Hydroxyurea

**Class:**
Antineoplastic agent, Antimetabolite

**Indications:**
Chronic myeloid leukemia
Solid tumors (head and neck cancer, melanoma, ovarian cancer)
Sickle cell anemia
*(Unlabeled use):*  
Acute myeloid leukemia (AML), cytoreduction
Essential thrombocythemia, high-risk
Head and neck cancer
Hypereosinophilic syndrome
Meningioma
Polycythemia Vera

**Available dosage form in the hospital:**
500 mg CAP

**Trade Names:**
Droxia
Hydrea

**Doses:** **Note:** Doses should be based on ideal or actual body weight, whichever is less (per manufacturer).

- **Antineoplastic uses:** Titrate dose to patient response; if WBC count falls to <2500/mm$^3$, or the platelet count to <100,000/mm$^3$, therapy should be stopped for at least 3 days and resumed when values rise toward normal

- **Chronic myeloid leukemia (resistant):** Oral: Continuous therapy: 20-30 mg/kg once daily

- **Solid tumors (head and neck cancer, melanoma, ovarian cancer):** Oral:
  - Intermittent therapy: 80 mg/kg as a single dose every third day
  - Continuous therapy: 20-30 mg/kg once daily
  - Concomitant therapy with irradiation (head and neck cancer): 80 mg/kg as a single dose every third day starting at least 7 days before initiation of irradiation

- **Sickle cell anemia:** Oral: Initial: 15 mg/kg/day; if blood counts are in an acceptable range, may increase by 5 mg/kg every 12 weeks until the maximum tolerated dose of 35 mg/kg/day is achieved or the dose that does not produce toxic effects (do not increase dose if blood counts are between acceptable and toxic ranges). Monitor for toxicity every 2 weeks; if toxicity occurs, withhold treatment until the bone marrow recovers, then restart with a dose reduction of 2.5 mg/kg/day; if no toxicity occurs over the next 12 weeks, then the subsequent dose may be increased by 2.5 mg/kg/day every 12 weeks to a maximum tolerated dose (dose which does not produce hematologic toxicity for 24 consecutive weeks). If hematologic toxicity recurs a second time at a specific dose, do not retry that dose.

  - **Acceptable hematologic ranges:** Neutrophils ≥2500/mm$^3$; platelets ≥95,000/mm$^3$; hemoglobin >5.3 g/dL, and reticulocytes ≥95,000/mm$^3$ if the hemoglobin concentration is <9 g/dL
  - **Toxic hematologic ranges:** Neutrophils <2000/mm$^3$; platelets <80,000/mm$^3$; hemoglobin <4.5 g/dL; and reticulocytes <80,000/mm$^3$ if the hemoglobin concentration is <9 g/dL

- **Acute myeloid leukemia (AML), cytoreduction (unlabeled use):** Oral: 50-100 mg/kg/day until WBC <100,000/mm$^3$ or 50-60 mg/kg/day until WBC <10,000-20,000/mm$^3$

- **Essential thrombocythemia, high-risk (unlabeled use):** Oral: 500-1000 mg daily; adjust dose to maintain platelets <400,000/mm$^3$ (Harrison, 2005)
-Head and neck cancer (unlabeled dosing; with concurrent radiation therapy and fluorouracil):
  Oral: 1000 mg every 12 hours for 11 doses per cycle (Garden, 2004)
-Hypereosinophilic syndrome (unlabeled use): Oral: 1000-3000 mg/day
-Meningioma (unlabeled use): Oral: 20 mg/kg once daily (Newton, 2000; Rosenthal, 2002)
-Polycythemia Vera, high-risk (unlabeled use): Oral: 15-20 mg/kg/day

Geriatric
Refer to adult dosing. May require lower doses.

Renal Impairment:
**The manufacturer’s labeling recommends the following adjustments:
- Sickle cell anemia:
  - $\text{Cl}_\text{cr} \geq 60 \text{ mL/minute}$: No dosage adjustment (of initial dose) necessary.
  - $\text{Cl}_\text{cr} < 60 \text{ mL/minute}$: Reduce initial dose to 7.5 mg/kg/day (Yan, 2005); titrate to response/avoidance of toxicity (refer to usual dosing).
- ESRD: Reduce initial dose to 7.5 mg/kg/dose (administer after dialysis on dialysis days); titrate to response/avoidance of toxicity.
- Other approved indications: Reduction in initial dose is recommended; however, no specific adjustments are available.

