NEXTSTEPS IN DERM | GW School of Medicine & Health Sciences

Cyclophosphamide Therapeutic Cheat Sheet

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TRADE NAME[1]

- Cytoxan

MECHANISM OF ACTION[1,2,6]

- Cyclophosphamide is a prodrug metabolized by hepatic cytochrome P450 enzymes into phosphoramide mustard (active) and acrolein (toxic).
  - Phosphoramide mustard cross-links DNA, impairing replication and transcription, leading to apoptosis of rapidly dividing cells.
  - Immunosuppressive effects: preferential suppression of proliferating B and T lymphocytes, reducing autoantibody production and immune-mediated inflammation.
  - Acrolein causes bladder toxicity, the basis of hemorrhagic cystitis.

FDA-APPROVED INDICATIONS[1]

- Approved for malignant diseases (lymphomas, leukemias, breast/ovarian cancer, neuroblastoma, retinoblastoma) and pediatric nephrotic syndrome refractory to corticosteroids.

OFF-LABEL DERMATOLOGIC USES[2,3,4,5,6,7,8,9]

- Autoimmune blistering diseases: pemphigus vulgaris, pemphigus foliaceus, cicatricial pemphigoid — pulse regimens (e.g., dexamethasone–cyclophosphamide) show efficacy in refractory cases.
- Dermatomyositis: used for severe cutaneous/systemic forms refractory to steroids and other immunosuppressants.
- Systemic sclerosis with skin involvement: sometimes used in progressive cutaneous disease when other agents fail.
- Cutaneous lupus erythematosus and vasculitis: considered for refractory CLE or systemic vasculitides with major skin involvement.

DOSING[1,2,3]

- Oral: ~1–2 mg/kg/day (max 5 mg/kg/day) adjusted to clinical response and leukocyte nadir.
- IV pulse regimens: 500–1000 mg/m^2 every 4 weeks in pemphigus and severe autoimmune disease cohorts.

WARNING AND PRECAUTIONS[1]

- Administer in the morning with hydration and frequent voiding.
- Use mesna or forced diuresis for high-dose IV regimens to prevent hemorrhagic cystitis.

SIDE EFFECTS[1,2,5,7]

- Cyclophosphamide is associated with multiple dose- and duration-dependent adverse effects.
  - Myelosuppression (leukopenia, neutropenia, thrombocytopenia) occurs in up to 60–70% of patients; febrile neutropenia may occur in 5–10%.
  - Infections complicate treatment in approximately 20–25% of patients, particularly in those receiving high cumulative doses or combination immunosuppression.
  - Hemorrhagic cystitis due to acrolein occurs in 10–20% without uroprotection; risk falls to <5% with mesna and hydration.
  - Secondary bladder cancer risk increases with cumulative doses >20–30 g, with reported incidence of ~5% after long-term use.
  - Gonadal toxicity/infertility occurs in 30–60% of women (premature ovarian failure) and up to 50% of men (azoospermia) depending on age and dose.
  - Alopecia (30–40%) and mucosal toxicity (10–15%) are common but reversible.
  - Nausea/vomiting occurs in 30–50%, mitigated with antiemetics.
  - Pulmonary fibrosis and cardiotoxicity are rare (<2%) but potentially fatal complications.

DRUG INTERACTIONS[1]

- Additive marrow suppression with other cytotoxics.
- Avoid live vaccines during therapy.

CONTRAINDICATIONS[1]

- Hypersensitivity, severe marrow suppression, active severe infection, urinary outflow obstruction. [1]

PREGNANCY & BREASTFEEDING[1]

- Category D: teratogenic and embryotoxic.
- Contraindicated in breastfeeding due to excretion in milk.
- Effective contraception required for both sexes.

MONITORING[1,2,4]

- Baseline: CBC with differential, renal and hepatic function, urinalysis.
- Ongoing: frequent CBCs, urinary sediment monitoring for hematuria, and long-term surveillance for fertility and bladder malignancy.

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