Cytarabine (sy-tar-a-been)
Cytosine arabinoside
Cyto: Cytarabine, Cytosar-U, DepoCyt
Pharmacologic: antimetabolites

Indications

Pharmacokinetics
Absorption: Absorption occurs from subcut sites, but blood levels are lower than with IV administration; IT administration results in negligible systemic exposure.
Distribution: Widely distributed; IV- and subcut-administered cytarabine crosses the blood-brain barrier but not in sufficient quantities. Crosses the placenta.
Metabolism and Excretion: Metabolized mostly by the liver; 10% excreted unchanged by the kidneys. Metabolism to inactive drug in the CSF is negligible because the enzyme that metabolizes it is present in very low concentrations in the CSF.

Contraindications/Precautions
Contraindicated in: Hypersensitivity; OB, Lactation: Pregnancy or lactation; Active meningeal infection (IT only).

Use Cautiously in: Active infections; bone marrow reserve; Renal/hepatic impairment; Other chronic debilitating illnesses; OR: Patients withchildbearing potential.

Adverse Reactions/Side Effects

Interactions
Drug-Drug: May inhibit bone marrow depression with other antineoplastics or radiation therapy. May increase risk of cardiomyopathy when used in high-dose regimens with cyclophosphamide. May decrease antibody response to live-virus vaccines and risk of adverse reactions. May decrease absorption of digoxin tablets. May decrease the efficacy of gentamicin when used to treat K. pneumoniae infections. Recent treatment with asparaginase may decrease antibody response to live-virus vaccines. May decrease toxicity with concurrently administered TNF antineoplastics (IT only).

Route/Dosage
Dose regimens vary widely.
IV (Adults): Induction dose—200 mg/m²/day for 5 days (1 wk as a single agent or 2–6 mg/kg/day) as a single daily dose or in 2–3 divided doses for 5–10 days or until remission occurs as part of combination chemotherapy. Maintenance—70–200 mg/m²/day for 2–5 days monthly. Hypoxanthine-xanthine oxidase (IT only)—1 g/m² q 12 hr for 16–22 doses.
Subcut (Adults): Maintenance—1–2.5 mg/kg q 1–4 wk.
IT (Adults): Dose (Induction)—50 mg (intraventricular or lumbar puncture) q 14 days for 3 doses (weeks 1, 5, and 9), followed by one additional dose at week 13; consolidation—50 mg (intraventricular or lumbar puncture) q 14 days for 4 doses (weeks 17, 21, 25, and 29). If drug-related neurotoxicity occurs, dose should be reduced to 25 mg or discontinued. Dexamethasone 4 mg PO/IV twice daily for 5 days should be started concurrently with IT cytarabine.

Contraindications
High Alert
Cytarabine is a high-alert medication due to the potential for serious patient harm if not administered correctly. Patients at risk for harm include those with bone marrow depression, renal impairment, and neurotoxicity.

Therapeutic Effects:
Death of rapidly replicating cells, particularly malignant ones.

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Half-life: IV, subcut—1–3 hr; IT—100–236 hr.

TIME/ACTION PROFILE (IV, subcut—effects on WBCs; IT—levels in CSF)
ROUTE ONSET PEAK DURATION
Subcut, IV (1st phase) 24 hr 7–9 days 12 days
Subcut, IV (2nd phase) 15–24 days 15–24 days 25–34 days
IT rapid 5 hr 14–28 days

Adverse Reactions:
GI:
nausea, vomiting, severe GI ulceration (high dose), stomatitis.
GU:
urothelial toxicity (high dose), hemorrhagic conjunctivitis (high dose), visual disturbances.
Neuro:
neurotoxicity, headache, ataxia, visual disturbances.
Resp:
PULMONARY EDEMA (high dose).
CV:
edema.
Derm:
alopecia, rash.
Endo:
sterility.
Hemat:
anemia, leukopenia, thrombocytopenia.
Metab:
hyperuricemia.
Neuro:
intrathecal—CHEMICAL ARACHNOIDITIS, abnormal gait.
Misc:
cytarabine syndrome, fever.
NURSING IMPLICATIONS

Assessment
- Monitor for bone marrow depression. Assess for bleeding (bloody stools, bruising, petechiae, purpuric spots, urine, and rectum) and avoid IM injections and taking rectal temperatures if platelet count is low. Apply pressure to skin puncture sites for 10 min. Assess for signs of infection during neutropenia. Anemia may occur. Monitor for increased fatigue, dyspnea, and orthostatic hypotension.
- Monitor intake and output and daily weights. Report significant changes in fluid balance.
- Monitor for symptoms of urticaria (urticarial rash, pruritus, angioedema). Urticaria may occur. Monitor for increased fatigue, dyspnea, and orthostatic hypotension.
- Monitor patient for signs of anaphylaxis (rash, dyspnea, swelling). Epinephrine, corticosteroids, and resuscitation equipment should be readily available.
- ID: Cytarabine should be administered with extreme caution to patients with known or suspected sensitivity to uracil nucleoside analogs. Anaphylactic reactions have been reported in patients who are sensitized to uracil nucleoside analogs. Cytarabine may be given subcut, direct IV, intermittent IV, continuous IV, or IT.

