For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Cyclophosphamide For Injection USP

NEOPHOS

Composition

NEOPHOS-200

Each vial contains
Cyclophosphamide USP equivalent to
anhydrous Cyclophosphamide ..... 200 mg
Sodium Chloride USP ..... 90 mg
As a sterile powder for reconstitution

NEOPHOS-500

Each vial contains:
Cyclophosphamide USP equivalent to
anhydrous Cyclophosphamide ..... 500 mg
Sodium Chloride USP ..... 225 mg
As a sterile powder for reconstitution

NEOPHOS-1000

Each vial contains:
Cyclophosphamide USP equivalent to
anhydrous Cyclophosphamide .... 1 gm
Sodium Chloride USP ..... 450 mg
As a sterile powder for reconstitution

Description

Cyclophosphamide belongs to the group of alkylating agents, which bind to DNA – usually via the binding of alkyl groups. As a result, a reactive intermediary is formed which binds to DNA and causes single or double stranded DNA breaks and may cross link the chains of DNA thus disturbing the fundamental mechanisms concerned with cell growth, mitotic activity, differentiation and function.

The effects of alkylating agents although dependent on proliferation, are not cell cycle specific and hence the drug may act on cells at any stage of cycle.

Indications

Cyclophosphamide is commonly used as a single agent or in combination in the treatment of indolent lymphomas and in combination chemotherapy for intermediate and aggressive non Hodgkins lymphoma. It is used in combination with other antineoplastic agents in the treatment of acute lymphoblastic leukemias in adults and in children, small cell lung cancer, Ewing's sarcoma, neuroblastoma, breast cancer, ovarian cancer and endometrial carcinoma. It is also used in postoperative adjuvant therapy and in autoimmune diseases like rheumatoid arthritis.

Dosage and Administration

Initial treatment is given by intravenous injection. After satisfactory remission has occurred, maintenance therapy with tablets is recommended. Individual dosage should take into account the general state of the patient and the WBC count. Initial treatment is recommended with:

1. Daily I.V. injection of **NEOPHOS** 3-6 mg/kg body weight (120-240 mg/m2) twice weekly.
2. Massive Intermittent therapy – **NEOPHOS** 10-15 mg/kg body weight (400 – 600 mg/m2) with therapy free intervals of 7-10 days.
3. Massive Intermittent therapy – **NEOPHOS** 20 – 40 mg/kg body weight (800 – 1600 mg/m2) in divided doses over a period of 2-5 days with therapy free intervals of 10-20 days.

The I.V. preparation is dissolved in sterile water for injection to yield a concentration of 20 mg/ml. The vials should be shaken until complete dissolution of the dry substance is obtained. A solution thus prepared is added to 250 ml 5% glucose and administered as a brief infusion of 30 min.

The Solution is chemically stable for 48 hrs, if stored under refrigeration between 4-8°C.

Contraindications

Cyclophosphamide should not be taken in patients with known hypersensitivity to oxazaphosphorines and in cases of severe bone marrow depression.

Warnings and Precautions

1. Since **NEOPHOS** (Cyclophosphamide) is a cytotoxic anticancer drug, procedures for proper handling and disposal of such drugs should be followed.
2. Myelosuppression is frequently encountered with **NEOPHOS** (Cyclophosphamide) therapy. Therefore, during treatment, the haematologic profile especially neutrophils and platelets should be monitored regularly to determine the degree of haematologic suppression.
3. The urinary sediment should be monitored regularly for redcells, which may precede hemorrhagic cystitis. To prevent toxicity of the urinary bladder, large quantities of fluid should be taken during or immediately after administration of **NEOPHOS** (Cyclophosphamide).
4. Prior to initiation of therapy, all conditions of hampered urinary flow in the efferent urinary passage should be excluded and disturbance of electrolyte balance should be corrected.
5. Patients of both sexes of reproductive age should take contraceptive measures throughout treatment with **NEOPHOS** (Cyclophosphamide) and for at least six months after its termination so as to preclude any risk of conception.
6. Patients with impaired renal and hepatic function must be monitored carefully. In cases of patients with severe renal impairment cyclophosphamide dosage reduction may be

required.

7. Patients should be advised to maintain oral and dental hygiene to prevent infections.

Drug Interactions

Concomitant use of antidiabetic drugs with cyclophosphamide, may potentiate the reduction in blood sugar level.

If **NEOPHOS** (Cyclophosphamide) and allopurinol are given concomitantly, there may be an increase in bone marrow depression.

NEOPHOS (Cyclophosphamide) treatment causes a marked persistent inhibition of cholinesterase activity and potentiate the effect of succinyl choline chloride.

Pregnancy

Cyclophosphamide can cause fetal harm when administered to a pregnant woman. Therefore, if this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. Women of child bearing potential should be advised to avoid pregnancy during cyclophosphamide therapy.

Lactation

Cyclophosphamide is excreted in breast milk. Therefore, nursing should be discontinued while the patient is on cyclophosphamide therapy.

Side Effects

Hematologic

Prolonged use of high dose may induce myelosuppression especially leucopenia. Leukocyte counts < 2000 cells/mm^3 develops commonly in patients treated with an initial loading dose of the drug and loss frequently in patients maintained on small doses. Thrombocytopenia and anaemia develop occasionally in patients treated with cyclophosphamide. These effects can be reversed by reducing the drug dose or by interrupting treatment. Recovery from leukopenia usually begins after 7-10 days of cessation of therapy.

Gastrointestinal

Nausea and vomiting commonly occur with cyclophosphamide therapy. Anorexia and less frequently, abdominal discomfort or pain and diarrhea may occur. Antiemetic therapy should be initiated to reduce the incidence of nausea and vomiting.

Dermatologic

Alopecia occurs commonly in patients treated with cyclophosphamide but is reversible. Pigmentation of the skin and changes in nails can occur.

Urologic

Haemorrhagic cystitis may develop in patients treated with cyclophosphamide. These adverse effects appear to depend on dose of cyclophosphamide and the duration of therapy and are thought to be due to cyclophosphamide metabolites excreted in urine. Ample fluid intake during or immediately after administration of cyclophosphamide and increased diuresis help to prevent the development of haemorrhagic cystitis. Haematuria usually resolves in a few days after cyclophosphamide treatment is stopped but may persist in few cases. In patients receiving doses of 10 mg/kg or more and in high risk patients, concomitant administration of **NEOPHOS** for protection of urinary bladder, is advisable.

Interference with gonadal function

Cyclophosphamide interferes with oogenesis and spermatogenesis. It may cause sterility in both sexes. Development of sterility appears to depend on the dose of cyclophosphamide, duration of therapy and the state of gonadal function at the start of treatment.

Infections

Treatment with cyclophosphamide may cause significant suppression of immune response. Serious, sometimes fatal infections may develop in severely immunosuppressed patients. Cyclophosphamide treatment may not be indicated or should be interrupted or the dose reduced in patients who have or who develop viral, bacterial, fungal, protozoal or helminthic infections.

Others

Rare instances of anaphylactic reactions have been reported but are not typical for cyclophosphamide.

Over dosage

No specific antidote for **NEOPHOS** (Cyclophosphamide) over dosage is known. It should be managed with supportive measures including appropriate treatment for any concurrent infection, which may occur.

Storage:

Store below 25°C. Avoid long exposure to temperatures above 30°C.

Presentation:

NEOPHOS-200 mg	15 ml vial
NEOPHOS-500 mg	30 ml vial
NEOPHOS-1000 mg	50 ml vial

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