

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

Equituz, 440 mg powder and solvent for solution for injection

Trastuzumab

Sugar free

Solvent for Equituz contains 1,1 % *m/v* benzyl alcohol, as preservative.

Read all of this leaflet carefully before you are given Equituz

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet

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

1. What Equituz is and what it is used for

Equituz contains the active substance trastuzumab, which is a humanised monoclonal antibody.

Equituz is used for the treatment of breast and gastric cancer when:

- You have early breast cancer, with high levels of a protein called HER2

- You have metastatic breast cancer (breast cancer that has spread beyond the original tumour) with high levels of HER2. Equituz may be prescribed in combination with the chemotherapy medicine paclitaxel or docetaxel as first treatment for metastatic breast cancer or it may be prescribed alone if other treatments have proved unsuccessful. It is also used in combination with medicines called aromatase inhibitors with patients with high levels of HER2 and hormone receptor-positive metastatic breast cancer (cancer that is sensitive to the presence of female sex hormones).
- You have metastatic gastric cancer with high levels of HER2, when it is in combination with the other cancer medicines capecitabine or 5-fluorouracil and cisplatin.

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

Equituz should not be administered to you if:

- if you are hypersensitive (allergic) to trastuzumab, to murine (mouse) proteins or to any other ingredients of Equituz (listed in section 6).
- if you have breathing problems at rest or if you need oxygen treatment.
- if you are pregnant or breastfeeding your baby.

Warnings and precautions

Your doctor will closely supervise your therapy.

Heart checks

Treatment with Equituz alone or with a taxane may affect the heart, especially if you have ever used an anthracycline (taxanes and anthracyclines are two other kinds of medicine used to treat cancer). The effects may be moderate to severe and could cause death. Therefore, your heart function will be checked before, during (every three months) and after (up to two to five years) treatment with Equituz. If you develop any signs of heart failure (inadequate pumping of blood by the heart), your heart function may be checked more frequently (every six to eight weeks), you may receive treatment for heart failure or you may have to stop Equituz treatment.

Tell your doctor or healthcare provider before being given the injection if:

- If you have or have had heart failure, coronary artery disease, heart valve disease (heart murmurs), high blood pressure, taken any high blood pressure medicine or are currently taking any high blood pressure medicine. This is because Equituz can cause heart failure.
- If you have ever had chemotherapy with a medicine called doxorubicin or epirubicin (medicines used to treat cancer). These medicines (or any other anthracyclines) can damage heart muscle and increase the risk of heart problems with Equituz.
- If you suffer from breathlessness, especially if you are currently using a taxane. Equituz can cause breathing difficulties, especially when it is first given. This could be more serious if you are already breathless. Less frequently, patients with severe breathing difficulties before treatment have died when they were given Equituz.
- If you have ever had any other treatment for cancer.

If you receive Equituz with any other medicine to treat cancer, such as paclitaxel, docetaxel, an aromatase inhibitor, capecitabine, 5-fluorouracil, or cisplatin you should also read the patient information leaflets for these medicines.

Children and adolescents

Equituz is not recommended for anyone under the age of 18 years.

Other medicines and Equituz

Always tell your healthcare provider if you are taking any other medicine.

(This includes all complementary or traditional medicines.)

It may take up to 7 months for Equituz to be removed from the body. Therefore, you should tell your doctor, pharmacist or nurse that you have had Equituz if you start any new medicine in the 7 months after stopping treatment.

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 healthcare provider for advice before receiving Equituz.

If you are a woman or a man receiving Equituz, you are advised to use a highly effective form of contraception, including a barrier method, while receiving Equituz and for at least 7 months after your last Equituz dose.

You must not use Equituz if you are pregnant. Equituz can cause harm to the foetus (unborn baby), in some cases death to the foetus, when taken by a pregnant woman.

Do not breastfeed your baby during Equituz therapy and for 7 months after the last dose of Equituz.

Driving and using machines

Equituz may affect your ability to drive a car or operate machinery. If during treatment you experience symptoms, such as dizziness, sleepiness, chills or fever, you should not drive or use machines until these symptoms disappear.

