Package leaflet: Information for the patient

Cyclophosphamide Seacross 500 mg powder for solution for injection/infusion
Cyclophosphamide Seacross 1000 mg powder for solution for injection/infusion
Cyclophosphamide Seacross 2000 mg powder for solution for injection/infusion
cyclophosphamide

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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

Important things to know about Cyclophosphamide Seacross
Your doctor has prescribed Cyclophosphamide Seacross because you have cancer that can be treated. Cyclophosphamide Seacross 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 Seacross 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 Seacross:
- 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 Seacross or for at least 3 to 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 Seacross that might be especially important for you.

What is in this leaflet

1. What Cyclophosphamide Seacross is and what it is used for

Cyclophosphamide Seacross contains an active substance called cyclophosphamide. Cyclophosphamide is a cytotoxic medicine or anti-cancer medicine. It works by killing cancer cells, this is sometimes called ‘chemotherapy’.

Cyclophosphamide is often used alone or together with other anti-cancer drugs or radiotherapy in the treatment of various cancers. These include:
- certain types of cancer of the white blood cells (acute lymphoblastic leukaemia, chronic lymphocytic leukaemia);
- different forms of lymphomas that affect the immune system (Hodgkin's disease, non-Hodgkin's

lymphoma and multiple myeloma);
- ovarian cancer and breast cancer;
- Ewing's sarcoma (a form of bone cancer);
- small cell lung cancer;
- in the treatment of advanced or metastatic tumour of the central nervous system (neuroblastoma).

Furthermore, cyclophosphamide is used in preparation for bone marrow transplantation to treat certain types of cancer of the white blood cells (acute lymphoblastic leukemia, chronic myeloid leukemia and acute myeloid leukemia)

Occasionally, some doctors may prescribe cyclophosphamide for other conditions not related to cancer:
- life threatening autoimmune diseases: severe progressive forms of lupus nephritis (inflammation of the kidney caused by a disease of the immune system) and Wegener's granulomatosis (a rare form of vasculitis).

2. What you need to know before you are given Cyclophosphamide Seacross

You will not be given Cyclophosphamide Seacross
- if you are allergic to cyclophosphamide or any of its metabolites. An allergic reaction can include shortness of breath, wheezing, rash, itching or swelling of the face and lips.
- if you currently have any infections.
- if 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.
- if you have a urinary tract infection, which can be recognised as pain when passing urine (cystitis).
- if you have ever had kidney or bladder problems as a result of previous chemotherapy or radiotherapy.
- if you have a condition which decreases your ability to urinate (urinary outflow obstruction).
- if you are breast-feeding.

Warnings and precautions
Talk to your doctor before being given Cyclophosphamide Seacross if you:
- have low blood cell counts;
- have severe infections;
- are already having, or have recently had, radiotherapy or chemotherapy;
- have diabetes;
- have liver or kidney problems. Your doctor will check how well your liver and kidneys are working by doing a blood test;
- have had your adrenal glands removed;
- have heart problems or have had radiotherapy in the area of your heart;
- have poor general health or are frail;
- are elderly;
- have had surgery less than 10 days ago.

Potentially life threatening allergic reactions (anaphylactic reaction) may occur during treatment with cyclophosphamide.

Take special care with Cyclophosphamide Seacross

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 receiving 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 receiving Cyclophosphamide and will stay low until a few days after you

finish the course of treatment. 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 effect 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 it 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 being given 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.

- Your doctor will ensure you are well hydrated and will monitor your fluid balance so that an adequate flow of urine is maintained.

- 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. Your doctor is aware of this and can give you treatments to reduce this risk.

- Cyclophosphamide can cause damage to your heart or affect the rhythm of its beating. This increased 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 yellowing of the skin or whites of the eyes (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.

Other medicines and Cyclophosphamide Seacross

Tell your doctor or nurse if you are taking, have recently taken or might take 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)
- ondansetron (used to prevent being sick)

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)
- 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)
  - dabrafenib (anti-cancer drug)
- medicines that can increase of the toxic effects on your blood cells and immunity:
  - other anti-cancer medicines (used to treat cancer)
  - clozapine (used to treat symptoms of some psychiatric disorders)
  - zidovudine (used to treat viruses)
  - ACE inhibitors (used to treat high blood pressure)
  - natalizumab (used to treat multiple sclerosis)
  - thiazide diuretics such as hydrochlorothiazide or chlortalidone (used to treat high blood pressure or water retention)

- 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)
- sulfonylurea derivatives (blood sugar levels may drop, if cyclophosphamide and sulfonylurea derivatives are used concomitantly)

Cyclophosphamide Seacross with food, drink and alcohol

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

Grapefruit (fruit or juice) should not be consumed while taking Cyclophosphamide. It can interfere with the usual effect of your medicine and may alter the effectiveness of Cyclophosphamide.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Pregnancy

Cyclophosphamide can cause miscarriage or damage your unborn baby.

