

**Rivotril® 1 mg/ml**

Roche

Concentrate for solution for injection or infusion

Clonazepam

**Please read all of this leaflet carefully before you start taking this medicine.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If any of the side effects become serious or troublesome, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

**In this leaflet:**

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**1. What Rivotril is and what it is used for**

Rivotril 1 mg/ml sterile concentrate contains a medicine called clonazepam. This belongs to a group of medicines called 'benzodiazepines'.

- Rivotril sterile concentrate is used to treat severe epilepsy (status epilepticus) in infants, children and adults.
- It lowers the number and length of fits (seizures) that you have.

**2. Before you are given Rivotril****You must not be given Rivotril if you are allergic (hypersensitive) to:**

- Clonazepam or any of the other ingredients of Rivotril (listed in Section 6: Further information).
- Other 'benzodiazepine' medicines. These include diazepam, flurazepam and temazepam.

You must not be given Rivotril if any of the above apply to you. If you are not sure, talk to your doctor or nurse before having Rivotril.

**Rivotril must not be given if:**

- You have breathing problems or lung disease.
- You have severe liver problems.
- You have a condition called 'myasthenia gravis' (where your muscles become weak and get tired easily).
- You have a condition called 'sleep apnoea syndrome' (where your breathing stops when you are asleep).
- The patient is a premature or newborn baby (less than 1 month old).
- You have problems with alcohol or drug (prescription or recreational) use.

Rivotril must not be given if any of the above apply to you. If you are not sure, talk to your doctor or nurse before having Rivotril.

**Take special care with Rivotril**

A small number of people being treated with anti-epileptics such as clonazepam have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.

Check with your doctor or nurse before having Rivotril if:

- You have liver, kidney or lung problems.
- You have ever had depression.

- You have ever tried to kill yourself.
- A close friend or relative has recently died.
- You regularly drink alcohol or take recreational drugs or you have had problems with alcohol or drug use in the past.
- You have spinal or cerebellar ataxia (where you may become shaky and unsteady, have slurred speech or rapid eye movements).
- You have a rare, inherited blood problem called 'porphyria'.
- You are elderly or debilitated (weak); your doctor may adjust your dose.

If any of the above apply to you, or if you are not sure, talk to your doctor or nurse before you are given Rivotril.

### **Taking other medicines**

Please tell your doctor or nurse if you are taking or have recently taken any other medicines. This includes medicines that you buy without a prescription and herbal medicines. This is because Rivotril can affect the way some other medicines work. Also some other medicines can affect the way Rivotril works.

In particular, tell your doctor or nurse if you are taking any of the following medicines:

- Other medicines to treat epilepsy, such as carbamazepine, hydantoins, phenobarbital, phenytoin, primidone or sodium valproate.
- Cimetidine (used to treat stomach problems and heartburn).
- Rifampicin (an antibiotic used to treat infections).
- Medicines used to make you sleep (hypnotics).
- Medicines that help with anxiety (tranquillisers).
- Pain-killers (analgesics) and medicines to relax your muscles (muscle relaxants).

### **Operations**

If you are going to have an anaesthetic for an operation or for dental treatment, it is important to tell your doctor or dentist that you are being given Rivotril.

### **Taking Rivotril with Alcohol**

Do not drink alcohol while you are being given Rivotril. This is because it may cause side effects or cause your fits to return.

### **Pregnancy and breast-feeding**

You must not take Rivotril if you are pregnant, might become pregnant or are breast-feeding, unless your doctor tells you to. Rivotril is known to have harmful effects on the unborn child.

### **Driving and using machines**

Talk to your doctor about driving and using machines or tools, whilst you are having Rivotril. This is because it can slow down your reactions. If you are in any doubt about whether you can do a particular activity, talk to your doctor.

### **Dependence**

When taking this medicine there is a risk of dependence which increases with the dose and duration of treatment and also in patients with a history of alcohol and/or drug abuse.

### **Important information about some of the ingredients of Rivotril**

Rivotril sterile concentrate contains 20% v/v of ethanol. Each ampoule contains up to 0.16 g of alcohol. If you suffer from liver disease, alcoholism, brain injury or disease, or are pregnant, Rivotril sterile concentrate may be harmful.

Rivotril sterile concentrate contains benzyl alcohol. Each ampoule contains 30 mg of benzyl alcohol, which may cause toxic reactions and allergic reactions in infants and children up to 3 years old.

If you are in any doubt about whether you should have this medicine, talk to your doctor.

### 3. How Rivotril will be given

Rivotril will be given to you by a doctor or nurse in one of two ways.

- Slow injection into one of your veins. This may take between 2 and 4 minutes.
- Through a small tube into one of your veins (called an 'intravenous infusion').

The dose of Rivotril varies from one patient to another. It depends on your age and how well you respond to the medicine. The doctor will work out how much to give you. The dose you are given should be less than 20 mg.

#### **If you are given more Rivotril than you should**

Because Rivotril is given by a doctor or nurse, it is unlikely that you or your child will be given too much or that you or your child will miss a dose. However, if you are worried talk to your doctor or nurse.

