Regimen Monograph

A - Regimen Name

DASA Regimen

Dasatinib

Disease Site

Hematologic
Leukemia - Chronic Myeloid (CML)

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

- Treatment of adult patients with Philadelphia chromosome positive (Ph+) chronic, accelerated, or blast phase chronic myeloid leukemia (CML) with resistance or intolerance to prior therapy, including imatinib mesylate
- Treatment of adults with newly diagnosed Philadelphia chromosome positive (Ph+) CML in chronic phase.

Note: Health Canada approval was based on hematologic and cytogenetic response rates; overall survival benefit has not been demonstrated.

Supplementary Public Funding

daSATinib
Exceptional Access Program (daSAtinib - Ph+ CML in the chronic phase, with specific criteria) (EAP Website) (does not exclude treatment-naïve patients)

daSATinib
Exceptional Access Program (daSAtinib - Accelerated phase or blast phase Ph+ CML with documented resistance or intolerance to imatinib, with specific criteria) (EAP Website)

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B - Drug Regimen

Chronic Phase:

daSATinib	100 mg	PO	Daily

If an adequate hematologic or cytogenetic response is not observed, the dose of dasatinib may be increased to 140 mg PO daily.

Accelerated Phase or Blast Crisis:

daSATinib	140 mg	PO	Daily

If an adequate hematologic or cytogenetic response is not observed, the dose of dasatinib may be increased to 180 mg PO daily.

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

Other Supportive Care:

- Also refer to CCO Antiemetic Recommendations.
- **Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.

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E - Dose Modifications

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

Hypokalemia and hypomagnesemia should be corrected before starting dasatinib.

Patients should be evaluated for signs and symptoms of underlying cardiopulmonary disease prior to initiating treatment.

Patients should be tested for HBV infection prior to initiating treatment. Carriers of HBV must be monitored for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy.

Dosage with toxicity

Dose Level	Dasatinib Dose (mg; PO once daily)	
	Chronic phase CML	Accelerated, blast phase CML
0	100	140
-1	80	100
-2	50	80

Dosage with Myelosuppression:

Indication	Blood Counts (x 10^9/L)	Action (Blood Counts x 10^9/L)
Chronic phase CML	ANC <0.5 and/or Platelets <50	1. Hold until ANC ≥ 1 and platelets ≥ 50 2. Resume at same dose level 3. If platelets < 25 and/or recurrence of ANC < 0.5 for > 7 days, repeat step 1 and resume at ↓ 1 dose level for second episode 4. Third episode: further ↓ by 1 dose level (newly diagnosed patients) or discontinue (patients resistant or intolerant to prior therapy including imatinib) 5. Fourth episode: Discontinue
Accelerated or blast phase CML	ANC <0.5 and/or Platelets <10	If related to leukemia (bone marrow biopsy), consider ↑ to 180 mg OD. If unrelated: 1. Hold until ANC ≥ 1 and platelets ≥ 20 2. Resume at same dose level 3. Second episode: repeat step 1 and resume at ↓ 1 dose level 4. Third episode: repeat step 1 and resume by further ↓ 1 dose level 5. Fourth episode: Discontinue

Dosage with non-hematologic toxicity:

Toxicity	Grade	Action
Fluid retention	Any	Hold if appropriate until recovery and treat with diuretics, short courses of steroids or other supportive measures. Consider dose reduction or treatment discontinuation.
Pulmonary hypertension	Any	Hold and investigate. Discontinue if confirmed.
Mucocutaneous skin reactions	Severe or any grade SJS	Discontinue (if no other etiology).
Other non-hematologic toxicity	Grade 2	Hold until recovery. First occurrence: resume at same dose level. Second occurrence: resume at ↓ 1 dose level.
	≥ Grade 3	Hold until recovery. Restart at a reduced dose if appropriate.

Dose Reduction for concomitant use of strong CYP3A4 inhibitors:

Current Dasatinib Dose (mg/daily)	Reduced Dasatinib Dose (mg/daily)*
140	40
100	20
70	20
60	Hold until the inhibitor is discontinued. Allow a washout period of approximately 1 week after the inhibitor is stopped before restarting dasatinib.
40	

*If dasatinib is not tolerated after dose reduction, discontinue the strong CYP3A4 inhibitor or hold dasatinib until the inhibitor is discontinued. Allow a washout period of approximately 1 week after the inhibitor is stopped before dasatinib dose is increased.

Hepatic Impairment

Dasatinib has not been studied in hepatic impairment within the indicated dosing range. Hepatic metabolism / excretion is significant; caution should be exercised and dose modification considered especially for moderate or severe hepatic impairment.

Renal Impairment

Studies in renal impairment have not been conducted. However, since <4% of dasatinib and metabolites are renally excreted and a reduction in dasatinib clearance is not expected.

Dosage in the Elderly

No dose adjustment is required. Patients ≥ 65 years of age are more likely to experience commonly reported adverse events, such as diarrhea, fatigue, cough, dyspnea, fluid retention (including pericardial and pleural effusion), dizziness, pneumonia, hypertension, arrhythmia, heart failure, and gastrointestinal bleeding, as well as less frequently reported events such as pulmonary edema, lung infiltration, arthritis and urinary frequency. Imatinib resistant or intolerant chronic phase CML patients are less likely to have major cytogenetic response. Monitor closely.