Implementation
- High alert: Adjudicate all ambiguous orders, double-check single, daily, and course-of-therapy dose limits; have second practitioner independently double-check original order, calculations, and infusion pump settings.
- High alert: Do not confuse high-dose and regular therapy. Fatalities have occurred with chemotherapeutic agents. Before administering, clarify all ambiguous orders, double-check single, daily, and course-of-therapy dose limits; have second practitioner independently double-check original order, calculations, and infusion pump settings.
- Lab Test Considerations: Monitor CBC with differential and platelet count prior to and frequently during therapy. Leukocyte counts begin to drop within 24 hr of administration. The initial nadir occurs in 7–9 days. After a small peak in the count, the second, deeper nadir occurs 15–24 days after administration. Platelet counts begin to decrease 4–5 days after a dose, with a nadir at 12–15 days. Leukocyte and thrombocyte counts usually begin to rise 7–10 days after the nadir. Therapy is usually withdrawn if leukocyte count is 1000/mm³ or platelet count is 50,000/mm³. Bone marrow aspirations are recommended every 2 wk until remission occurs.
- Monitor renal (BUN and creatinine) and hepatic function (AST, ALT, bilirubin, alkaline phosphatase, and LDH) prior to and frequently during therapy.
- Monitor nutritional status. Nausea and vomiting may occur within 1 hr of administration. Avoid IM injections and taking rectal temperatures if platelet count is low. Apply pressure to skin puncture sites for 10 min. Assess for signs of infection during neutropenia. Anemia may occur. Monitor for increased fatigue, dyspnea, and orthostatic hypotension.
- Monitor for symptoms of urticaria (urticarial rash, pruritus, angioedema). Urticaria may occur. Monitor for increased fatigue, dyspnea, and orthostatic hypotension.
- Monitor for respiratory distress and pulmonary edema. Occurs with high doses rarely; may be fatal.
- Monitor patient for signs of anaphylaxis (rash, dyspnea, urticaria). Epinephrine, corticosteroids, and resuscitation equipment should be readily available.
- High Alert: Patients have received multiple chemotherapy agents. Before administering, ensure that all ambiguous orders, double-check single, daily, and course-of-therapy dose limits; have second practitioner independently double-check original order, calculations, and infusion pump settings.
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IV Administration

- pH: 7.4–9.0
- Direct IV: Diluent: Administer undiluted. Concentration: 100 mg/mL. Rate: Administer each 100 mg over 1–3 min.
- Interim: Infusion: Diluent: May be further diluted in 0.9% NaCl, D5W, D5/0.9% NaCl, Ringer's solution, LR, or D5LR. Concentration: Dilute doses in 100 mL of diluent. Rate: Infuse over 30–60 min.
- Continuous Infusion: Rate and concentration for IV infusion are ordered individually.

Y-Site Compatibility:

- Continuous Infusion:
  - Direct IV:
    - pH:

Y-Site Incompatibility:

- Trimethoprim/sulfamethoxazole, vancomycin, vasopressin, vecuronium, verapamil, vincristine, vinorelbine, voriconazole, zidovudine.
- L-Ascorbic acid, loratadine, melphalan, meropenem, mesna, metoclopramide, metoprolol, methotrexate, mexitelene, midazolam, minocycline, mitoxantrone, morphine, nalbuphine, naloxone, nesiritide, nicardipine, nipecotic acid, nitroglycerin, nitroprusside, norepinephrine, octreotide, ondansetron, oxycodone, piperacillin/tazobactam, potassium acetate, potassium chloride, potassium phosphate, potassium sulfate, potassium chloride, potassium acetate.
- Trimethoprim/sulfamethoxazole, vancomycin, vasopressin, vecuronium, verapamil, vincristine, vinorelbine, voriconazole, zidovudine.
- Calcium gluconate, carboplatin, carmustine, cephalotaxine, cephalosporin, chloramphenicol, chlorpromazine, cisplatin, cladribine, clindamycin, cyclophosphamide, cyclosporine, dexamethasone, doxorubicin, doxorubicin liposome, doxycycline, droperidol, enalaprilat, ephedrine, epinephrine, docetaxel, doxacurium, doxorubicin hydrochloride, dexmedetomidine, dexrazoxane, diethyl ether, diphenhydramine, diltiazem, diltiazem hydrochloride, dexamethasone, doxycycline, dexamethasone hydrochloride, doxorubicin, dopamine, daptomycin, diazepam, ganciclovir, phenytoin.
- Allopurinol, amiodarone, amphotericin B colloidal, aminophylline, amphotericin B cholesteryl, aminocaproic acid, aminophylline, amphotericin B.
- Carboplatin, carmustine, cephalotaxine, ceftazidime, ceftriaxone, cefuroxime, chlorpromazine, ciprofloxacin, cisatracurium, cisplatin, cladribine, clindamycin, cyclophosphamide, cyclosporine, doxorubicin, doxorubicin liposome, doxycycline, droperidol, enalaprilat, ephedrine, epinephrine, docetaxel, doxacurium, doxorubicin hydrochloride, dexmedetomidine, dexrazoxane, diethyl ether, diphenhydramine, diltiazem, diltiazem hydrochloride, dexamethasone, doxycycline, dexamethasone hydrochloride, doxorubicin, dopamine, daptomycin, diazepam, ganciclovir, phenytoin.
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● Instruct patient not to receive any vaccinations without advice of health care professional.

● Advise patient that this medication may have teratogenic effects. Contraception should be used during therapy and for at least 4 mo after therapy is concluded.

● Emphasize the need for periodic lab tests to monitor for side effects.

● IT: Inform patient about the expected side effects (headache, nausea, vomiting, fever) and about early signs of neurotoxicity. Instruct patient to notify health care professional if these signs occur.

● Emphasize the importance of taking dexamethasone with liposomal cytarabine.

Evaluation/Desired Outcomes

● Improvement of hematopoietic values in leukemias.

● Decrease in size and spread of the tumor in non-Hodgkin’s lymphomas. Therapy is continued every 2 wk until patient is in complete remission or thrombocyte count or leukocyte count falls below acceptable level.

● Treatment of lymphomatous meningitis.

Why was this drug prescribed for your patient?