PACKAGE INSERT

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

GLYPRESSIN® 0,1 mg/ml (Solution for Injection)

COMPOSITION

One ampoule of 8,5 ml solution contains 1 mg terlipressin acetate, corresponding to 0,85 mg terlipressin free base. The concentration of the solution is 0,12 mg terlipressin acetate per ml, corresponding to 0,1 mg terlipressin free base per ml.

Excipients:

The excipients are sodium chloride, acetic acid, sodium acetate and water for injection.

One ampoule contains 1,33 mmol (or 30,7 mg) sodium.

PHARMACOLOGICAL CLASSIFICATION

A. 21.13 Other.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Terlipressin is a prodrug of vasopressin that is converted in the circulation to lysine vasopressin by exoperoxidase enzymes. Lysine-vasopressin causes splanchnic vasoconstriction by stimulating vasopressin V1 receptors on vascular smooth muscle. Vasoconstriction of the mesenteric circulation leads to decreased portal venous inflow and therefore reduced portal venous pressure.

Doses of 1 mg and 2 mg terlipressin acetate reduce the portal venous pressure and produce marked vasoconstriction. The lowering of portal pressure and azygos blood flow is dependent on dose. The effect of the low dose is reduced after 3 hours, while haemodynamic data show that 2 mg is more effective than 1 mg as the higher dose produces a dependable effect throughout the period of treatment (4 hours).

Pharmacokinetic properties

The pharmacokinetics exhibits a two-compartment model with a terminal half-life of approximately 40 minutes. The plasma clearance is approximately 9 ml/kg/min and the volume of distribution is approximately 0,5 l/kg. The desired concentration of lysine vasopressin in plasma is achieved at approximately 30 minutes and reaches a peak value at 60 to 120 minutes after administration of Glypressin® injection.

INDICATIONS

Bleeding oesophageal varices.

CONTRAINDICATIONS

Hypersensitivity to terlipressin or any other excipient of GLYPRESSIN®

Contraindicated in pregnancy.

WARNINGS AND SPECIAL PRECAUTIONS

Blood pressure, heart rate and fluid balance should be monitored during treatment.

To avoid local necrosis at the injection site, GLYPRESSIN® must be given intravenously. Caution should be exercised in administering GLYPRESSIN® to patients with hypertension or recognised heart disease.

In patients with septic shock with a low cardiac output, GLYPRESSIN® should not be used.

This medicinal product contains 1,33 mmol (or 30,7 mg) of sodium per ampoule. To be taken into consideration in patients on a controlled sodium diet.

Elderly population:

Particular caution should be exercised in the treatment of elderly patients, as experience is limited in this group. There is no data available regarding dosage recommendation in this special patient category.

Paediatric population

GLYPRESSIN® should not be used in children.

Use of GLYPRESSIN® should be confined to specialist supervision in units with facilities for regular monitoring of the cardiovascular system, haematology and electrolytes.

Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

INTERACTIONS

The hypotensive effect of non-selective β-blockers on the portal vein is increased by GLYPRESSIN®. Concomitant administration of GLYPRESSIN® with medicines with a known bradycardiac effect (e.g. propranolol or other beta-blockers) may cause lowering of the heart rate and cardiac output. These effects are due to the reflexogenic inhibition of the cardiac activity via the vagus nerve due to the elevated blood pressure.

GLYPRESSIN® must not be mixed with other medicinal products.

PREGNANCY AND LACTATION

Pregnancy

Treatment with GLYPRESSIN® during pregnancy is contraindicated. GLYPRESSIN® has been shown to cause uterine contractions and increased intrauterine pressure in early pregnancy and may decrease uterine blood flow. GLYPRESSIN® may have harmful effects on pregnancy and the foetus.

Lactation

Information on transfer of GLYPRESSIN® to breast milk is insufficient. GLYPRESSIN® should not be used in breastfeeding women.

DOSAGE AND DIRECTIONS FOR USE

Bleeding oesophageal varices

Initially an intravenous injection of 17 ml (2 ampoules) GLYPRESSIN® solution for injection (1,7 mg terlipressin is equivalent to 2 mg terlipressin acetate) is given every 4 hours.
The treatment should be maintained until the bleeding has been controlled for 24 hours, but up to a maximum of 48 hours.

After the initial dose, the dose can be adjusted to 8,5 ml (1 ampoule) GLYPRESSIN® solution for injection (0,85 mg terlipressin is equivalent to 1 mg terlipressin acetate) intravenously every 4 hours in patients with a body weight of less than 50 kg or if adverse effects occur.

SIDE EFFECTS

The most commonly reported side-effects of GLYPRESSIN® are paleness, increased blood pressure, abdominal pain, nausea, diarrhoea and headache.

The antidiuretic effect of GLYPRESSIN® may cause hyponatraemia unless the fluid balance is controlled.

Common (≥ 1/100 to < 1/10)

Uncommon (≥ 1/1 000 to < 1/100)

Rare (≥ 1/10 000 to < 1/1 000)

Not known: cannot be estimated from the available data.

Metabolism and nutrition disorders

Uncommon: Hyponatraemia if fluid balance is not monitored

Nervous system disorders

Common: Headache

Cardiac disorders

Common: Bradycardia,

Uncommon: Atrial fibrillation, ventricular extrasystoles, tachycardia, chest pain, myocardial infarction, fluid overload with pulmonary oedema

Not known: Torsade de pointes, cardiac failure

Vascular disorders

Common: Peripheral vasoconstriction, peripheral ischaemia, facial pallor, hypertension

Uncommon: Intestinal ischaemia, peripheral cyanosis, hot flushes

Respiratory, thoracic and mediastinal disorders

Uncommon: Respiratory distress, respiratory failure

Rare: Dyspnoea

Gastrointestinal disorders

Common: Transient abdominal cramps, transient diarrhoea

Uncommon: Transient nausea, transient vomiting

Skin and subcutaneous tissue disorders

Not known: Skin necrosis

Pregnancy, puerperium and perinatal conditions

Not known: Uterine constriction, decreased uterine blood flow

General disorders and administrative site conditions

Uncommon: Injection site necrosis

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

The recommended dose (2 mg/4 hours) should not be exceeded as the risk of severe circulatory adverse effects is dose-dependent.

Elevated blood pressure in patients with recognised hypertension can be controlled with 150 microgram clonidine i.v.

Bradycardia may be treated with atropine.

Treatment is symptomatic and supportive.

IDENTIFICATION

Clear, colourless solution for injection.

PRESENTATION

8,5 ml GLYPRESSIN® Solution for Injection is filled into clear, type I glass ampoules. Each pack

contains 5 ampoules in a plastic tray.

STORAGE INSTRUCTIONS

Store in a refrigerator (2 °C to 8 °C).

Store the ampoules in the outer container in order to protect from light.

KEEP OUT OF REACH OF CHILDREN.

For single use only

Discard any unused portion

REGISTRATION NUMBER

43/21.13/0829

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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