Baxter

PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Cyclophosphamide Injection 500 mg and 1 g Cyclophosphamide monohydrate

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

Throughout this leaflet, Cyclophosphamide Injection will be called Cyclophosphamide.

Important things to know about Cyclophosphamide

Your doctor has prescribed Cyclophosphamide because you have cancer that can be treated.

Cyclophosphamide is a medicine that kills cancer cells but, as a result, also attacks normal cells. It can therefore have a number of side effects. Your doctor will not give you Cyclophosphamide unless he or she thinks that your cancer is more of a risk to you than any possible side effects. Your doctor will check you regularly and treat any side effects where possible.

Cyclophosphamide:

- will reduce your blood cell count, which may make you feel tired and be more likely to get infections.
- can affect your kidneys and bladder. You may be given another medicine called Mesna to help prevent any damage. If you notice blood in your urine, tell your doctor immediately.
- like most anti-cancer or chemotherapy medicines, you may lose your hair (anything from thinning to total loss), although it should start to grow back once your treatment has finished. It may also make you feel sick or be sick. Your doctor can give you advice or medicines to help.
- Men or women should not have a child during treatment with Cyclophosphamide or for at least 6 months after treatment. You should use an effective contraceptive. Ask your doctor for advice.

Now read the rest of this leaflet. It includes other important information on the use of Cyclophosphamide that might be especially important for you.

In this leaflet:

1 What Cyclophosphamide is and what it is used for

Cyclophosphamide is a cytotoxic drug or anti-cancer drug. It works by killing cancer cells, this is sometimes called 'chemotherapy'.

It is used to treat lots of different cancers. Cyclophosphamide is often used together with other anti-cancer drugs or radiotherapy. Occasionally, some doctors may prescribe Cyclophosphamide for other conditions not related to cancer, your doctor will tell you if this applies to you.

2 What you need to know before you are given Cyclophosphamide

You will not be given Cyclophosphamide if:

- you have ever had an allergic reaction to Cyclophosphamide. An allergic reaction can include shortness of breath, wheezing, rash, itching or swelling of the face and lips
- your bone marrow is not working properly (especially if you have previously had chemotherapy or radiotherapy). You will have blood tests to check how well your bone marrow is working
- you have a urinary tract infection, which can be recognised as pain when passing urine (cystitis)
- you currently have any infections
- you have ever had kidney or bladder problems as a result of previous chemotherapy or radiotherapy
- you have a condition which decreases your ability to urinate (Urinary outflow obstruction).

Tell your doctor if:

- you are already having, or have recently had, radiotherapy or chemotherapy
- you have diabetes
- you have liver or kidney problems. Your doctor will check how well your liver and kidneys are working by doing a blood test
- you have had your adrenal glands removed
- you have heart problems or have had radiotherapy in the area of your heart
- you have poor general health or are frail
- you are elderly.

