Package Leaflet: Information for the user

Flumazenil 0.1 mg/ml solution for injection
(flumazenil)

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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse . This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Flumazenil is and what it is used for

Flumazenil is a counteragent (antidote) for the complete or partial reversal of the central sedative effects of benzodiazepines (specific group with sedative, sleep inducing, muscle relaxing and anxiolytic properties).
It may therefore be used in anaesthesia to wake you up after certain diagnostic tests or in intensive care if you have been hold under sedative conditions. Flumazenil may also be used for the diagnosis and treatment of intoxications or overdose with benzodiazepines.

Flumazenil is also used in children (more than 1 year old) to wake them up after they have been given a 'benzodiazepine' medicine to make them sleepy during a medical procedure.

2. What you need to know before you use Flumazenil

Do not use Flumazenil
- if you are **allergic** to flumazenil or any of the other ingredients (listed in section 6).
- if benzodiazepines have been administered to you to control a **potentially life-threatening situation** (for example control of pressure in the brain or a serious epileptic seizure).
- in mixed **intoxications** with benzodiazepines and certain types of other antidepressants (so called tricyclic and tetracyclic antidepressants like Imipramin, Clomipramin, Mirtazepine or Mianserin). The toxicity of these antidepressants can be masked by protective benzodiazepine effects. If you are showing signs of a significant overdose of these antidepressants, Flumazenil must not be used to reverse benzodiazepine effects.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using Flumazenil.

- If **you do not wake up** after Flumazenil is administered, another reason for this will be considered because Flumazenil specifically reverses the effects of benzodiazepines.
- If Flumazenil is administered to you at the **end of** your **operation** to wake you up, it should not be given until the effects of muscle relaxants have gone away.
- As the action of flumazenil is usually shorter than that of benzodiazepines, **sedation may possibly recur**. You will be closely observed, possibly in the intensive care unit until the effects of flumazenil have gone away.
- If you have received high dose and/or long-term (chronic) treatment with benzodiazepines at any time within the weeks preceding flumazenil administration, **rapid injection** of high doses of flumazenil (more than 1 mg) should be avoided since this may cause **withdrawal symptoms** (see section 4. Possible side effects).
- If you have been treated **for long periods with high doses** of benzodiazepines, the advantages of the use of Flumazenil should be carefully weighed against the risk of **withdrawal symptoms**.
- In children previously sedated with **Midazolam**. These children should be closely observed in intensive care units for at least 2 hours after administration of Flumazenil because **repeated sedation or difficulty with breathing can occur**. In case of sedation by other benzodiazepines, the monitoring must be adjusted according to their expected duration.
- If you are **epileptic** and have received benzodiazepine treatment for a long period of time, the administration of flumazenil is not recommended as flumazenil can cause **seizures**.
- Seizures or other toxic effects can be more severe in cases of mixed drug overdose (e.g. intoxication with benzodiazepines and cyclic antidepressents)
- If you have **serious brain injury** (and/or instable pressure in your brain) care willl be taken as Flumazenil can cause an **increased pressure** in your brain.
- As Flumazenil is not recommended for the treatment of **benzodiazepine-dependence** or for the treatment of **benzodiazepines-withdrawal-symptoms.**
- If you have experienced **panic attacks** in the past Flumazenil can cause new attacks.
- If you are dependent on alcohol or medicines as you have a higher risk of benzodiazepine tolerance and dependence.
- If your liver is not working well Flumazenil elimination can be delayed.

Children

- Children should only receive Flumazenil after **deliberate sedation**. There are unsufficient data for any other indications. The same applies for children below the age of 1 year.

Other medicines and Flumazenil

Tell your doctor if you are taking, have recently taken or might take any other medicines.

When using Flumazenil in cases of an accidental overdose it has to be taken into account that the toxic effects of other psychotropic medicinal products (especially tricyclic antidrepressants like Imipramin) taken concurrently, may increase with the subsidence of the benzodiazepine effect.

Interaction with other central nervous system depressants has not been observed.

Flumazenil with alcohol

There is no known interaction between ethanol and flumazenil.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask you doctor or pharmacist for advice before taking this medicine.

Because of insufficient experience during pregnancy Flumazenil should only be used if the **advantage** for you is higher than the potential **risk** for the unborn baby. The administration of Flumazenil during pregnancy is not contraindicated in an emergency situation.

It is not known whether flumazenil is excreted in breast milk. Therefore it is **recommended not to breast-feed 24 hours** after administration of Flumazenil.

