PACKAGE LEAFLET: INFORMATION FOR THE USER
Flumazenil 0.1 mg/ml solution for injection

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. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Flumazenil is and what it is used for

Flumazenil is a counteragent (antidote) for a specific group of medicines called benzodiazepines. Benzodiazepines have sedative, sleep inducing and muscle relaxing properties. They are used to make you sleepy and tranquillize you if you are anxious. Flumazenil may completely or partially reverse these effects.

Flumazenil may therefore be used
- in anaesthesia to wake you up after surgery or certain diagnostic tests
- if you have been held under sedative conditions in intensive care.

Flumazenil may also be used for the diagnosis and treatment of intoxications or overdose with benzodiazepines.

Flumazenil is used in children older than 1 year to wake them up after they have received benzodiazepines 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 of this medicine (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).

Warnings and precautions

Special care has to be taken
- if you are epileptic and have received benzodiazepine treatment for a long period of time. In this case the administration of Flumazenil can cause seizures.
- if you have a serious brain injury (and/or instable pressure in your brain) as Flumazenil can cause an increased pressure in your brain.
- if you suffer from liver disease. Your doctor will carefully adjust the dosage of Flumazenil.
- if you have experienced panic attacks in the past as Flumazenil can cause new attacks.

- if you are very nervous about having your operation or have a history of anxiety. Your doctor will carefully adjust the dosage of Flumazenil.
- if you have been treated for long periods with high doses of benzodiazepines as there is a risk of withdrawal symptoms (Withdrawal symptoms are listed in section 4. “Possible side effects”).
- if you are dependent on alcohol or medicines. In this case you have a higher risk of benzodiazepine tolerance and dependence.
- if you have a coronary heart disease. Your doctor should be informed as she / he might decide to keep you longer under sedation.

Your alertness and vital signs (like blood pressure, heart and breathing rate) will be controlled for an adequate period of time after you received Flumazenil. As the action of Flumazenil is usually shorter than that of benzodiazepines, sedation may recur. You will be closely observed, possibly in the intensive care unit, until the effects of Flumazenil have gone away.

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.

Your doctor will consider postoperative pain before giving you 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.

Your doctor will avoid rapid injection of Flumazenil. If you have received long-term (chronic) treatment with benzodiazepines, rapid injection of high doses of Flumazenil (more than 1 mg) may cause withdrawal symptoms.

Flumazenil is not recommended for the treatment of benzodiazepine-dependence or benzodiazepines-withdrawal-symptoms.

Your doctor will administer Flumazenil only with particular caution in case of mixed intoxications with benzodiazepines and certain types of other antidepressants (so called cyclic antidepressants like Imipramin, Clomipramin, Mirtazapine or Mianserin). The toxicity of these antidepressants can be masked by protective benzodiazepine effects (see also section 2 “Other medicines and Flumazenil”).
Signs of a significant overdose with cyclic antidepressants include:

- dilation of the pupil, inability to urinate, dry mouth,
- severe or potentially life threatening conditions like agitation, breathing problems, convulsions, heart problems and coma.

Children
Children previously sedated with midazolam should be closely observed in intensive care units for at least 2 hours after administration of Flumazenil. 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.

Children of 1 year and younger should only receive Flumazenil if the risks have been carefully weighed against the advantages of the therapy.

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

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

Flumazenil counteracts the effect of all medicines that act via the benzodiazepine receptor. This includes medicines that do not belong to the group of benzodiazepines, but that have the same active principle such as zopiclone (like Zimovane), triazolopyridazine and others.

Benzodiazepines can mask the toxic effects of certain psychotropic medicinal products (especially tricyclic antidepressants like Imipramin, see also section 2 "Warnings and precautions"). When using Flumazenil in cases of an accidental overdose it has to be taken into account that the toxic effects of such medicines taken concurrently may increase with the subsidence of the benzodiazepine effect.

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

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your 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 you should not breastfeed for 24 hours after administration of Flumazenil. The administration of Flumazenil during lactation is not contraindicated in an emergency situation.

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 medicinal product contains 3.7 mg sodium per ml (18.5 mg / 5 ml ampoule size or 37 mg / 10 ml ampoule size) solution for injection. To be taken into consideration by patients on a controlled sodium diet.

3. How to use Flumazenil

Flumazenil will be given by your anaesthetist or experienced physician. Flumazenil is administered as intravenous injection (into a vein) or diluted as intravenous infusion (over a longer period).

Flumazenil may be used at the same time as other resuscitative measures.

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.
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	If drowsiness recurs, a second bolus injection may

0.6 mg, but may deviate depending on the patients characteristics and the benzodiazepine used.	be administered. An intravenous infusion of 0.1-0.4 mg/h may be useful. The rate of infusion should be adjusted individually to achieve the desired level of consciousness

The infusion should be stopped every 6 hours to check if sedation recurs.