Take special care with Cyclophosphamide

- Cyclophosphamide can have effects on your blood and immune system.
- Blood cells are made in your bone marrow. Three different types of blood cell are made:
  - red blood cells, which carry oxygen around your body
  - white blood cells, which fight infection, and
  - platelets, which help your blood to clot.
- After taking Cyclophosphamide, your blood count of the three types of cells will drop. This is an unavoidable side effect of Cyclophosphamide. Your blood count will reach its lowest level about 5 to 10 days after you start taking Cyclophosphamide and will stay low until a few days after you finish the course. Most people recover to a normal blood count within 21 to 28 days. If you have had a lot of chemotherapy in the past, it may take a little longer to return to normal.
- You may be more likely to get infections when your blood count drops. Try to avoid close contact with people who have coughs, colds and other infections. Your doctor will treat you with appropriate medicine if they think you have, or are at risk, of an infection.
- Your doctor will check that the number of red blood cells, white blood cells and platelets is high enough before and during your treatment with Cyclophosphamide. They may need to reduce the amount you are given or delay your next dose.
- Cyclophosphamide can affect wound healing. Keep any cuts clean and dry, and check they are healing normally.
- It is important to keep your gums healthy, as mouth ulcers and infections can occur. Ask your doctor about this if you are unsure.
- Cyclophosphamide can damage the lining of your bladder, causing bleeding into your urine and pain on urination. Your doctor knows this can happen and, if necessary, he or she will give you a medicine called Mesna which will protect your bladder.
- Mesna can either be given to you as a short injection, or mixed into the drip solution with your Cyclophosphamide, or as tablets.
- More information on Mesna can be found in the Patient Information Leaflet for Mesna Injection and Mesna tablets.
- Most people having Cyclophosphamide with Mesna do not develop any problems with their bladder, but your doctor may want to test your urine for the presence of blood using a 'dipstick' or microscope.
- If you notice that you have blood in the urine, you must tell your doctor straight away as they may need to stop giving you Cyclophosphamide.
- Cancer medicines and radiation therapy can increase the risk of you developing other cancers; this can be a number of years after your treatment has stopped. Cyclophosphamide has an increased risk of causing cancer in the area of your bladder.
- Cyclophosphamide can cause damage to your heart or affect the rhythm of it beating. This increases with higher doses of Cyclophosphamide, if you are being treated with radiation or other chemotherapy medicines or if you are elderly. Your doctor will monitor your heart closely during treatment.
- Cyclophosphamide can cause inflammation or scarring in your lungs. This can occur more than six months after your treatment. If you start having difficulty breathing tell your doctor straight away.
- Cyclophosphamide can have life threatening effects on your liver.
  If you have sudden weight gain, liver pain and jaundice tell your doctor straight away.
- Hair thinning or baldness can occur. Your hair should grow back normally though it may be different in texture or colour.
- Cyclophosphamide can make you feel sick or be sick. This can last for about 24 hours after taking Cyclophosphamide. You may need to be given medicines to stop feeling or being sick. Ask your doctor about this.

Using other medicines and treatments

Tell your doctor or nurse if you are taking or have recently taken any other medicines, including medicines you have bought yourself. In particular, tell them about the following medicines or treatments as they may not work well with Cyclophosphamide:

The following medicines can reduce how effective Cyclophosphamide is:

- aprepitant (used to prevent being sick)
- bupropion (an anti-depressant)
- busulfan, thiotepa (used to treat cancer)
- ciprofloxacin, chloramphenicol (used to treat bacterial infections)
- fluconazole, itraconazole (used to treat fungal infections)
- Prasugrel (used to thin the blood)
- Sulfonamides, such as sulfadiazine, sulfasalazine, sulfamethoxazole (used to treat bacterial infections).

The following medicines can increase the toxicity of Cyclophosphamide:

- allopurinol (used to treat gout)
- azathioprine (used to reduce the activity of the immune system)
- chloral hydrate (used to treat insomnia)
- cimetidine (used to reduce stomach acid)
- disulfiram (used to treat alcoholism)
- glyceraldehyde (used to treat warts)
- protease inhibitors (used to treat viruses)
- ondansetron (used to prevent being sick)
- medicines that increase liver enzymes such as:
  - rifampicin (used to treat bacterial infections)
  - carbamazepine, phenobarbital, phenytoin (used to treat epilepsy)
  - St. John's wort (a herbal remedy for mild depression)
  - Corticosteroids (used to treat inflammation)
- medicines that can increase the toxic effects on your blood cells and immunity
  - ACE inhibitors (used to treat high blood pressure).
  - natalizumab (used to treat multiple sclerosis)
  - paclitaxel (used to treat cancer)
  - thiazide diuretics such as hydrochlorothiazide or chlortalidone (used to treat high blood pressure or water retention)
  - zidovudine (used to treat viruses)
  - Clozapine (used to treat symptoms of some psychiatric disorders)
- medicines that can increase the toxic effects on your heart
  - anthracyclines such as bleomycin, doxorubicin, epirubicin, mitomycin (used to treat cancer)
  - cytarabine, pentostatin, trastuzumab (used to treat cancer)
  - radiation in the area of your heart
- medicines that can increase the toxic effects on your lungs
  - amiodarone (used to treat irregular heart beat)
  - G-CSF, GM-CSF hormones (used to increase white blood cell numbers after chemotherapy)
- medicines that can increase the toxic effects on your kidneys
  - amphotericin B (used to treat fungal infections)
  - Indomethacin (used to treat pain and inflammation).