If you are a woman, you should not get pregnant during treatment with cyclophosphamide or up to 6 months after treatment.
If you are a man, you should take adequate precautions, including use of an effective contraceptive to ensure that you do not father a child during your treatment with cyclophosphamide or up to 3 months after treatment.

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

Fertility
Cyclophosphamide can affect your ability to have children in the future. Talk to your doctor about cryo-preservation (freezing) of sperm or eggs prior to treatment because of the possibility of irreversible infertility due to therapy with cyclophosphamide. If you are considering becoming parents after the treatment please discuss this with your doctor.

Driving and 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 Seacross.

3. How to use Cyclophosphamide Seacross

Method of administration
For intravenous use

Cyclophosphamide Seacross will be given to you by a doctor or nurse experienced in the used of cancer chemotherapy.
Cyclophosphamide Seacross will be given to you by a doctor or nurse.
- It 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.
- Cyclophosphamide Seacross is often given with other anti-cancer drugs or radiotherapy.

The recommended 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 medicines or having radiotherapy.

It is advisable to get cyclophosphamide administered in the morning. Before, during and after the administration, it is important that you get adequate amounts of fluid, to avoid potential adverse effects on the urinary tract.
Cyclophosphamide Seacross is usually given as a series of courses of treatment. After each course there is a break (a period when no Cyclophosphamide Seacross 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.

Use in children and adolescents
Cyclophosphamide has been administered to children. The safety profile of cyclophosphamide in paediatric patients is similar to that of the adult population.

If you use more Cyclophosphamide Seacross than you should
As cyclophosphamide is given to you under the supervision of your doctor, it is very unlikely that you will receive too much. However, if you experience any side effects after being given cyclophosphamide, tell your doctor immediately or go to Accident and Emergency at your nearest hospital. You may need urgent medical attention.
Symptoms of a cyclophosphamide overdose include the side effects listed below in the 'Side Effects' section, but are usually of a more severe nature.
If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine 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, increased heart rate, decreased blood pressure (extreme tiredness), rash, itching or swelling of the face and lips. Severe allergic reactions could lead to difficulty in breathing or shock, with a possible fatal outcome (anaphylactic shock, anaphylactic/ anaphylactoid reaction).
- 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
- severe pain in the chest
- symptoms like weakness, vision loss, impaired speech, loss of sense of touch

Other possible side effects may be:

Very common: may affect more than 1 in 10 people
- decrease in the number of blood cells (myelosuppression)
- loss of hair (alopecia)
- burning sensations during urination and frequent need to urinate (cystitis)
- fever
- suppression of the immune system

Common: may affect up to 1 in 10 people
- infections
- inflammation of mucous membranes (mucositis)
- abnormal liver function
- infertility in men
- chills
- generally feeling unwell
- decrease in white blood cells and fever (febrile neutropenia)

Uncommon: may affect up to 1 in 100 people
- inflammation of the lung (pneumonia)
- sepsis
- infertility in women (rarely irreversible)
- fast heart beat
- heart problems
- changes in the results of some blood tests
- redness of the skin (flush)
- damage to the nerves which can cause numbness, pin, and weakness (neuropathy)
- pain in the distribution of a nerve (neuralgia)
- anorexia
- deafness
- ECG changes
- decreased LVEF
- lower levels of female sex hormones

Rare: may affect up to 1 in 1,000 people
- increased risk of cancer of the white blood cells (acute leukaemia) and some other cancers (bladder cancer, ureter cancer)
- ineffective production of the myeloid class of blood cells (myelodysplastic syndrome)
- increase in the release of antidiuretic hormone from the pituitary gland (syndrome of inappropriate antidiuretic hormone secretion). This affects the kidneys causing the low levels of sodium in your blood (hyponatremia) and water retention resulting in swelling of the brain due to too much water in your blood. Signs of this can be headache, changes in personality or behaviour, confusion, drowsiness
- changes in heart beat
- inflammation of the liver
- rash
- inflammation of the skin