Infants and toddlers, children and adolescents (from 1 to 17 years)
Reversal of deliberate sedation
Dosage level:
Injection of 0.01 mg/kg body weight (up to 0.2 mg) administered intravenously over a period of 15 seconds. If after a waiting period of 45 seconds the required level of consciousness is not obtained, a follow-up injection of 0.01 mg/Kg (up to 0.2 mg) may be administered. Where necessary repeated injections at 60-second intervals (up to a maximum of 4 times) to a maximum dose of 0.05 mg/kg or 1 mg, depending on which is the lowest dose can be injected.

Newborn infants, infants and toddlers 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 (see also section 2 "Warnings and precautions, Children").

Patients with renal (kidney) or hepatic (liver) impairment
In patients with impaired liver function, the elimination of Flumazenil may be delayed and therefore careful adjustment of dosage is recommended.
No dosage adjustments are required in patients with impaired kidney function.

If you have any further questions on the use of this medicine, 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.

The following side effects may be serious. If any of the following side effects occur, stop using this medicine and consult a doctor immediately:

Common (may affect up to 1 in 10 people):
- allergic reactions,
- abnormal rapid and deep respiration (hyperventilation),
- speech disorder.

Uncommon (may affect up to 1 in 100 people):
- slow or rapid heart rate, premature beat of your heart (extrasystole),
- difficulty in breathing,
- chest pain.

Not known (frequency cannot be estimated from the available data):
- convulsions (in patients suffering from epilepsy or severe liver insufficiency, mainly after long-term treatment with benzodiazepines or multiple medicinal products abuse).

Other side effects include:

Common (may affect up to 1 in 10 people):
- agitation (after rapid injection, not requiring treatment), strong emotional lability,
- having problems in initiating and maintaining sleep (insomnia), feeling sleepy (somnolence),
- dizziness, headache,
- involuntary trembling or quivering (tremor),
- dry mouth,
- sensations on the skin (e.g. cold, warmth, tingling, pressure, etc.) in the absence of stimulation (paresthesia),
- double vision, squinting (strabismus), increased production of tear fluid (increased lacrimation),
- sweating,
- low blood pressure, drop of blood pressure on transition from lying to standing (orthostatic hypotension),
- feeling sick: vomiting (after surgery), hiccups,
- fatigue,
- pain at the injection site.

Uncommon (may affect up to 1 in 100 people)*:*
- anxiety and fear (occurring after rapid injection, not requiring treatment),
- being aware of your heart rate (palpitations, occurring after rapid injection, not requiring treatment),
- abnormal hearing,
- cough, nasal congestion,
- reddening of the skin,
- shivering.

Not known (frequency cannot be estimated from the available data):
- panic attacks in patients that already showed panic reactions,
- transient increased blood pressure (on awaking),
- abnormal crying, agitation and aggressive reactions.

If you were treated for a long period with benzodiazepines Flumazenil can induce withdrawal symptoms (frequency not known). The symptoms include: agitation, anxiety, emotional lability, confusion, tension, hallucinations and abnormal sensory perception.

In general the undesirable effects in children are generally similar to those in adults. When Flumazenil is used to wake up your child from sedation, abnormal crying, agitation and aggressive reactions might occur.

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

5. How to store Flumazenil

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

Flumazenil must not be used 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.

The solution should be inspected visually prior to use. Do not use Flumazenil if the solution is not clear, colourless 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. Content 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 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 and Manufacturer:

B. Braun Melsungen AG
Carl-Braun-Strasse 1
34212 Melsungen
Germany

Postal address:
34209 Melsungen
Germany

Phone: +49 5661/71-0
Fax: +49 5661/71-4567

Additional Manufacturer:

hameln pharmaceuticals gmbh
Langes Feld 13, 31789 Hameln
Germany

Tel.: +49 5151/581-0
Fax: +49 5151/581-258

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

Austria	Flumazenil B. Braun 0,1 mg/ml Injektionslösung und Konzentrat zur Herstellung einer Infusionslösung
Belgium	Flumazenil B. Braun 0,1 mg/ml oplossing voor injectie
Germany	Flumazenil B. Braun 0,1 mg/ml Injektionslösung und Konzentrat zur Herstellung einer Infusionslösung
Spain	Flumazenil B. Braun 0,1 mg/ml solución inyectable EFG
Finland	Flumazenil B. Braun 0,1 mg/ml injektioneste, liuos
Ireland	Flumazenil 0.1 mg/ml solution for injection
Italy	Flumazenil B. Braun 0,1 mg/ml soluzione iniettabile
Luxembourg	Flumazenil B. Braun 0,1 mg/ml Injektionslösung und Konzentrat zur Herstellung einer Infusionslösung
The Netherlands	Flumazenil B. Braun 0,1 mg/ml, oplossing voor injectie
Norway	Flumazenil B. Braun 0,1 mg/ml injeksjonsvæske, oppløsning
Poland	Flumazenil B. Braun 0,1 mg/ml roztwór do wstrzykiwań
Portugal	Flumazenilo B. Braun 0,1 mg/ml solução injectável
Sweden	Flumazenil B. Braun 0,1 mg/ml injektionsvätska, lösning
United Kingdom	Flumazenil 0.1 mg/ml solution for injection

This leaflet was last revised in 05/2012

The following information is intended for healthcare professionals only:

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.