Medicines & Healthcare products Regulatory Agency

MHRA

# Public Assessment Report

# National Procedure

# Byfavo 20 mg powder for solution for injection remimazolam besylate

# PLGB 54212/0001

# PAION Netherlands B.V.

# LAY SUMMARY

## Byfavo 20 mg powder for solution for injection
## remimazolam besylate

This is a summary of the Public Assessment Report (PAR) for Byfavo 20 mg powder for solution for injection. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

For practical information about using Byfavo 20 mg powder for solution for injection, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

**What is Byfavo 20 mg powder for solution for injection and what is it used for?**
This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 26 March 2021 (EMEA/H/C/005246/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

Byfavo 20 mg powder for solution for injection is a sedative given before a medical test or procedure to make the patient feel relaxed and sleepy (sedated).

This is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indications.

**How does Byfavo 20 mg powder for solution for injection work?**
This medicine contains the active substance remimazolam, which belongs to a class of sedative medicines called benzodiazepines. Remimazolam attaches to a specific site on the receptor for the neurotransmitter gamma-amino butyric acid (GABA) in the brain. By activating the GABA-A receptor, remimazolam reduces brain activity, helping the patient feel calm and sleepy.

**How is Byfavo 20 mg powder for solution for injection used?**
The pharmaceutical form of this medicine is a powder for solution for injection and the route of administration is intravenous (injection into a vein).

Remimazolam must only be administered by health care professionals experienced in sedation. The patient should be monitored throughout by a separate healthcare professional, who is not involved in the conduct of the procedure, and whose sole task is to monitor the patient.

Remimazolam dosing should be individually titrated to an effective dose which provides the desired level of sedation and minimises adverse reactions (see PIL). Additional doses can be administered as needed to induce or maintain the desired level of sedation. At least 2 minutes should elapse prior to administration of any supplemental dose in order to fully assess the sedative effect. Adding or switching to another sedative should be considered if 5 doses of remimazolam within 15 minutes do not result in the desired level of sedation. Remimazolam is associated with fast onset and offset of sedation. In clinical trials, peak sedation occurred 3 - 3.5 minutes after the initial bolus and patients became fully alert 12 - 14 minutes from last dose of remimazolam.

For further information on how Byfavo 20 mg powder for solution for injection is/are used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning the medicine.

**What benefits of Byfavo 20 mg powder for solution for injection have been shown in studies?**
This medicine was shown to be effective at sedating patients in two main studies involving adult patients undergoing colonoscopy or bronchoscopy. In both studies, the sedative effect of Byfavo started and wore off within minutes.

**What are the possible side effects of Byfavo 20 mg powder for solution for injection?**
For the full list of all side effects reported with this medicine medicines, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

The most common side effects with Byfavo 20 mg powder for solution for injection (which may affect more than 1 in 10 people) are low blood pressure and unusually slow or shallow breathing (and low oxygen level in blood).

**Why was Byfavo 20 mg powder for solution for injection approved?**
MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

**What measures are being taken to ensure the safe and effective use of Byfavo 20 mg powder for solution for injection?**
A Risk Management Plan (RMP) has been developed to ensure that Byfavo 20 mg powder for solution for injection is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

**Other information about Byfavo 20 mg powder for solution for injection**
A marketing authorisation was granted in Great Britain on 28 June 2021.

The full PAR for Byfavo 20 mg powder for solution for injection follows this summary.

This summary was last updated in August 2021

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## I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Byfavo 20 mg powder for solution for injection (PLGB 54212/0001) could be approved.

The product is indicated in adults for procedural sedation.

The name of the active substance is remimazolam, which is an ultra-short acting benzodiazepine sedative. The effects of remimazolam on the central nervous system are dependent on the dose administered intravenously and the presence or absence of other medicinal products. Remimazolam binds to benzodiazepine sites of gamma amino butyric acid type A [GABAA] receptors with high affinity, while its carboxylic acid metabolite (CNS7054) has approximately 300 times lower affinity for these receptors. Remimazolam does not show clear selectivity between subtypes of the GABAA receptor.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 26 March 2021 (EMEA/H/C/005246/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A Marketing Authorisation was granted on 28 June 2021.

## II. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

## PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

## LABEL

The labelling is in line with current guidelines and is satisfactory.

