoma. Experience with 109 patients. Cancer. 1985;56(12):2751
3. Doxorubicin 2mg/ml Concentrate for Solution for Infusion. Summary of Product Characteristics. Last updated 29/05/2019. Accessed Jan 2020Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA22766-004-001_29052019171647.pdf

Version	Date	Amendment	Approved By
1	20/12/2016		Prof Maccon Keane
2	26/11/2018	Updated to new NCCP template. Standardisation of dosing in hepatic impairment	Prof Maccon Keane
3	15/01/2020	Reviewed. Update of haematological dose modifications and emetogenic potential.	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