

## **PACKAGE LEAFLET: INFORMATION FOR THE USER**

### **Variquel 1 mg powder and solvent for solution for injection** Terlipressin acetate

#### **Read all of this leaflet carefully before you start using this medicine.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

#### **In this leaflet:**

1. What Variquel is and what it is used for
2. Before you use Variquel
3. How to use Variquel
4. Possible side effects
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### **1. WHAT VARIQUEL IS AND WHAT IT IS USED FOR**

Variquel is a synthetic pituitary hormone.

Variquel is used for treatment of bleeding from dilated veins in the food pipe leading to your stomach (bleeding oesophageal varices).

### **2. BEFORE YOU USE VARIQUEL**

#### **Do not use Variquel**

- if you are hypersensitive (allergic) to terlipressin or any of the other ingredients of Variquel.

#### **Take special care with Variquel**

This medicine is administered to you if you have severe or life-threatening bleeding in your food pipe (oesophagus). It is used under continuous monitoring of your heart and blood circulation. If you are able to then tell your doctor if you suffer from the conditions shown below:

- if you are suffering from a severe infection known as septic shock.
- if you suffer from bronchial asthma or other conditions that affect your breathing
- if you suffer from uncontrolled high blood pressure, insufficient blood circulation in the heart vessels (e.g. angina), have previously had a heart attack (myocardial infarction), or you have hardening of your arteries (arteriosclerosis)
- if you suffer from irregular heart beats (cardiac arrhythmias)
- if you have poor blood circulation to your brain (e.g. you have had a stroke) or to your limbs (peripheral vascular disease)
- if you suffer from impaired kidney function (renal insufficiency)
- if you suffer from disturbances in the level of salt (electrolytes) in your blood
- if you are suffering from reduced amount of fluid in your circulation or have already lost a large amount of blood
- if you are pregnant.

### **Using other medicines**

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without prescription.

Please inform your doctor immediately if you use the following medicines

- drugs that have an effect on your heart rate (e.g. beta-blockers or propofol)
- drugs that can trigger irregular beating of the heart (arrhythmia) such as the following:
  - anti-arrhythmic drugs known as Class IA (quinidine, procainamide, disopyramide) and Class III (amiodarone, sotalol, ibutilide, dofetilide)
  - an antibiotic called erythromycin
  - antihistamines (mainly used to treat allergies but also found in certain cough and cold remedies)
  - a type of medicine used to treat depression called tricyclic antidepressants
  - medicines that may alter the level of salt or electrolytes in your blood, particularly diuretics (used to treat high blood pressure and heart failure).

### **Using Variquel with food and drink**

There are no limitations.

### **Pregnancy and Breast-feeding**

Ask your doctor or pharmacist for advice before taking any medicine.

Variquel should only be used during pregnancy if it is vital to treat your condition.

It is not known if Variquel is present in breast milk, therefore it is not known if there may be an effect on your baby. You should discuss the potential risk to your baby with your doctor.

### **Driving and using machines**

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

### **Important information about some ingredients of Variquel**

After reconstitution with the accompanying solvent, this medicinal product contains less than 1 mmol (23 mg) of sodium per 5 ml, i.e. essentially "sodium-free".

## **3. HOW TO USE VARIQUEL**

This medicine is not to be used by yourself but will always be administered to you by your doctor. Please ask your doctor for further information regarding its use.

#### Adults

Initially 1-2 mg terlipressin acetate equivalent to 1-2 vials of Variquel are administered. Your dose will depend on your body weight.

After the initial injection, your dose may be reduced to 1 mg every 4 to 6 hours.

The maximum dose you can receive each day is approximately 120 micrograms/kg body weight.

#### Elderly

If you are over 70 years of age speak with your doctor before you receive Variquel.

#### Children and adolescents

Variquel is not recommended for use in children and adolescents due to insufficient experience.

