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Study of Cytotoxic Responses of Anticancer Drug Cyclophosphamide

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Abstract: *It is widely accepted that cancer, the second leading cause of death, is a morbidity with big impacts on the global health. In the last few years, chemo- therapeutic treatment continually induces alone most lengthy consequents, which is extremely harmful for the physiological and psychological health of the patients. In the present research, we discuss the recent techniques for employed for extraction, and quantitative determination of such compounds in pharmaceutical, and biological specimens. In the frame of this information, this review aims to provide basic principles of chromatography, spectroscopy. Anticancer drugs research and development have been largest market area in pharmaceuticals industry in terms of the numbers of project and clinical trials and spending. Our goals to improve cancer treatment by increasing our understanding of the mechanism by which anti-cancer treatments kill susceptible tumor cells. This articles provides an overview of current knowledge of anticancer drug their pharmacology, mechanism of action, uses, side effects,precautions, and contraindication. This mini review outlined the current status of anticancer drugs development and hinted the opinions of how to further increase the accuracy and efficacy of discovery for cancer treatment.*

Keywords: Anticancer Drugs, Cancer, Drug discovery

I. INTRODUCTION

Cancer is one of the leading causes of human death which is estimated at 8.2 million and will likely rise to 13 million worldwide per year till 2030, and oncology has become the largest therapeutic area in the pharmaceutical industry in terms of the number of project. Cancer is a disease characterized byuncontrolled proliferation abnormally transformed cells.There are more than 100 types of cancer . A multifactorial disease. Induction of proto-oncogenes and inhibition of tumor suppressor genes has been implicated in the pathogenesis of cancer. Anticancer drugs are developed from variety of sources ranging from natural products to synthetic molecules.{1}There are about 200 different types of cancer. It can start in any type of body tissue. What affects one body tissue may not affect another for example, tobacco smokes that you breath in may help to cause lung cancer. overexposing your skin to the sun could cause a melanoma on your leg. But the sun won't give you lung cancer and smoking won't give you melanoma. Apart from infection disease, most illnesses (including cancer) are multifactorial. This means that there are many factors involved. In other words, there is no single cause for any one type of cancer.{2}Cancer is a disease in which a person's cells grow out of control and spread to other parts of thebody.Cancer can develop in almost any region of the human body. Normally, human cells grow and multiply (through a process called cell division) to produce new cells when the body needs them. Cells in the body die when they complete their life cycle or become damaged, and new cells replace them. Cancer is a group of conditions where the body's cells begin to grow and reproduce in an uncontrolled manner. These cells can then invade and destroy healthy tissues. The cells become cancerous or malignant because of DNA damage. This damage can be inherited, or can be caused by mistakes happening while the normal cell is reproducing or by an environmental stimulus like tobacco.Cancer cells may travel to other parts of the body, where they begin to grow and form new tumors. Approximately 12,00,000 new cancer cases are diagnosed in India every year. As per the latest National Cancer Registry data, one in eight men and one in nine women in India will develop some form of cancer.The incidence of cancer and cancer types are influenced by many factors such as age, sex, race, local environmental factors, diet, and genetics. In

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males, lung followed by oral cavity and throat cancers is the most common, while cervical cancers and breast cancers are the commonest ones diagnosed in females in India.{3}

II. CANCER

Cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs. This process is referred to as metastasis. Metastase are the major cause of death from cancer. (WHO) Cancer known medically as a malignant neoplasm, is a broad group of diseases involving unregulated cell growth. In cancer, cellsdivide and grow uncontrollably, forming malignant tumors, and invading nearby

parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Not all tumors are cancerous; benign tumors do not invade neighboring tissues and do not spread throughout the body. There are over 200 different known cancers that affect humans. Cancer is one of the leading causes of human death which is estimated at 8.2 million and will likely rise to 13 million worldwide per year till 2030. Cancer is a large group of diseases that can start in almost any organ or tissue of the body when abnormal cells grow uncontrollably, go beyond their usual boundaries to invade adjoining parts of the body and/or spread to another organs.{4}

2.1 TYPES CANCER

- Bladder Cancer Breast Cancer Colorectal CancerKidney Cancer
- Lung Cancer - Non-Small CellLymphoma - Non-Hodgkin Melanoma
- Oral and Oropharyngeal CancerPancreatic Cancer
- Prostate Cancer Thyroid Cancer Uterine Cancer{5}

