**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:
- $Cl_{cr}$ ≥60 mL/minute: No dosage adjustment (of initial dose) necessary.
- $Cl_{cr}$ <60 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:
- $Cl_{cr}$ >50 mL/minute: No dosage adjustment necessary
- $Cl_{cr}$ 10-50 mL/minute: Administer 50% of dose.
- $Cl_{cr}$ <10 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:
- $Cl_{cr}$ 46-60 mL/minute: Administer 85% of dose.
- $Cl_{cr}$ 31-45 mL/minute: Administer 80% of dose.
- $Cl_{cr}$ <30 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/$mm^3$ or platelets <100,000/$mm^3$: Interrupt treatment (for at least 3 days), may resume when values rise toward normal
  2.Sickle cell anemia: Neutrophils <2000/$mm^3$, platelets <80,000/$mm^3$, hemoglobin <4.5 g/dL, or reticulocytes <80,000/$mm^3$ with hemoglobin <9 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