#### **Stopping Rivotril**

If you receive long term treatment with Rivotril (are given the medicine for a long time) you may become dependent upon this medicine and get withdrawal symptoms (see Section 4).

- Treatment with Rivotril must not be stopped suddenly. If this happens, your fits may return and you may get withdrawal symptoms (see Section 4: Possible side effects).
- If the dose of Rivotril you are being given has to be reduced, or stopped, this must be done gradually. Your doctor will explain how this will be done.

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

### 4. Possible side effects

Like all medicines Rivotril can cause side effects, although not everybody will get them.

#### **Important side effects to look out for:**

##### **Allergic reactions**

If you get an allergic reaction, **see a doctor straight away.**

The signs may include:

- Sudden swelling of the throat, face, lips and mouth. This may make it difficult to breathe or swallow.
- Sudden swelling of the hands, feet and ankles.
- Skin rash or itching.

##### **Effects on the heart**

If you notice any of the following effects, **see a doctor straight away.**

The signs may include:

- Breathlessness, swelling of the ankles, cough, tiredness and a racing heart.
- Chest pain which may spread to your neck and shoulders and down your left arm.

##### **Effects on behaviour**

If you notice any of the following effects, **talk to your doctor** as they may want you to stop taking Rivotril.

The signs may include:

- Being aggressive, excited, irritable, nervous, agitated, hostile or anxious.
- Problems sleeping, nightmares and vivid dreams.
- Mental problems such as seeing or hearing things that are not really there (hallucinations), delusions (believing in things that are not real) and problems with your speech.
- Types of fits (seizures) that you have not had before.

##### **Infants and children**

- If an infant or small child is being given Rivotril, watch them carefully. This is because they could develop breathing problems, coughing or choking. This can be caused by too much saliva being made.
- Early puberty in children. This is reversible after stopping treatment with Rivotril.

### **Elderly patients**

Older patients taking benzodiazepine medicines have a higher risk of falling and breaking bones.

### **Other possible side effects**

**When you start being given Rivotril** you may notice the following effects:

- Feeling drowsy and tired.
- Feeling dizzy and light-headed.
- Weak or floppy muscles or jerky movements (poor co-ordination).
- Feeling unsteady when walking.

If you notice any of these effects, talk to your doctor. Your doctor may be able to help you by giving you a lower dose of Rivotril and then increasing it slowly.

### **The following may occur at any time during your treatment**

#### **Injection site**

- Pain and inflammation of the vein into which Rivotril was given, which may lead to blood clots.

#### **Mind and nervous system**

- Poor concentration, confusion and a feeling of being lost (disorientation).
- Feeling restless.
- Difficulty remembering new things.
- Headache.
- Depression.
- Slowing or slurring of speech.
- Poor co-ordination, including feeling unsteady when walking.
- An increase in how often you have fits.

#### **Liver, kidney and blood**

- Changes in how well your liver is working (shown by blood tests).
- Loss of bladder control.
- Blood problems. The signs include feeling tired, bruising easily, being short of breath and nose bleeds. Your doctor may want you to have blood tests from time to time.

#### **Stomach and gut**

- Feeling sick (nausea).
- Stomach upset.

#### **Eyes**

- Double vision.
- Jerky movements of the eyes (nystagmus).

#### **Breathing**

- Breathing problems (respiratory depression). Early signs include suddenly noisy, difficult and uneven breathing. Your skin may become blue.

#### **Skin and hair**

- Skin rashes, hives (lumpy rash) and itchy skin.
- Changes to the colour of your skin.
- Hair loss (the hair usually grows back).

## **Sexual**

- Loss of sex drive.
- Difficulty getting or keeping an erection (erectile dysfunction).

## **Withdrawal symptoms**

Using benzodiazepines like Rivotril may make you dependent on the medicine. This means that if treatment is stopped quickly, or the dose reduces too quickly, you may get withdrawal symptoms. The symptoms can include:

- Problems sleeping.
- Muscle pain, shaking (tremor) and feeling restless.
- Feeling very anxious, tense, confused, irritable or agitated, or changes in your mood.
- Increased sweating.
- Headache.

Less common withdrawal symptoms include:

- Feeling sensitive to light, noise and physical contact.
- Seeing or hearing things that are not really there (hallucinations).
- Tingling and feeling numb in your arms and legs.
- A feeling of losing contact with reality.

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

## **5. How to store Rivotril**

- Your doctor or pharmacist is responsible for storing Rivotril sterile concentrate. They are also responsible for disposing of any unused Rivotril correctly.
- Keep out of the reach and sight of children.
- Do not use Rivotril sterile concentrate after the expiry date printed on the pack.
- Keep the ampoules of Rivotril sterile concentrate in the original packaging to protect them from light.
- Rivotril sterile concentrate should not be stored above a temperature of 30°C.

## **6. Further information**

### **What Rivotril contains**

The active substance in Rivotril 1 mg/ml sterile concentrate is clonazepam. Each 1 ml of liquid medicine contains 1 mg (milligram) of clonazepam.

The other ingredients in Rivotril sterile concentrate are ethanol absolute, glacial acetic acid, benzyl alcohol, propylene glycol and pure nitrogen.