Other medicines that can affect or be affected by Cyclophosphamide include:

- etanercept (used to treat rheumatoid arthritis)
- metronidazole (used to treat bacterial or protozoal infections)
- tamoxifen (used to treat breast cancer)
- bupropion (used to help stop smoking)
- coumarins such as warfarin (used to thin the blood)
- cyclosporine (used to reduce the activity of the immune system)
- succinylcholine (used to relax muscles during medical procedures)
- digoxin, ß-acetyldigoxin (used to treat heart conditions)
- vaccines
- verapamil (used to treat high blood pressure, angina or irregular heart beat).

Cyclophosphamide with food and drink

Drinking alcohol can increase the nausea and vomiting caused by Cyclophosphamide.

Pregnancy, breast-feeding and fertility

Do not become pregnant while taking Cyclophosphamide. This is because it can cause miscarriage or damage your unborn baby. Tell your doctor if you are pregnant, think you might be pregnant or are trying to become pregnant.

- Men or women should not try to have a child during or for at least 6 to 12 months after treatment. You should use an effective contraceptive. Ask your doctor for advice.
- Cyclophosphamide can affect your ability to have children in the future. Talk to your doctor about freezing sperm samples or eggs before your treatment starts.

Do not breast-feed while being treated with Cyclophosphamide. Ask your doctor for advice.

Driving or using machines

Some of the side effects of treatment with Cyclophosphamide might affect your ability to drive and use machines safely. Your doctor will decide if it is safe for you to do so.

What to do if you see a different doctor, or have to go to hospital

If you see any other doctor or have to go to hospital for any reason, tell them what medicines you are taking. Do not take any other medicines unless your doctor knows you are taking Cyclophosphamide.

3 How Cyclophosphamide is given

Cyclophosphamide will be given to you by a doctor or nurse.

- It can be given as an injection or by mouth.
- When Cyclophosphamide is given as an injection, it will normally be added to a large bag of fluid and will be slowly injected (infused) directly into your vein. The vein can be in your arm, the back of your hand or a large vein under your collar bone. Depending on your dose, it will usually take between a few minutes to an hour to be given.
- When Cyclophosphamide is given by mouth, it will usually be made in to a solution with some flavourings (called an 'elixir') which will make it taste pleasant and easier to swallow.
- Cyclophosphamide is often given with other anti-cancer drugs or radiotherapy.

The usual dose

- Your doctor will decide how much of the medicine you need and when you should be given it.
- The amount of Cyclophosphamide you will be given depends on:
  - the type of illness you have
  - how big you are (a combination of your height and weight)
  - your general health
  - whether you are being given other anti-cancer drugs or having radiotherapy.

Cyclophosphamide is usually given as a series of courses of treatment. After each course there is a break (a period when no Cyclophosphamide is given) before the next course.

Your doctor may need to change the amount of medicine you are given and monitor you more closely if you:

- have problems with your liver or kidneys
- you are elderly.

If you take too much Cyclophosphamide

In the event of an overdose, or if a child swallows any of your tablets, talk to your doctor or local hospital emergency department immediately. Hospital admission for special treatment may be needed.

4 Possible side effects

Like all medicines, Cyclophosphamide can cause side effects, although not everybody gets them. Side effects can sometimes occur after ending the treatment. The following side effects may happen with this medicine.

Tell your doctor straight away, if you notice any of the following serious side effects:

- allergic reactions, signs of this would be shortness of breath, wheezing, rash, itching or swelling of the face and lips
- getting bruises without knocking yourself, or bleeding from your gums. This may be a sign that the platelet levels in your blood are getting too low
- a lowering of your white blood cell count, your doctor will check this during your treatment. It will not cause any signs, but you will be more likely to get infections. If you think you have an infection (a high temperature, feeling cold and shivery, or hot and sweaty, or any signs of infection such as a cough, or stinging on passing water) you may need antibiotics to fight infections because your blood count is lower than usual

- very pale, lethargic and tired. This may be a sign of low red blood cells (anaemia). Usually, no treatment is required, your body will eventually replace the red blood cells. If you are very anaemic, you may need a blood transfusion
- blood in your urine, pain while passing urine, or less urine being passed.

