

Package leaflet: Information for the patient**Byfavo 50 mg powder
for concentrate for solution
for injection/infusion**

remimazolam

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effect you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given 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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Byfavo is and what it is used for

Byfavo is a medicine that contains the active substance remimazolam. This is one of a group of medicines known as benzodiazepines. Byfavo is given to make you lose consciousness (sleep) when you have surgery.

2. What you need to know before you are given Byfavo**You must not be given Byfavo if:**

- you are allergic to remimazolam or other benzodiazepines (such as midazolam) or any of the other ingredients of this medicine (listed in section 6).
- you have an unstable form of a condition called myasthenia gravis (weakness of muscles) in which your chest muscles that help you breathe get weak

Warnings and precautions

Talk to your doctor or nurse before using Byfavo if you have any severe illness or condition and in particular if:

- you have very low or very high blood pressure or tend to faint
- you have heart problems especially a very slow and/or irregular (arrhythmic) heart rate
- you have any breathing problems including shortness of breath
- you have severe liver problems
- you have a condition called myasthenia gravis in which your muscles are weak
- you regularly take recreational drugs or you have had problems with drug use in the past.

Byfavo can cause temporary loss of memory. Your doctor will assess you before you leave the hospital or clinic and give you necessary advice.

Some patients undergoing surgical operations may experience sudden mental confusion (delirium) after the operation. This is more common in patients who have major surgeries, are older, have memory problems, are exposed to anaesthesia/sedation which is deep and/or for a long period, or have infections. Patients with delirium may find it difficult to follow a conversation, be confused at some times more than others, become agitated and

restless or sleepy and very slow, and have vivid dreams or hear noises or voices which do not exist. Your doctor will assess your condition and organise the necessary treatment to manage it.

Benzodiazepines sometimes cause effects which are the opposite of the medication is meant to do. You may hear these referred to as 'paradoxical' effects. They include e.g. aggressive behaviour, agitation, anxiety. These are more common in older people when receiving high doses of the drug or when the drug is given rapidly.

Children and adolescents

Byfavo should not be given to patients under the age of 18 years because it has not been tested in children and adolescents.

Other medicines and Byfavo

Tell your doctor if you are taking, have recently taken or might take any other medicines, in particular about:

- opioids (including painkillers such as morphine, fentanyl and codeine or certain cough medicines or medicines for use in drug substitution therapy)
- antipsychotics (medicines to treat certain psychiatric illnesses)
- anxiolytics (tranquilizers or medicines that reduce anxiety)

– medicines that cause sedation (for example temazepam or diazepam),

- antidepressants (medicines to treat depression)
- certain antihistamines (medicines to treat allergies)
- certain antihypertensives (medicines to treat high blood pressure)

It is important to tell your doctor or nurse if you are taking other medicines, as using more than one at the same time can change the effect of the medicines involved.

Byfavo with alcohol

Alcohol can change the effect of Byfavo. Tell your doctor or nurse how much alcohol you drink regularly or if you have had problems with alcohol use.

Do not drink alcohol for 24 hours before you are given Byfavo.

Pregnancy and breast-feeding

You should not use Byfavo if you are pregnant or think you may be pregnant. Tell your doctor or nurse if you are pregnant or think you may be pregnant. If you are a breastfeeding mother, do not breastfeed for 24 hours after you are given this medicine.

Driving and using machines

Byfavo makes you sleepy, forgetful and affects your

ability to concentrate. Even though these effects wear off rapidly, you must not drive and operate machinery until these effects are completely gone. Ask your doctor about when you can drive or operate machinery again.

Byfavo contains dextran 40 for injection

This medicine contains 198 mg of dextran 40 for injection in each vial. Rarely, dextrans can cause severe allergic reactions. If you have breathing difficulty or swelling or you feel faint, get medical help at once.

3. How Byfavo is given

Your doctor will decide on the right dose for you.

Your breathing, heart rate and blood pressure will be monitored during the procedure and the doctor will adjust the dose if needed.

A doctor or nurse will give you Byfavo by injection into your vein (blood stream) before and during surgery. Byfavo is mixed with sterile sodium chloride solution to make a solution before it is used. You may need several medicines to keep you asleep, free from pain, breathing well with a steady blood pressure. The doctor will decide which medicines you need.

Time to recovery after end of administration is expected to be 12-15 min.

If you are given too much Byfavo

If you are given too much Byfavo, you may have the following symptoms:

- your blood pressure may drop
- your heartbeat may slow down
- your breathing may become slow and shallow

Your doctor will know how to treat you.

Ask your doctor or nurse if you have any questions about the use of this medicine.

