

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

ENDOXAN 50 mg Tablets

Cyclophosphamide monohydrate

ENDOXAN tablets contain 24,6 mg lactose monohydrate in the tablet core and 51,11 mg sucrose in the tablet coating.

Read all of this leaflet carefully before you start taking ENDOXAN

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- ENDOXAN has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

Important things to know about ENDOXAN

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

- will reduce your blood cell count, which may make you feel tired and be more likely to get infections.

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

- 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 ENDOXAN or for at least 6 to 12 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 ENDOXAN that might be especially important for you.

What is in this leaflet

1. What ENDOXAN is and what it is used for
2. What you need to know before you take ENDOXAN
3. How to take ENDOXAN
4. Possible side effects
5. How to store ENDOXAN
6. Contents of the pack and other information

1. What ENDOXAN is and what it is used for

ENDOXAN is a cytostatic or anti-cancer medicine. It works by killing cancer cells, this is sometimes called 'chemotherapy'. It is used to treat lots of different cancers. ENDOXAN is often used together with other anti-cancer medicines or radiotherapy.

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

2. What you need to know before you take ENDOXAN

Do not take ENDOXAN if:

- you are hypersensitive (allergic) to cyclophosphamide, any of its metabolites or excipients.
- have severely reduced bone-marrow function (especially if you have previously had chemotherapy or radiotherapy).
- you have a urinary tract infection, which can be recognised as pain when passing urine (cystitis).
- you currently have any infections.
- you have a condition which decreases your ability to urinate (Urinary outflow obstruction).
- you have recently been vaccinated.
- you are pregnant or breastfeeding.

Warnings and precautions

Tell your doctor if:

- you are elderly.
- 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 problem or have had radiotherapy in the area of your heart.
- you have poor general health or are frail.

Take special care with ENDOXAN

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

- ENDOXAN can have effects on your blood and immune system
- After taking ENDOXAN, your blood count will drop and will stay low for a few days after you finish the course.
- 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 your blood count is high enough before and during your treatment with ENDOXAN. They may need to reduce the amount you are given or delay your next dose.
- ENDOXAN 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.
- ENDOXAN 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.
- More information on Mesna can be found in the Patient Information Leaflet for Mesna Injection and Mesna tablets.
- Most people having ENDOXAN 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 ENDOXAN.

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous 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. ENDOXAN has an increased risk of causing cancer in the area of your bladder.
- ENDOXAN can cause damage to your heart or affect the rhythm of it beating. This increases with higher doses of ENDOXAN, 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.
- ENDOXAN 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.
- ENDOXAN 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.
- ENDOXAN can make you feel sick or be sick. This can last for about 24 hours after taking ENDOXAN. You may need to be given medicines to stop feeling or being sick. Ask your doctor about this.

Other medicines and ENDOXAN

Always tell your healthcare professional if you are taking any other medicine (this includes complementary or traditional medicines).

If you are taking medicines together with ENDOXAN, which may increase the likelihood or severity of the side effects, or which may reduce the efficacy of ENDOXAN, your treatment will be closely monitored by your doctor to ensure that your ENDOXAN dose is adjusted when required. Tell your

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

doctor or nurse especially if you are taking the following medicines as they may not work well with ENDOXAN:

The following medicines can reduce how effective ENDOXAN is:

- Aprepitant (used for nausea and vomiting).
- Bupropion (an antidepressant and used to stop smoking).
- Busulfan, thiopeta (used to treat cancer).
- Ciprofloxacin, chloramphenicol (used to treat bacterial infections).
- Fluconazole, itraconazole (used to treat fungal infections).
- Prasugrel (used to thin blood).
- Sulphonamides, such as sulfadiazine, sulfasalazine, sulfamethoxazole (used to treat bacterial infections).
- Ondansetron (used to treat nausea and vomiting).