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F - Adverse Effects

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

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Headache • Musculoskeletal pain • Infection (including atypical infections, HBV re-activation) • Diarrhea (may be severe) • Fatigue • Myelosuppression (may be severe) • Cough/dyspnea • Rash/pruritus (may be severe) • Fluid retention (may be severe) • Hemorrhage (may be severe)	• Abdominal pain • Nausea/vomiting • Constipation • Dizziness • Neuropathy • Insomnia • Appetite disturbances/weight changes • Depression • Abnormal electrolytes • Mucositis • Hyperhidrosis	• Arrhythmia, prolonged QTc • Venous/arterial thromboembolism • Cardiotoxicity • Pericardial effusion • Myocarditis/pericarditis • Pulmonary hypertension • Hypersensitivity • Pneumonitis • Pancreatitis • Tumour lysis syndrome • Increased LFTs • Renal failure • Nephrotic syndrome • Thrombotic microangiopathy • Rhabdomyolysis • Pure red cell aplasia • Stevens-Johnson syndrome • Erythema multiforme

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G - Interactions

Refer to daSATinib drug monograph(s) for additional details.

- Avoid strong CYP3A4 inhibitors as they may increase dasatinib exposure; if the strong CYP3A4 inhibitor cannot be discontinued, consider a dasatinib dose reduction. See Dosage with Toxicity for dasatinib dose reductions.
- Avoid strong CYP3A4 inducers as they may decrease dasatinib exposure. Consider alternative agents with less enzyme induction potential.
- Avoid use with other drugs that prolong the QT interval.
- Avoid concomitant use with H2 blockers/ proton pump inhibitors; consider the use of antacid instead (e.g. aluminum hydroxide/magnesium) ≥ 2hrs before or after dasatinib.

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H - Drug Administration and Special Precautions

Refer to daSATinib drug monograph(s) for additional details.

Administration

- Swallow tablet whole with or without food once daily.
- Tablets should not be crushed or cut.
- Antacids should be avoided; if required, they should be taken up to 2 hours before or 2 hours after the administration of dasatinib.
- Avoid grapefruit, starfruit, Seville oranges, their juices or products during treatment.
- If a dose is missed, skip this and give the next dose as scheduled. Do not double the dose to make up for the forgotten one.
- Pregnant women should avoid exposure to crushed and/or broken tablets.
- Store at room temperature (15°C to 30°C).

Contraindications

- Patients with hypersensitivity to dasatinib or its components
- Breastfeeding women

Other Warnings/Precautions

- Contains lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- Consultation with a liver disease expert is recommended prior to starting dasatinib in chronic HBV carriers (including those with active disease), and for patients who test positive for HBV infection while on treatment.
- Dasatinib and its metabolite may prolong the QT interval, and should be used with caution in patients at risk, such as those with hypokalemia, hypomagnesemia, congenital long QT syndrome, on antiarrhythmic therapy or other medications that may lead to QT prolongation, or in patients who have received cumulative high-dose anthracyclines.
- Use with caution in patients with uncontrolled or significant cardiovascular disease as they were excluded from clinical trials. Adverse cardiac events were more frequent in patients with cardiovascular risk factors or a previous medical history of cardiac disease.
- Exercise caution in patients at risk of bleeding or who are taking concurrent anticoagulants, as dasatinib has been shown to inhibit platelet aggregation and increase bleeding time. Patients with a history of significant bleeding disorder unrelated to CML were excluded from dasatinib clinical studies.
- Patients with pre-existing pleural effusion were excluded from phase III studies.
- Use with extreme caution when fluid loading/transfusing.

Pregnancy/Lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is **contraindicated** during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Probable

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; Chronic phase CML: Baseline and every 2 weeks for 12 weeks, then every 3 months or as clinically indicated
- CBC; Advanced phase CML: Baseline and weekly for the first 8 weeks, then monthly or as clinically indicated
- Liver and renal function tests (including electrolytes), creatine kinase; Baseline and every 2 weeks for the first 2 months, then monthly and as clinically indicated
- LVEF evaluation, in patient with cardiac risk factors; Baseline and as clinically indicated
- ECG; Baseline and as clinically indicated
- Signs and symptoms of active HBV infection (in HBV carriers); During treatment and for several months after treatment discontinues
- Clinical toxicity assessment for signs and symptoms of bleeding, infection, cardiotoxicity, muscle pain, rash, GI, pulmonary hypertension, pleural effusion, dermatological and auditory effects and fluid retention; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Consider LVEF evaluation in patients without cardiac risk factors; baseline and as clinically indicated

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Cortes J, Rousselot P, Kim DW, et al.Dasatinib induces complete hematologic and cytogenetic responses in patients with imatinib-resistant or -intolerant chronic myeloid leukemia in blast crisis. Blood 2007; 109: 3207-3213. doi:10.1182/blood-2006-09-046888

Dasatinib drug monograph, Ontario Health (Cancer Care Ontario).

Guilhot F, Apperley J, Kim DW, et al. Dasatinib induces significant hematologic and cytogenetic responses in patients with imatinib-resistant or -intolerant chronic myeloid leukemia in accelerated phase. Blood 2007; 109: 4143-4150. doi:10.1182/blood-2006-09-046839

Kantarjian H, Shah NP, Hochhaus A, et al. Dasatinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med. 2010 Jun 17;362(24):2260-70.

Shah NP, Kantarjian HM, Kim DW, et al. Intermittent target inhibition with dasatinib 100 mg once daily preserves efficacy and improves tolerability in imatinib-resistant and -intolerant chronic-phase chronic myeloid leukemia. Blood 2008; 26(19); 3204-12.

February 2025 Updated Pregnancy and Lactation section

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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.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

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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