- lack of menstruation (periods)
- lack of spermia
- dizziness
- changes in the colour of your nails and skin
- dehydration
- convulsion
- bleedings

Very rare: may affect up to 1 in 10,000 people
- breakup of red blood cells and kidney failure (Hemolytic uremic syndrome)
- blood clots form throughout the body's small blood vessels (Disseminated intravascular coagulation)
- shock
- complications that can occur after cancer treatment caused by break-down products of dying cancer cells (tumour lysis syndrome)
- low levels of sodium in your blood (hyponatremia)
- high blood pressure (hypertension)
- low blood pressure (hypotension)
- angina
- heart attack
- occlusion of a blood vessel due to a blood clot in the circulatory system (thromboemboembolism)
- injury of the lung (acute respiratory distress syndrome)
- scarring of the lungs which causes shortness of breath (chronic pulmonary interstitial fibrosis)
- difficulty breathing with wheezing or coughing (bronchospasm)
- breathlessness (dyspnoea)
- a condition in which the body or a region of the body is deprived of adequate oxygen supply (hypoxia)
- cough
- soreness or ulcers in the mouth (stomatitis)
- feeling sick (nausea) being sick (vomiting) or diarrhoea
- constipation
- inflammation of the intestine
- inflammation of the pancreas
- blood clot in the liver (veno-occlusive liver disease)
- enlargement of the liver (hepatomegaly)
- yellow eyes or skin
- severe hypersensitivity reactions with (high) fever, red spots on the skin, joint pain and/or eye infection (Stevens-Johnson syndrome)
- severe sudden (hypersensitive) reaction with fever and blisters on the skin/peeling of the skin (toxic epidermal necrolysis)
- radiation erythema
- itching
- impairment of the sense of taste (dysgeusia, hypogeusia)
- sensation of tingling, tickling, prickling, pricking, or burning (paraesthesia)
- impairment of the sense of smell (parosmia)
- abnormal muscle breakdown which can lead to kidney problems (rhabdomyolysis)
- cramps
- problems with your bladder
- kidney problems, including kidney failure
- headache
- multi organ failure
- injection/infusion site reactions
- weight gain
- confusion
- conjunctivitis, eye oedema
- respiratory failure due to fluid accumulation in the lung (pulmonary oedema)
- accumulation of fluid in the abdominal cavity (ascites)
- ventricular fibrillation
- pericarditis
- atrial fibrillation

- suburethral haemorrhage
- myocardial infarction
- blood creatinine increased

Not known: frequency cannot be estimated from the available data
- different kinds of cancer e.g. blood cancer (Non-Hodgkin's lymphoma), kidney cancer
- thyroid cancer
- sarcoma
- different kind of blood disorders (agranulocytosis, lymphopenia, haemoglobin decreased)
- occlusion of a blood vessel due to a blood clot in the circulatory system (thromboembolic events), including the possibility of occlusion of the lung vessels (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
- increased tear formation (lacrimation)
- ringing in the ears (tinnitus)
- impaired hearing
- blockage of the nasal passages (nasal congestion)
- oropharyngeal pain
- rhinorrhea
- sneezing
- pulmonary veno-occlusive disease
- obliterative bronchiolitis
- alveolitis allergic
- pneumonitis
- pleural effusion
- abdominal pain
- bleeding in stomach or guts
- intestinal problems/bleeding
- liver impairment
- rash, skin reddening, blistering of lips, eyes or mouth, skin peeling (erythema multiforme, urticaria, erythema)
- hand-foot syndrome
- facial swelling
- increased sweating
- hardening of skin (scleroderma)
- muscle spasm and pain
- joint pain
- inflammation, scarring and contraction of your bladder
- damage or death of the foetus
- changes in the results of some blood tests (glucose level, hormone levels)
- disorder of the brain (encephalopathy), neurotoxicity manifested as a syndrome characterised by headache, confusion, seizures and visual loss (posterior reversible encephalopathy syndrome), abnormal sensation (dysesthesia, hypoesthesia), tremor, impairment of the sense of taste (dysgeusia, hypogeusia), impairment of the sense of smell (parosmia)
- different kind of heart disorders (ventricular tachycardia, cardiogenic shock, pericardial effusion, bradycardia, palpitations, electrocardiogram QT prolonged)
- infertility in women and men
- changes in the frequency of menstruation
- intra-uterine death
- foetal malformation
- foetal growth retardation
- carcinogenic effect on offspring
- salivary gland inflammation (usually in cheek area; parotid gland inflammation)
- reddening of the skin (flushing) which may be accompanied by feeling hot or sweating (hot flushing)
- increased blood pressure in the lungs which can cause shortness of breath, fatigue, cough, angina, fainting, peripheral oedema (pulmonary hypertension)