Other possible side effects may be:

Immune system and Infections
- allergic reactions, signs of this would be shortness of breath, wheezing, rash, itching or swelling of the face and lips (hypersensitivity). Severe allergic reactions could lead to difficulty in breathing or shock, with a possible fatal outcome (anaphylactic shock, anaphylactic/anaphylactoid reaction)
- reduction in the effectiveness of your immune system (immunosuppression)
- increased risk and severity of bacterial, fungal, viral, protozoal or parasitic infections due to the effect of cyclophosphamide on your immune system
- reactivation of infections you have had before (latent infections)
- severe infection spreading through the blood which may lead to a dangerous drop in blood pressure with a possible fatal outcome (sepsis, shock).

Cancers
- cancer of your blood (leukaemia)
- cancer of the bone marrow (myelodysplastic syndrome)
- cancer of the lymphatic system (Non-Hodgkin's lymphoma)
- secondary tumours in various parts of the body, often in the area of the bladder
- changes to your metabolism caused by the breakdown of the dying cancer cells (Tumour lysis syndrome).

Blood and Lymphatic System
- decrease in the activity of your bone marrow (myelosuppression). This can cause a decrease in the number of cells in your blood:
  - white cells – which fight infection (leucopenia, agranulocytosis, granulocytopenia, lymphopenia, neutropenia). This may be associated with fever (febrile neutropenia)
  - platelets – which help your blood clot (thrombocytopenia)
  - red cells – which carry oxygen around the body (anaemia). This may be associated with a decrease in their ability to carry oxygen (decreased haemoglobin)
  - red cells, white cells and platelets at the same time (pancytopenia)
- formation of small blood clots in your blood vessels disrupting the normal blood flow around your body (disseminated intravascular coagulation)
- haemolytic uremic syndrome – a condition causing abnormal break down of the red blood cells, decreased numbers of platelets in the blood and kidney failure.

Endocrine System
- swelling of the brain due to too much water in your blood (water intoxication). Signs of this can be headache, changes in personality or behaviour, confusion, drowsiness
- increase in the release of antidiuretic hormone from the pituitary gland. This affects the kidneys causing the low levels of sodium in your blood (hypernatremia) and water retention.

Metabolism and Nutrition
- low blood levels of sodium which can cause tiredness and confusion, muscle twitching, fits and coma (hyponatremia)
- accumulation of fluid in the body (water retention), which may been seen as fluid beneath the skin or swelling in you limbs
- high blood sugar levels which can cause thirst, tiredness and irritability (hyperglycaemia)
- low blood sugar levels which can cause confusion and sweating (hypoglycaemia)
- loss of appetite (anorexia)
- dehydration.

Digestive system
- feeling sick and being sick (nausea, vomiting).
- inflammation of your intestines or bowel which may resulting in bleeding (enteritis, cecitis, hemorrhagic enterocolitis)
- bleeding in your stomach or intestines (gastrointestinal haemorrhage)
- tummy discomfort or severe tummy and back pain, this may be caused by inflammation of the pancreas (acute pancreatitis)
- Inflammation which causes abdominal pain or diarrhoea (colitis)
- constipation or diarrhoea
- ulcers in the lining of your digestive system (mucosal ulceration)
- inflammation of the lining of your mouth including ulcers (stomatitis)
- swelling of the glands in your neck (parotid gland inflammation).

Psychiatric Disorders
- Confusion

Nervous System
- effects on the brain (encephalopathy), signs of this can be problems in thinking or concentrating, reduced alertness, changes in personality, tiredness, fits, muscle twitching, and shaking
- fits (convulsions)
- dizziness
- a syndrome called Reversible posterior leukoencephalopathy syndrome, which can cause swelling of the brain, headache, confusion, fits and loss of sight
- effects on the spinal cord (Myelopathy), which can cause numbness, weakness and tingling in the hands, loss of motor skills
- a disorder of the nerves which can cause weakness, tingling or numbness (peripheral neuropathy). This could be in more than one set of nerves (polyneuropathy)
- pain from your nerves, which can also feel like an aching or burning sensation (neuralgia)
- tingling or numbness, often in the hands or feet (paresthesia)
- shaking (tremor)
- changes in your sense of touch (dysesthesia) or loss of sensation (hypoesthesia)
- changes in your sense of taste (dysgeusia) or loss of taste (hypogeusia)
- changes in your sense of smell (parosmia).