#### Method and route of administration

The powder should be dissolved in the accompanying solvent and is slowly injected intravenously.

#### Duration of treatment

The use is limited to 2 – 3 days, depending on the course of your condition.

### **If you use more Variquel than you should**

You must not use more Variquel than the recommended dose. If you are given too much then you may have a rapid increase in your blood pressure, especially if you already suffer with high blood pressure. If this happens then you need another medicine called an alpha blocker (e.g. clonidine) to control your blood pressure.

You may also experience a low heart rate. This can be treated with a medicine called atropine.

### **If you forget to use Variquel**

You will be given Variquel in hospital under the supervision of your doctor.

### **If you stop using Variquel**

If you have any further questions on the use of this product, ask your doctor, pharmacist or nurse.

## **4. POSSIBLE SIDE EFFECTS**

Like all medicines, Variquel can cause side effects, although not everybody gets them.

The assessment of side effects is based on the following frequencies:

<b>very common:</b>	more than 1 of 10 treated
<b>common:</b>	1 to 10 of 100 treated
<b>uncommon:</b>	1 to 10 of 1,000 treated
<b>rare:</b>	1 to 10 of 10,000 treated
<b>very rare:</b>	less than 1 of 10,000 treated
<b>not known:</b>	cannot be estimated from the available data

### **Important side effects or signs you should pay attention to, and measures to be taken if you are affected:**

In very rare cases severe side effects are possible when you are given Variquel. If you are affected by one of the following side effects, please tell your doctor immediately if you are able to. Your doctor should not give any more Variquel to you.

Severe shortness of breath due to an asthma attack, severe difficulty with or stopping breathing, severe pain in the chest (angina), severe and persistent irregular heart beats, locally dead skin (necrosis), convulsions (seizure), kidney failure.

### **Other possible side effects:**

#### Metabolism and nutrition disorders

Uncommon: too little sodium in the blood (hyponatraemia)

Very rare: too much sugar in the blood (hyperglycaemia)

#### Nervous system disorders

Common: headache

Uncommon: triggering of a fit

Very rare: stroke

#### Cardiac disorders

Common: irregular heart beats, too slow heart rate, signs of insufficient blood circulation in the heart vessels in the ECG

Uncommon: chest pain due to insufficient blood circulation in the heart vessels (angina pectoris), rapid increase in blood pressure, irregular heart rate, too fast heart rate (palpitations), chest pain, heart attack, excess fluid on the lungs

Very rare: severe angina

Not known: heart failure

#### Vascular disorders

Common: high blood pressure, low blood pressure, insufficient blood circulation in arms, legs and skin, paleness of face

Uncommon: insufficient blood flow to the intestines, bluish colouration of the skin or lips, hot flushes

#### Respiratory, thoracic and mediastinal disorders

Uncommon: pain in the chest, shortness of breath due to spasm in the bronchial muscles, severe difficulty with or stopping breathing

Rare: shortness of breath

#### Gastrointestinal disorders

Common: temporary abdominal cramps, temporary diarrhoea

Uncommon: temporary nausea, temporary vomiting

#### Skin and subcutaneous tissue disorders

Common: pale skin

Uncommon: inflammation of the lymph vessels

Not known: dead skin (necrosis) not related to the injection site

#### Reproductive system and breast disorders

Common: abdominal cramps (in women)

#### Pregnancy and postnatal conditions

Not known: uterine cramps, decreased blood flow to the uterus

#### General disorders and administration site conditions

Uncommon: locally dead skin (necrosis)

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

### **5. HOW TO STORE VARIQUEL**

Keep out of the reach and sight of children.

Do not store above 25°C.

Keep the vial in the outer carton in order to protect from light.

The reconstituted Variquel-solution has to be used immediately.

Do not use Variquel after the expiry date which is stated on the carton and the vial after 'EXP'. The expiry date refers to the last date of that month.