- 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)
- death of the cells and tissues (necrosis), ulceration or scaring (fibrosis) of the bladder
- ovarian disorder
- general physical deterioration
- localised swelling(oedema)
- 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 (nephropathy toxic)
- inflammation of the urethra which causes pain and bleeding (haemorrhagic ureteritis)
- glucose in the urine (nephrogenic diabetes insipidus)
- increase in the levels of urea nitrogen in your blood. Your doctor will do blood tests to test for these.
- Premature labour
- Nail disorder
- Toxic skin eruption
- Blister
- 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

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cyclophosphamide Seacross

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial label after EXP. The expiry date refers to the last day of that month.

Do not store above 25℃.

After reconstitution for intravenous administration
After reconstitution/dilution:
Chemical and physical in-use stability has been demonstrated for 24 hours at 2℃ - 8℃ for the reconstituted solution and for the diluted solution.

From a microbiological point of view, the reconstituted and diluted solution should be used immediately, unless reconstitution has taken place in controlled and validated aseptic conditions. If not used immediately, in-use storage times and conditions before use are the responsibility of the user and would normally not be longer than 24 hours at 2 – 8℃, unless reconstitution /dilution has taken place in controlled and validated aseptic conditions.

Do not throw away any medicines via wastewater. Ask your doctor how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Cyclophosphamide Seacross contains
- The active substance is cyclophosphamide.

Each Cyclophosphamide Seacross 500 mg powder for solution for injection/infusion contains 534.5 mg

cyclophosphamide monohydrate equivalent to 500 mg cyclophosphamide.
Each Cyclophosphamide Seacross 1000 mg powder for solution for injection/infusion contains 1069.0 mg cyclophosphamide monohydrate equivalent to 1000 mg cyclophosphamide.
Each Cyclophosphamide Seacross 2000 mg powder for solution for injection/infusion contains 2138.0 mg cyclophosphamide monohydrate equivalent to 2000 mg cyclophosphamide.
- There are no other ingredients

What Cyclophosphamide Seacross looks like and contents of the pack
Cyclophosphamide Seacross is a white crystal or crystalline powder.

Cyclophosphamide Seacross 500 mg powder for solution for injection/infusion is a white crystal or crystalline and is supplied in a colourless 50 ml glass vial sealed with butyl rubber stopper and aluminium flip-off seal with a red polypropylene plastic button, containing 500mg cyclophosphamide.
Cyclophosphamide Seacross 1000 mg powder for solution for injection/infusion is a white crystal or crystalline and is supplied in a colourless 100 ml glass vial sealed with butyl rubber stopper and aluminium flip- off seal with a green polypropylene plastic button, containing 1000 mg cyclophosphamide.
Cyclophosphamide Seacross 2000 mg powder for solution for injection/infusion is a white crystal or crystalline and is supplied in a colourless 100 ml glass vial sealed with butyl rubber stopper and aluminium flip- off seal with a purple polypropylene plastic button, containing 2000 mg cyclophosphamide.

Each pack contains one vial of Cyclophosphamide Seacross.

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The following information is intended for healthcare professionals only:

Cyclophosphamide Seacross should only be used by clinicians experienced in the use of cancer chemotherapy. Cyclophosphamide Seacross should only be administered where there are facilities for regular monitoring of clinical, biochemical and haematological parameters before, during, and after administration and under the direction of a specialist oncology service.

Posology and mode of administration
Dosage must be individualised. Doses and duration of treatment and/or treatment intervals depend on the therapeutic indication, the scheme of a combination therapy, the patient's general state of health and organ function, and the results of laboratory monitoring (in particular, blood cell monitoring).

In combination with other cytostatics of similar toxicity, a dose reduction or extension of the therapy-free intervals may be necessary.

Use of hematopoiesis stimulating agents (colony-stimulating factors and erythropoiesis stimulating agents) may be considered to reduce the risk of myelosuppressive complications and/or help facilitate the delivery of the intended dosing.

Prior, during and 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 Seacross should be administered in the morning.

Cyclophosphamide is inert until activated by enzymes in the liver. However, as with all cytotoxic agents, it is recommended that reconstitution should be performed by trained personnel, in a designated area.