2.2 ANTICANCER

Definition

Anticancer, or antineoplastic, drugs are used to treat malignancies, or cancerous growths. Drug therapy may be used alone, or in combination with other treatments such as surgery or radiation therapy. Anti cancer drugs kill the cancer cell by first order kinetic means concentration dependent killing is done by Anti cancer drugs.For complete cure of cancer all cancerous cells must be killed as single cell capable of producing cancer. The anticancer drug either kill cancer cells or modify their growth. Discovery of anticancer agents started after 1940's (when nitrogen mustard was used). Most of the agents were discovered in 1950-1970.{6}

CYCLOPHOSPHAMIDE:

Introduction: Cyclophosphamide is a synthetic antineoplastic drug also known as cytophosphane, a nitrogen mustard alkylating agent from the oxazophorines group. It is a prodrug, converted in the liver to active forms that have chemotherapeutic activity. Soluble in water, saline and ethanol.

Brand Names : Procytox.

Generic Name: Cyclophosphamide.{8}Mechanism of action:

Alter DNA structure by misreading DNA code, initiating breaks in the DNA molecule.

Alkylating metabolites (Phosphoramide mustard) interfere with the growth of susceptible rapidly proliferating malignant cells and forms cross linking of DNA strands of tumor cell thereby blockingsynthesis of DNA, RNA, and protein

Attachment of alkyl groups to DNA bases, resulting in the DNA being fragmented by repair enzymes

in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA.

Cyclophosphamide is an alkylating agent of the nitrogen mustard type.2 An activated form of cyclophosphamide,phosphoramide mustard, alkylates, or binds, to DNA. Its cytotoxic effect is mainly due to cross-linking of strands of DNA and RNA, and to inhibition of protein synthesis.3These actions do not appear to be cell-cycle specific.

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Cyclophosphamide is a type of nitrogen mustard drug which exerts its effects through the alkylationof DNA. The drug is not cell-cycle phase-specific and metabolizes to an active form capable of inhibiting protein synthesis through DNA and RNA crosslinking.

The majority of the antineoplastic effects of cyclophosphamide are due to the phosphoramide mustard formed from the metabolism of the drug by liver enzymes like cytochrome P-450. Hepatic enzymes first convert cyclophosphamide to hydroxycyclophosphamide and then subsequently metabolized to aldophosphamide. Aldophosphamide is cleaved to the active alkylating agent phosphoramide mustard and acrolein. The phosphoramide metabolite forms cross-linkages within and between adjacent DNA strands at the guanine N-7 position. These modifications are permanent and eventually lead to programmed cell death.

In addition to antimitotic and antineoplastic effects, cyclophosphamide has immunosuppressive effects and selectivity for T cells. High-dose cyclophosphamide is used in eradication therapy of malignant hematopoietic cells, while lower dosages have shown merit for use in selective immunomodulation of regulatory T cells. The drug decreases the secretion of interferon-gamma and IL-12 while increasing the secretion of Th2 cytokines like IL-4 and IL-10 in the CSF and peripheral blood.Due to these effects, cyclophosphamide is considered as a valuable addition to tumor vaccination protocols, post-transplant alloreactivity management.{9}

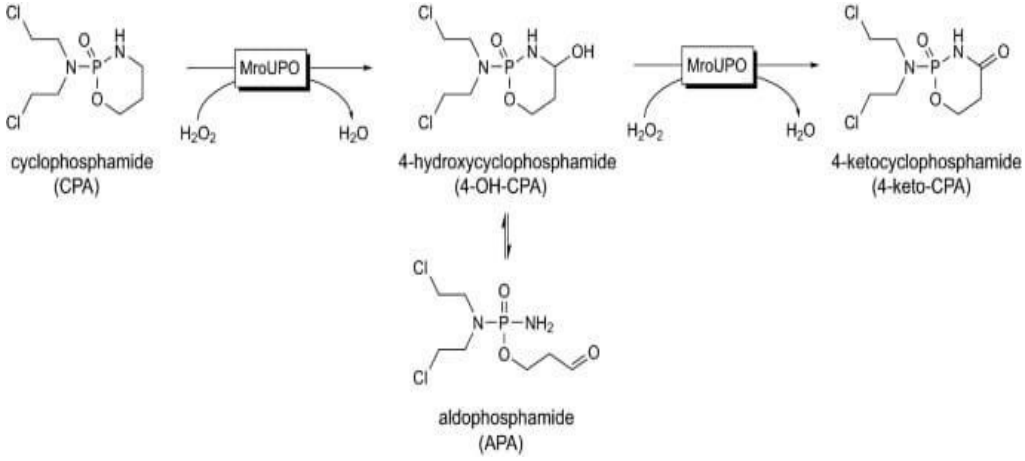

Fig. Structure of cyclpho

PHARMCOKINETIC:

Absorption: Readily absorbed from GI tract and Peak: 1 h PO.

