

Applicant/HCR:	Baxter Healthcare South Africa (Pty) Ltd
Product Name:	Holoxan 500 mg Injection, Holoxan 1g Injection & Holoxan 2 g Injection
	Intravenous injections containing 500 mg, 1 g or 2 g ifosfamide as dry substance

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: **S4**

HOLOXAN 500 mg Injection

HOLOXAN 1 g Injection

HOLOXAN 2 g Injection

ifosfamide

Sugar free

Read all of this leaflet carefully before you are given HOLOXAN

- 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.

What is in this leaflet

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

1. What HOLOXAN is and what it is used for

HOLOXAN contains the active substance Ifosfamide,

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HOLOXAN is a cytotoxic or anti-cancer medicine. It works by killing cancer cells. Treatment with HOLOXAN is sometimes called “chemotherapy”. It is used to treat lots of different cancers. HOLOXAN is often used together with other anti-cancer medicines or radiotherapy.

2. What you need to know before you are given HOLOXAN

HOLOXAN should not be administered to you if:

- you are hypersensitive (allergic) to ifosfamide. An allergic reaction can include shortness of breath, wheezing, rash, itching or swelling of the face and lips.
- 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 severe kidney problems. Your doctor will check how well your kidneys are working by doing regular tests.
- if you have a condition which decreases your ability to urinate (urinary outflow obstruction).
- if you have a urinary tract infection, which can be recognised as pain when passing urine (cystitis).
- if you currently have any infections.
- if you are pregnant or breastfeeding.
- if you have a nervous system condition called advanced cerebral sclerosis.
- if you have a blood platelet count below 50000 platelets per mm³ (this will be confirmed with a blood test).

Warnings and precautions

Tell your doctor or health care provider before being given the injection:

- If you are already having, or have recently had, radiotherapy, chemotherapy, any other medicines which suppress your immune system, medicines which affect your kidneys or

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medicines which affect your bladder.

- If you are receiving dialysis.
- If you have blood in your urine or experience pain whilst urinating.
- If you have heart problems.
- If you have or had cancer.
- If you have poor general health or are frail.
- If you are elderly.
- If you have diabetes.

Take special care with HOLOXAN

- HOLOXAN can have effects on your bone marrow, blood and immune system.
- After taking HOLOXAN, your white blood cell 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 white blood cell 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 white blood cell count and other blood component levels are high enough before and during your treatment with HOLOXAN. Depending on the test results, your dose may need to be reduced or your next dose may need to be delayed.
- HOLOXAN can affect wound healing. Ensure that all cuts or wounds are treated carefully and check regularly to ensure that 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.
- HOLOXAN can affect your nervous system and may cause confusion, sleepiness (somnolence), coma, hallucinations, blurred vision, psychotic behaviour, involuntary muscle movements (extrapyramidal symptoms), inability to control urinating (urinary incontinence), seizures, pain in the extremities (peripheral neuropathy).

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- Nervous system effects may occur within a few hours to a few days after the first administration and usually stop within 48 to 72 hours after HOLOXAN has been discontinued. Sometimes the symptoms may occur for longer and occasionally, recovery is not complete. Fatal outcome to nervous system toxicity has been reported.
- HOLOXAN may cause encephalopathy, a condition affecting the brain function and structure.
- HOLOXAN is nephrotoxic and urotoxic, which means that it can damage your kidneys and bladder. Your kidney function and urine should be tested before, during and after treatment with HOLOXAN.
- HOLOXAN 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.
- 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 HOLOXAN.
- HOLOXAN can affect your kidneys so that they do not work properly. This is more likely to happen if you only have one kidney or if your kidneys are already damaged. This is often temporary and they return to normal once HOLOXAN therapy is stopped. Occasionally the damage is permanent and more severe.
- 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. HOLOXAN has an increased risk of causing cancer in the area of your bladder.
- HOLOXAN can cause damage to your heart or affect the rhythm of it beating. The risk of your heart being affected is increased with higher doses of HOLOXAN, with concurrent radiation treatment in the area of the heart, or medicines which present with cardiac (heart) toxicity, or other chemotherapy medicines. Your doctor will monitor your heart closely during treatment.

