For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

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Terlipressin Injection 1 mg/10 mL

Biocon

For I.V. Use Only

THINWES® थिनवेस

COMPOSITION
Each mL contains:
Terlipressin Acetate
Equivalent to Terlipressin 100 mcg
Water for Injections I.P q.s.

PHARMACEUTICAL FORM
Solution for injection

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties
Pharmacotherapeutic group: posterior pituitary lobe hormones (vasopressin and vasopressin analoges)

ATC code: H01BA04

Terlipressin is N-triglycyl-b-lysine-vasopressin, a synthetic analogue of vasopressin, naturally occurring pituitary hormone. It may be regarded as a circulating depot of lysine-vasopressin.

Mechanism of Action
Terlipressin has significant vasoconstrictive and anti-hemorrhagic effect. The most significant change is reduced blood flow in the splanchnic area followed by the reduction of hepatic blood flow and portal blood pressure. Pharmacodynamic studies have shown that, like other similar peptides, terlipressin causes intra-arteriolar, intravenous and intravenular constrictions primarily in the splanchnic area, as well as the constriction of esophageal unstripped muscles, and increase in tonus and intestinal peristaltic activity. In addition to its vasopressor effects, terlipressin stimulates myometrial activity, even in non-pregnant uterus.

The anti-shock effect of terlipressin has been confirmed not only for hemorrhagic but also for endotoxic and histaminic shocks. There are no clinical manifestations of the antidiuretic effect of terlipressin.

Pharmacokinetic Properties
General

Following the intravenous injection of terlipressin, three glycyl moieties are enzymatically cleaved from the N-terminus to release lysine-vasopressin. The intravenous pharmacological profile can be described using a two compartment model.

Distribution and Metabolism

Estimated lysine-vasopressin concentration can be found in the plasma 30 minutes after the administration of terlipressin, with peak values after 60 to 120 minutes. The duration of action is about 4 to 6 hours. The volume of distribution is about **0.5 L/Kg** and the half-life of distribution is about 8 to 10 minutes.

Excretion

Lysine-vasopressin is subject to the usual biodegradation in liver, kidneys and other tissues. The excretion half-life of terlipressin is about 40 minutes and the metabolic clearance is about 9 mL/kg x min.

Preclinical Safety Data
There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the package insert.

CLINICAL PARTICULARS

Therapeutic Indications
Terlipressin is indicated in the treatment of:

- Bleeding esophageal varices

Posology and Method of Administration

Bleeding from esophageal varices:
2 mg of terlipressin should be administered by intravenous bolus, followed by 1 to 2 mg every 4 to 6 hours until bleeding is controlled, up to a maximum of 72 hours.

Special Populations

Paediatric use
Children and the Elderly Because of limited experience, special precaution should be taken during treatment of children and elderly patients. No data are available regarding dosage recommendation in these special patient categories.

Geriatric use
Children and the Elderly Because of limited experience, special precaution should be taken during treatment of children and elderly patients. No data are available regarding dosage recommendation in these special patient categories.

Contraindications
Contraindicated in pregnancy, hypersensitivity to terlipressin or any other excipients of the product.

Special Warnings and Precautions for Use
Since terlipressin has antidiuretic and pressor activity it should be used with great caution in patients with hypertension, atherosclerosis, cardiac dysrhythmias or coronary insufficiency. Constant monitoring of blood pressure, serum sodium and potassium, and fluid balance is essential when terlipressin is administered in higher doses (≥800 mcg). Special care and precautions should be taken when administering to elderly patients, pediatrics, patients with ischemia, serious hypertension, cardiac arrhythmia or asthma bronchiale.

Terlipressin is not a replacement of blood substitution in patients with blood volume deficit.

Drug Interactions
Both oxytocin and methylergometrine increases the vasoconstrictive and uterotonic effects. Terlipressin enhances the hypotensive effect of non-selective blockers in the portal vein. Parallel medications with substances lowering heart rate can result in serious bradycardia.

Pregnancy and Lactation
Terlipressin causes rise in myometrial activity (contractions of smooth muscle) and decrease in uteral blood flow. Reproduction studies in rabbits and rats with higher doses showed increased abortion rate or embryo deaths. In infants lower birth weight as well as increased anomaly rate has been found. Terlipressin is

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contraindicated in pregnancy.

The data for terlipressin distribution in breast milk is not available; however significant absorption of unchanged peptides in gastrointestinal system of children seems not to be probable. There is no definite data on terlipressin use in lactating women.

Effects on Ability to Drive and Use Machines
Not applicable

Undesirable Effects
Potentially fatal effects: myocardial infarction, cardiac failure.

The most frequent effects in the course of administration of terlipressin are: skin pallor, hypertension, accelerated defecation or abdominal colics, nausea, diarrhea, transient blanching and headache, and in less frequent cases bradycardia. Serious adverse effects are rare. Individual cases of heart attack, heart failure, dyspnoea and local necrosis at the site of injection were also reported.

Overdose
The recommended dose (2 mg/4 hours) should not be exceeded, as the risk of severe circulatory adverse effects is dose-dependent. In case of hypertension resulting from terlipressin, clonidine or other sympatholytic should be administered. In case of bradycardia, atropine should be administered.

PHARMACEUTICAL PARTICULARS

Shelf Life: Please refer carton/label.

Storage and Precautions
Store at temperature between 2°C to 8°C. Protect from Light. Do not freeze.
Keep out of reach of children.

Special Precautions for Disposal and Other Handling
Unused drug and waste should be destroyed in accordance with local requirements.

Nature and Contents of Container
Each pack of THINWES® contains Terlipressin 1 mg in 10 mL ampoule.

Marketed by:
Biocon Biologics India Limited
Biocon House, Semicon Park,
Electronics City, Phase - II,
Bengaluru - 560 100, India.

BF/LL/3990/01

® - Registered trademark

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To report adverse events and/or product complaints visit our website **www.biocon.com** or call the toll free number: **1800 102 9465** or e-mail us at **drugsafety@biocon.com.**