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 users*)

- Slow heart rate
- Low blood pressure
- Feeling sick (nausea)
- Being sick (vomiting)

Common (*may affect up to 1 in 10 users*)

- Feeling agitated
- Headache
- Feeling dizzy
- Unusually slow or shallow breathing (and low oxygen level in blood)

– Prolonged sleepiness or being unconscious after the operation

– Chills

Uncommon (*may affect up to 1 in 100 users*)

- Hiccups
- Abnormal positioning of the tongue in the mouth (higher, toward the roof, and further back in the mouth than usual)
- Feeling cold

Not known (*frequency cannot be estimated from the available data*)

- Sudden, severe allergic reaction

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, website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Byfavo

Professionals in the hospital or clinic are responsible for storing this medicine.

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 carton and vial label. The expiry date refers to the last day of that month.

Chemical and physical in-use stability has been demonstrated for 24 h at 20 - 25°C.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user (see SmPC section 6.3).

Do not use this medicine if you notice visible particulate matter or discolouration.

6. Contents of the pack and other information**What Byfavo contains**

– The active substance is remimazolam. Each vial contains remimazolam besylate equivalent to 50 mg of remimazolam. After reconstitution each mL contains 5 mg of remimazolam which is further diluted before use. Your doctor will decide the exact amount that is right for you.

– The other ingredients are:

- Dextran 40 for injection
- Lactose monohydrate
- Hydrochloric acid
- Sodium hydroxide

See section 2, "Byfavo contains dextran 40 for injection".

What Byfavo looks like and contents of the pack

Byfavo is a white to off-white powder for concentrate for solution for injection/infusion (powder for concentrate).

Pack sizes
10 vial pack

Approval by Regulatory Affairs:

Approval Date:

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The following information is intended for healthcare professionals only:

Byfavo 50 mg powder for concentrate for solution for injection/infusion

FOR INTRAVENOUS USE ONLY

Must be reconstituted and further diluted before use with Sodium chloride 9 mg/mL (0.9%) solution for injection

Read the summary of product characteristics (SmPC) carefully before use.

Remimazolam must only be given in hospitals or adequately equipped day therapy units by physicians trained in anaesthesia.

Circulatory and respiratory functions should be constantly monitored (e.g. ECG, pulse oximetry) and facilities for maintenance of patent airways, artificial ventilation, and other resuscitation facilities should be immediately available at all times.

Instructions for use

General precautions

Each vial is for single use only. Reconstitution and dilution of the product should be conducted using aseptic

techniques. Once opened the contents of the vial should be used immediately (SmPC section 6.3). To prevent coring, the needle should be inserted at a 45–60° angle with the opening of the needle tip facing up (i.e., away from the stopper), sometimes referred to as “bevel up”. A small amount of pressure is applied, and the angle is gradually increased as the needle enters the vial. The needle should be at a 90° angle just as the needle bevel passes through the stopper.

Instructions for reconstitution

Byfavo should be reconstituted by adding 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection and swirled gently until the powder has entirely dissolved. Reconstituted Byfavo will be clear and colourless to light yellow. The solution is to be discarded if visible particulate matter or discolouration is observed.

Instructions for dilution

For administration, the reconstituted solution must be further diluted. The appropriate volume of reconstituted remimazolam solution must be withdrawn from the vial(s) and added to a syringe or infusion bag containing sodium chloride 9 mg/mL (0.9%) solution for injection in order to achieve a final concentration of 1-2 mg/mL remimazolam (Table 2).

Table 2 Dilution instructions

Reconstituted solution	Final concentration 2 mg/ml	Final concentration 1 mg/ml
5 mg/mL (50 mg reconstituted with 10 mL)	Dilute 10 mL of reconstituted solution with 15 mL of sodium chloride (0.9%) solution for injection	Dilute 10 mL of reconstituted solution with 40 mL of sodium chloride (0.9%) solution for injection

Administration with other fluids

When Byfavo is reconstituted and diluted for use in sodium chloride (0.9%) as described above, compatibility has been shown with:

Glucose 5% intravenous infusion, Glucose 20% w/v solution for infusion, Sodium Chloride 0.45% w/v and Glucose 5% w/v solution for infusion, Sodium Chloride 0.9% intravenous infusion, Ringers Solution (Sodium Chloride 8.6 g/L, Potassium Chloride 0.3 g/L, Calcium Chloride dihydrate 0.33 g/L)

This medicinal product must not be mixed or co-administered through the same infusion line with medicinal products other than those fluids described in this section

Incompatibilities

Incompatibilities between Byfavo and co-administered solutions may result in precipitation/turbidity which may cause occlusion of vascular access site. Byfavo is incompatible with Lactated Ringer's Solution (also known as Compound Sodium Lactate Solution or Hartmann's Solution), Acetated Ringer's Solution, and Bicarbonated Ringer's Solution for infusion and other alkaline solutions since the solubility of the product is low at pH of 4 or higher.

This medicinal product must not be mixed or co-administered through the same infusion line with other medicinal products except those mentioned in "Administration with other fluids".

In-use stability after reconstitution

Chemical and physical in use stability has been demonstrated for 24 hours at 20°C to 25°C.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of


microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Special precautions for storage

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

Approval by Regulatory Affairs:

Approval Date:

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