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- HOLOXAN can cause inflammation or scarring in your lungs. If you start having difficulty breathing tell your doctor straight away.
- HOLOXAN can have life threatening effects on your liver. If you have sudden weight gain, liver pain and jaundice (yellowing of the skin and eyes) tell your doctor straight away.
- If you are planning to have children, as HOLOXAN may negatively affect the baby. Men should not father a child for up to six months after end of therapy. Sexually active women and men should use effective methods of contraception during these periods of time. If you are being treated with HOLOXAN and plan to have a child, speak to your doctor.
- Treatment with HOLOXAN interferes with the normal development of eggs in women and sperm in men. The absence of periods (amenorrhea), absence of sperm in semen (azoospermia) and sterility may occur, which may sometimes be irreversible.
- Hair thinning or baldness can occur. Your hair should grow back normally though it may be different in texture or colour.
- HOLOXAN can cause vomiting or nausea. You may need to be given medicines to stop you from vomiting or feeling nauseous. Speak to your doctor if you are vomiting or feeling nauseous.
- Drinking alcohol whilst being treated with HOLOXAN may increase the occurrence of nausea and vomiting.
- If you have reduced kidney function, as this could result in you being exposed to higher concentrations of HOLOXAN. If you have reduced kidney function, your doctor may adjust your HOLOXAN dose.
- If you have reduced liver function, as this could reduce the effectiveness of your treatment with HOLOXAN, as well as the possible increase of a metabolite, which could increase the blood levels of a metabolite that could cause or contribute to nervous system effects. If you have reduced liver function, your doctor may adjust your HOLOXAN dose.

Other medicines and HOLOXAN

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

Your doctor will carefully assess the other medicines you are taking whilst being treated with HOLOXAN to ensure that your HOLOXAN dose and administration frequency is such, that the interaction of HOLOXAN with your other medicines is minimised, particularly with respect to increased side effects and reduced efficacy of HOLOXAN or any of the other medicines. Tell your doctor or nurse if you are taking any of the following medicines as they may not work well with HOLOXAN:

The following medicines can increase the toxicity of HOLOXAN:

- 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).
 - Cisplatin (used to treat cancer).
 - Carboplatin (used to treat cancer).
 - Natalizumab (used for the treatment of multiple sclerosis and Crohn's Disease).
- Medicines that can increase the toxic effects on your heart:
 - Anthracyclines (used to treat cancer).
 - Radiation therapy in the area of your heart.
- Medicines that can increase the toxic effects on your lungs:
 - Amiodarone (used to treat irregular heartbeat).
 - G-CSF (granulocyte colony-stimulating factor) and GM-CSF (granulocyte macrophage colony-stimulating factor) (used to increase white blood cell numbers after chemotherapy).

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- Medicines that can increase the toxic effects on your kidneys:
 - Cisplatin (used to treat cancer).
 - Aminoglycosides (used to treat bacterial infections).
 - Acyclovir (used to treat viruses).
 - Amphotericin B (used to treat fungal infections).
 - Carboplatin (used to treat cancer).

- Medicines that can increase the toxic effects on your bladder:
 - Busulfan (used to treat cancer).
 - Irradiation of the bladder.

- Medicines that can cause additive effects on your central nervous system when combined with HOLOXAN:
 - Anti-emetics (used to control vomiting and nausea).
 - Sedatives (medicines used to treat depression, anxiety, sleeping tablets, etc.).
 - Narcotics (pain medication with an effect on the central nervous system).
 - Antihistamines (used to treat allergic reactions).

- Medicines that increase liver enzymes such as:
 - Phenobarbital, phenytoin, carbamazepine, primidone (used to treat epilepsy).
 - Benzodiazepines (used to treat anxiety).
 - Rifampicin (used to treat bacterial infections).
 - Chloral hydrate (used to treat insomnia (inability to sleep)).
 - Corticosteroids (used to treat inflammation).
 - St. John's wort (a herbal remedy for mild depression).
 - Aprepitant (used to treat nausea and vomiting).

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The following medicines can reduce how effective HOLOXAN is:

- Ketoconazole, fluconazole, itraconazole (used to treat fungal infections).
- Aprepitant (used for nausea and vomiting).