Distribution: Widely distributed, including brain, breast milk; crosses placent. Metabolism: Metabolized in liver.

Elimination: Excreted in urine as active metabolites and unchanged drug Half-Life: 4-6 h. {10}

HOW CYCLOPHOSPHAMIDE:

Cyclophosphamide works by interfering with the DNA of cancer cells, preventing them from dividing and growing. It also suppresses the immune system by reducing the number of white blood cells in the body. This can help prevent the immune system from attacking healthy tissues in autoimmune diseases. Cyclophosphamide is in a class of medications called alkylating agents. When cyclophosphamide is used to treat cancer, it works by slowing or stopping the growth of cancer cells in your body. When cyclophosphamide is used to treat nephrotic syndrome, it works by suppressing your body's immune system. 15 Aug 2018Cyclophosphamide is a medication primarily used in the management and treatment of neoplasms, including multiple myeloma, sarcoma, and breast cancer. Cyclophosphamide is a nitrogen mustard that exerts its anti- neoplastic effects through alkylation. 3 Jul 2023The ability of cyclophosphamide to kill cancer cells depends on its ability to halt cell division. Usually, the drug works by damaging the RNA or DNA that tells the cell how to copy itselfin division. If the cells are unable to divide, they die. Cyclophosphamide is an antineoplastic agent metabolized to active alkylating metabolites with properties similar to those of chlormethine. It also possesses marked immunosuppressant properties. It is widely used, often in

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combination with other agents, in the treatment of several malignant diseases.Oral cyclophosphamide is rapidly absorbed and then converted by mixed-function oxidase enzymes (cytochrome P450 system) in the liver to active metabolites.{11}Cyclophosphamide is a strong immunosuppressant and puts patients at risk of infections. It is extremely important that patients report any signs of infection while using cyclophosphamide. We often need to prescribe an antibiotic (Bactrim) to prevent fungal pneumonia in patients taking cyclophosphamide.You usually have docetaxel and cyclophosphamide as cycles of treatment. This means that you have these drugs and then a rest to allow your body to recover. You have up to 4 cycles.Hepatic enzymes first convert cyclophosphamide to hydroxycyclophosphamide and then subsequently metabolized to aldophosphamide. Aldophosphamide is cleaved to the active alkylating agent phosphoramide mustard and acrolein. 3 Jul 2023The dose for the injectable form is either calculated based on height, weight and kidney function or it's given
as a fixed dose of 1g every 4 weeks, or 500 mg IV every two weeks for six weeks. It may take several weeks for symptoms to improve and the full effect may take several months or longer. Cyclophosphamide works in all phases of cell cycle and can be used for the treatment of different types of cancers.{12}The dose you're prescribed will depend on your bodyweight and may change, depending on how you respond to the drug. Cyclophosphamide doesn't work straight away. Itmaytake several weeks before you notice an improvement.
The mentioned solvent-free process for the preparation of cyclophosphamide comprises reacting phosphoryl chloride, bis(2-chloroethyl)amine hydrochloride, 3-aminopropanol and base for producing cyclophosphamide. According to this invention, there could be no solvent used in the reaction for producing cyclophosphamide.{13}

III. DOSAGE AND ADMINISTRACTION:

Cyclophosphamide is typically given as an intravenous infusion or taken orally in tablet form. The dosage and duration of treatment depend on the type of cancer or autoimmune disease being treated,as well as the patient's overall health. Patients receiving cyclophosphamide should be closely monitored for side effects.During or immediately after the administration, adequate amounts of fluid should be ingested or infused to force diuresis in order to reduce the risk of urinary tract toxicity. Therefore, cyclophosphamide should be administered in the morning.{14}