Eyes and Ears
- blurring, reduction or loss of sight
- inflammation of the eye (conjunctivitis)
- increased tear formation (lacrimation).
- deafness or hearing impairment
- ringing in the ears (tinnitus).

Heart and Circulation
- heart attack (myocardial infarction)
- changes in your heart rhythm (arrhythmia) which may be noticeable (palpitations):
  - irregular heart beat (fibrillation)
  - faster heart beat (tachycardia), which may be life threatening (ventricular tachycardia)
  - slower heart beat (bradycardia)
- decrease in your hearts ability to pump enough blood around your body which may be life threatening (cardiogenic shock, heart failure or cardiac arrest)
- disease of the heart muscle (cardiomyopathy)
- inflammation of the tissues in or around your heart (myocarditis, pericarditis)
- build up of fluid in the sac around your heart (pericardial effusion). Increased pressure from this fluid can stop the heart filling properly (cardiac tamponade)
- abnormal ECG heart tracing (Electrocardiogram QT prolonged).
- blood clot in the lungs which causes chest pain and breathlessness (pulmonary embolism)
- blood clot, usually in a leg, which causes pain swelling or redness (venous thrombosis)
- inflammation of the blood vessels (vasculitis)
- reduced blood supply to your hands and feet (peripheral ischemia). This may cause pain, weakness, numbness, ulcers, changes in skin colour or temperature
- low or high blood pressure (hypotension, hypertension)
- reddening of the skin (flushing) which may be accompanied by feeling hot or sweating (hot flushing).

Lungs
- life-threatening decrease of your lungs ability to transfer oxygen in to your blood (respiratory failure)
- blood clot in the lungs which causes chest pain and breathlessness (pulmonary veno-occlusive disease)
- scarring of the lungs which causes shortness of breath (pulmonary fibrosis)
- conditions causing inflammation of the lungs which can cause breathlessness, cough and raised temperature or scarring of the lungs (pneumonitis, acute respiratory distress syndrome, obliterative bronchiolitis, organizing pneumonia, alveolitis allergic)
- fluid in or around the lungs (pulmonary oedema, pleural effusion)
- increased blood pressure in the lungs which can cause shortness of breath, fatigue, cough, angina, fainting, peripheral oedema (pulmonary hypertension)
- difficulty in breathing or wheezing (bronchospasm)
- shortness of breath (dyspnea)
- decrease levels of oxygen in your body (hypoxia)
- cough
- blocked or runny nose
- pain at the back of your throat.

Liver
- increased liver size (hepatomegaly)
- yellowing of the skin or whites of the eyes (jaundice)
- blockage of the small veins in your liver (veno-occlusive liver disease) which can cause weight gain, increased liver size, pain and jaundice
- conditions causing inflammation of the liver which can cause jaundice, weight loss and malaise (hepatitis),
- disruption of the formation of bile by the liver which can cause itchiness, jaundice, pale coloured stools, dark urine (cholestasis)
- a build up of toxins in the body due to liver failure (hepatotoxicity). This may affect the brain causing confusion, reduced consciousness or coma (hepatic encephalopathy)
- a build up of fluid in the abdomen causing swelling of the tummy and shortness of breath (ascites)
- increased levels of certain proteins produced by your liver called enzymes. Your doctor will do blood tests to test for these.

Skin and Subcutaneous Tissue
- life threatening conditions which cause rash, ulcers, sore throat, fever, conjunctivitis, separation of skin layers (toxic epidermal necrolysis, Stevens-Johnson syndrome)
- swelling, numbness, red lumps and peeling of skin on the hands and feet (Palmar-plantar erythrodysesthesia syndrome)
- dark red raised itchy rash (urticaria)
- inflammation of this skin which may cause rash, blisters, itching, sores, oozing and scarring (dermatitis)
- redness and blistering of the skin appearing months or years after treatment (Radiation recall dermatitis)
- itchy, red rash which can develop in to sores (erythema multiforme)
- changes in colour of your fingernails and skin.
- separation of the nail bed which can cause nails to fall off
- dehydration
- excessive sweating (hyperhidrosis)
- swelling of the face
- hair loss (alopecia).