Do not use Variquel if you notice

- that the powder does not dissolve in the accompanying solvent
- that the solution discolours after dissolving the powder.

## 6. FURTHER INFORMATION

### What Variquel contains

- The active substance is terlipressin acetate.  
Each vial of powder contains: 1 mg terlipressin acetate equivalent to 0.85 mg terlipressin.  
1 ml of reconstituted solution contains 0.2 mg terlipressin acetate.
- The other ingredients are:  
The powder contains mannitol, acetic acid (for pH adjustments).  
The solvent contains sodium chloride, water for injections.

### What Variquel looks like and contents of the pack

This medicine is presented as a powder and solvent for solution for injection (a powder which is made into a solution and then given as an injection). It is supplied in clear glass vials containing a white to off-white solid powder together with a clear glass ampoule containing solvent. The powder must be dissolved in the solvent prior to use.

Each vial contains 11 mg of powder  
Each ampoule contains 5 ml of solvent

This medicine is available in pack sizes of:  
1 vial with powder and 1 ampoule of solvent  
5 vials with powder and 5 ampoules of solvent  
Not all pack sizes may be marketed.

### Marketing Authorisation Holder and Manufacturer

#### Marketing authorisation holder

IS Pharmaceuticals Limited  
Office Village, Chester Business Park  
Chester  
CH4 9QZ  
United Kingdom

#### Manufacturer:

BAG Health Care GmbH, Amtsgerichtsstrasse 1-5, D-35423 Lich, Germany

### **This medicinal product is authorised in the Member States of the EEA under the following names:**

Belgium:	Variquel 1 mg
Denmark:	Variquel 1 mg
Finland:	Stemflova 1 mg
France:	Haemopressin 1 mg, poudre et solvant pour solution injectable
Germany:	Haemopressin 1 mg
Greece:	Haemopressin 1 mg
Ireland:	Haemopressin 1 mg
Italy:	Variquel 1 mg
Luxembourg:	Variquel 1 mg
Netherlands:	Haemopressin 1 mg
Norway:	Stemflova 1 mg
Portugal:	Variquel 1 mg

Spain: Variquel 1 mg  
Sweden: Variquel 1 mg  
United Kingdom: Variquel 1 mg

**This leaflet was last approved in 08/2010.**

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**The following information is intended for medical or healthcare professionals only**

Posology

Initially 1-2 mg terlipressin acetate (equivalent to 1-2 vials of Variquel) are administered.

Depending on the patient's body weight the dose can be adjusted as follows:

- Weight less than 50 kg: 1 mg.
- Weight 50 kg to 70 kg: 1.5 mg.
- Weight exceeding 70 kg: 2 mg.

After the initial injection, the dose can be reduced to 1 mg every 4 to 6 hours.

The approximate value for the maximum daily dose of Variquel is 120 micrograms/kg body weight.

The therapy is to be limited to 2 – 3 days in adaptation to the course of the disease.

Variquel is injected intravenously and should be given over a period of one minute.

Variquel should only be used with caution in patients over 70 years, and patients with chronic renal failure.

Variquel is not recommended in children and adolescents due to insufficient experience on safety and efficacy.

A dose adjustment is not required in patients with liver failure.

**Preparation of the injection:**

Reconstitute the powder only with the solvent provided. The entire contents of the solvent ampoule should be slowly added to the powder vial and the vial rolled gently until the powder is completely dissolved. The powder should dissolve within 10 seconds. A clear colourless solution results.

A further dilution to 10 ml with sterile sodium chloride 9 mg/ml (0.9%) solution for injection is possible.

The solution should be inspected visually for particles and discolouration prior to administration.

Do not use Variquel if you notice

- that the powder does not dissolve in the accompanying solvent
- that the solution discolours after dissolving the powder.

Do not store the medicinal product above 25°C.

Keep the vial in the outer carton to protect from light.

After reconstitution the solution should be used immediately.

For single use only. Discard any unused solution.