Dosing for Malignant Diseases Adults and Pediatric Patients
Intravenous
When used as the only oncolytic drug therapy, the initial course of cyclophosphamide for patients withno hematologic deficiency usually consists of 40 mg per kg to 50 mg per kg given intravenously in divided doses over a period of 2 to 5 days. Other intravenous regimens include 10 mg per kg to 15 mg per kg given every 7 to 10 days or 3 mg per kg to 5 mg per kg twice weekly.
OralOral cyclophosphamide dosing is usually in the range of 1 mg per kg per day to 5 mg per kg per day for both initial and maintenance dosing. Many other regimens of intravenous and oral cyclophosphamide have been reported. Dosages must be adjusted in accord with evidence of antitumor activity and/or leukopenia. The total leukocyte count is a good, objective guide for regulatingdosage. When cyclophosphamide is included in combined cytotoxic regimens, it may be necessary to reduce the dose of cyclophosphamide as well as that of the other drugs

Dosing for Minimal Change Nephrotic Syndrome in Pediatric Patients
An oral dose of 2 mg per kg daily for 8 to 12 weeks (maximum cumulative dose 168 mg per kg) is recommended. Treatment beyond 90 days increases the probability of sterility in males
Preparation, Handling and AdministrationHandle and dispose of cyclophosphamide in a mannerconsistent with other cytotoxic drugs.1 Cautionshould
be exercised when handling and preparing Cyclophosphamide for Injection, USP (Iyophilized powder), or Cyclophosphamide for Injection.{15}Cyclophosphamide for Injection,
USP Intravenous AdministrationParenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use cyclophosphamide vials if there are signs of melting. Melted cyclophosphamide is a clear or yellowish viscous liquid usually found as a connected

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phase or in droplets in the affected vials.Cyclophosphamide does not contain any antimicrobial preservative and thus care must be taken to assure the sterility of prepared solutions. Use aseptic technique. For Direct
Intravenous Injection Reconstitute Cyclophosphamide with 0.9% Sodium Chloride Injection, USP only, using the volumes listed below in Table 1. Gently swirl the vial to dissolve the drug completely. Do not use Sterile Water for Injection, USP because it results in a hypotonic solution and should not be injected directly.{16}

A COMPREHENSIVE REVIEW OF USES AND SIDE EFFECTS:

USES:

- Cyclophosphamide is a chemotherapy drug used to treat various types of cancer and autoimmune diseases. It works by slowing or stopping the growth of cancer cells and suppressing the immune system. However, it can cause several side effects, including nausea, hair loss, and increased risk of infection.
- Cyclophosphamide is used to treat a variety of cancers, including lymphoma, leukemia, and breast cancer. It is also used to treat autoimmune diseases, such as lupus and rheumatoid arthritis. In addition, it may be used in combination with other drugs to prepare patients for a stem cell transplant.
- Cyclophosphamide is used to treat cancer of the ovaries, breast, blood and lymph system, and nerves (mainly in children).
- Cyclophosphamide is also used for retinoblastoma (a type of eye cancer mainly in children)
- It is also used in the treatment of multiple myeloma (cancer in the bone marrow)
- Used in the treatment of mycosis fungoides (tumors on the skin). It belongs to the group of cancer medicines called alkylating agents.
- Cyclophosphamide is also used for some kinds of kidney disease.
- Cyclophosphamide interferes with the growth of cancer cells, which are then destroyed by the body.
- Take this medication by mouth exactly as directed by your doctor. The dosage is based on your medical condition, weight, response to treatment, and other treatments (such as other chemotherapy drugs, radiation) you may be receiving. Be sure to tell your doctor and pharmacist about all the products you use (including prescription drugs, nonprescription drugs, and herbal products).
- During treatment with this medication, you must drink more fluids than usual and pass urine often to help avoid kidney and bladder side effects. Ask your doctor how much you should drink and how often to empty your bladder each day, and follow these instructions carefully.
- Cyclophosphamide is also sometimes used to treat a certain type of lung cancer (small cell lung cancer; SCLC). It is also used to treat rhabdomyosarcoma (a type of cancer of the muscles) and Ewing's sarcoma (a type of bone cancer) in children. Talk to your doctor about the risks of using this medication for your condition.
- This medication may be prescribed for other uses; ask your doctor or pharmacist for more information.{17}

SIDE EFFECTS:

Cyclophosphamide can cause several side effects, including nausea, vomiting, diarrhea, hair loss, and increased risk of infection. It may also cause bladder irritation and an increased risk of developing secondary cancers. Patients receiving cyclophosphamide should report any side effects to their healthcare provider.How often and how severe the side effects are can vary from person to person. They also depend on what other treatments you're having.

