SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Argipressin AOP 20 I.U. / ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

20 I.U. / ml
One ampoule Argipressin AOP 20 I.U. / ml contains 1 ml of solution for injection equivalent to 20 International Units (I.U.) of argipressin (as argipressin acetate)

Excipient(s) with known effect: Contains less than 1mmol sodium (23 mg) per ml.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution and free from visible particles, with a pH of 3.3 - 4.5 and an osmolality of 200 – 400 mOsm/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Argipressin AOP is indicated in adults for the treatment of 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 Argipressin AOP should be given intravenously. Argipressin AOP 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 successfully used at normal dosage in the elderly.

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.

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

Vascular disease (especially disease of coronary arteries), chronic nephritis (until reasonable blood nitrogen concentrations attained).

4.4 Special warnings and precautions for use

Argipressin 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.

Argipressin may produce water intoxication. The early signs of drowsiness, listlessness, and headaches should be recognised 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.

Argipressin 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.

Chronic nephritis with nitrogen retention contraindicates the use of argipressin injection until reasonable nitrogen blood levels have been attained.

4.5 Interaction with other medicinal products and other forms of interaction

The following drugs may potentiate the antidiuretic effect of argipressin when used concurrently: carbamazepine, chlorpropamine, clofibrate, fludrocortisone, urea or tricyclic antidepressants.

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

Ganglion blocking agents may produce a marked increase in sensitivity to the pressor effect of argipressin.

4.6 Fertility, Pregnancy and lactation

Fertility

Effects of vasopressin on fertility are unknown.

Pregnancy

No animal reproduction studies have been performed with argipressin. Oxytocic effect in third trimester has been reported. However, argipressin has been used successfully during pregnancy for the treatment of diabetes insipidus with no adverse effects on the fetus 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 fetus.

Breastfeeding

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

4.7 Effects on ability to drive and use machines

Argipressin AOP 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 Argipressin with the following frequency:

The undesirable effects are listed below by organ class and the following frequency convention:

Very common: (≥1/10)

Common: (≥1/100, <1/10)

Uncommon: (≥1/1,000, <1/100)

Rare: ((≥1/10,000, <1/1,000)

Very rare: (<1/10,000),

Not known – frequency cannot be estimated from the available data.

The frequency of the following side effects is not known.

Immune system disorders

- Hypersensitivity
- anaphylaxis

Metabolism and nutrition disorders

- hyperhydration / water intoxication

Nervous system disorders

- headache
- vertigo
- tremor

Cardiac disorder

- chest pain due to angina
- cardiac arrest

Vascular disorders

- peripheral ischaemia
- pallor
- hypertension

Respiratory, thoracic and mediastinal disorders

- bronchospasm

Gastrointestinal disorders

- flatulence
- nausea
- vomiting
- diarrhoea
- abdominal pain

Skin and subcutaneous tissue disorders

- gangrene
- hyperhidrosis
- 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 the yellow card scheme at www.yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 Argipressin AOP, amyl nitrite by inhalation or glyceryl trinitrate sublingually, may be given.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vasopressin and analogues ATC code: H01BA06

The antidiuretic action of argipressin is ascribed to increase in reabsorption of water by the renal tubules. Argipressin 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 antagonised by adrenergic blocking agents nor prevented by vascular denervation.

5.2 Pharmacokinetic properties

Following subcutaneous or intramuscular administration of argipressin injection, the duration of antidiuretic activity is variable, but effects are usually maintained for 2-8 hours. The majority of the dose of argipressin is metabolised and rapidly destroyed in the liver and kidneys. Argipressin has a plasma half-life of about 10 to 20 minutes.
Approximately 5% of a subcutaneous dose of argipressin is excreted unchanged in the urine four hours after dosing.

5.3 Preclinical safety data

Preclinical safety data does not add anything of further significance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, Glacial acetic acid (for pH adjustment), water for injections.

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.
Diluted solutions should be used immediately.

6.4 Special precautions for storage

Store refrigerated (2°C – 8°C). Do not freeze.

6.5 Nature and contents of container

1 mL clear glass ampoules (Type I) containing 1 ml solution for injection.

Pack size: 5, 10, 50 ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Single use ampoules, discard any remaining solution.
The solution should be checked for visible particles and discolouration prior to the use. Only clear and colourless solutions should be used.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7 MARKETING AUTHORISATION HOLDER

AOP Orphan Pharmaceuticals GmbH
Leopold-Ungar-Platz 2
1190 Vienna
Austria

8 MARKETING AUTHORISATION NUMBER(S)

PL 21344/0024

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

08/01/2019

10 DATE OF REVISION OF THE TEXT

20/04/2022