cyclophosphamide (sy-e-kloe-fos-fa-mide)

**Classification**
Therapeutic: antineoplastics, immunosuppressants
Pharmaceutical: alkylating agents

**Pregnancy Category D**

**Indications**
Cyclophosphamide is used alone or with other modalities in the management of:
- Hodgkin's disease
- Malignant lymphomas
- Multiple myeloma
- Leukemias
- Mycosis fungoides
- Neuroblastoma
- Ovarian carcinoma
- Breast carcinoma
- A variety of other tumors

**Unlabeled Use:**
- Severe active rheumatoid arthritis
- Granulomatosis with polyangiitis

**Action**
- Interferes with DNA replication and RNA transcription, ultimately disrupting protein synthesis (cell-cycle phase–nonspecific).

**Therapeutic Effects:**
- Death of rapidly replicating cells, particularly malignant ones.
- Also has immunosuppressant action in smaller doses.

**Pharmacokinetics**
- **Absorption:** Inactive parent drug is well absorbed from the GI tract. Converted to active drug by the liver.
- **Distribution:** Widely distributed. Limited penetration of the blood-brain barrier.
- **Crosses the placenta; enters breast milk.**
- **Metabolism and Excretion:** Converted to active drug by the liver; 30% eliminated unchanged by the kidneys.
- **Half-life:** 4–6.5 hr.

**TIME/ACTION PROFILE (effects on blood counts)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO, IV</td>
<td>7 days</td>
<td>7–15 days</td>
<td>21 days</td>
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**Contraindications/Precautions**
- **Contraindicated in:** Hypersensitivity.
- **Cautions:**
  - Active infections
  - Bone marrow depression
  - Other chronic debilitating illnesses
  - OB: Patients with childbearing potential

**Adverse Reactions/Side Effects**
- **Resp:** Pulmonary fibrosis.
- **CV:** Myocardial fibrosis, hypotension.
- **GI:** Anorexia, nausea, vomiting.
- **GU:** Hemorrhagic cystitis, hematuria.
- **Derm:** Alopecia.
- **Endo:** Gonadal suppression, syndrome of inappropriate antidiuretic hormone (SIADH).
- **Hemat:** Leukopenia, thrombocytopenia, anemia.
- **Metab:** Hyperuricemia.

**Interactions**
- **Drug-Drug:**
  - Phenobarbital or rifampin may q toxicity of cyclophosphamide.
  - Concurrent anticholinergic or diuretics may exacerbat bone marrow depression.
  - May potentiate the effects of other cardiotoxic agents (e.g., etoposide, daunorubicin, doxorubicin).
  - Additive bone marrow depression with other antineoplastics or radiation therapy.
  - May potentiate the effects of warfarin. May decrease serum digoxin levels.
  - May potentiate the effects of other antineoplastics or radiation therapy.

**Route/Dosage**
- Many regimens are used.

**PO (Adults):**
- 1–5 mg/kg/day.

**PO (Children):**
- **Induction:** 2–8 mg/kg/day (60–250 mg/m²/day) in divided doses for 6 days or longer.
- **Maintenance:** 2–5 mg/kg (50–150 mg/m²/day) twice weekly.

**IV (Adults):**
- 40–50 mg/kg in divided doses over 2–5 days or 10–15 mg/kg q 7–10 days or 5–10 mg/kg twice weekly or 1.5–3 mg/kg/day. Other regimens may use larger doses.

**IV (Children):**
- **Induction:** 2–8 mg/kg/day (60–250 mg/m²/day) in divided doses for 6 days or longer. Total dose for 7 days may be given as a single weekly dose.
- **Maintenance:** 10–15 mg/kg every 7–10 days or 30 mg/kg q 3–4 wk.

**NURSING IMPLICATIONS**

**Assessment**
- Monitor BP, pulse, respiratory rate, and temperature frequently during administration. Report significant changes.

**Contraindications/Precautions**
- **Contraindicated in:**
  - Hypersensitivity.
  - **Cautions:**
    - Active infections
    - Bone marrow depression
    - Other chronic debilitating illnesses
    - OB: Patients with childbearing potential
Monitor urinary output frequently during therapy. To reduce the risk of hemorrhagic cystitis, fluid intake should be at least 3000 mL/day for adults and 1000–2000 mL/day for children. May be administered with mesna.

Monitor for bone marrow depression. Assess for bleeding (bleeding gums, bruising, guaiac stools, urine, and emesis) and avoid IM injections and taking rectal temperatures if platelet count is low. Apply pressure to venipuncture sites for 10 min. Assess for signs of infection during neutropenia. Anemia may occur. Monitor for increased fatigue, dyspnea, and orthostatic hypotension.

Assess nausea, vomiting, and appetite. Weight loss. Anorexia may be given 30 min before administration of medication to minimize GI effects. Anemia and weight loss can be minimized by feeding frequent light meals.

Encourage patient to drink 2000–3000 mL/day to promote excretion of uric acid. Alkalinization of the urine may be used to help prevent uric acid nephropathy.

Assess cardiac and respiratory status for dyspnea, rales/crackles, cough, weight gain, edema. Pulmonary toxicity may occur after prolonged therapy. Cardiotoxicity may occur early in therapy and is characterized by symptoms of HF.