## III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.
The grant of a marketing authorisation is recommended.

## IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation is recommended.

## V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.
The grant of a marketing authorisation is recommended.

## VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

## VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

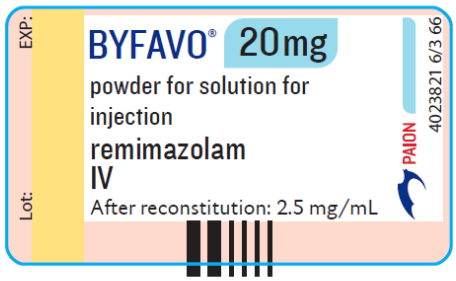
## VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

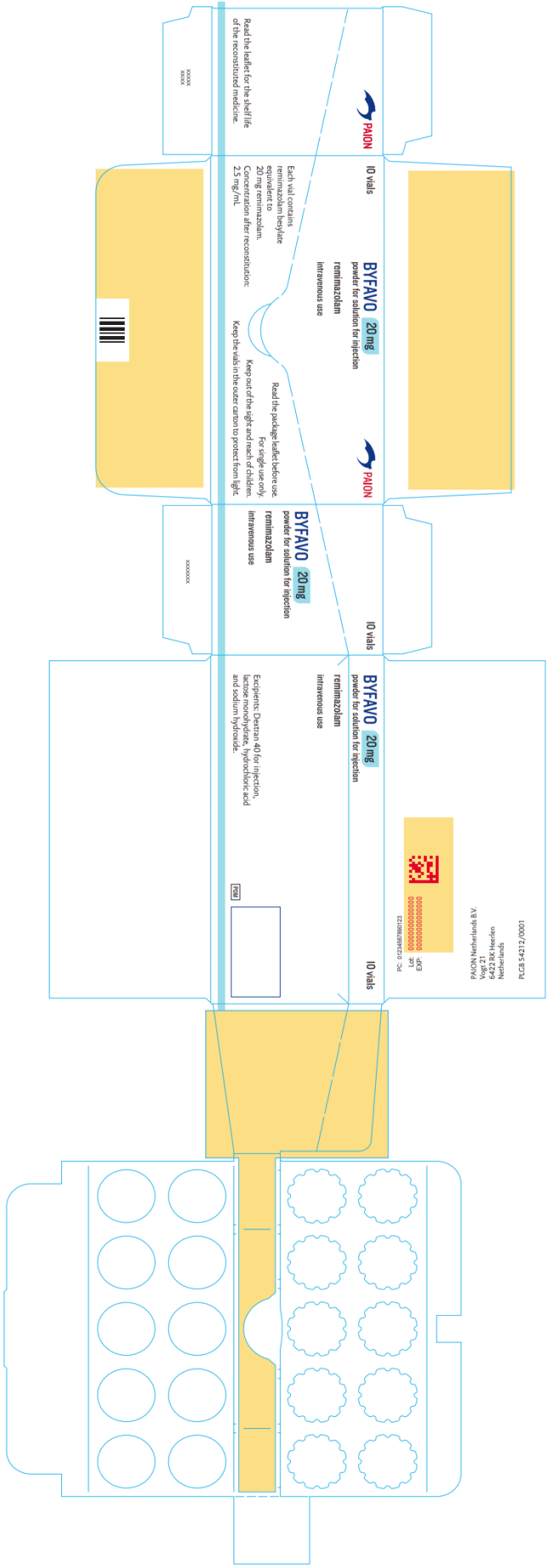
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

Representative copies of the labels at the time of UK licensing are provided below.




PAION
10 vials
BYFAVO 20 mg
powder for solution for injection
remimazolam
intravenous use
Each vial contains remimazolam besylate equivalent to 20 mg remimazolam.
Concentration after reconstitution: 2.5 mg/mL
Read the leaflet for the shelf life of the reconstituted medicine.
Read the package leaflet before use.
For single use only.
Keep out of the sight and reach of children.
Keep the vials in the outer carton to protect from light.
Excipients: Dextran 40 for injection, lactose monohydrate, hydrochloric acid and sodium hydroxide.
PAION Netherlands B.V.
Vogt 21
6422 PK Heerlen
Netherlands
PLGB 54212/0001

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

| **Application type** | **Scope** | **Product information affected** | **Date of grant** | **Outcome** | **Assessment report attached Y/N** |
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