Common Side Effects

These side effects happen in more than 10 in 100 people (more than 10%). You might have one or more of them. They include:{18}Increased Risk Of Infection Increased risk of getting an infection is due to a drop in white blood cells. Symptoms include a change in temperature, aching muscles, headaches, feeling cold and shivery and generally unwell. You might have other symptoms depending on where the infection is.Infections can sometimes be life threatening..Breathlessness and looking paleYou might be breathless and look pale due to a drop in red blood cells. This is called anaemia Bruising, bleeding gums or nose bleedsThis is due to a drop in the number of platelets in your

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blood. These blood cells help the blood to clot when we cut ourselves. You may have nosebleeds or bleeding gums after brushing your teeth. Or you may have lots of tiny red spots or bruises on your arms or legs (known as petechiae).{19}

Hair Loss

You could lose all your hair. This includes your eyelashes, eyebrows, underarms, legs and sometimespubic hair. Your hair will usually grow back once treatment has finished but it is likely to be softer. It may grow back a different colour or be curlier than before.Inflammation of the bladderInflammation of the bladder (cystitis) can cause pain and occasionally blood when passing urine.Depending on the dose of cyclophosphamide you have, you might have extra fluids through a drip toprevent

bladder irritation. Or you might have a drug called mesna to protect your bladder.{20}High temperature (fever)If you get a high temperature.Occasional Side EffectsThese side effects happen inbetween 1 and 10 out of every 100 people (between 1 and 10%). You might have one or more of them. They include: liver changes that are usually mild you have regular blood tests to check this inflammation and soreness of the mouth, throat, gut and bowels{21}

chillslack of energy and strengthRare Side Effects

This side effects happens in fewer than 1 in 100 people (fewer than 1%). You might have one or moreof them. They include:an allergic reaction that can cause a rash, shortness of breath, redness or swelling of the face and dizziness. Some allergic reactions can be life threatening.

heart problems such as changes to the heart muscle or rhythmnerve pain or changes that can cause a lack of sensation and strength in the hands and feetloss of appetitehearing loss

lung changes that can cause a cough or shortness of breathblood clots that are life threatening; signs are pain, swelling and redness where the clot is. Feeling breathless can be a sign of a blood clot on the lung.eye problems causing vision changes and discomfortskin and nail problems including a rash and colour changesa second cancer many years after treatment. This could be a blood cancer like leukaemia. or a solid cancer like bladder cancer{22}

Other Side Effects

There isn't enough information to work out how often these side effects might happen. You might have oneor more of them. They include:ringing in the ears (tinnitus)changes in blood sugar levels.feeling confusedinflammation of the lining of the large bowel (colitis)inflammation of the lungs causing breathlessness and a cough. {23}Nausea, vomiting, loss of appetite, stomach ache, diarrhea, or darkening of the skin/nails may occur. Nausea and vomiting can be severe. In some cases, drug therapy may be necessary to prevent or relieve nausea and vomiting.

Serious side effects (such as change in the amount of urine, pink/bloody urine), mouth sores, joint pain, stopping of menstrual periods, existing wounds that are slow healing, black/bloody stools, severe stomach/abdominal pain, yellowing eyes or skin, dark urine, mental/mood changes, muscle weakness/spasm.This medication may rarely cause very serious effects on the heart, especially when used in high doses, or in combination with radiation treatment or certain other chemotherapy drugs (such as doxorubicin), chest pain, jaw/left arm pain, trouble breathing, irregular heartbeat, symptoms of heart failure (such as shortness of breath, swelling ankles/feet, unusual tiredness, unusual/sudden weight gain).{24}

INFECTION RISK:

1. Cyclophosphamide can increase the risk of infection by suppressing the immune system. Patients should avoid contact with people who are sick and practice good hygiene, such as washing their hands
2. frequently. Patients should also report any signs of infection, such as fever or chills, to their healthcare provider.
3. A common side effect of cyclophosphamide is feeling or being sick. Your doctor may prescribe anti- sickness medication to control this. Because of its effects on the immune system, cyclophosphamide can make you more likely to develop symptoms of a cold or to pick up infections.
4. Cyclophosphamide can temporarily lower the number of white blood cells in your blood, increasing the chance of getting an infection. It can also lower the number of platelets, which are necessary for proper blood clotting. 1 Nov 2023