### **What Rivotril Sterile concentrate looks like and contents of the pack**

- The medicine in Rivotril sterile concentrate is a clear, colourless to slightly green-yellow liquid ('concentrate for solution for injection or infusion'). This liquid will be diluted with 'water for injections' before it is given to you.
- Rivotril is supplied in amber coloured glass ampoules with separate clear glass ampoules of 'water for injections' to dilute it with. They are supplied in packs of 5 or 10 medicine ampoules (with 5 or 10 ampoules of water). Not all packs may be marketed.

**Marketing Authorisation Holder**

Roche Products Limited  
6 Falcon Way  
Shire Park  
Welwyn Garden City, AL7 1TW  
United Kingdom

**Manufacturer (UK only)**

Roche Products Limited  
6 Falcon Way  
Shire Park  
Welwyn Garden City, AL7 1TW  
United Kingdom

**Manufacturer (Ireland only)**

Roche Pharma AG  
Emil-Barell-Str. 1  
D-79639 Grenzach-Wyhlen  
Germany

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This information is intended for medical or healthcare professionals only:  
The tear-off portion above is intended for the patient.

**INFORMATION FOR HEALTHCARE PROFESSIONALS****Rivotril® 1 mg/ml**

concentrate for solution for injection or infusion

Clonazepam

Please refer to the Summary of Product Characteristics for full prescribing information.

**Therapeutic indications**

Administered intravenously, Rivotril quickly controls status epilepticus in all clinical forms.

**Presentation**

Amber glass ampoules containing 1 ml clonazepam solution supplied with clear glass ampoules containing 1 ml solvent (water for injections). The clonazepam solution is clear, colourless to slightly green-yellow. Excipients are ethanol absolute, glacial acetic acid, benzyl alcohol, propylene glycol and nitrogen pure. Cartons of 5 or 10 clonazepam ampoules (with 5 or 10 solvent ampoules). Not all pack sizes may be marketed.

***Important information about the excipients in Rivotril sterile concentrate 1 mg/ml.***

Each ampoule (1 mg clonazepam) contains 30 mg benzyl alcohol, 159 mg (equivalent to 0.2 ml) ethanol absolute and 802 mg propylene glycol.

***Posology and method of administration***

Rivotril sterile concentrate is for intravenous administration. Either slow intravenous injection or intravenous infusion.

### ***Adults***

1 mg (one ampoule of active substance mixed with one ampoule of solvent for parenteral use) by slow intravenous injection.

### ***Elderly***

Care should be taken with the elderly.

### ***Children***

0.5 mg (equivalent to half an ampoule (0.5 ml) of active substance mixed with half an ampoule of solvent (0.5 ml) for parenteral use) by slow intravenous injection.

### ***Special dosage instructions***

Rivotril can be administered with one or several other antiepileptic agents, in which case the dosage of each drug must be adjusted to achieve optimum effect.

### ***Mode of administration***

Rivotril must be diluted prior to administration in order to avoid irritation of the veins, see *Instructions for use*.

Intravenous injection of Rivotril should be into a large vein of the antecubital fossa. The injection should be given slowly - in adults, the rate of injection must not exceed 0.25 mg – 0.5 mg (0.5 – 1.0 ml of the prepared solution) per minute – and should be administered with continuous monitoring of EEG, respiration and blood pressure. This will greatly diminish the rare possibility of hypotension or apnoea occurring. Nevertheless, facilities for resuscitation should always be available. A total dose of 20 mg should not be exceeded.

Rivotril sterile concentrate solution may be diluted when given in intravenous infusions of saline or glucose, such as are customary in the treatment of status epilepticus, see *Instructions for use*.

### **Incompatibilities**

Do not prepare Rivotril infusions using sodium bicarbonate solution, as precipitation of the solution may occur.

### ***Instructions for use***

#### ***Preparation of Rivotril intravenous injection:***

The contents of the solvent ampoule, which contains 1 ml Water for Injection, **must** be added to the contents of the other ampoule, which contains 1 mg clonazepam in 1 ml, **immediately before** injection.

#### ***Preparation of Rivotril intravenous infusion:***

Up to 3 mg (3 ampoules) in 250 ml of the following solutions is permissible:

Sodium chloride intravenous infusion 0.9% w/v

Glucose intravenous infusion 5% and 10%

Sodium chloride and glucose intravenous infusion (0.45% sodium chloride and 2.5% glucose)

The active ingredient clonazepam can be absorbed on PVC. It is therefore recommended either glass containers be used or, if PVC infusion bags are used, that the mixture be infused straight-away over a period of no longer than 2 hours.

**DO NOT prepare Rivotril infusions using sodium bicarbonate solution, as precipitation of the solution may occur.**

***Shelf life***

Unopened: 4 years.

Shelf-life of diluted product: From a chemical and physical stability point of view the diluted product is stable for up to 12 hours. However, it should be used immediately after dilution in order to reduce the possibility of microbial contamination unless it is diluted under validated aseptic conditions.

***Special precautions for storage***

Do not store above 30°C. Keep the ampoules in the outer carton to protect from light.

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