Those handling the preparation should wear protective gloves. Care should be taken to avoid splashing material into the eyes. The material should not be handled by women who are pregnant or who are breast-feeding.

Handling

The choice of solvent for reconstituting Cyclophosphamide Seacross containing cyclophosphamide depends on the route of administration to be used.

Infusion:

If the solution is to be used for IV infusion, Cyclophosphamide Seacross (containing cyclophosphamide) is reconstituted by adding sterile water for injection or sodium chloride 9 mg/mL (0.9%) solution for injection.
Reconstituted Cyclophosphamide Seacross should be further diluted in 5% glucose or sodium chloride 9 mg/mL (0.9%) solution for infusion prior to infusion.

Direct injection:
If the solution is to be used for direct injection, Cyclophosphamide Seacross (containing cyclophosphamide) is reconstituted by adding sodium chloride 9 mg/mL (0.9%) solution for injection. Please note that only Cyclophosphamide Seacross reconstituted in sodium chloride 9 mg/mL (0.9%) solution for injection is suitable for bolus injection.
Cyclophosphamide Seacross (containing cyclophosphamide) reconstituted in water is hypotonic and should not be injected directly.

The following quantities of water for injections or sodium chloride 9 mg/mL (0.9%) solution for injection are added to the vials containing Cyclophosphamide Seacross, powder for solution for injection/infusion

Vial of 500 mg: 25 ml
Vial of 1000 mg: 50 ml
Vial of 2000 mg: 100 ml

Injecting the solvent into the vial for injection creates an abnormally high pressure, which disappears as soon as the second sterile needle has been inserted in the rubber stop of the vial for injection. The powder easily dissolves when the vial for injection is shaken vigorously to produce a clear solution. If the powder does not immediately dissolve, continue to shake the vial vigorously for up to several minutes until complete dissolution of the powder. The solution must be administered as soon as possible following its reconstitution.

After reconstitution the solution is clear and colourless to light yellow. Please check the vial before further use. Only clear solutions must be used.

Infusion:
Reconstituted Cyclophosphamide Seacross should be further diluted in 5% glucose or sodium chloride 9 mg/mL (0.9%) solution for infusion prior to infusion, the solution should be diluted to a minimum

concentration of 2 mg per ml.

The rules and regulations for handling cytostatics in general must be observed when reconstituting or handling Cyclophosphamide Seacross. Reconstitution must, to the extent possible, be performed in a *laminar air flow safety* cabinet. The person handling the product must wear a protective mask and protective gloves. In case of spills, the area must be thoroughly rinsed with water. If Cyclophosphamide Seacross, powder for solution for injection/infusion is stored (e.g. during transport) at the temperature exceeding the maximum temperature, cyclophosphamide may melt. Vials for injections containing melted cyclophosphamide can be visually recognised. Cyclophosphamide is a white powder. Melted cyclophosphamide is a clear or yellowish viscous liquid (usually found as droplets in the affected vials.). Vials for injections containing melted cyclophosphamide may no longer be used.

Guidelines for the Safe Handling of Antineoplastic Agents
The rules and regulations for handling cytotoxic in general must be observed when reconstituting or handling Cyclophosphamide Seacross.
Reconstitution must, to the extent possible, be performed in a laminar air flow safety cabinet. Cytotoxic preparations should not be handled by pregnant staff. Trained personnel should dilute the drug. This should be performed in a designated area. The work surface should be covered with disposable plastic-backed absorbent paper.
Adequate protective gloves, masks and clothing should be worn. Precautions should be taken to avoid the drug accidentally coming into contact with skin or mucous membranes, the affected area should be cleaned thoroughly with soap and water. If accidental contamination occurs with the eyes, they should be washed with water thoroughly and immediately.
Use Luer-lock fittings on all syringes and sets. Large bore needles are recommended to minimise pressure and the possible formation of aerosols. The latter may also be reduced by the use of a venting needle.
Any unused contents should be discarded. Adequate care and precaution should be taken in the disposal of items used to dilute cyclophosphamide. Any unused product or contaminated materials should be placed in a high-risk waste bag. Sharp objects (needles, syringes, vials, etc.) should be placed in a suitable rigid container. Personnel concerned with the collection and disposal of this waste should be aware of the hazard involved.

<u>Disposal</u>
Any unused medicinal product or waste material should be disposed of in accordance with local requirements for cytotoxic agents.