Lab Test Considerations: Monitor CBC with differential and platelet count before and periodically during therapy. The nadir of leukopenia occurs in 7–12 days (recovery in 17–21 days). Leukocytes should be maintained at 2500–4000/mm$^3$. May also cause thrombocytopenia (nadir 10–15 days), and rarely causes anemia.

Monitor BUN, creatinine, and uric acid before and frequently during therapy to detect nephrotoxicity.

Monitor ALT, AST, LDH, and serum bilirubin before and frequently during therapy to detect hepatotoxicity.

Urinalysis should be evaluated before initiating therapy and frequently during therapy to detect hematuria or change in specific gravity indicative of SIADH.

May suppress positive reactions to skin tests for Candida, mumps, Trichophyton, and tuberculin purified-protein derivative (PPD). May also produce false-positive results in Papanicolaou smears.

### Potential Nursing Diagnoses

- Risk for infection (Side Effects)
- Disturbed body image (Side Effects)

### Implementation

**High Alert:** Fatalities have occurred with chemotherapeutic agents. Before administration, 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.

**PO:** Administer in the morning. Swallow tablets whole; do not crush, break, or chew.

**IV:** Prepare solution for IV administration in a biologic cabinet. Wear gloves, gown, and mask while handling IV medication. Discard IV equipment in specially designated containers.

#### IV Administration

**pH:** 3.0–9.0.

**Direct IV:** Reconstitute each 100 mg with 5 mL 0.9% NaCl. Swirl gently to dissolve. Do not reconstitute with sterile water for injection, results in a hypotonic solution not suitable for direct IV. Concentration: 20 mg/mL, administer reconstituted solution undiluted. Rate: Inject very slowly.

**Intermittent Infusion:** Reconstitute each 100 mg with 5 mL of 0.9% NaCl or Sterile Water for injection. Swirl gently to dissolve. Use solutions reconstituted with Sterile Water for injection immediately. Solution reconstituted with 0.9% NaCl may be stored at room temperature for 24 hrs or if refrigerated for 6 days. Do not administer solutions that contain clear of yellow viscous liquids. Diluent: May be further diluted in up to 250 mL of D5W, D5/0.9% NaCl, or 0.45% NaCl. Concentration: minimum 2 mg/mL. Rate: Infuse very slowly. May reduce drug-dependent adverse reactions (facial swelling, headache, nasal congestion, scalp burning).

**Y-Site Compatibility:** acetaminophen, albuterol, allopurinol, aminoglycoside, amphotericin B lipid complex, amphotericin B liposome, ampicillin, ampicillin/sulbactam, antidiabetes, argatroban, arsenic trioxide, atracurium, aztreonam, bevacizumab, bivalirudin, bleomycin, bumetanide, buprenorphine, butorphanol, calcium chloride, calcium gluconate, canareamidine, capsaicinoids, celastrol, celiprolol, cefazolin, cefepime, cefoperazone, cefotaxime, cefotetan, cefoxitin, ceftazidime, ceftriaxone, cefuroxime, chloramphenicol, chloropromazine, clindamycin, cyclophosphamide, cyclosporine, cyclosporine, cyproterone, daunorubicin, daunomycin, deoxycorticosteroids, dexamethasone, di-
Y-Site Incompatibility: amphotericin B cholesteryl, amphotericin B colloidal, diazepam, phenytoin.

Patient/Family Teaching
- Instruct patient to take dose in early morning. Emphasize need for adequate fluid intake for 72 hr after therapy. Patient should void frequently to decrease bladder irritation from metabolites excreted by the kidneys. Report hematuria immediately. If dose is missed, consult health care professional. Inform patient to use gloves when handling tablets. If broken tablets occur, wash hands thoroughly.

- Patient should notify health care professional promptly if fever; sore throat; signs of infection; lower back or side pain; difficulty or painful urination; nausea; itching; yellow discoloration of skin or eyes; bleeding gums; bruising; pain; blood in urine, stool, or vomit; unusual swelling of ankles or knees; joint pain; shortness of breath; cough, palpitations, or weight gain of more than 5 lbs in 24 hrs; loss of consciousness or confusion occurs. Caution patient to avoid crowds and persons with known infections. Instruct patient to use soft toothbrush and electric razor and to avoid falls. Patient should also be cautioned not to drink alcoholic beverages or to take products containing aspirin or NSAIDs; may precipitate GI hemorrhage.
- Discuss with patient the possibility of hair loss. Explore methods of coping. May also cause darkening of skin and nails.
- Instruct patient not to receive any vaccinations without advice of health care professional.
- Advise patient that this medication may cause sterility and menstrual irregularities or cessation of menses. This drug is also teratogenic; females should use highly effective contraceptive measures for up to 1 yr after completion and men should continue to use condoms for at least 6 mo after completion of therapy.

Evaluation/Desired Outcomes
- Decrease in size or spread of malignant tumors.
- Improvement of hematologic status in patients with leukemia. Maintenance therapy is instituted if leukocyte count remains between 2500 and 4000/mm³ and if patient does not demonstrate serious side effects.
- Management of minimal change nephrotic syndrome in children.

Why was this drug prescribed for your patient?