Musculoskeletal and Connective Tissue
- abnormal muscle breakdown which can lead to kidney problems (rhabdomyolysis)
- serious illness which causes thickening of the skin and the connective tissue in your internal organs (scleroderma)
- muscle spasms
- muscle pain (myalgia) or joint pain (arthralgia).

Renal and Urinary
- life threatening decrease in the abilities of your kidney to adequately remove toxins and waste products from the blood (kidney failure)
- changes to the tissues within your kidneys which prevent them from working correctly (renal tubular necrosis, renal tubular disorder)
- damage to the kidneys by toxins in the blood (toxic nephropathy)
- pain and difficultly passing urine (cystitis)
- blood in the urine (haematuria)
- glucose in the urine (nephrogenic diabetes insipidus)
- inflammation of the bladder lining which causes pain, bleeding, blood in the urine, reduced urine flow (haemorrhagic cystitis)
- inflammation of the urethra which causes pain and bleeding. (haemorrhagic ureteritis)
- death of the cells and tissues (necrosis), ulceration or scaring (fibrosis) of the bladder
- decrease in the size of the bladder (bladder contracture)
- changes to the cells in the lining of your bladder
- increase in the levels of creatinine or urea nitrogen in your blood. Your doctor will do blood tests to test for these.

Pregnancy and Fertility
- premature labour.
- infertility. Sperm production in men and egg production in women may be reduced or stop. In some cases this can be permanent
- absence of menstrual periods (amenorrhea) or reduced frequency (oligomenorrhea)
- decrease in testicle size (testicular atrophy)
- decrease in the hormone oestrogen in the blood
- increase in the hormone gonadotrophin in the blood.
- use in young patients may result in some impairments of future fertility.

Congenital, Familial and Genetic Disorders
- reduction in growth, deformity or death of a foetus while in the womb
- toxic effects on the foetus such as myelosuppression and gastroenteritis.

General Disorders and Administrative Site Conditions
- life threatening failure of multiple organs
- general physical deterioration
- flu-like symptoms such as headache, fever, chills, joint and muscle pain, weakness, tiredness
- chest pain
- swelling
- Injection/infusion site reactions such as swelling, redness, pain, inflammation, tissue damage, tissue death, clot formation
- inflammation of the linings of your body cavities (mucosal inflammation).

Reporting of side effects

If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

UK

Yellow Card Scheme
www.mhra.gov.uk/yellowcard

5 How to store Cyclophosphamide

Because Cyclophosphamide is usually given in hospital it will be stored safely and correctly by the hospital staff. If you do need the storage conditions they are given below:
- Keep this medicine out of the sight and reach of children.
- Do not use Cyclophosphamide after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.
- Do not store above 25ºC. Store in the original container.

6 Contents of the pack and other information

What Cyclophosphamide contains

The active substance is Cyclophosphamide and each vial contains 500 mg or 1 g.
There are no other ingredients.

What Cyclophosphamide looks like and contents of the pack

Cyclophosphamide is a dry, white powder supplied in clear glass vials. Each carton contains one vial.

Nature and contents of container

Vials are packed with or without a protective plastic overwrap. Protective plastic overwrap does not come into contact with the medicinal product and provides additional transport protection, which increases the safety for the medical and pharmaceutical personnel.

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisation holder is:
Baxter Healthcare Ltd
Caxton Way, Thetford, Norfolk, IP24 3SE
United Kingdom
Send all enquiries to this address.

Cyclophosphamide is manufactured by:
Baxter Oncology GmbH
Kantstrasse 2, 33790 Halle/Westfalen
Germany

This leaflet was last revised in 01/2019.

**For information about Cyclophosphamide or to request this leaflet in formats such as audio or large print please contact the Marketing Authorisation Holder:
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