Regimen Monograph

A - Regimen Name

DCRB Regimen

Dacarbazine

Disease Site
Sarcoma - Soft Tissue
Skin - Melanoma

Intent
Palliative

Regimen Category
Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses

- For the treatment of patients with metastatic melanoma.
- For the treament of patients with metastatic leiomyosarcoma and liposarcoma

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B - Drug Regimen

dacarbazine	1000 mg /m²	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Other Supportive Care:

Also refer to CCO Antiemetic Summary

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Toxicity	Action[1]	Dose
Grade 3 (with fever or systemic infection) or Grade 4 hematological toxicity	Hold	↓ 25%
Grade 3 non-hematological	Hold	↓ 25%; discontinue if recurs after 2 dose reductions
Grade 4 non-hematological	Discontinue	Not applicable

[1] Before retreatment, major organ toxicities should recover to ≤ Grade 2, platelets ≥ 100 x 10^9/L, and ANC ≥ 1.5 x 10^9/L.

Hepatic Impairment

Adjustment required; no details found.

Renal Impairment

Creatinine Clearance (mL/min)	Dose*
>50	100% of dose
30-50	75% of dose
10-30	50% or discontinue
<10	discontinue

* modified from Kintzel et al 1995

Dosage in the Elderly

Safety and efficacy not established.

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F - Adverse Effects

Refer to dacarbazine drug monograph(s) for additional details of adverse effects

Very common (≥ 50%)	Common (25-49%)	Less common (Up to 24%)	Uncommon (< 10%), but may be severe or life-threatening
• Anorexia • Nausea, vomiting	• Fatigue	• Constipation • Diarrhea • Myelosuppression (may be severe) • Mucositis • Flu-like symptoms	• Hepatic necrosis • Veno-occlusive disease • Nephrotoxicity • Hypersensitivity • Photosensitivity • Rash • Injection site reaction • Seizure • Blurred vision

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G - Interactions

Refer to dacarbazine drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to dacarbazine drug monograph(s) for additional details

Administration

- Administration of concentrated dacarbazine solutions may cause severe perivenous pain; therefore, it is recommended to give dacarbazine as a diluted IV infusion.
- Extreme care should be taken to avoid extravasation as this may result in tissue damage and severe pain.
- May be mixed in 500 mL to 1000 mL normal saline or D5W bag and infused IV over 1 to 2 hours.
- Keep dacarbazine vials refrigerated (2 to 8ºC); protect the undiluted drug, infusion bags and tubing from light.

Contraindications

- patients with known hypersensitivity to dacarbazine, or any component of its formulation
- patients who have previously had severe myelosuppression.

Warnings/Precautions

- Dacarbazine is a moderate immunosuppressive agent. Avoid the use of live vaccines during treatment and for at least 3 months after the last dose. Response to inactivated vaccines may be decreased.

Pregnancy/Lactation:

- Dacarbazine is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during therapy and for at least 6 months after treatment cessation.
- Breast feeding is not recommended due to the potential secretion into breast milk.
- Effects on fertility: Probable

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; Baseline and before each cycle
- Liver and renal function tests; Baseline and as clinically indicated
- Clinical toxicity assessment including GI, infection, bleeding, hypersensitivity, skin, injection site reactions, flu-like symptoms; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	1 - 2 hours
Pharmacy Workload (average time per visit)	22.2 minutes
Nursing Workload (average time per visit)	36.667 minutes

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K - References

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Therapy for metastatic malignant melanoma using high dose single agent dacarbazine. BC Cancer Agency, Feb 1, 2020.

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Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. N Engl J Med 2011;364:2507-16.

Chapman PB, Einhorn LH, Meyers ML, et al. Phase III multicentre randomized trial of the Dartmouth regimen versus dacarbazine in patients with metastatic melanoma. J Clin Oncol 1999; 17(9): 2745-

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Demetri GD, von Mehren M, Jones RL, et al. Efficacy and safety of trabectedin or dacarbazine for metastatic liposarcoma or leiomyosarcoma after failure of conventional chemotherapy: results of a phase III randomized multicentre clinical trial.

Middleton MR, Grob JJ, Aaronson N, et al. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. J Clin Oncol 2000; 18(1): 158-66.

Pritchard KI, Quirt IC, Cowan DH, et al. DTIC therapy in metastatic malignant melanoma: a simplified dose schedule. Cancer Treat Rep, 1980; 64: 1123-26.

Sileni VC, Nortilli R, Aversa SML, et al. Phase II randomized study of dacarbazine, carmustine, cisplatin and tamoxifen versus dacarbazine alone in advanced melanoma patients. Melanoma Research 2001; 11: 189-96.

August 2020 added liposarcoma and leiomyosarcoma as ST-QBP approved indications

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

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Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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