Driving and using machines
After receiving Flumazenil for the reversal of the sedative effects of benzodiazepines you must not drive a **car**, operate **machinery** or engage in any other physically or mentally demanding **activity** for at least 24 hours since sedation may possibly recur.

Flumazenil contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 5 ml ampoule, that is to say essentially 'sodium-free'**.**

This medicine contains 3.7 mg sodium (main component of cooking/table salt) in each 10 ml ampoule. This is equivalent to 1.9% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Flumazenil

Flumazenil is administered as intravenous **injection** (into a vein) or diluted as intravenous **infusion** (over a longer period).
Flumazenil will be given by your anaesthetist or experienced physician. Flumazenil may be used at the same time as other resuscitative measures.
This medicinal product is for single use only. Any unused solution should be discarded. The solution should be inspected visually prior to use. It should only be used if the solution is clear, colourless and practically free from particles.

The recommended dose is described as follows:

Adults	
Anaesthesia	**Intensive Care**
Dosage level:	
Starting dose: 0.2 mg administered intravenously over a period of 15 seconds.	Starting dose: 0.3 mg administered intravenously over a period of 15 seconds.
A further dose of 0.1 mg can be injected and repeated at 60 second intervals, if required level of consciousness is not obtained within 60 seconds, up to a maximum dose of 1.0 mg.	A further dose of 0.1 mg can be injected and repeated at 60 second intervals, if required level of consciousness is not obtained within 60 seconds, up to a maximum dose of 2.0 mg..
The usual dose required lies between 0.3 and 0.6 mg, but may deviate depending on the	If drowsiness recurs a second bolus injection may be administered. An intravenous

patients characteristics and the benzodiazepine used.	infusion of 0.1- 0.4 mg/h has also been shown useful. The dosage and rate of infusion should be adjusted individually to achieve the desired level of consciousness
	The infusion can be given additionally to the maximum dose of 2 mg by injection.

Patients with renal (kidney) or hepatic (liver) impairment
In patients with impaired liver function, the elimination of flumazenil may be delayed and therefore careful **titration of dosage** is recommended.

No dosage adjustments are required in patients with impaired kidney function.

Use in Children

Children above 1 year of age
Reversal of deliberate sedation
Dosage level:
The recommended initial dose is 10 micrograms/kg (up to 200 micrograms), administered intravenously over 15 seconds. If the desired level of consciousness is not obtained after waiting an additional 45 seconds, further injection of 10 micrograms//kg may be administered (up to 200 micrograms) and repeated at 60 second intervals where necessary (a maximum of 4 times) to a maximum total dose of 50 micrograms/kg or 1 mg, whichever is lower.

Children under the age of 1 year
There are insufficient data on the use of Flumazenil in children under 1 year. Therefore Flumazenil should only be administered in children under 1 year if the potential **benefits** to the patient outweigh the possible **risk**.

If you have any further questions on the use of this product, ask your doctor or pharmacist.
For information intended for healthcare professionals please see accordant section below.

4. Possible side effects

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

Very common (may affect more than 1 in 10 people)
Nausea

Common (may affect up to 1 in 10 people)
Hypersensitivity reactions (allergic reactions), anxiety (after rapid injection, not requiring treatment), emotional lability, having problems in initiating and maintaining sleep (insomnia), feeling sleepy (somnolence), vertigo, headache, agitation (after rapid injection, not requiring treatment), unvoluntary trembling or quivering (tremor), dry mouth, abnormal rapid and deep respiration (hyperventilation), speech disorder, subjective cutaneous sensations (e.g. cold, warmth, tingling, pressure, etc.) in the absence of stimulation (paresthesia), double vision, strabismus (squinting), lacrimation (production of tear fluid) increased, heart palpitations (after rapid injection, not requiring treatment), reddening of the skin (flushing), low blood pressure on transition from lying to standing, transient increased blood pressure (on awaking), vomiting, hiccup, sweating, fatigue, injection site pain.

Uncommon (may affect up to 1 in 100 people)
Fear (after rapid injection, not requiring treatment), convulsions (in patients suffering from epilepsy or severe liver insufficiency, mainly after long-term treatment with benzodiazepines or mixed drug overdose (see section 2 warnings and precautions), abnormal hearing, slow or rapid heart rate, premature beat of your heart (extrasystole), difficulty breathing (dyspnoea), cough, nasal congestion, chest pain, shivering (after rapid injection, not requiring treatment).

