**Cyclophosphamide for Injection, USP**

**CLINICAL PHARMACOLOGY**

Cyclophosphamide is a nitrogen mustard, a widely used alkylating agent. It is available as a white or almost white, odorless, crystalline powder. It is freely soluble in water and almost insoluble in chloroform or ether. The solubility of cyclophosphamide in water is about 3 mg/mL at pH 7.4. Its powder is stable for at least 2 years when stored at room temperature in airtight, light-resistant containers.

**Pharmacokinetics**

Cyclophosphamide is metabolized in the liver to active alkylating metabolites by a mixed function microsomal enzyme system. The major route of elimination is via the urine. The plasma half-life of cyclophosphamide is about 2 hours. The plasma half-life of the N-oxide metabolite is about 10 hours. The terminal plasma half-life of the major metabolite, phosphoramide mustard, is about 24 hours. The plasma half-life of the major metabolite, phosphoramide mustard, is about 24 hours. The plasma half-life of the major metabolite, phosphoramide mustard, is about 24 hours. The plasma half-life of the major metabolite, phosphoramide mustard, is about 24 hours.

**Indications and Usage**

Cyclophosphamide is useful in the treatment of a variety of neoplastic disorders, including lymphomas, leukemias, myelomas, certain solid tumors, and some types of nonmalignant disease in which immune processes are involved. Cyclophosphamide is useful in the treatment of a variety of neoplastic disorders, including lymphomas, leukemias, myelomas, certain solid tumors, and some types of nonmalignant disease in which immune processes are involved.

**Contraindications**

Cyclophosphamide is contraindicated in patients with a known hypersensitivity to it. See WARNINGS and PRECAUTIONS sections.

**NURSING MOTHERS**

Cyclophosphamide may interfere with normal wound healing. Wound Healing

Cyclophosphamide may interfere with normal wound healing. Wound healing may be impaired during cyclophosphamide treatment. Urinary System

Cyclophosphamide treatment, which causes a marked and persistent inhibition of cholinesterase activity, potentiates the effect of succinylcholine chloride. Cyclophosphamide treatment, which causes a marked and persistent inhibition of cholinesterase activity, potentiates the effect of succinylcholine chloride.

**Adrenalectomy**

If a patient has been treated with cyclophosphamide within 10 days of general anesthesia, the anesthesiologist should be alerted. If a patient has been treated with cyclophosphamide within 10 days of general anesthesia, the anesthesiologist should be alerted.

**Laboratory Tests**

7. Impaired renal function

5. Previous therapy with other cytotoxic agents

1. Leukopenia

if any of the following conditions are present.

**Cardiac Toxicity**

Cyclophosphamide has been reported to potentiate doxorubicin-induced cardiotoxicity. No residual cardiac abnormalities, as evidenced by electrocardiogram or echocardiogram, appear to be present in patients with transplantation procedures. In a few instances with high doses of cyclophosphamide, severe, and sometimes fatal, cardiac toxicity has occurred. The possibility of cyclophosphamide-induced malignancy should be considered in any patient who has received cyclophosphamide in high doses.

**Infections**

Cyclophosphamide may cause opportunistic infections of usual infectious agents. Septicemia and urinary tract infections have been reported. Septicemia and urinary tract infections have been reported.

**Hematopoietic Suppression**

Infections

Cyclophosphamide may cause severe, and occasionally fatal, infections. Certain infections, such as myeloblastosis or mononucleosis, may precede the onset of hematologic suppression. Urinary System

Cyclophosphamide treatment is stopped, but it may persist. Medical and/or surgical supportive treatment may be required, especially for those with renal impairment and for those with metastatic disease. Urinary System

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**Adverse Reactions**

Other reactive hematopoietic changes, death, have been reported in association with the use of cyclophosphamide. Possible cutaneous reactions of cyclophosphamide have been reported. Other reactive hematopoietic changes, death, have been reported in association with the use of cyclophosphamide.

**WARNINGS**

Cyclophosphamide is contraindicated in patients who have demonstrated a previous hypersensitivity to it. See WARNINGS and PRECAUTIONS sections.