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

- Docetaxel (used to treat cancer).
- Coumarins such as warfarin (used to thin the blood).
- Vaccines.
- Tamoxifen: (used to treat breast cancer).
- Cisplatin: (used to treat cancer).
- Irinotecan: (used to treat cancer).
- Allopurinol (used to treat gout and kidney stones).
- Hydrochlorothiazide (used to treat high blood pressure).
- Disulfiram (used to treat alcoholism).
- Chlorpromazine (used to treat psychosis).
- Triiodothyronine (used to treat thyroid).
- Succinylcholine (used to relax muscles during medical procedures).
- Sulphonylureas (used to treat diabetes).
- Suxamethonium (used as a muscle relaxant).
- Bupropion (used to treat depression and to stop smoking).
- Orphenadrine (used to treat muscle pain and motor control in Parkinson's disease).

HOLOXAN with food, drink and alcohol

Drinking alcohol whilst being treated with HOLOXAN may increase the occurrence of nausea and vomiting.

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Grapefruit contains a compound that may reduce the effectiveness of HOLOXAN. Accordingly, neither grapefruit nor grapefruit juice should be consumed whilst you are being treated with HOLOXAN.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

If you are pregnant or breastfeeding your baby, you should not receive HOLOXAN.

If you are a woman receiving HOLOXAN, you should not become pregnant during treatment. This is because HOLOXAN 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 with HOLOXAN. You should use an effective contraceptive. Ask your doctor for advice.
- HOLOXAN can affect your ability to have children in the future. Talk to your doctor about freezing sperm samples or eggs before your treatment starts.
- Also refer to 'Take special care with HOLOXAN' for additional information relating to the effect of HOLOXAN on fertility.
- HOLOXAN may pass into your breastmilk and may affect your baby. You should not breastfeed whilst being treated with HOLOXAN. Ask your doctor for advice.

Driving and using machines

Some of the side effects of treatment with HOLOXAN might affect your ability to drive and use machines safely. Ask your doctor for advice.

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3. How you will be given HOLOXAN

You will not be expected to give yourself HOLOXAN. It will be given to you by a person qualified to do so.

HOLOXAN should only be administered by doctors experienced with this medicine and the treatment of cancer.

The dosage, duration of treatment and treatment frequency of HOLOXAN 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 and how well your organs are functioning.
- your laboratory test results.
- your age.
- whether you are being given other anti-cancer medicines or are having radiotherapy.

HOLOXAN will be administered via the intravenous (into a vein) route. The administration may be a slow injection or a slow infusion over a longer period of time.

Whilst receiving treatment with HOLOXAN, you should ingest adequate amounts of fluid.

HOLOXAN is usually given as a series of courses of treatment. After a course there is a break (a period when no injections are given) before the next course. Your doctor will determine how many courses you require and how long the breaks between courses will be.

If you receive more HOLOXAN than you should

Since a healthcare professional will administer this medicine, he/she will control the dosage. However, in the event of overdosage, your doctor will manage the overdosage.

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If you forget to take HOLOXAN

Since a health care provider will administer HOLOXAN, it is unlikely that the dose will be missed.

4. Possible side effects

HOLOXAN can have side effects.

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

If any of the following happens after you have received HOLOXAN, tell your doctor immediately or go to the casualty department at 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 HOLOXAN. You may need urgent medical attention or hospitalisation.

Frequent side effects are:

- effects on the brain (encephalopathy), signs of this can range from mild, such as subtle personality changes, memory loss to severe, such as seizures, coma and death.
- central nervous system toxicity presenting with the following signs and symptoms: abnormal behaviour, irregular emotional response (affect lability), aggression, agitation, anxiety, inability to communicate (aphasia), abnormal lack of energy (asthenia),

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movement disorders and gait disturbances (ataxia, cerebellar syndrome), mental health disorders that affect cognitive abilities including learning, memory, perception, and problem solving, coma, confusion, convulsions (fits), ability to decrease in your ability to remain awake and aware, depression, disorientation, dizziness, abnormal brain function (EEG test), severe reduction in emotional expressiveness (flat affect), hallucinations, headache, abnormal thoughts, lifelessness, memory impairment, mood change, muscle and nerve dysfunction, muscle spasms or twitching (myoclonus), loss of reflexes, psychosis, restlessness, feeling drowsy (somnolence), tremor, urinary incontinence,

