SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Terlipressin Acetate 0.12 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml contains 0.12 mg terlipressin acetate, corresponding to 0.1 mg terlipressin.

One ampoule or vial of 8.5 ml contains 1 mg terlipressin acetate in 8.5 ml solution for injection, corresponding to 0.85 mg terlipressin.

Excipients with known effect

Sodium acetate trihydrate: 0.27 mg/ml

Sodium chloride: 9.00 mg/ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless liquid with pH between 4.5 – 5.5 and osmolality between 270 to 330 mOsmol/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Terlipressin Acetate is indicated in the treatment of bleeding oesophageal varices.

4.2 Posology and method of administration

Posology

In acute variceal bleeding:

Adults:

Initially an i.v. injection of 2 mg Terlipressin Acetate is given every 4 hours. The treatment should be maintained until 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 1 mg i.v. every 4 hours in patients with body weight < 50 kg or if adverse effects occur.

Paediatric population:

There is no relevant use of Terlipressin Acetate in paediatric population.

Method of administration

Intravenous injection use

4.3 Contraindications

Contraindicated in pregnancy.

Hypersensitivity to terlipressin or any other excipient (see section 6.1).

4.4 Special warnings and precautions for use

Monitoring during treatment

During treatment regular monitoring of blood pressure, ECG or heart rate, oxygen saturation, serum levels of sodium and potassium, as well as fluid balance are required.

Particular care is required in the management of patients with cardiovascular or pulmonary disease since terlipressin may induce ischaemia and pulmonary vascular congestion.

Caution should also be exercised in treating patients with hypertension.

Injection site reaction

To avoid local necrosis at the injection site, the injection must be given i.v.

Septic shock

In patients with septic shock with a low cardiac output Terlipressin Acetate should not be used.

Skin necrosis

During post-marketing experience with terlipressin several cases of cutaneous ischaemia and necrosis unrelated to the injection site have been reported (see section 4.8). Patients with diabetes mellitus and obesity seem to have a greater tendency to this reaction. Therefore, caution should be exercised when administering terlipressin in these patients.

Torsade de pointes

During clinical trials and post-marketing experience, several cases of QT interval prolongation and ventricular arrhythmias including “Torsade de pointes” have been reported (see section 4.8). In most cases, patients had predisposing factors such as basal prolongation of the QT interval, electrolyte abnormalities (hypokalemia, hypomagnesemia) or medications with concomitant effect on QT prolongation.

Therefore, extreme caution should be exercised in the use of terlipressin in patients with a history of QT interval prolongation, electrolyte abnormalities, or concomitant medications that can prolong the QT interval (see section 4.5).

Children and the elderly:

Particular caution should be exercised in the treatment of children and elderly patients, as experience is limited in these groups. There is no data available regarding dosage recommendation in these special patient categories.

Sodium

This medicinal product contains 31 mg of sodium in each 8.5 ml vial/ampoule, equivalent to 1.6% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

The hypotensive effect of non-selective beta-blockers on the portal vein is increased with terlipressin. Concomitant treatment with medicinal products with a known bradycardic effect (e.g. propofol, sufentanil) may lower the heart rate and cardiac output. These effects are due to reflexogenic inhibition of cardiac activity via the vagus nerve due to the elevated blood pressure.

Terlipressin can trigger “torsade de pointes” (see sections 4.4 and 4.8). Therefore, extreme caution should be exercised in the use of terlipressin in patients with concomitant medications that can prolong the QT interval, such as class IA and III antiarrhythmics, erythromycin, certain antihistamines and tricyclic antidepressants or medications that may cause hypokalaemia or hypomagnesemia (e.g. some diuretics).

4.6 Fertility, pregnancy and lactation

Pregnancy

Treatment with Terlipressin during pregnancy is contraindicated (ref. 4.3 and 5.3).

Terlipressin has been shown to cause uterine contractions and increased intrauterine pressure in early pregnancy and may decrease uterine blood flow. Terlipressin may have harmful effects on pregnancy and foetus.

Spontaneous abortion and malformation have been shown in rabbits after treatment with Terlipressin.

