SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Terlipressin Acetate AFT 0.12 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial contains 1 mg terlipressin acetate in 8.5 ml solution for injection, corresponding to 0.85 mg terlipressin. Each ml contains 0.12 mg terlipressin acetate, corresponding to 0.1 mg terlipressin.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Terlipressin Acetate AFT 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 AFT in paediatric population.

Method of administration

Intravenous injection use

4.3 Contraindications

Contraindicated in pregnancy.

Hypersensitivity to terlipressin acetate or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

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

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

Caution should be exercised in treating patients with hypertension or recognised heart disease.

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

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.

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 Acetate AFT 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 Acetate AFT 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

Frequency of undesirable effects

System organ class	**Frequency**		
	Common ≥1/100 to <1/10	**Uncommon ≥ 1/1,000 to < 1/100**	**Rare ≥1/10,000 to ≤1/1,000**

System organ class	Frequency		
	Common ≥1/100 to <1/10	**Uncommon ≥ 1/1,000 to < 1/100**	**Rare ≥1/10,000 to ≤1/1,000**
Metabolism and nutrition disorders		Hyponatraemia if fluid not monitored	
Nervous system Disorders	Headache		
Cardiac disorders	Bradycardia	Atrial fibrillation Ventrical extrasystoles Tachycardia Chest pain Myocardial infarction Fluid overload with pulmonary oedema Torsade de pointes Cardiac failure	
Vascular disorders	Peripheral vasoconstriction Peripheral ischaemia Facial pallor Hypertension	Intestinal ischaemia Peripheral cyanosis Hot flushes	
Respiratory thoracic and mediastinal disorders		Respiratory distress Respiratory failure	Dyspnoea
Gastrointestinal disorders	Transient abdominal cramps Transient diarrhoea	Transient nausea Transient vomiting	
Skin and subcutaneous tissue disorders		Skin necrosis	
Pregnancy, puerperium and perinatal conditions		Uterine hypertonus Uterine ischemia	
General disorders and administration site disorders		Injection site necrosis	

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 the 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 (2 mg/4 hours) 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) (H 01 BA 04)

Terlipressin Acetate AFT may be regarded as a circulating depot of lysine vasopressin. Following intravenous injection, three glycyl moieties are enzymatically cleaved from the N-terminus to release lysine vasopressin.

The slowly released vasopressin reduces blood flow in the splanchnic circulation in a prolonged manner, thereby helping to control bleeding from ruptured oesophageal varices.

5.2 Pharmacokinetic properties

Terlipressin is administered by bolus intravenous injection. It shows a biphasic plasma level curve which indicates that a two-compartment model can be applied.

The half-life of distribution ($T_{1/2\alpha}$) is about 8 -10 minutes.

The half-life of elimination ($T_{1/2\beta}$) is about 50 -70 minutes.

Lysine vasopressin reaches maximum plasma levels about 1-2 hours following intravenous administration and has a duration of activity of 4-6 hours.

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 chloride

Sodium acetate

Acetic acid

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

36 months

6.4 Special precautions for storage

Store in a refrigerator (2-8 °C).

6.5 Nature and contents of container

Terlipressin Acetate AFT solution for injection is packed in a 10 mL borosilicate clear glass vial type I with a rubber stopper and aluminium-plastic overseal.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

AFT Pharma UK Limited
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United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 57592/0008

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/09/2024

10 DATE OF REVISION OF THE TEXT

21/11/2024