- infections.
- decrease in the activity of your bone marrow (myelosuppression).
- decrease or low levels of various white blood cells - which fight infection. This may be associated with fever (leukopenia, granulocytopenia, neutropenia, lymphopenia).
- decrease in red and white blood cells, as well as platelets (pancytopenia).
- decrease of platelets - which help your blood clot (thrombocytopenia).
- decrease of red blood cells - which carry oxygen around the body (anaemia).
- increase of acidity of body fluids (metabolic acidosis).
- anorexia (weight loss).
- drowsiness.
- feeling sick (nausea).
- being sick (vomiting).
- increases of liver enzymes in the blood (hepatotoxicity).
- hair loss (alopecia).
- blood in the urine (haematuria).
- inflammation of the bladder lining which causes pain, bleeding, blood in the urine, reduced urine flow (haemorrhagic cystitis).
- life threatening decrease in the abilities of your kidney to adequately remove toxins and waste products from the blood (renal dysfunction, renal failure).

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- changes to the structure of your kidneys which prevent them from working correctly (renal structural damage).
- kidney diseases (nephropathies, tubular dysfunction).
- impairment in the development of the sperm cells.
- feeling weak (asthenic conditions).
- inflammation of the vein where administration occurred (phlebitis).
- fever due to decrease in certain white blood cells than fights infection (neutropenic fever).

Less frequent side effects are:

- pneumonia.
- severe infection spreading through the blood which may have a possible fatal outcome (sepsis).
- secondary tumours in various parts of the body, often in the area of the bladder.
- progression of underlying cancers (myelodysplastic syndrome, acute leukaemia).
- a condition causing abnormal break down of the red blood cells, decreased numbers of platelets in the blood and kidney failure (haemolytic uremic syndrome).
- formation of small blood clots in your blood vessels disrupting the normal blood flow around your body (disseminated intravascular coagulation).
- allergic and hypersensitivity reactions, which may include rash, fever, low blood pressure, hypotension, angioedema (swelling of the skin around the face, inside of the mouth and throat), immunosuppression (inhibition of the immune system), urticaria (skin rash or red itchy swellings). These reactions may develop to anaphylactic shock (a systemic reaction to an allergy) and death.
- irreversible ovulation disturbances.
- increase in the release of antidiuretic hormone from the pituitary gland (SIADH). This affects the kidneys, causing low levels of sodium in your blood (hyponatraemia), water

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retention and associated symptoms such as confusion and cramps.

- dehydration.
- electrolyte imbalance.
- low blood levels of potassium (hypokalaemia).
- depression accompanied by psychotic symptoms.
- disorientation.
- restlessness.
- confusion.
- feeling drowsy (somnolence).
- forgetfulness.
- dizziness.
- a disorder of the nerves which can cause weakness, tingling or numbness of the extremities (peripheral neuropathy, polyneuropathy).
- cerebellar syndrome (a condition where the blood flow in the brain is reduced).
- coma.
- seizures.
- blurring, reduction or loss of sight.
- changes in your heart rhythm (dysrhythmia).
- decrease in your hearts ability to pump enough blood around your body which may be life threatening (cardiac failure or cardiac arrest).
- increase in heartrate (tachycardia).
- heart attack (myocardial infarction).
- fluid in the lungs, which can cause breathing problems (pulmonary oedema).
- bleeding.
- low blood pressure (hypotension), that can lead to shock and death.
- thromboembolism (the formation of a blood clot in a blood vessel).
- ongoing lung diseases.

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	Intravenous injections containing 500 mg, 1 g or 2 g ifosfamide as dry substance

- cough.
- shortness of breath and breathing difficulty (dyspnoea).
- conditions causing inflammation of the lungs (pneumonitis) which can cause breathlessness and cough.
- scarring of the lungs which causes shortness of breath (interstitial lung disease, pulmonary fibrosis).
- life-threatening decrease of your lungs ability to transfer oxygen into your blood (respiratory failure).
- toxic allergic pulmonary oedema (increased fluid in the lungs).
- diarrhoea.
- constipation.
- inflammation of the lining of your mouth, including ulcers (stomatitis).
- inability to control bowel movements.
- severe tummy and back pain which may be from inflammation of the pancreas (pancreatitis).
- disturbances in the liver function.
- skin eruption or reaction consisting of small, round, raised bumps that have clear borders (popular rash).
- inflammation of this skin which may cause rash, blisters, itching, sores, oozing and scarring (dermatitis).
- toxic skin reactions.
- muscle cramps.
- partial or complete fractures and muscle weaknesses (osteomalacia, rickets).
- abnormal muscle breakdown which can lead to kidney problems (rhabdomyolysis).
- loss of bladder control.
- painful or difficult urination.
- disturbance in urinary frequency.

