Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

HYDR Regimen

Hydroxyurea

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

- For upfront treatment to improve blood counts and reduce the risk of leukostasis in patients with chronic myeloid leukemia (CML); same rationale for end of life care in refractory patients
- For bridge therapy prior to tyrosine kinase inhibitor (TKI) initiation in patients with CML

Supplementary Public Funding

hydroxyurea
ODB - General Benefit (hydroxyurea) (ODB Formulary)

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B - Drug Regimen

hydroxyurea	20 to 30 mg /kg	PO	Daily

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C - Cycle Frequency

Up to a usual total of 6 months of treatment

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

- 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.

Other Supportive Care:

- Patients at risk of tumour lysis syndrome (i.e. high tumour burden) should have appropriate prophylaxis and be monitored closely.
- Skin cancer has been reported in patients on long-term hydroxyurea. Patients should be advised to protect skin from sun exposure.

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E - Dose Modifications

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

Severe anemia must be corrected prior to initiation of treatment with hydroxyurea.

Dosage with toxicity

If no guidelines available for dose modifications, refer to Dosage Modification for Hematologic and Non-Hematologic Toxicities.

Toxicity	Action
Mild to moderate anemia	Transfuse if symptomatic; do not interrupt.
Worsening or persistent anemia	Consider hold, and evaluate for hemolysis. If hemolytic anemia is confirmed, discontinue.
Severe mucositis or gastric distress (e.g., nausea, vomiting, and anorexia)	Hold until ≤ grade 1.
Vasculitis	Discontinue.
Hepatitis or cholestasis	Discontinue.
Interstitial lung disease	Discontinue. Manage with corticosteroids.

Hepatic Impairment

No data available; close hematologic monitoring recommended.

Renal Impairment

Hydroxyurea should be used with caution in patents with renal impairment; close hematologic monitoring is recommended. In patients with CrCl < 60 mL/min (or ESRD), there was an approximate 64% increase in mean hydroxyurea exposure.

Creatinine Clearance (mL/min)	Starting Dose (% usual dose)
> 60	100%
10-60	50%
<10	20%* or Discontinue

*Give hydroxyurea after dialysis on dialysis days.

Dosage in the Elderly

May be more sensitive to toxic effects. Consider dosage adjustment.

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F - Adverse Effects

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

Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Myelosuppression +/- infection, bleeding • Anorexia • Diarrhea • Nausea, vomiting • Rash (may be severe) • Fever • Fatigue	• ILD/Pneumonitis • Secondary malignancies • Pancreatitis • Hepatic failure • Cholestasis • Cutaneous vasculitis/ulcers, gangrene • CNS effects (hallucinations, seizure) • Systemic or cutaneous lupus • Radiation recall • Dermatomyositis • Tumour lysis syndrome • Hemolytic anemia

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G - Interactions

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

- Avoid antiretrovirals (didanosine +/- stavudine) given increased incidence of pancreatitis, liver failure and neurotoxicity.
- Adjust dose of uricosuric agents as necessary as hydroxyurea may increase uric acid levels.
- Hyrdoxyurea may interfere with enzymatic assays (unknown clinical relevance).

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H - Drug Administration and Special Precautions

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

Administration

- To minimize the risk of exposure, always wash hands before and after handling hydroxyurea. Always wear impervious gloves when handling hydroxyurea capsules or packaging.
- If patient is unable to swallow capsules, capsule contents may be emptied into a glass of water and taken immediately. Some inert material used as vehicle in the capsule may not dissolve and float on the surface.
- Patients should not allow the drug powder to come in contact with their skin or mucous membranes and avoid inhaling the powder when opening the capsules.
- Store at room temperature (15 - 30°C) and protect from excessive heat and moisture.

Contraindications

- Patients with marked myelosuppression (WBC < 2.5 x 10^9/L or platelets < 100 x 10^9/L), or severe anemia
- Patients who have demonstrated a previous hypersensitivity to hydroxyurea or any other component in its formulation

Warnings/Precautions

- Avoid the use of live vaccines.
- Patient's antibody response to inactivated vaccines may be suboptimal.
- Avoid combination of hydroxyurea with antiretrovirals, particularly didanosine and/or stavudine, due to risk of serious toxicities. (Refer to interactions.)
- Use with caution in patients who have recently received extensive radiotherapy or chemotherapy.
- Exercise caution when driving or using machinery since hydroxyurea may cause drowsiness or other neurologic effects.
- Some brands of hydroxyurea contain lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

Pregnancy/Lactation

- Hydroxyurea is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **6 months** after the last dose (for

females) and **12 months** after the last dose (for males).
- Breastfeeding is not recommended.
- Fertility effects: Probable
    - Sperm banking should be offered for males due to effects on fertility.

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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; Baseline and as clinically indicated
- Liver function tests; Baseline and as clinically indicated
- Renal function tests; Baseline and as clinically indicated
- Clinical assessment of fever, infection, bleeding, TLS, secondary malignancies (including skin), respiratory, skin, gastrointestinal and neurologic effects; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Serum folic acid; Baseline and as clinically indicated

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Hehlmann R, Heimpel H, Hasford J, et al. Randomized comparison of interferon-α with busulfan and hydroxyurea in chronic myelogenous leukemia. Blood 1994; 84: 4064-4077.

Hehlmann R, Heimpel H, Hasford J, et al. Randomized comparison of busulfan and hydroxyurea in chronic myelogenous leukemia: prolongation of survival by hydroxyurea. The German CML Study Group. Blood 1993; 82: 393-407.

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

March 2023 Modified Premedication/Supportive care, Dosage with toxicity, Adverse effects and Monitoring sections

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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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