The following medicines can increase the toxicity of ENDOXAN:

- Allopurinol (used to treat gout and kidney stones).
- Azathioprine (used to reduce the activity of the immune system).
- Chloral hydrate (used to treat insomnia (inability to sleep)).
- Cimetidine (used for the treatment of stomach ulcers and the reduction of stomach acid production).
- Disulfiram (used to treat alcoholism).
- Medicines that increase liver enzymes such as:
 - rifampicin (used to treat bacterial infections).
 - carbamazepine, phenobarbital, phenytoin (used to treat epilepsy).

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

- St. John’s Wort (a herbal remedy for mild depression).
- corticosteroids (used to treat inflammation).
- Protease inhibitors (a class of medicines used in the treatment of HIV/AIDS).
- Medicines that can increase the toxic effects on your blood cells and immunity:
 - ACE inhibitors (a class of medicine used to treat high blood pressure).
 - Natalizumab (used for the treatment of multiple sclerosis and Crohn’s Disease).
 - Paclitaxel (used to treat cancer).
 - Zidovudine (used in the treatment of HIV/AIDS).
 - Carbimazole (used to treat an overactive thyroid).
 - Thiazide diuretics such as hydrochlorothiazide or chlorthalidone (used to treat high blood pressure or water retention).
- Medicines that can increase the toxic effects on your heart:
 - Anthracyclines (used to treat cancer).
 - Cytarabine, pentostatin, trastuzumab (used to treat cancer).
 - Radiation therapy of the area of your heart.
- Medicines that can increase the toxic effects on your lungs:
 - Amiodarone (used to control the rhythm of the heartbeat).
 - G-CSF (granulocyte colony-stimulating factor) and GM-CSF (granulocyte macrophage colony-stimulating factor) (used to stimulate the production of stem cells and various blood cells).
- Medicines that can increase the toxic effects on your kidneys:
 - Amphotericin B (used to treat fungal infections).
 - Indomethacin (a non-steroidal anti-inflammatory drug (NSAID) used for the treatment of fever, pain, stiffness and swelling).

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

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

- Etanercept (used to rheumatoid arthritis).
- Metronidazole (used to bacterial or protozoal infections).
- Tamoxifen (used to treat breast cancer).
- Bupropion (an antidepressant used to stop smoking).
- Warfarin (used to thin the blood).
- Ciclosporin (used to reduce the activity of the immune system).
- Succinylcholine (used to relax muscles during medical procedures).
- Digoxin (used to treat heart conditions).
- Vaccines.
- Verapamil (used to treat high blood pressure, angina or irregular heartbeat).

ENDOXAN with food, drink and alcohol

In general, alcoholic beverages should be avoided during treatment with ENDOXAN as it can increase the nausea and vomiting caused by ENDOXAN.

Because grapefruit contains a compound that may impair the activation of ENDOXAN and thereby its efficacy, no grapefruit or grapefruit juice should be consumed.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before receiving this medicine.

The use of ENDOXAN is contraindicated in pregnancy and breastfeeding.

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

If you are a woman receiving ENDOXAN, you should not become pregnant during treatment. This is because it can cause a 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.

ENDOXAN 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 breastfeed while being treated with ENDOXAN. Ask your doctor for advice

Driving and using machines

Whilst undergoing treatment with ENDOXAN, you may experience undesirable effects (including e.g. dizziness, blurred vision, visual impairment), which could affect your ability to drive or use machines. The decision to drive or operate machinery should be made on an individual basis and you should discuss this with your doctor.

ENDOXAN contains sucrose and lactose monohydrate

ENDOXAN contains sucrose and lactose monohydrate (milk sugar) which may have an effect on your blood sugar if you have diabetes mellitus. Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not take ENDOXAN. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking ENDOXAN.

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

3. How to take ENDOXAN

Do not share medicines prescribed for you with any other person.

Always take ENDOXAN exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

ENDOXAN should only be prescribed by doctors experienced with this medicine.