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- bladder irritation.
- dysfunction of the kidneys.
- accumulation of acid in the body due to a failure of the kidneys.
- kidney malfunction leads to excessive urine production and excessive thirst, resulting in deficits of water, calcium, potassium, magnesium, and other substances in the body (Fanconi syndrome).
- the absence of menstruation (amenorrhoea).
- reduced levels of female sex hormones.
- low sperm count (oligospermia) or no sperm count (azoospermia) in male semen.
- kidney malfunction causing increase of total urine amino acids into urine (aminoaciduria).
- fatigue (feeling tired).
- inflammation and ulceration of the lining of the digestive system (mucositis).
- appearance of skin changes and irritation at the site of injection or infusion, including swelling, inflammation, pain, tenderness, redness and itching.
- death.
- kidney malfunction causing urine to appear cloudy or murky colour (phosphaturia).
- intensified reaction on radiotherapy.

The frequency of the following side effects are unknown:

- general feeling of discomfort (malaise).
- increased risk and severity of bacterial, fungal, viral, protozoal or parasitic infections due to the effect of HOLOXAN on your immune system.
- changes to your metabolism caused by the breakdown of the dying cancer cells (Tumour lysis syndrome).
- low blood levels of calcium (hypocalcaemia) which can cause muscle cramps and twitching, irregular heartbeat, overactive reflexes, and burning or tingling sensations in

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the hands and feet.

- low blood levels of phosphate (hypophosphataemia) which can cause bone pain, confusion and muscle weakness.
- high blood sugar levels (hyperglycaemia) which can cause thirst, tiredness and irritability.
- excessive thirst that is also accompanied by excessive fluid intake (polydipsia).
- psychiatric effects including panic attack, catatonia (motionless and unresponsive to stimuli), mania (feeling overly excited), paranoia (feeling paranoid and that people are “out to get you”), delusion (believing something that is not real), delirium (feeling confused and unsure about your surroundings), bradyphrenia (slow thinking and processing of information), mutism (inability to speak), echolalia (repeating words), logorrhoea (excessive and often incoherent talkativeness), perseveration (constantly repeating a task).
- convulsive and non-convulsive status epilepticus (a syndrome characterised by one continuous seizure (fit) lasting longer than 5 minutes, or recurring seizures without regaining consciousness between seizures for greater than 5 minutes).
- flapping tremor of the hand (asterixis).
- movement and muscle control problems throughout your body (extrapyramidal disorder).
- impairment of the senses, especially of the sense of touch (dysesthesia).
- loss of sense of touch or sensation (hypoesthesia).
- tingling or numbness, often in the hands or feet (paresthesia).
- pain from your nerves, which can also feel like an aching or burning sensation (neuralgia).
- having difficulties in controlling or coordinating the muscles you use when you speak, or weakness of those muscles (dysarthria).
- inflammation (conjunctivitis) or irritation of the eyes.

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- deafness or hearing impairment (hypoacusis).
- dizziness or feeling of spinning and disorientation (vertigo).
- ringing in the ears (tinnitus).
- damage to the heart muscle (cardiotoxicity).
- irregular (atrial or ventricular fibrillation, palpitations), slow (bradycardia) or early (premature atrial contractions) heartbeat.
- blockage of electrical impulses in the heart.
- accumulation of too much fluid around the heart.
- bleeding into the muscles of the heart (myocardial haemorrhage).
- chest pain from reduced blood supply to the heart (angina pectoris).
- disease of the heart muscle (cardiomyopathy, congestive cardiomyopathy).
- inflammation for the heart muscle (myocarditis) or pericardium (pericarditis).
- abnormal ECG heart tracing (a test to measure the electrical activity of the heart).
- 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 (deep vein thrombosis).
- leaking of fluid from the circulation into surrounding tissues (capillary leak syndrome).
- inflammation of the blood vessels (vasculitis).
- high blood pressure (hypertension).
- reddening of the skin (flushing).
- acute respiratory distress syndrome, a rapid onset of widespread inflammation in the lungs, which include shortness of breath, rapid breathing, and bluish skin coloration.
- increased blood pressure in the lungs which can cause shortness of breath, fatigue, cough, angina, fainting, peripheral oedema (pulmonary hypertension).
- inflammation of the alveoli of the lungs caused by the inhalation of an allergen (alveolitis allergic).

