Fludarabine

Class:
Antineoplastic agent, Antimetabolite (Purine Analog)

Indications:
_Chronic lymphocytic leukemia
_Non-Hodgkin lymphomas
Unlabeled use:
_Acute myeloid leukemia (AML), high-risk patients
_AML, refractory
_Waldenstron's macroglobulinemia
_Stem cell transplant (allogeneic) conditioning regimen, reduced-intensity
_Stem cell transplant (allogeneic) non myeloablative conditioning regimen

Available dosage form in the hospital:
50 mg VIAL

Trade names: Fludara

Doses: Details concerning dosing in combination regimens should also be consulted.

-Chronic lymphocytic leukemia (CLL):
-I.V.: 25 mg/m^2/day for 5 days every 28 days
-Oral (Canadian labeling; not available in U.S.): 40 mg/m^2 once daily for 5 days every 28 days

-CLL combination regimens (unlabeled dosing): I.V.:
-CFAR: 20 mg/m^2/day for 3 days every 28 days for 6 cycles (in combination with cyclophosphamide, rituximab and alemtuzumab)

-FC: 30 mg/m^2/day for 3 days every 28 days for 6 cycles (in combination with cyclophosphamide) **or** 20 mg/m^2/day for 5 days every 28 days for 6 cycles (in combination with cyclophosphamide)
-FCR: 25 mg/m^2/day for 3 days every 28 days for 6 cycles (in combination with cyclophosphamide and rituximab)
-FluCam: 30 mg/m^2/day for 3 days every 28 days for 4-6 cycles (in combination with alemtuzumab)
-FR: 25 mg/m^2/day for 5 days every 28 days for 6 cycles (in combination with rituximab)
-OFAR: 30 mg/m^2/day for 2 days every 28 days for 6 cycles (in combination with oxaliplatin, cytarabine, and rituximab)

-Acute myeloid leukemia (AML), high-risk patients (unlabeled use): I.V.: 30 mg/m^2/day for 5 days induction therapy, followed by post remission therapy of 30 mg/m^2/day for 4 days every other cycle (in combination with cytarabine with or without filgrastim)

-AML, refractory (unlabeled use): I.V.: 30 mg/m^2/day for 5 days (in combination with cytarabine and filgrastim), may repeat once for partial remission **or** 30 mg/m^2/day for 5 days for 1 or 2 cycles (in combination with cytarabine, idarubicin, and filgrastim)

-Non-Hodgkin lymphomas: I.V.: Canadian labeling: 25 mg/m^2 for 5 days every 28 days; dosage adjustment may be necessary for hematologic or non hematologic toxicity.

**Follicular lymphoma (unlabeled use):
-FCR: 25 mg/m^2/day for 3 days every 21 days for 4 cycles (in combination with cyclophosphamide and rituximab)
-FCMR: 25 mg/m^2/day for 3 days every 28 days for 4 cycles (in combination with cyclophosphamide, mitoxantrone, and rituximab)
-FND: 25 mg/m^2/day for 3 days every 28 days for up to 8 cycles (in combination with mitoxantrone and dexamethasone)
-FNDR: 25 mg/m^2/day for 3 days every 28 days for up to 8 cycles (in combination with mitoxantrone, dexamethasone, and rituximab) (McLaughlin, 2000)
-FR: 25 mg/m^2/day for 5 days every 28 days for 6 cycles (in combination with rituximab)

******Mantle cell lymphoma (unlabeled use):
-FC: 20 mg/m^2/day for 4-5 days or 25 mg/m^2/day for 3-5 days (in combination with cyclophosphamide) (Cohen, 2001)
-FCMR: 25 mg/m^2/day for 3 days every 28 days for 4 cycles (in combination with cyclophosphamide, mitoxantrone, and rituximab)

-Waldenstron's macroglobulinemia (unlabeled use): I.V.:25 mg/m^2/day for 5 days every 28 days **or** 25 mg/m^2/day for 5 days every 28 days for 6 cycles (in combination with rituximab)

-Stem cell transplant (allogeneic) conditioning regimen, reduced-intensity, (unlabeled use): I.V.: 30 mg/m^2/dose for 6 doses beginning 10 days prior to transplant **or** 30 mg/m^2/dose for 5 days beginning 6 days prior to transplant (in combination with busulfan with or without antithymocyte globulin)

-Stem cell transplant (allogeneic) nonmyeloablative conditioning regimen (unlabeled use): I.V.: 30 mg/m^2/dose for 3 doses beginning 5 days prior to transplant (in combination with cyclophosphamide and rituximab) **or** 30 mg/m^2/dose for 3 doses beginning 4 days prior to transplant (in combination with total body irradiation) .

Geriatric

Refer to adult dosing

Renal Impairment:

U.S. labeling: Adults:
-CLL: I.V.:

- Cl_{cr} 50-79 mL/minute: Decrease dose to 20 mg/m^2.
- Cl_{cr} 30-49 mL/minute: Decrease dose to 15 mg/m^2.
- Cl_{cr} <30 mL/minute: Avoid use.

Canadian labeling:
- (Oral, I.V.), NHL (I.V.):

- Cl_{cr} 30-70 mL/minute: Reduce dose by up to 50%.
- Cl_{cr} <30 mL/minute: Use is contraindicated.

The following guidelines have been used by some clinicians: Aronoff, 2007: I.V.:

- Cl_{cr} 10-50 mL/minute: Administer 75% of dose.
- Cl_{cr} <10 mL/minute: Administer 50% of dose.
- Hemodialysis: Administer after dialysis
- Continuous ambulatory peritoneal dialysis (CAPD): Administer 50% of dose.
- Continuous renal replacement therapy (CRRT): Administer 75% of dose.

Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling.

Dosing: Obesity

*ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer (**Note:** Excludes HSCT dosing):* 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).

Dosing: Adjustment for Toxicity

-Hematologic or nonhematologic toxicity (other than neurotoxicity): Consider treatment delay or dosage reduction.
-Hemolysis: Discontinue treatment.

-Neurotoxicity: Consider treatment delay or discontinuation.

Common side effect:

Cardiovascular: Edema (8% to 19%), Angina (≤6%), arrhythmia (≤3%), cerebrovascular accident

Central nervous system: Fever (60% to 69%), fatigue (10% to 38%), pain (20% to 22%), chills (11% to 19%)

Dermatologic: Rash (15%)

Gastrointestinal: Nausea/vomiting (31% to 36%), anorexia (7% to 34%), diarrhea (13% to 15%), gastrointestinal bleeding (3% to 13%), Stomatitis (≤9%), esophagitis (≤3%), constipation (1% to 3%), mucositis.

Genitourinary: Urinary tract infection (2% to 15%)

Hematologic: Myelosuppression (nadir: 10-14 days; recovery: 5-7 weeks; dose-limiting toxicity), anemia (60%), neutropenia (grade 4: 59%; nadir: ~13 days), thrombocytopenia (55%; nadir: ~16 days)

Neuromuscular & skeletal: Weakness (9% to 65%), myalgia (4% to 16%), paresthesia (4% to 12%)

Ocular: Visual disturbance (3% to 15%)

Respiratory: Cough (10% to 44%), pneumonia (16% to 22%), dyspnea (9% to 22%), upper respiratory infection (2% to 16%)

Miscellaneous: Infection (33% to 44%), diaphoresis

Pregnancy Risk Factor: D