Package leaflet: Information for the user

GLYPRESSIN 1 mg Powder and Solvent for Solution for Injection

Terlipressin acetate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
• Keep this leaflet. You may need to use 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.

What is in this leaflet

1. What GLYPRESSIN is and what it is used for

GLYPRESSIN consists of a powder and solvent for solution for injection. The white, freeze-dried powder contains the active component terlipressin acetate. This medicinal product contains up to 1.54 mmoles of sodium per dose, therefore please tell your doctor if you are on a controlled sodium diet.

GLYPRESSIN is used in the treatment of bleeding oesophageal varices.

Oesophageal varices are enlarged blood vessels that form in the stomach or oesophagus (gullet) as a complication of liver disease. They may burst and bleed which is a serious and life- threatening condition.

When injected into the bloodstream, the active ingredient, terlipressin acetate, is broken down to release a substance called lysine vasopressin. This acts on the walls of the blood vessels, causing them to narrow and restrict blood flow to the affected veins so that bleeding is reduced.

GLYPRESSIN is also used as an emergency treatment of type 1 hepatorenal syndrome in patients with liver cirrhosis and ascites.

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

Do not use GLYPRESSIN
- if you are **allergic** to terlipressin acetate or any of the other ingredients of this medicine (listed in section 6)
- if you are **pregnant**

Take special care with GLYPRESSIN
- if you have **high blood pressure**
- if you have **heart disease**
- if you have **renal (kidney) dysfunction**
- if you have **septic shock**. Septic shock is a serious condition that occurs when a major infection leads to low blood pressure and low blood flow.
- if you have **atherosclerosis** (a disease of the arteries in which fatty plaques develop on the inner lining of the arteries, preventing blood from flowing normally)
- if you have **asthma**
- if you have **respiratory failure or difficulty breathing,** GLYPRESSIN can increase your risk of developing respiratory failure that may be life-threatening. If you experience difficulty breathing, or symptoms of fluid overload, before GLYPRESSIN is given or during treatment, immediately inform your doctor.
- in **children and elderly** patients as experience is limited in these age groups.

If you are treated for very severe liver and kidney disease (type 1 hepatorenal syndrome), your doctor should ensure that your heart function and fluid and electrolyte balance are monitored during the treatment. Particular care is required if you have prior heart or lung disease since GLYPRESSIN can induce heart ischemia (decrease in the amount of blood flow to the heart) and respiratory failure (severe breathing difficulties). Treatment with GLYPRESSIN should be avoided if you have liver failure with multiple organ failures and/or kidney failure with very high levels of creatinine (a waste product) in the blood, as it increases your risk of adverse outcomes.

If you are treated for very severe liver and kidney disease, GLYPRESSIN can increase your risk of developing sepsis (bacteria in the blood and the body's extreme response to an infection) and septic shock (a serious condition that occurs when a major infection leads to low blood pressure and low blood flow). Your doctor will take additional precautions should this apply to you.

Tell your doctor if any of these apply to you.

During treatment with GLYPRESSIN, **your blood pressure, heart rate, oxygen levels and fluid balance should be monitored constantly.**

GLYPRESSIN contains sodium as an excipient
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

Other medicines and GLYPRESSIN
Tell your doctor or other healthcare personnel if you are taking, have recently taken or might take any other medicines.

It is most important to tell your doctor if you are taking any kind of heart medication (e.g. beta-blockers) as their effect could be increased if used at the same time as GLYPRESSIN.

Please inform your doctor immediately if you take any of the following medicines:
Drugs that can trigger irregular beating of the heart (arrhythmia) such as the following:

- anti-arryhthmic drugs known as Class IA (quinidine, procainamide, disopyramide) and Class III (amiodarone, sotalol, ibutilide, dofetilide)
- erythromycin (an antibiotic)
- antihistamines (mainly used to treat allergies but also found in certain cough and cold remedies)
- tricyclic antidepressants used to treat depression
- medicines that may alter the level of salt or electrolytes in your blood, particularly diuretics (water tablets used to treat high blood pressure and heart failure).

Pregnancy and breast-feeding
GLYPRESSIN should not be used during pregnancy. GLYPRESSIN should not be used during breastfeeding as it is not known if GLYPRESSIN is transferred into breast milk.

Driving and using machines
Not applicable. GLYPRESSIN is a medicine that is only used in hospitals.

3. How you will be given GLYPRESSIN
GLYPRESSIN is a medicine that is used in hospitals and should only be given by qualified staff. Solvent is mixed with the powder for injection via the rubber stopper of the glass vial. Immediately after mixing, the clear solution is injected or infused intravenously (directly into the bloodstream).