**PRECAUTIONS**

Cyclophosphamide is useful in carefully selected cases of biopsy proven “minimal change” nephrotic syndrome in children but should be used with caution in elderly patients. These elderly patients may require more cautious dose adjustment, which should be determined by the degree of hematopoietic suppression. Urinary System

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Unopened vials of cyclophosphamide are stable until the date indicated on the package when stored at or below 25°C (77°F).

- Sodium Chloride Injection, USP (0.45% Sterile Sodium Chloride Injection, USP)
- Dextrose and Sodium Chloride Injection, USP (5% dextrose and 0.9% Sterile Sodium Chloride Injection, USP)
- Dextrose Injection, USP (5% dextrose)

For Intravenous Infusion should not be is hypotonic and

For Direct Intravenous Injection

The total leukocyte count is a good, objective guide for regulating intravenous regimens include 10 to 15 mg/kg given every 7 to 10 days or 3 to 5 mg/kg twice weekly.

- Deficiency usually consists of 40 to 50 mg/kg given intravenously in divided doses over a period of 2 to 5 days. Other

Adults and Children appropriate treatment for any concurrent infection, myelosuppression, or cardiac toxicity should it occur.

- Malaise and asthenia have been reported as part of the postmarketing experience. Sensitivity with other alkylating agents has been reported. SIADH (syndrome of inappropriate ADH secretion) has been reported with the use of cyclophosphamide.

Carcinogenesis

See Infections

Hemorrhagic ureteritis and renal tubular necrosis have been reported to occur in patients treated with cyclophosphamide. Such effects usually can be reversed by reducing the drug dose or by interrupting treatment. Recovery from leukopenia usually begins in 1 to 2 weeks. Leukopenia of less than 2000 cells/mm3 develops commonly in patients treated with an initial loading dose of the drug, and granulocytopenia.

- Thrombocytopenia or anemia develop occasionally in patients treated with cyclophosphamide. These hematologic effects and less frequently in patients maintained on smaller doses. The degree of neutropenia is particularly important because it

WARNINGS

- Oral Administration

in the above table.

- Cyclophosphamide is chemically and physically stable for the period of time as shown in the above table.

Reconstituted solution in Sterile Water for Injection, USP must be further diluted and stored as described below

- Further Diluted Solutions

- 2% (20 mg per mL) 1 g

REFERENCES

1. NIOSH Alert: Preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings. 2004.


References:

- Blood

- Chemotherapeutic agents. To minimize the risk of dermal exposure, always wear gloves when handling vials containing cyclophosphamide sterile powder for injection. More information is available in the references listed below.

Prepared solutions. USE ASEPTIC TECHNIQUE.

Reconstituted solution in Sterile Water for Injection, USP must be further diluted and stored as described below:

- Further Diluted Solutions

- 2% (20 mg per mL) 1 g

Manufactured by:

Baxter Healthcare

For Institutional Use Only

USA

Product and manufacturer information (institutional use only) (2nd. ed.) Pittsburgh, PA: Oncology Nursing Society.

Infections

Stevens-Johnson syndrome and toxic epidermal necrolysis have been received during postmarketing surveillance; due to the

ADVERSE REACTIONS

1. NIOSH Alert: Preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings. 2004.

- The degree of neutropenia is particularly important because it

- Nausea and vomiting commonly occur with cyclophosphamide therapy. Anorexia and, less frequently, abdominal discomfort or

- Pain and diarrhea may occur. There are isolated reports of hemorrhagic colitis, oral mucosal ulceration and jaundice occurring during therapy. These adverse drug effects generally remit when cyclophosphamide treatment is stopped.

- Doses of MTD-100 mg/m2 (or 100 mg/kg) were explored in phase II and III trials in hematologic malignancies.

- Toxicity was evaluated in solid tumor patients (not shown in the table). Toxicity included myelosuppression as well as nephrotoxicity, nausea, vomiting, and stomatitis. Cyclophosphamide was well tolerated in patients with NHL at doses that exceeded the MTD. However, severe oral mucositis was observed in patients treated with cyclophosphamide.