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5. Infection occurred in more CYC-treated patients taking concomitant steroids than in those treated with
6. high-dose steroids alone (45% versus 12%; P = 0.001). Fatal and opportunistic infections during CYC therapy were associated with a low WBC nadir and a high maximum corticosteroid dose.
7. Cyclophosphamide also increases the risk of developing some kinds of cancer, includinglymphoma,
8. skin and bladder cancer (periodic urine tests screen for this).
9. The long-term side effects of cyclophosphamide (Cytoxan) are damage to the bladder and the bone marrow. Bladder cancer is a well-known risk and continues to arise at least 10- 15 years after the drug was given. 1 Dec 2012
10. Fertility in women. The major threat to women is cyclophosphamide exposure. This drug is used to control vasculitis activity and is directly toxic to the ovaries. This can result in permanent infertility, also known as primary ovarian failure.
11. Clinically, damage to the bladder (haemorrhagic cystitis), immunosuppression (when not desired)and alopecia are
12. the most significant toxicities associated with cyclophosphamide. Cardiotoxicity is also a possibility when very high doses are given.
13. If blood levels of cyclophosphamide are too high, kidney function may decrease. This is why blood work is done frequently so that the dose of cyclophosphamide can be adjusted. Your doctor may want the bladder emptied every two hours and may also want the bladder emptied during the night.
14. Possible Side Effects (More Common)
15. These symptoms may happen within a few hours after your treatment and may last up to 72 hours. Medicines are available to stop or lessen these side effects. Bone marrow depression. This is a decrease in the number of white blood cells, red blood cells, and platelets.
16. Cyclophosphamide therapy in idiopathic membranous nephropathy gives a threefold increase in cancer risk. For the average patient, this finding translates into an increase in annual risk from approximately 0.3% to 1.0%. The increased risk of malignancy must be balanced against the improved renal survival.{25}
17. Cyclophosphamide can increase the risk of developing secondary cancers, such as bladder cancer and leukemia. However, the risk of developing a secondary cancer is generally low and must be weighed against the benefits of treatment. Patients receiving cyclophosphamide should be closely monitored for signs of a secondary cancer.
18. The lung toxicity caused by cyclophosphamide is accelerated when cyclophosphamide is combined with amiodarone, an antiarrhythmic agent also capable of lung toxicity.
19. Cyclophosphamide increased the risk of causing hearing loss. Complaints of tinnitus and speech understanding difficulty were observed.
20. Sinusoidal obstructive syndrome (SOS) which may cause damage to the liver, yellowing of eyes and skin, swelling. Constipation, bloating, weight loss. Loss or absence of sperm which may lead to an inability to father children.
21. Blood in the urine warning: When cyclophosphamide is broken down by your body, it creates substances that irritate your kidneys and bladder. These substances can cause your kidneys or bladder to bleed. If you have blood in your urine and bladder pain, tell your doctor.{26}

IV. PRECAUTIONS AND CONTRAINDICATION:

Cyclophosphamide should not be used in patients with severe bone marrow suppression, severe kidney disease, or a history of allergic reaction to the drug. It should be used with caution in patients with a history of heart disease or liver disease. Patients receiving cyclophosphamide should avoid livevaccines and should use effective contraception during treatment.It is very important that your doctor check your progress at regular visits to make sure that this medicine is working properly and to check for unwanted effects.While you are being treated with cyclophosphamide, and after you stop treatment with it, do not have any immunizations (vaccines) without your doctor's approval. Cyclophosphamide may lower your body's resistance and the vaccine may not work as well or you might get the infection the vaccine is meant to prevent. In addition, you should not be around other persons living in your household who receive live virus

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vaccines because there is a chance. they could pass the virus on to you. Some examples of live vaccines include measles, mumps, influenza (nasal flu vaccine), poliovirus (oral form). rotavirus, and rubella. Do not get close to them and do not stay in the same room with them for very long. If you have questions about this, talk to your doctor.