Short term management of bleeding oesophageal varices
The usual starting dose of GLYPRESSIN in sudden bleeding from oesophageal varices is 2 mg terlipressin acetate. Further doses are usually 1-2 mg terlipressin acetate every 4 hours until bleeding has been controlled for 24 hours. Treatment should last a maximum of 48 hours.

After the starting dose your dose may be adjusted according to your body weight or if you experience any side effects.

Type I hepatorenal syndrome
The usual dose of GLYPRESSIN in Type 1 hepatorenal syndrome is 3 to 4 mg terlipressin acetate every 24 hours as 3 or 4 administrations. In the absence of any reduction of serum creatinine after 3 days of treatment your doctor should stop your treatment with GLYPRESSIN. When a reduction in serum creatinine is seen, treatment with GLYPRESSIN should be continued with the standard average duration of treatment being 10 days.

You may also be given GLYPRESSIN as a drip (continuous intravenous infusion) usually starting with 2 mg terlipressin acetate per day and increased in a stepwise manner to a maximum of 12 mg terlipressin acetate per day.

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor or other healthcare professional straight away:

- If you develop breathing difficulties or experience a worsening of breathing ability (signs or symptoms of respiratory failure). This side effect is very common if you are treated for type 1 hepatorenal syndrome - may affect more than 1 in 10 people.

- If you develop signs or symptoms of infection of the blood (sepsis/septic shock), which may include fever and chills or very low body temperature, pale and/or bluish skin, severe breathlessness, urinating less than usual, fast heartbeat, nausea and vomiting, diarrhoea, fatigue and weakness, and feeling dizzy. This side effect is common if you are treated for type 1 hepatorenal syndrome - may affect up to 1 in 10 people.

Other side effects that may occur with different frequencies depending on the disease that you have.

Very commonly reported side effects: (may affect more than 1 in 10 people)
If you have type 1 hepatorenal syndrome:
- Shortness of breath (dyspnoea)

Commonly reported side effects (affect between 1 and 10 of every 100 patients treated):
- Headache
- Bradycardia (very slow heart rate)
- Increased blood pressure
- Constriction of blood vessels
- Decreased blood flow to the limbs
- Paleness
- Stomach pain
- Diarrhoea

Commonly reported side effects (affect between 1 and 10 of every 100 patients treated):
If you have type 1 hepatorenal syndrome:
- Fluid in the lungs (pulmonary oedema)
- Difficulties in breathing (respiratory distress)

Uncommonly reported side effects (affect between 1 and 10 of every 1,000 patients treated):
- Low blood sodium
- Irregular heart beat
- Increased pulse rate
- Chest pain
- Myocardial infarction (heart attack)
- Pulmonary oedema (excess fluid in the lungs)
- Torsade de pointes (acute cardiac event)
- Heart failure. Symptoms include shortness of breath, tiredness and swollen ankles
- Decreased blood flow to the guts
- Cyanosis (bluish discolouration of the skin caused by lack of oxygen)
- Hot flush
- Respiratory distress and respiratory failure (difficulties in breathing)
- Nausea
- Vomiting
- Skin necrosis (tissue damage)
- Uterine constriction (constriction of the womb)

- Decreased uterine blood flow
- Injection site necrosis (tissue damage)

Rarely reported side effects (affect between 1 and 10 of every 10,000 patients treated):
- Dyspnoea (shortness of breath)

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie.

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

5. How to store GLYPRESSIN

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

Do not store above 25°C. Keep container in outer carton in order to protect from light.

The clear reconstituted solution must be used immediately after mixing of the powder with solvent. For single use only. Discard any unused solution.

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

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

6. Contents of the pack and other information

What GLYPRESSIN contain

Glypressin 1mg powder and solvent for solution for injection contains:

- one vial of freeze-dried powder containing 1mg of the active ingredient, terlipressin acetate. The other ingredients are mannitol and hydrochloric acid to adjust the acidity.
- one ampoule of liquid (solvent) containing a 5 ml solution of sodium chloride in water for injection. Hydrochloric acid is added to adjust the acidity to make it suitable for injection.

The concentration of the reconstituted solution is 0.2mg terlipressin acetate/ml.

What GLYPRESSIN looks like and contents of the pack

The product is a powder and solvent for solution for injection. The powder is white in colour. When dissolved in the solvent provided, a clear, colourless solution should be obtained.

GLYPRESSIN is available in one pack size: 5 sets of 1 vial + 1 ampoule

Marketing Authorisation Holder
Ferring Ireland Ltd., United Drug House, Magna Drive, Magna Business Park, Citywest Road, Dublin 24.
PA 1009/4/1

Manufacturer:
Ferring GmbH, Wittland 11, 24109 Kiel, Germany.

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