It is not always possible to predict to what extent Equituz may interfere with your daily activities. You should ensure that you do not engage in driving a vehicle or using machines until you are aware of the measure to which Equituz affects you.

Benzyl alcohol

The solvent for Equituz contains bacteriostatic water for injection with 11 mg/ml benzyl alcohol as preservative, which is equivalent to 1,1 % *m/v*. Benzyl alcohol may cause allergic reactions.

Ask your doctor or pharmacist for advice if you have a liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called “metabolic acidosis”).

3. How to use Equituz

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

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

Equituz is given as intravenous infusion (“drip”) directly into your veins. Your doctor will prescribe a dose and treatment regimen that is right for you. The number of infusions you receive will depend on how you respond to the treatment. Your doctor will discuss this with you.

Your doctor will tell you how long your treatment with Equituz will last. If you have the impression that the effect of Equituz is too strong or too weak, tell your doctor or pharmacist.

If you use more Equituz than you should

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

If you forget to use Equituz

Since a healthcare provider will administer Equituz, it is unlikely that the dose will be missed.

4. Possible side effects

Equituz can have side effects.

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

If any of the following happens, stop receiving Equituz and tell your doctor immediately:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting.

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

During a Equituz infusion, chills, fever and other flu-like symptoms may occur. These are very frequent. Other infusion-related symptoms are feeling sick (nausea), vomiting, pain, increased muscle tension and shaking, headache, dizziness, breathing difficulties, high or low blood pressure, heart rhythm disturbances (palpitations, heart fluttering or irregular heartbeat), swelling of the face and lips, rash and feeling tired. Some of these symptoms can be serious and some patients have died (see section 2 under “Warnings and precautions”).

These effects mainly occur with the first intravenous infusion (“drip” into your vein) and during the first few hours after the start of the infusion. They are usually temporary. You will be observed by a healthcare professional during the infusion and for at least six hours after the start of the first infusion and for two hours after the start of other infusions. If you develop a reaction, they will slow down or

stop the infusion and may give you treatment to counteract the side effects. The infusion may be continued after the symptoms improve.

Occasionally, symptoms start later than six hours after the infusion begins. If this happens to you, contact your doctor immediately. Sometimes, symptoms may improve and then get worse later.

Serious side effects

Other side effects can occur at any time during treatment with Herceptin, not just related to an infusion. **Tell a doctor or nurse straight away, if you notice any of the following side effects:**

- Heart problems can occur during treatment and occasionally after treatment has stopped and can be serious. They include weakening of the heart muscle possibly leading to heart failure, inflammation of the lining around the heart and heart rhythm disturbances. This can lead to symptoms such as breathlessness (including breathlessness at night), cough, fluid retention (swelling) in the legs or arms, palpitations (heart fluttering or irregular heartbeat) (see section 2. Heart checks).

Your doctor will monitor your heart regularly during and after treatment but you should tell your doctor immediately if you notice any of the above symptoms.

- serious and potentially deadly lung problems, including:
 - a severe shortness of breath
 - too little oxygen in the body
 - weakening of the heart valve between the heart and the lungs
 - swelling of the lungs
 - scarring of the lungs
 - excess fluid in the lungs
 - an abnormal accumulation of fluid and swelling in the tissues of the larynx
- Tumour lysis syndrome (a group of metabolic complications occurring after cancer treatment characterised by high blood levels of potassium and phosphate, and low blood levels of calcium).

Symptoms may include kidney problems (weakness, shortness of breath, fatigue and confusion), heart problems (fluttering of the heart or a faster or slower heartbeat), seizures, vomiting or diarrhoea and tingling in the mouth, hands or feet.

