

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 because it contains important information for you.

- 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What Variquel is and what it is used for
2. What you need to know before you use Variquel
3. How to use Variquel
4. Possible side effects
5. How to store Variquel
6. Contents of the pack and other information

1. What Variquel is and what it is used for

Variquel is a synthetic pituitary hormone.

Variquel is used for the treatment of:

- bleeding from dilated (widening) veins in the food pipe leading to your stomach (bleeding oesophageal varices).

2. What you need to know before you use Variquel**You should NOT be given Variquel if you:**

- are hypersensitive (allergic) to terlipressin or any of the other ingredients of Variquel (see section 6).

Warnings and precautions

This medicine is administered to you if you have:

- severe or life-threatening bleeding in your food pipe (oesophagus).

It is given under continuous monitoring of your heart and blood circulation.

If you are able, please tell the doctor if you have any of 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
- if you are over the age of 70 years.

Other medicines and Variquel

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 take any of the following medicines

- drugs that have an effect on your heart rate (e.g. beta-blockers, sufentanil 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).

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.

Variquel contains sodium

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 slowly injected intravenously.

Duration of treatment

The use of this medicine 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 a doctor.

If you stop using Variquel

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

4. Possible side effects

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

Important side effects which need immediate attention:

In very rare cases, there may be severe side effects 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.

Frequency of possible side effects:

Common (affects less than 1 in 10 people):

Heart and circulation

- very slow heart rate
- signs of insufficient blood circulation in the heart vessels in the ECG
- high or low blood pressure
- insufficient blood circulation in arms, legs and skin
- paleness of face
- pale skin

General

- headache

Stomach and gut

- temporary abdominal cramps
- temporary diarrhoea
- abdominal cramps (in women)

Uncommon (affects less than 1 in 100 people):

Mind and nervous system

- triggering of a fit

Heart and circulation

- chest pain
- rapid increase in blood pressure
- heart attack
- irregular heart rate
- too fast heart rate (palpitations)
- bluish colouration of the skin or lips
- hot flushes
- heart failure (Torsade de Pointes)

Lungs and breathing

- excess fluid on the lungs
- shortness of breath due to spasm in the bronchial muscles
- severe difficulty with or stopping breathing

Stomach and gut

- temporary nausea
- temporary vomiting

General

- inflammation of the lymph vessels
- reduced blood supply to the intestinal system
- uterine cramps
- decreased blood flow to the uterus
- dead skin (necrosis) not related to the injection site

Results of blood tests

- too little sodium in the blood (hyponatraemia) if not monitored

Rare (affects less than 1 in 1000 people):

Lungs and breathing

- shortness of breath

Very rare (affects less than 1 in 10,000 people):

Heart and circulation

- stroke
- severe angina

Results of blood tests

- too much sugar in the blood (hyperglycaemia)

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme at

www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

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. Contents of the pack and other 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

Alliance Pharmaceuticals Limited
Avonbridge House, Bath Road
Chippenham
Wiltshire
SN15 2BB
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 revised in 06/2017.

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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.