The dosage of ENDOXAN will be calculated specifically for you by your doctor and depends on:

- the type of illness you have.
- how big you are (combination of your height and weight).
- your general health.
- whether you are being given other anti-cancer medicines or having radiotherapy.

ENDOXAN tablets should be taken in the morning. During or immediately after taking your dose, adequate amounts of fluid should be ingested. It is important to ensure that you empty your bladder at regular intervals.

The usual dose for continuous therapy is 1 - 4 tablets (50 – 200 mg) daily. The dose may be increased or decreased by your doctor if necessary, depending on your blood test results, how you respond to the treatment, and whether you are receiving combination treatment with other medicines.

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

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

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

ENDOXAN sugar-coated tablets should always be handled with caution, as they are cytostatic (anti-cancer) agents. The coating of the tablets prevents direct contact of the person handling the tablets with the active substance. To prevent unintentional exposure of the active substance to other people, tablets should be taken whole and should not be divided or crushed.

If you take more ENDOXAN than you should

In the event of an overdose, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre. Hospital admission for special treatment may be needed.

If you forget to take ENDOXAN

If you forget to take a dose at the usual time, take it as soon as you remember if it is on the same day. If you have forgotten to take the whole day's tablets, then you should talk to your doctor.

Never take more tablets in one day that you were meant to – so never take two days worth of tablets on the same day in order to 'catch up'.

4. POSSIBLE SIDE EFFECTS

ENDOXAN can have side effects.

Not all side effects reported for ENDOXAN are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking ENDOXAN, please consult your health care provider for advice.

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

If any of the following happens, stop taking ENDOXAN and tell your doctor immediately or go to the casualty department of your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting,
- yellowing of the skin and eyes, also called jaundice.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to ENDOXAN. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the nearest casualty department at your nearest hospital if you notice any of the following:

- Infections.
- Allergic and hypersensitivity reactions.
- Anaphylactic shock (a systemic reaction to an allergy).
- Blood glucose increased or decreased.
- Peripheral neuropathy (pain or numbness in the hands and feet as a result of damage to the peripheral nerves).
- Neuralgia (pain which occurs as a result of a damaged nerve).
- Abnormal sensation (e.g. a changed sense of touch), including dysesthesia and hypoesthesia.
- Convulsions (fits).

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

- Cardiogenic shock (a condition where the heart can't pump enough blood for the body's needs).
- Myocardial infarction (heart attack).
- Myocardial haemorrhage (bleeding of the heart).
- Tachycardia (increased heartrate).
- Bradycardia (low heartrate).
- Palpitations (a feeling that the heart is racing or pounding).
- Dysrrhythmias (hear rhythm conditions), including atrial and ventricular fibrillation.
- Angina pectoris (chest pain or discomfort due to coronary heart disease) and chest pain.
- Bleeding.
- Vasculitis (inflammation of the blood vessel).
- Peripheral ischemia (poor blood flow to the extremities (hands and feet)).
- Thromboembolism (the formation of a blood clot in a blood vessel).
- Changes in blood pressure.
- Bronchospasm (a spasm of the muscles in the lungs).
- Dyspnoea (shortness of breath and breathing difficulty).
- Respiratory distress (breathing difficulty).
- Gastrointestinal ulceration (ulceration of the stomach or intestines).
- Liver function disorders.
- Hepatitis (inflammation of the liver) and activation of virus hepatitis.
- Dermatitis (inflammation of the skin).
- Severe skin reactions, including rash, blistering, urticaria (a skin rash with raised, itchy lumps) and itching.
- Erythema in the irradiated field (reddening of the skin due to inflammation).

