Dacarbazine (1.2 g/m^2) Therapy – 21 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement status
Treatment of metastatic soft tissue sarcoma	C43	00511	Hospital

**If the reimbursement status[i] is not defined, the indication has yet to be assessed through the formal HSE reimbursement process.*

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.

Dacarbazine is administered on day 1 of a 21 day cycle for 4 cycles or until disease progression or unacceptable toxicity develops.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Dacarbazine	1.2 g/m^2	IV infusion	1000mls NaCl 0.9% over 1 hour	Every 21 days
Dacarbazine is sensitive to light exposure. All reconstituted solutions should be suitably protected from light also during administration (light-resistant infusion set)					

ELIGIBILTY:

- Indications as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to the active substance or to any of the excipients
- Pregnancy or breastfeeding
- Leukopenia and/or thrombocytopenia
- Severe liver or kidney diseases.

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile

Regular tests:

- FBC, renal and liver profile prior to each treatment

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 dacarbazine in haematological toxicity

ANC ($x10^9$ /L)		Platelets ($x10^9$ /L)	Dose
>1.5	and	>100	100%
1– 1.5	or	70 – 100	80 %
< 1	or	< 70	Delay one week

If the patient was admitted with an episode of neutropenic sepsis during the interval, give 80% of the previous dose.

Renal and Hepatic Impairment:

Table 2: Dose modifications in renal and hepatic impairment

Renal Impairment		Hepatic Impairment
Cr Cl (ml/min)	**Dose**	Can be hepatotoxic. Consider dose reduction.
45-60	**80%**	
30-45	**75%**	
<30	**70%**	

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.
- **Vein Irritation:** Dacarbazine often causes pain during administration that usually responds to slowing the infusion rate.
- **Hepatotoxic drugs** and alcohol should be avoided during chemotherapy.

DRUG INTERACTIONS:

- Dacarbazine is metabolised by cytochrome P450 (CYP1A1, CYP1A2, and CYP2E1). This has to be taken into account if other medicinal products are co-administered which are metabolised by the same hepatic enzymes.

- Concomitant use of phenytoin and dacarbazine should be avoided since there is a risk of exacerbation of convulsions resulting from the decrease of phenytoin digestive absorption.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Dacarbazine - L01AX04

REFERENCES:

1. Buesa JM, M., van Oosterom AT, Verweij J, et al. High-dose DTIC in advanced soft-tissue sarcomas in the adult. A phase II study of the E.O.R.T.C Soft Tissue and Bone Sarcoma Group. Ann Oncol 1991;2:307-9.
2. BCCA Protocol Summary for High Dose Single Agent Dacarbazine (DTIC) for Metastatic Soft Tissue Sarcoma SADTIC Revised 1 May 2016
3. Dosage Adjustment for Cytotoxics in Renal Impai*rment* January 2009; North London Cancer Network. Available at http://londoncancer.org/media/65600/renal-impairment-dosage-adjustment-for-cytotoxics.pdf
4. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009;North London Cancer Network. Available at http://londoncancer.org/media/65594/hepatic-impairment-dosage-adjustment-for-cytotoxics.pdf
5. Dacarbazine Summary of Product Characteristics. Accessed August 2018. Available at https://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1760-001-002_21082017143042.pdf

Version	Date	Amendment	Approved By
1	10/10/2018		Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/