

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Pitressin 20 PU/ml Solution for Injection

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml contains 0.4 mg of synthetic vasopressin (50 pressor unit per mg) which is equivalent to argipressin 20 pressor units.

For the full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Solution for injection.

A clear, sterile, colourless solution.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

For use in diabetes insipidus, when this is not of nephrogenic origin and control of bleeding from oesophageal varices.

### 4.2 Posology and method of administration

#### Posology

##### Adults

##### Diabetes Insipidus:

A dose of 0.25ml to 1ml (5 to 20 units) by subcutaneous or intramuscular injection every four hours.

##### Oesophageal Varices:

For the initial control of variceal bleeding Pitressin should be given intravenously. Pitressin, 20 units diluted in 100ml dextrose 5% w/v may be infused over a 15 minute period.

##### Elderly (over 65 years):

As for adults, no clinical or pharmacokinetic data specific to this age group are available. However, the drug has been used successfully at normal dosage in the elderly.

##### Patients with renal impairment:

Pitressin should not be used in patients with chronic nephritis with nitrogen retention (see Section 4.3).

##### Paediatric population:

Not recommended in children below 18 years.

#### Method of administration

Subcutaneous, intravenous or intramuscular injection.

### 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Anaphylaxis to the active substance or to any of the excipients listed in section 6.1.

Patient with coronary artery disease, or those intended to receive halogenated anaesthetic agents.

Chronic nephritis with nitrogen retention contra-indicates the use of Pitressin until reasonable blood urea nitrogen levels have been attained.

Vascular disease (especially disease of coronary arteries).

#### **4.4 Special warnings and precautions for use**

This drug should not be used in patients with systemic hypertension or vascular disease, especially disease of the coronary arteries, except with extreme caution. In such patients, even small doses may precipitate pain and with larger doses, the possibility of myocardial infarction should be considered. If this drug must be used in patients with peripheral vascular disease then the skin should be observed carefully for signs of ischaemia.

Pitressin may produce water intoxication. The early signs of drowsiness, listlessness, and headaches should be recognized to prevent terminal coma and convulsions.

Adjustment of dosage in cases immediately post-hypophysectomy should be controlled on the basis of measurements of urine osmolality.

Pitressin should be used cautiously in the presence of epilepsy, migraine, asthma, heart failure, or any state in which a rapid addition to extracellular water may produce hazard for an already overburdened system.

Regular monitoring of blood urea nitrogen (BUN) levels is required in patients with chronic nephritis to ensure an adequate level is maintained (see section 4.3).

#### **4.5 Interaction with other medicinal products and other forms of interaction**

The following drugs may enhance the antidiuretic effect of pitressin when used concurrently: carbamazepine, chlorpropamide, clofibrate, fludrocortisone, urea or tricyclic antidepressants.

The following drug may decrease the antidiuretic effect of pitressin when given concurrently: demeclocycline, noradrenaline, lithium, heparin and alcohol.

Ganglion blocking agents may increase sensitivity to the pressor effect of pitressin.

#### **4.6 Fertility, pregnancy and lactation**

##### Pregnancy

No animal reproduction studies on Pitressin are available. Oxytocic effects in the third trimester have been reported. However, Pitressin has been used successfully during pregnancy for the treatment of diabetes insipidus with no adverse effects on the foetus being reported. Nevertheless, as with all medicines, use during pregnancy should be avoided if possible and the potential benefit to the patient weighed against any possible risk to the foetus.

##### Breast-feeding

Pitressin has been administered to breast feeding women without apparent adverse effect on the infant.

#### **4.7 Effects on ability to drive and use machines**

Pitressin has moderate influence on the ability to drive and use machines and may cause vertigo (see section 4.8).

#### **4.8 Undesirable effects**

The following undesirable effects have been observed and reported during treatment with Pitressin with the following frequencies:

Not known –cannot be estimated from the available data.

**Immune system disorders:**

- hypersensitivity
- Anaphylaxis

**Metabolism and nutrition disorder:**

- Hyperhydration/ Water intoxication

**Nervous system disorders:**

- headache
- vertigo
- tremor

**Cardiac disorder:**

- Chest pain due to angina
- Cardiac arrest

**Vascular disorders:**

- Pallor
- peripheral ischaemia
- Hypertension

**Respiratory, thoracic and mediastinal disorders:**

- bronchospasm

**Gastrointestinal disorders:**

- flatulence
- nausea
- vomiting
- diarrhoea
- abdominal pain

**Skin and subcutaneous tissue disorders:**

- hyperhidrosis
- gangrene
- urticaria

**Renal and urinary disorders:**

- fluid retention

**General disorders and administration site conditions:**

- Non-cardiac chest pain

### 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: [www.hpra.ie](http://www.hpra.ie); e-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

## **4.9 Overdose**

If water intoxication occurs, no fluids should be given. In severe cases, small amounts of hypertonic saline may be administered. Urea and mannitol infusions may be helpful in cases of cerebral oedema. If a patient should experience anginal pain after administration of Pitressin, amyl nitrate by inhalation, or glyceryl trinitrate sublingually, may be given.

## **5 PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Vasopressin and analogues  
ATC code: H01BA01

#### Mechanism of action

The antidiuretic action of Pitressin is ascribed to increase in reabsorption of water by the renal tubules. Pitressin can cause contraction of smooth muscle of the gastrointestinal tract, gall bladder, urinary bladder and all parts of the vascular bed, especially the capillaries, small arterioles and venules with less effect on the smooth musculature of the large veins. The direct effect on the contractile elements is neither antagonized by adrenergic blocking agents nor prevented by vascular denervation.

### **5.2 Pharmacokinetic properties**

#### Absorption

Following subcutaneous or intramuscular administration of Pitressin injection, the duration of antidiuretic activity is variable, but effects are usually maintained for 2-8 hours.

#### Biotransformation

The majority of a dose of Pitressin is metabolized and rapidly destroyed in the liver and kidneys. Pitressin has a plasma half-life of about 10 to 20 minutes.

#### Elimination

Approximately 5% of a subcutaneous dose of Pitressin is excreted unchanged in the urine four hours after dosing.

### **5.3 Preclinical safety data**

Pre-clinical safety data does not add anything of further significance to the prescriber.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Glacial Acetic Acid and Water for Injection.

### **6.2 Incompatibilities**

Not applicable.

### 6.3 Shelf life

2 years.  
Once opened, use immediately.

### 6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.

Store in the original package in order to protect from light.

### 6.5 Nature and contents of container

White neutral glass ampoules with two **orange** break bands. Available in packs of 10 x 1 ml ampoules. Glass ampoule Type I Ph. Eur. (ampoule 1cc oil break type I straight stem flint).

### 6.6 Special precautions for disposal and other handling

Single use only. Discard any remaining contents after use. Any unused medicinal product or waste material should be disposed of in accordance with local requirements

## 7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals Ltd  
Capital House  
85 King William Street  
London EC4N 7BL  
United Kingdom

## 8 MARKETING AUTHORISATION NUMBER

PA0899/001/001

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first Authorisation: 1<sup>st</sup> April 1979

Date of last renewal: 1<sup>st</sup> April 2009

## 10 DATE OF REVISION OF THE TEXT

October 2016