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

- Radiation recall dermatitis (an inflammatory skin reaction of an area previously exposed to radiation).
- Facial swelling.
- Palmar-plantar erythrodysesthesia syndrome (redness, swelling and pain in the palms of the hands and the soles of the feet)
- Haemorrhagic cystitis a lower urinary tract condition which may include painful urinating and blood in urine).
- Haematuria (blood in the urine).
- Nephrogenic diabetes insipidus (a condition, whereby the kidney cannot concentrate the urine and is characterised by excessive urination).
- Multi-organ failure and general physical deterioration.
- Premature labour.
- Inter-uterine death (death of the foetus in the womb).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

- Ovulation disorders.
- Irreversible ovulation disturbances.
- Infertility.
- Testicular atrophy (a reduction in testicle size).
- Amenorrhoea (the absence of menstruation).
- Flushing (a condition whereby the skin becomes red).
- Anorexia (weight loss).

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

- Weight gain.
- Dehydration.
- Water retention.
- Confusion.
- Dizziness.
- Paraesthesia (tingling feeling of the arms, legs, hands or feet).
- Taste disturbances.
- Smelling disturbances.
- Blurred vision or difficulty in seeing.
- Conjunctivitis (pink eye) and eye oedema (fluid accumulation in the eye), together with hyper-sensitivity.
- Increased secretion of tears.
- Reduced hearing and deafness.
- Tinnitus (ringing in the ears).
- Cough.
- Flu-like illness.
- Nasal congestion (blocked nose) and nasal discomfort.
- Oropharyngeal pain (pain in the middle part of the throat).
- Rhinorrhoea (runny nose).
- Sneezing.
- Nausea and vomiting.
- Diarrhoea.
- Stomatitis (inflammation of the mouth and lips).
- Constipation.

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

- Stomach (abdominal) pain and discomfort.
- Alopecia (hair loss) and baldness.
- Scleroderma (hardening and tightening of the skin).
- Skin discolouration.
- Nail disorder.
- Increased sweating.
- Cramp.
- Fever.
- Chills.
- Tremor.
- Muscle spasms.
- Muscle and joint pain.
- Asthenic conditions (feeling weak).
- Fatigue (feeling tired).
- Malaise (general feeling of discomfort).
- Headache.
- Pain.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the “**6.04 Adverse Drug Reaction Reporting Form**”, found online under SAHPRA’s publications: <https://www.sahpra.org.za/Publications/Index/8>.

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

By reporting side effects, you can help provide more information on the safety of ENDOXAN.

5. How to store ENDOXAN

ENDOXAN must be stored at or below 25 °C.

Protect from moisture.

Do not use ENDOXAN after the expiry date given on the package.

Store all medicines out of reach of children.

6. Contents of the pack and other information

What ENDOXAN contains

The active substance in ENDOXAN is cyclophosphamide monohydrate. Each ENDOXAN tablet contains cyclophosphamide monohydrate, which is equivalent to 50 mg anhydrous cyclophosphamide.

The other ingredients are:

Tablet: Calcium hydrogen phosphate dihydrate, gelatine, glycerol 85 %, lactose monohydrate, magnesium stearate, maize starch and talc.

Coating: Calcium carbonate, carboxymethyl cellulose sodium, colloidal silicon dioxide, montan glycol wax, polyethylene glycol 35000, polysorbate 20, polyvidone 25, sucrose, talc and titanium dioxide (E171).

What ENDOXAN looks like and contents of the pack

Aluminium foil (20 µm) suitable for heat-sealing with PVC and PVDC-coated PVC-sheet (7 g/m² coating).

Transparent PVC/PVDC deep-drawing sheet (200 µm), PVC coated with PVDC 40 g/m².

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Endoxan 50 mg Tablets
	Each tablet contains cyclophosphamide monohydrate equivalent to 50 mg anhydrous cyclophosphamide.

Pack sizes: Blister packs of 50 or 100 tablets.

Holder of Certificate of Registration

Baxter Healthcare South Africa (Pty) Ltd

The Campus – Eden Gardens

57 Sloane Street & Cnr Main Rd

Bryanston

2021

This leaflet was revised in

14 October 2022

Registration number

A38/26/0593