Not known (frequency cannot be estimated from the available data)
Withdrawal symptoms (see below); panic attacks (in patients with a history of panic reactions); abnormal crying, agitation, aggressive reaction, severe allergic reactions (anaphylaxis).

If you were treated for a long period with benzodiazepines flumazenil can induce **withdrawal symptoms**. The **symptoms** are: tension, agitation, anxiety, emotional lability confusion, hallucinations, involuntary trembling or quivering (tremor) and convulsions.
In general the **undesirable effects** in **children** do not differ much from that in adults. When using Flumazenil to awaken a child from sedation, abnormal crying, agitation and aggressive reactions have been reported.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below).

United Kingdom

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

Ireland

HPRA Pharmacovigilance
Earlsfort Terrace
IRL-Dublin 2
Tel: +353 1 6764971
Fax: +353 16762517
Website: www.hpra.ie

e-mail: medsafety@hpra.ie

5. How to store Flumazenil

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.

Do not store above 25 °C
This medicinal product is for single use only.
Shelf life after first opening: the medicinal product should be used immediately.
Shelf life after dilution: 24 hours.
Chemical and physical in-use stability has been demonstrated for 24 hours at 25 °C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Do not use this medicine if the solution is not clear and free from particles.
Any unused solution should be discarded in accordance with local requirements.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Flumazenil contains

- The **active substance** is flumazenil.

  Each millilitre contains 0.1 mg flumazenil.
  Each ampoule with 5 ml contains 0.5 mg flumazenil.
  Each ampoule with 10 ml contains 1.0 mg flumazenil.

- The **other ingredients** are disodium edetate, glacial acetic acid, sodium chloride, sodium hydroxide solution 4%, water for injections.

What Flumazenil looks like and contents of the pack

Flumazenil is a clear and colourless solution for injection and concentrate for solution for infusion in colourless glass ampoules.

Following packaging sizes are available:
Carton boxes with 5 or 10 ampoules containing 5 ml solution.
Carton boxes with 5 or 10 ampoules containing 10 ml solution

Not all packaging sizes may be marked.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
For UK:

Fresenius Kabi Ltd
Cestrian Court
Eastgate Way
Manor Park
Runcorn
Cheshire
WA7 1NT
UK

For IE:
Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1
Bad Homburg v.d.H 61352,
Germany

Manufacturer:
Fresenius Kabi Austria GmbH
Hafnerstrasse 36
A-8055 Graz
Austria

This medicinal product is authorised in the Member State of the EEA under the following names:

Austria	***Flumazenil 0,1 mg/ml Injektionslösung und Konzentrat zur Herstellung einer Infusionslösung***
Germany	***Flumazenil 0,1 mg/ml Injektionslösung und Konzentrat zur Herstellung einer Infusionslösung***
Denmark	***Flumazenil Fresenius Kabi***
Spain	***Flumazenilo Fresenius Kabi 0,1 mg/ml inyectable***
Finland	***Flumazenil Fresenius Kabi 0,1 mg/ml injektioneste, liuos***
Hungary	***Flumazenil 0,1 mg/ml oldatos injekció***
Ireland	***Flumazenil 0.1 mg/ml Solution for Injection***
Italy	***Flumazenil Kabi***
The Netherlands	***Flumazenil 0,1 mg/ml oplossing voor injectie***
Norway	***Flumazenil Fresenius Kabi 0,1 mg/ml injeksjonsvæske, oppløsning***
Poland	***Flumazenil 0,1 mg/ml roztwór do iniekcji***
Portugal	***Flumazenilo Fresenius Kabi 0,1 mg/ml solução injectável***
Sweden	***Flumazenil Fresenius Kabi 0,1 mg/ml injektionsvätska, lösning***
United Kingdom	***Flumazenil 0.1 mg/ml Solution for Injection***

This leaflet was last revised in Jan 2021.

The following information is intended for healthcare professionals only:

Detailed storage conditions can be found in section **5. How to store Flumazenil.**

When Flumazenil is to be used in infusion, it must be diluted prior to infusion. Flumazenil should only be diluted with sodium chloride 9 mg/ml (0.9 % w/v) solution, glucose 50 mg/ml (5 % w/v) or sodium chloride 4.5 mg/ml (0.45 % w/v) + glucose 25 mg/ml (2.5 % w/v) solution. Compatibility between flumazenil and other solutions for injection has not been established.
This medicinal product must not be mixed with other medicinal products except for those mentioned in this section.
For further information on dosage instructions please see section 3 of the Package Information Leaflet.