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- fluid around the lungs (pleural effusion).
- difficulty in breathing or wheezing (bronchospasm).
- decrease levels of oxygen in your body (hypoxia).
- inflammation of the bowel/cecum (cectitis).
- inflammation of the lining of the colon and/or small intestine (colitis, enterocolitis).
- decrease bowel activity which may lead to bowel obstruction (ileus).
- bleeding in your stomach or intestines (gastrointestinal haemorrhage).
- ulceration of the lining of the digestive system (mucosal ulceration).
- increased saliva production.
- liver failure.
- blockage of the small veins in your liver (veno-occlusive liver disease) which can cause weight gain, increased liver size, pain and jaundice.
- reduction of blood supply or blockage of the portal vein of the liver (portal vein thrombosis).
- inflammation of the liver which can cause jaundice, weight loss and malaise (cytolytic hepatitis).
- total or partial suppression of the flow of bile (cholestasis).
- 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).
- redness and blistering of the skin appearing months or years after treatment (radiation recall syndrome).
- loss or death of skin (necrosis).
- swelling of the face.
- small red or purple spots caused by bleeding into the skin (petechiae).
- itching (pruritus).

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Product Name:	Holoxan 500 mg Injection, Holoxan 1g Injection & Holoxan 2 g Injection
	Intravenous injections containing 500 mg, 1 g or 2 g ifosfamide as dry substance

- itchy, red rash which can develop into sores (erythema).
- darkening of an area of skin (hyperpigmentation).
- excessive sweating (hyperhidrosis).
- nail disorders.
- growth retardation.
- muscle pain (myalgia) or joint pain (arthralgia).
- pain in the extremities (shoulders, neck, wrists, legs, arms).
- muscle twitching.
- inflammation of the kidneys (tubulointerstitial nephritis).
- glucose in the urine (nephrogenic diabetes insipidus).
- condition usually defined as excessive or abnormally large production or passage of urine (polyuria).
- repeated inability to control urination (enuresis).
- feeling of residual urine.
- infertility (sperm production in men and egg production in women may be reduced or stop, which could be permanent in some cases).
- loss of ovarian function before age 40 (ovarian failure, premature menopause).
- absence of ovulation (ovulation disorder).
- reduction in growth, deformity or death of a foetus while in the womb.
- life threatening failure of multiple organs.
- general physical deterioration.
- chest pain.
- swelling.
- fever.
- chills.

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

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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>.

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

5. How to store HOLOXAN

Store at or below 25 °C.

The solution of HOLOXAN injection can be kept for up to 24 hours in the refrigerator at 5 °C.

Store all medicines out of reach of children.

6. Contents of the pack and other information

What HOLOXAN contains

The active substance is ifosfamide. Each vial of HOLOXAN injection contains either 500 mg, 1 g or 2 g ifosfamide as a dry substance for preparing an injectable solution.

HOLOXAN contains the active ingredient only and no inactive ingredients.

What HOLOXAN looks like and contents of the pack

HOLOXAN is a white, crystalline powder in clear glass vials.

Injection vials of 500 mg: Packs of 1 and 10.

Injection vials of 1 g: Packs of 1 and 10.

Injection vials of 2 g: Packs of 1 and 10.

Holder of Certificate of Registration

Baxter Healthcare South Africa (Pty) Ltd

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The Campus – Eden Gardens

57 Sloane Street & Cnr Main Rd

Bryanston

2021

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Registration numbers

HOLOXAN 500 mg Injection: K/26/32

HOLOXAN 1 g Injection: K/26/33

HOLOXAN 2 g Injection: K/26/34