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

Frequent side effects:

- infections
- throat infections
- bladder and skin infections
- infection of lungs
- diarrhoea
- constipation
- heartburn (dyspepsia)
- fatigue
- skin rashes
- chest pain
- abdominal pain
- joint pain
- low counts of red blood cells and white blood cells (which help fight infection) sometimes with fever
- muscle pain
- conjunctivitis
- watery eyes
- nose bleeds
- runny nose

- hair loss
- tremor
- hot flush
- dizziness
- nail disorder
- weight loss
- loss of appetite
- inability to sleep (insomnia)
- altered taste
- low platelet count
- bruising
- numbness or tingling of the fingers and toes
- redness, swelling or sores in your mouth and/or throat
- pain, swelling, redness or tingling of hands and/or feet
- breathlessness
- headache
- cough
- vomiting
- nausea
- allergic reactions
- inflammation of the breast
- inflammation of the liver
- kidney disorders
- increased muscle tone or tension (hypertonia)
- pain in the arms and/or legs
- itchy rash

- sleepiness (somnolence)
- haemorrhoids
- itchiness
- dry mouth and skin
- dry eyes
- sweating
- feeling weak and unwell
- anxiety
- depression
- asthma
- lung disorders
- back pain
- neck pain
- bone pain
- acne
- leg cramps

Less frequent side effects:

- deafness
- bumpy rash
- wheezing
- inflammation or scarring of the lungs
- jaundice
- anaphylactic reactions
- build-up of extra fluid in the space around the heart (pericardial effusion)

Other side effects that have been reported with unknown frequency:

- abnormal or impaired blood clotting
- high potassium levels
- swelling or bleeding at the back of the eyes
- shock
- abnormal heart rhythm
- respiratory distress
- respiratory failure
- acute accumulation of fluid in the lungs
- acute narrowing of the airways
- abnormally low oxygen levels in the blood
- difficulty in breathing when lying flat
- liver damage
- swelling of the face, lips and throat
- kidney failure
- abnormally low levels of fluid around baby in womb
- failure of the lungs of the baby to develop in the womb
- abnormal development of the kidneys of the baby in the womb
- meningitis
- progressive and uncontrolled growth of tumour cells
- tumour lysis syndrome
- abnormal thinking
- build-up of fluid around the brain

Some of the side-effects you experience may be due to your underlying cancer. If you receive Equituz in combination with chemotherapy, some of them may also be due to the chemotherapy

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

5. How to store Equituz

Store all medicines out of reach of children.

Store the unopened vials in a refrigerator (2 - 8 °C).

Do not freeze the reconstituted solution.

Keep the vial in the outer carton in order to protect from light.

Infusion solutions should be used immediately after dilution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user, and would not normally be longer than 24 hours at 2°C – 8°C.

Do not use Equituz if you notice any particulate matter or discolouration prior to administration.

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

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What Equituz contains

The active substance is trastuzumab.

Vial containing powder for concentrate for solution for infusion:

Each vial contains 440 mg of trastuzumab powder for concentrate for solution for infusion.

Reconstituted Equituz concentrate contains 21 mg/ml trastuzumab.

The other ingredients are α , α -trehalose dihydrate, L-histidine hydrochloride monohydrate, L-histidine, polysorbate 20.

Vial containing solvent:

Each vial contains 20 ml sterile bacteriostatic water for injection with 1,1 % m/v benzyl alcohol as preservative.

What Equituz looks like and contents of the pack

Equituz 440 mg powder for concentrate for solution for infusion is supplied in 50 ml colourless neutral hydrolytic class I glass vials, sealed with rubber bromobutyl stoppers, crimped with aluminium caps with red plastic "flip-off" lid. The powder is a porous mass from white to light yellow. Each vial is labelled with a self-adhesive label.

Solvent for Equituz is supplied in 20 ml neutral glass type I vials, sealed with rubber bromobutyl stoppers and crimped with aluminium flip-off caps with red plastic "flip-off" lid. The solvent is a clear colourless or with yellowish shade liquid.

Each carton contains one vial with powder and one vial with the solvent in a PVC blister.

Holder of Certificate of Registration

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Registration /Application number

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Access to the corresponding translated Patient Information Leaflet:

An electronic copy of the translated Patient Information Leaflet (PIL) is available on the Equity website:

<http://www.equitypharmaceuticals.co.za>