Package leaflet: Information for the patient
Erwinase
10,000 IU, Powder for solution for injection/infusion
Crisantaspase (L-asparaginase from *Erwinia chrysanthemi*)

Read all of this leaflet carefully before you start receiving 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 your pharmacist.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Erwinase is and what it is used for

How does Erwinase work
Erwinase is an anti-blood-cell-cancer treatment from the pharmacotherapeutic group: antineoplastic and immunomodulating agents. It works by lowering the levels of asparagine in your body, a substance the cancer cells need to survive.

What this medicine is used for
Erwinase is used for the treatment of a cancer of the white blood cells called Acute Lymphoblastic Leukaemia, in patients aged 4 months and above, who have developed allergic reactions to *E. coli* derived asparaginase.

Erwinase may be used alone or with other treatments.

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

You should not be given Erwinase if :
- you have previously had a severe allergic reaction to the active substance (Crisantapase L-asparaginase from *Erwinia chrysanthemi*) or are allergic to any of the other ingredients of this medicine (see section 6)
- You have, or have previously had, serious problems with your pancreas (severe pancreatitis) from using a medicine containing L-asparaginase
- You have serious problems with your pancreas (severe pancreatitis)

Warnings and precautions
Talk to your doctor or pharmacist or nurse before taking Erwinase.
The following complications may arise during treatment with Erwinase:
- Serious life-threatening allergic reactions. The hospital will have the necessary precautions in place to deal with such situations.
- Inflammation of the pancreas. If you experience abdominal pain this may be a sign of pancreatitis and should be reported to your doctor immediately. Fatal outcomes associated with pancreatitis have occurred.
- Increases in your blood sugar levels (hyperglycemia). This can be controlled by receiving insulin sometimes even to fatal amounts (hyperglycemia). This can be controlled by receiving insulin.

- Bleeding and blood clot disorders. During treatment your body's ability to prevent excessive bleeding may be affected. In the case you experience any significant bleeding your treatment will be stopped. Your doctor will determine if, and when, treatment can be restarted.
- Liver dysfunctions can be caused or worsened. Discontinuation of Erwinase will be considered in the event of a severe reaction. Treatment can be restarted under close monitoring, but only once at least near complete recovery is achieved.
- Neurological disorders have been reported with fatal outcomes. Posterior reversible encephalopathy syndrome (characterised by headache, confusion, seizures and visual loss) may require blood-pressure lowering medicines and in case of seizure, anti-epileptic treatment.
- Kidney impairment due to high levels of a substance called uric acid in your blood from the chemotherapy.
- Reduced immune system that may increase your chances of an infection.

Monitoring during treatment with Erwinase
You will be monitored closely during and after treatment with Erwinase for:
- Allergic reactions
- Pancreas, kidney and liver functions
- Normal blood content

For traceability purposes your health care professional will record the product name and batch number for each dose of Erwinase you receive.

Other medicines and Erwinase
Tell your doctor or your pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription, particularly any of the following:
- Types of medicines used to treat cancer called 'methotrexate' or 'cytarabine' as they can affect the way Erwinase works.
- Prednisone which is used in cancer treatment may increase the risk of a change in clotting.
- Vincristine, which is used in cancer treatment, can increase the toxic effects of both medicinal products and increase the risk of anaphylaxis.
- Oral contraceptives.

Your doctor or your nurse will not mix Erwinase with other medicines in the same infusion.

However, you will probably be given other medicines before, during or after Erwinase treatment as part of your course of therapy.

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

Breastfeeding
You must not breastfeed your baby during your treatment with Erwinase, there may be a risk to the feeding child.

Fertility & Family planning
Potential for a decrease in male fertility cannot be ruled out.

When appropriate both men and women should use necessary contraceptive measures before, and for at least three months after treatment with Erwinase. Women should use a form of contraception other than oral contraceptives.

Driving and using machines
Erwinase can cause dizziness and drowsiness. This can affect your coordination and therefore your ability to drive and operate machinery.

Erwinase contains sodium and glucose
Erwinase contains the following ingredients :
■ **sodium** (less than 23 mg per dose). You can consider this medicine as essentially sodium free if you are on a salt-free or low-salt diet.
■ **glucose**. If you are diabetic, please note that each bottle of Erwinase contains 5 mg glucose.

3. How Erwinase is given

Dosage
Erwinase will only be given to you by health care professionals who are experienced in giving chemotherapy.

Your doctor will decide what dose to administer, how often you will be given Erwinase and for how long. It varies according to your body weight, your specific condition being treated, and your response to therapy.

Method of administration
Erwinase can be given to you in one of the following ways:
a) Into a vein (intravenous use). This may be given over 1 to 2 hours.
b) Into a muscle (intramuscular use).

If you are given more Erwinase than you should
If you are concerned that you have been given too much Erwinase, contact your doctor or another healthcare professional immediately.

If you think you have missed a dose of Erwinase
If you are concerned that you have missed a dose, contact your doctor or another healthcare professional immediately.

If you have any further questions on this product, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, Erwinase can cause side effects, although not everybody gets them. Erwinase will be given under strict medical supervision and your doctor may give you other medicines to treat these side effects. Most of the side effects will stop once you stop taking Erwinase.