Breast-feeding

It is not known whether terlipressin is excreted in human breast milk. The excretion of terlipressin in milk has not been studied in animals. A risk to the suckling child cannot be excluded. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with terlipressin should be made taking into account the benefit of breast-feeding to the child and the benefit of terlipressin therapy to the woman.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of safety profile

The most frequently reported undesirable effects in clinical trials are abdominal pain, nausea, diarrhoea, pallor, vomiting and bradycardia.

Table: Frequency of undesirable effects

SYSTEM ORGAN CLASS	**Frequency**			
	VERY COMMON >1/10	**COMMON** ≥ 1/100 to < 1/10	**UNCOMMON** ≥ 1/1000 to < 1/100	**FREQUENCY NOT KNOWN***
Metabolism and nutrition disorders		Hyponatraemia		
Nervous system		Headache		

disorders				
Cardiac disorders		Chest pain Bradycardia Tachycardia	Atrial fibrillation Myocardial infarction Torsade de pointes Cardiac failure Ventrical extrasystoles**	
Vascular disorders		Vasoconstriction Peripheral ischaemia Pallor Cyanosis	Hot flush	
Respiratory thoracic and mediastinal disorders		Pulmonary oedema Dyspnoea	Respiratory failure Respiratory distress	
Gastrointestinal disorders	Abdominal pain	Diarrhoea Nausea Vomiting	Intestinal ischaemia	
Skin and subcutaneous tissue disorders			Skin necrosis (unrelated to the site of administration)**, ***	
Pregnancy, puerperium and perinatal conditions				Uterine hypertonus
Reproductive system and breast disorders				Uterine ischemia
General disorders and administration site conditions			Injection site necrosis	

* Frequencies of these adverse events cannot be estimated from the available data

** Adverse reactions identified from post-marketing sources are presented by frequency category based on a theoretically calculated frequency if not observed in clinical trials

*** See section 4.4 for further information

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The recommended dose in the specific patient population should not be exceeded as the risk of severe circulatory adverse effects is dose-dependent.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Posterior pituitary lobe hormones (vasopressin and analogues), ATC code: H01B A04

Terlipressin (Triglycyl-Lysine-Vasopressin) is a synthetic analogue of the natural posterior pituitary hormone vasopressin.

Terlipressin is a pro-drug with partial, intrinsic activity by itself. Terlipressin is transformed into the fully active metabolite lysine-vasopressin (LVP) by enzymatic cleavage. Doses of 1 and 2 mg terlipressin acetate effectively 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 with a sustained effect throughout the treatment period of 4 to 6 hours.

5.2 Pharmacokinetic properties

The pharmacokinetics follows a two-compartment model with a rapid distribution phase.

Absorption

Terlipressin is administered by the intravenous route resulting in instant systemic exposure.

Distribution

In patients with liver cirrhosis with or without hepatorenal syndrome the mean distribution volume was reported in the range 0.2 to 0.5 l/kg in two clinical trials in Japanese and Caucasian subjects, respectively.

Biotransformation

The concentration of the active metabolite, lysine-vasopressin, starts to increase approximately 30 minutes after bolus administration of terlipressin and peak levels are reached between 60 and 120 minutes after administration of terlipressin.

Elimination

The terminal elimination half-life of terlipressin is approximately 40 minutes in patients with liver cirrhosis with and without hepatorenal syndrome and the mean clearance was reported in the range 5 to 9 ml/kg/min in two clinical trials in Japanese and Caucasian subjects, respectively.

Linearity

Terlipressin demonstrated a dose-dependent and approximate proportional increase in total exposure (AUC) after single i.v. injections to healthy subjects (n=2-14 subjects per dose group) in a dose range between 5 and 30 μg/kg.

5.3 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 SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium acetate trihydrate

Acetic acid, glacial

Sodium chloride

Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Do not store above 25°C. Store in the original packaging to protect from light.

6.5 Nature and contents of container

8.5 ml in clear glass (Type 1) ampoules in packs of 1 or 5 ampoules.

8.5 ml in clear glass (Type 1) vials with bromobutyl rubber stoppers and crimped with aluminium seals with white flip-off caps in pack sizes of 1 or 5 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Farmak Pharmaceuticals UK Ltd

First Floor, 47 Queen Street

Hull

HU1 1UU

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 59209/0018

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/05/2026

10 DATE OF REVISION OF THE TEXT

01/05/2026