**The following adjustments have also been reported:
- Aronoff, 2007: Adults:
  - $\text{Cl}_\text{cr} > 50 \text{ mL/minute}$: No dosage adjustment necessary
  - $\text{Cl}_\text{cr} 10-50 \text{ mL/minute}$: Administer 50% of dose.
  - $\text{Cl}_\text{cr} < 10 \text{ mL/minute}$: Administer 20% of dose.
- Hemodialysis: Administer dose after dialysis on dialysis days.
- Continuous renal replacement therapy (CRRT): Administer 50% of dose.
- Kintzel, 1995:
  - $\text{Cl}_\text{cr} 46-60 \text{ mL/minute}$: Administer 85% of dose.
  - $\text{Cl}_\text{cr} 31-45 \text{ mL/minute}$: Administer 80% of dose.
  - $\text{Cl}_\text{cr} < 30 \text{ mL/minute}$: Administer 75% of dose.

Hepatic Impairment:
No dosage adjustment provided in the manufacturer’s labeling; closely monitor for bone marrow toxicity.

Dosing: Obesity
**ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer**: Utilize patient’s actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012). **Note**: The manufacturer recommends dosing based on ideal or actual body weight, whichever is less.

Dosing: Adjustment for Toxicity
- Cutaneous vasculitic ulcerations: Discontinue
- Gastrointestinal toxicity (severe nausea, vomiting, anorexia): Temporarily interrupt treatment
- Mucositis (severe): Temporarily interrupt treatment
- Pancreatitis: Discontinue permanently
- Hematologic toxicity:
  1. Antineoplastic uses (CML, head and neck cancer, melanoma, ovarian cancer): WBC $< 2500/\text{mm}^3$ or platelets $< 100,000/\text{mm}^3$: Interrupt treatment (for at least 3 days), may resume when values rise toward normal
  2. Sickle cell anemia: Neutrophils $< 2000/\text{mm}^3$, platelets $< 80,000/\text{mm}^3$, hemoglobin $< 4.5 \text{ g/dL}$, or reticulocytes $< 80,000/\text{mm}^3$ with hemoglobin $< 9 \text{ g/dL}$: Interrupt treatment; following recovery,
may resume with a dose reduction of 2.5 mg/kg/day. If no toxicity occurs over the next 12 weeks, subsequent dose may be increased by 2.5 mg/kg/day every 12 weeks to a dose which does not produce hematologic toxicity for 24 consecutive weeks. If hematologic toxicity recurs a second time at a specific dose, do not retry that dose.

**Common side effect:**

Cardiovascular: Edema  
Central nervous system: Chills, disorientation, dizziness, drowsiness (dose-related), fever, hallucinations, headache, malaise, seizure  
Dermatologic: Alopecia, cutaneous vasculitic toxicities, dermatomyositis-like skin changes, facial erythema, gangrene, hyperpigmentation, maculopapular rash, nail atrophy, nail discoloration, peripheral erythema, scaling, skin atrophy, skin cancer, skin ulcer, vasculitis ulcerations, violet papules  
Endocrine & metabolic: Hyperuricemia  
Gastrointestinal: Anorexia, constipation, diarrhea, gastrointestinal irritation and mucositis, (potentiated with radiation therapy), nausea, pancreatitis, Stomatitis, vomiting  
Genitourinary: Dysuria  
Hematologic: Myelosuppression (anemia, leukopenia/neutropenia [common], thrombocytopenia; hematologic recovery: within 2 weeks); macrocytosis, megaloblastic erythropoiesis, secondary leukemias (long-term use)  
Hepatic: Hepatic enzymes increased, hepatotoxicity  
Neuromuscular & skeletal: Peripheral neuropathy, weakness  
Renal: BUN increased, creatinine increased, renal tubular dysfunction  
Respiratory: Acute diffuse pulmonary infiltrates (rare), dyspnea, pulmonary fibrosis (rare)

**Pregnancy Risk Factor:** D