Serious side effects
Tell your doctor immediately if you experience:

- Severe allergic reactions including blue discolouration of the lips and extremities (possible symptoms of hypoxia), swelling of the face and/or, shortness of breath, increased heart rate, wheezing, difficulty swallowing, hay fever like symptoms, rash, chills, flushing, high or low blood pressure, vomiting
- Redness, pain, swelling, bruising, or hardening of the skin at the site of the injection
- Damage to the Central Nervous System symptoms may include coma, encephalopathy, hallucinations, muscle weakness, confusion, dizziness, drowsiness, agitation, difficulty speaking
- Arm, leg or calf pain with or without swelling (symptoms of blood clots in the arm or leg), abdominal pain (symptoms of a blood clot in the area of the stomach, intestines, and kidneys), chest pain spreading to the arms, neck, jaw, back or stomach, feeling sweaty and breathless (which may be symptoms of a heart attack/myocardial infarction)
- Pain near your stomach or in your back (this may be inflammation of your pancreas)
- High blood sugar levels (hyperglycemia)
- Increased frequency of bleeding events including bruising even if you have not been injured
- Changes in liver functions (identified by laboratory testing)

Other side effects
Talk to your doctor if you get any of the following:

Very common side effects (may affect more than 1 in 10 people):
- Infections, including blood infections caused by bacteria (sepsis). This may be due to low levels of white cells in your blood. You may experience fever, a rapid heart rate, confusion or a rash
- Decreases in normal blood content. Some of which may be due to reduced bone marrow activity
- Increase in blood fats, bilirubin, creatinine, urea levels and certain liver enzymes. Your doctor will monitor these
- Weight loss
- Generalised pain/muscle pains
- Nausea

Common (may affect up to 1 in 10 people) side effects include:
- Difficulty breathing or stopping breathing
- Mucositis (inflammation of the digestive tract)
- Diarrhoea
- Abdominal pain/discomfort
- Tiredness or headache
- High temperature

Uncommon (may affect up to 1 in 100 people) side effects include:
- Life-threatening complications of uncontrolled diabetes
- High blood levels of ammonia
- Fits (convulsions)
- Build-up of fats in the liver
- Kidney dysfunction

Rare (may affect up to 1 in 1,000 people) side effects include:
- Posterior reversible encephalopathy syndrome (a condition characterised by headache, confusion, seizures and visual loss)

Not known (frequency cannot be estimated from the available data):
- Inflammation of the salivary gland at the back of the throat
- Liver failure, increased mass of liver, jaundice
- Decreased albumin levels in the blood causing water retention
- Blistering and peeling of the skin (Toxic epidermal necrolysis)
- Joint pain

Additional side effects in children and adolescents
Liver, pancreas and blood clotting side effects may be higher in adults compared to children.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via MHRA Yellow Card in 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 Erwinase

Keep this medicine out of the sight and reach of children.
Erwinase will not be used after the expiry date printed on the label after "EXP". The expiry date refers to the last day of the month.

The unopened Erwinase vials will be stored in a refrigerator (between +2°C to +8°C) by the hospital.

After reconstitution, the product should be used within 15 minutes. If the delay is more than 15 minutes, the solution should be withdrawn into a glass or polypropylene syringe and used within 4 hours. The reconstituted product should be stored below 25°C.

6. Contents of the pack and other information

What Erwinase contains

The active substance is crisantaspase (L-asparaginase from *Erwinia chrysanthemi*). Each vial contains 10,000 International units of cristanaspase (L-asparaginase from *Erwinia chrysanthemi*).
The other excipients are sodium chloride (See section 2) and glucose monohydrate (See section 2).

What Erwinase looks like and contents of the pack

Erwinase is provided as a powder for solution for injection/infusion.
It comes as a white lyophilized powder in a clear glass bottle with a rubber stopper and an aluminium seal.
Each pack contains 5 glass bottles of powder.

Marketing Authorisation Holder and Manufacturer

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DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

The following information is intended for healthcare professionals only:

The contents of each vial should be reconstituted in 1 mL or 2 mL of saline solution (0.9%) for injection.

Slowly add the saline solution (0.9%) for injection against the inner vial wall, do not add it directly onto or into the powder. Allow the contents to dissolve by gentle mixing or swirling, maintaining the vial in an upright position. Avoid contact of the solution with the stopper. Avoid froth formation due to excessive or vigorous shaking.

The solution should be clear without any visible particles. Fine crystalline or thread-like particles of protein aggregates may be visible if shaking is excessive, resulting in visible foaming. If there are any visible particles or protein aggregates present, the reconstituted solution should be rejected.

The reconstituted solution for injection should be administered within 15 minutes of reconstitution. If a delay of more than 15 minutes between reconstitution and administration is unavoidable, then the solution should be withdrawn into an aseptic glass or polypropylene syringe under sterile conditions. The syringe containing the reconstituted solution should then be stored below 25°C and used within 4 hours.

For IV infusion, it is recommended to further dilute the reconstituted Erwinase solution in 100 ml saline solution (0.9%). To make preparation easier, the reconstituted Erwinase solution can be transferred directly to a bag prefilled with 100 ml saline (0.9%) for infusion.

It is recommended that the diluted solution for infusion should be used immediately after preparation. If not used immediately, the diluted solution for infusion can be stored in a polyvinylchloride (PVC) infusion bag. The infusion bag should be stored below 25°C and used within 4 hours.

From a microbiological point of view, the reconstituted solution for injection should be used immediately unless the reconstitution method precludes the risk of microbiological contamination. If not used immediately, the user is responsible for the storage times and conditions.

Erwinase is not a cytotoxic medicinal product and does not require the special precautions needed for manipulating such agents. Nevertheless, when preparing or administering Erwinase the fact should be taken into account that it can be sensitising.

Inhalation of the powder or the solution should be avoided. In the event of it coming into contact with the skin or mucous membranes, in particular with the eyes, these should be rinsed with plenty of water for at least 15 minutes.

Any unused product or waste material should be disposed of in accordance with local requirements.

In the absence of compatibility studies, this medicinal product should not be mixed with other medicinal products. Accordingly, other intravenous medicinal products must not be infused through the same intravenous line as when administering Erwinase.