Before having any kind of surgery, including dental surgery, or emergency treatment, make sure the medical doctor or dentist in charge knows that you are taking this medicine, especially if you have taken it within the last 10 days.Cyclophosphamide may cause a temporary loss of hair in some people. After treatment has ended, normal hair growth should return, although the new hair may be a slightly different color or texture.Cyclophosphamide can temporarily lower the number of white blood cells in your blood, increasing the chance of getting an infection. It can also lower the number of platelets, which are necessary for proper blood clotting. If this occurs, there are certain precautions you can take, especially when your blood count is low, to reduce the risk of infection or bleeding:

If you can, avoid people with infections. Check with your doctor immediately if you think you are getting an infection or if you get a fever or chills, cough or hoarseness, lower back or side pain, or painful or difficult urination. Check with your doctor immediately if you notice any unusual bleeding or bruising, black, tarry stools; blood in the urine or stools; or pinpoint red spots on your skin. Be careful when using a regular toothbrush, dental floss, or toothpick. Your medical doctor, dentist, or nurse mayrecommend other ways to clean your teeth and gums. Check with your medical doctor before having any dental work done. Do not touch your eyes or the inside of your nose unless you have just washedyour hands and have not touched anything else in the meantime. Be careful not to cut yourself when you are using sharp objects such as a safety razor or fingernail or toenail cutters. Avoid contact sportsor other situations where bruising or injury could occur.Before you have any medical tests, tell the medical doctor in charge that you are taking this medicine. The results of some tests may be affected by this medicine.{27}

V. PREGNANCY AND BREASTFEEDING:

Cyclophosphamide can harm a developing fetus and should not be used during pregnancy. Women of childbearing age should use effective contraception during treatment. It is not known if cyclophosphamide passes into breast milk, so women should avoid breastfeeding while receiving treatment.For pregnant women: Cyclophosphamide is a category D pregnancy drug. That means two things:

Studies show a risk of adverse effects to the fetus when the mother takes the drug.

The benefits of taking the drug during pregnancy may outweigh the potential risks in certain cases. This drug can harm a pregnancy. Women shouldn't become pregnant while taking this drug. If you're a woman, be sure to use effective birth control during treatment and for up to one year after you stop taking this drug. If you're a man and your partner could become pregnant, be sure to use a condomduring your treatment and for at least four months after your treatment ends.

Tell your doctor if you're pregnant or planning to become pregnant. Cyclophosphamide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

For women who are breastfeeding: Cyclophosphamide passes into breast milk and can cause serious effects in a child who is breastfed. You and your doctor may need to decide if you'll take cyclophosphamide or breastfeed.For seniors: As you age, your organs (such as your liver, kidneys, or heart) may not work as well as they did when you were younger. More of this drug may stay in your body and put you at risk for severe side effects.For children: Children who receive cyclophosphamide have a higher risk for: infertility ovarian fibrosis in girls who haven't reached puberty yet low sperm counts, immobile sperm, or smaller testes in boys who haven't gone through puberty yetThese conditions may be reversible in some people, but it may not happen for several years after stopping cyclophosphamide.{28}

VI. CONCLUSION

Cyclophosphamide is a chemotherapy drug used to treat various types of cancer and autoimmune diseases. It works by slowing or stopping the growth of cancer cells and suppressing the immune system. However, it can cause several side effects, including nausea, hair loss, and increased risk of infection. Patients receiving cyclophosphamide should be closely monitored for side effects and should report any concerns to their healthcare provider.A plan for the diagnosis and treatment of cancer is a key component of any overall cancer control plan. Its main goal is to cure cancer patients or prolong their life considerably, ensuring a good quality of life. In order for a diagnosis and treatment programme to be

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effective, it must never be developed in isolation. It needs to be linked to an early detection programme so that cases are detected at an early stage, when treatment is more effective and there is a greater chance of cure. It also needs to be integrated with a palliative care programme, so that patients with advanced cancers, who can no longer benefit from treatment, will get adequate relief from their physical, psychosocial and spiritual suffering. Furthermore, programmes should include a awareness-raising component, to educate patients, family and community members about the cancer risk factors and the need for taking preventive measures to avoid developing cancer.{29} Where resources are limited, diagnosis and treatment services should initially target all patients presenting with curable cancers, such as breast, cervical and oral cancers that can be detected early. They could also include childhood acute lymphatic leukaemia, which has a high potential for cure although it cannot be detected early. Above all, services need to be provided in an equitable and sustainable manner. As and when more resources become available, the programme can be extended to include other curable cancers as well as cancers for which treatment can prolong survival considerably. This module on diagnosis and treatment is intended to evolve in response to national needs and experience. WHO welcomes input from countries. wishing to share their successes in diagnosis and treatment. WHO also welcomes requests from countries for information relevant to their specific needs. Evidence on the barriers to diagnosis and treatment in country contexts-and the lessons learned in overcoming them would be especially welcome.{30}

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