

## Indication

Byfavo is a benzodiazepine indicated for the induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes or less.

## Important Safety Information

### **WARNING: PERSONNEL AND EQUIPMENT FOR MONITORING AND RESUSCITATION, AND RISKS FROM CONCOMITANT USE WITH OPIOID ANALGESICS AND OTHER SEDATIVE-HYPNOTICS**

#### **Personnel and Equipment for Monitoring and Resuscitation**

- Only personnel trained in the administration of procedural sedation, and not involved in the conduct of the diagnostic or therapeutic procedure, should administer Byfavo.
- Administering personnel must be trained in the detection and management of airway obstruction, hypoventilation, and apnea, including the maintenance of a patent airway, supportive ventilation, and cardiovascular resuscitation.
- Byfavo has been associated with hypoxia, bradycardia, and hypotension. Continuously monitor vital signs during sedation and during the recovery period.
- Resuscitative drugs, and age- and size-appropriate equipment for bag-valve-mask-assisted ventilation must be immediately available during administration of Byfavo.

#### **Risks From Concomitant Use With Opioid Analgesics and Other Sedative-Hypnotics**

Concomitant use of benzodiazepines, including Byfavo, and opioid analgesics may result in profound sedation, respiratory depression, coma, and death. The sedative effect of intravenous Byfavo can be accentuated by concomitantly administered CNS depressant medications, including other benzodiazepines and propofol. Continuously monitor patients for respiratory depression and depth of sedation.

## Contraindication

Byfavo is contraindicated in patients with a history of severe hypersensitivity reaction to dextran 40 or products containing dextran 40.

## Personnel and Equipment for Monitoring and Resuscitation

Clinically notable hypoxia, bradycardia, and hypotension were observed in Phase 3 studies of Byfavo. Continuously monitor vital signs during sedation and through the recovery period. Only personnel trained in the administration of procedural sedation, and not involved in the conduct of the diagnostic or therapeutic procedure, should administer Byfavo. Administering personnel must be trained in the detection and management of airway obstruction, hypoventilation, and apnea, including the maintenance of a patent airway, supportive ventilation, and cardiovascular resuscitation. Resuscitative drugs, and age- and size-appropriate equipment for bag-valve-mask-assisted ventilation must be immediately available during administration of Byfavo. Consider the potential for worsened cardiorespiratory depression prior to using Byfavo concomitantly with other drugs that have the same potential (eg, opioid analgesics or other sedative-hypnotics). Administer supplemental oxygen to sedated patients through the recovery period. A benzodiazepine reversal agent (flumazenil) should be immediately available during administration of Byfavo.

## Risks From Concomitant Use With Opioid Analgesics and Other Sedative-Hypnotics

Concomitant use of Byfavo and opioid analgesics may result in profound sedation, respiratory depression, coma, and death. The sedative effect of IV Byfavo can be accentuated when administered with other CNS depressant medications (eg, other benzodiazepines and propofol). Titrate the dose of Byfavo when administered with opioid analgesics and sedative-hypnotics to the desired clinical response. Continuously monitor sedated patients for hypotension, airway obstruction, hypoventilation, apnea, and oxygen desaturation. These cardiorespiratory effects may be more likely to occur in patients with obstructive sleep apnea, the elderly, and ASA III or IV patients.

## Hypersensitivity Reactions

Byfavo contains dextran 40, which can cause hypersensitivity reactions, including rash, urticaria, pruritus, and anaphylaxis. Byfavo is contraindicated in patients with a history of severe hypersensitivity reaction to dextran 40 or products containing dextran 40.

## Neonatal Sedation and Withdrawal Syndrome

Receiving benzodiazepines late in pregnancy can result in sedation (respiratory depression, lethargy, hypotonia) and/or withdrawal symptoms (hyperreflexia, irritability, restlessness, tremors, inconsolable crying, and feeding difficulties) in the neonate. Monitor neonates exposed to benzodiazepines, including Byfavo, during pregnancy or labor for signs of sedation and monitor neonates exposed to benzodiazepines during pregnancy for signs of withdrawal and manage these neonates accordingly.

## Pediatric Neurotoxicity

Published animal studies demonstrate that anesthetic and sedation drugs that block NMDA receptors and/or potentiate GABA activity increase neuronal apoptosis in the developing brain and result in long-term cognitive deficits when used for longer than 3 hours. The clinical significance of this is not clear. However, the window of vulnerability to these changes is believed to correlate with exposures in the third trimester of gestation through the first several months of life but may extend out to approximately 3 years of age in humans.

Anesthetic and sedation drugs are a necessary part of the care of children needing surgery, other procedures, or tests that cannot be delayed, and no specific medications have been shown to be safer than any other. Decisions regarding the timing of any elective procedures requiring anesthesia should take into consideration the benefits of the procedure weighed against the potential risks.

## Adverse Reactions

The most common adverse reactions reported in >10% of patients (N=630) receiving Byfavo 5-30 mg (total dose) and undergoing colonoscopy (two studies) or bronchoscopy (one study) were: hypotension, hypertension, diastolic hypertension, systolic hypertension, hypoxia, and diastolic hypotension.

## Use in Specific Populations

### *Pregnancy*

Neonates born to mothers using benzodiazepines late in pregnancy have been reported to experience symptoms of sedation and/or neonatal withdrawal. Available data from published observational studies of pregnant women exposed to benzodiazepines do not report a clear association with benzodiazepines and major birth defects.

Benzodiazepines cross the placenta and may produce respiratory depression, hypotonia, and sedation in neonates. Monitor neonates exposed to Byfavo during pregnancy or labor for signs of sedation, respiratory depression, hypotonia, and feeding problems. Monitor neonates exposed to Byfavo during pregnancy for signs of withdrawal. Manage these neonates accordingly.

### *Lactation*

There are reports of sedation, poor feeding, and poor weight gain in infants exposed to benzodiazepines through breast milk. Infants exposed to Byfavo through breast milk should be monitored for sedation, poor feeding, and poor weight gain. A lactating woman may consider interrupting breastfeeding and pumping and discarding breast milk during treatment and for 5 hours after Byfavo administration.

### *Pediatric Use*

Safety and effectiveness in pediatric patients have not been established. Byfavo should not be used in patients less than 18 years of age.

### *Geriatric Use*

No overall differences in safety or effectiveness were observed between these subjects and younger subjects. However, there is a potential for greater sensitivity (eg, faster onset, oversedation, confusion) in some older individuals. Administer supplemental doses of Byfavo slowly to achieve the level of sedation required and monitor all patients closely for cardiorespiratory complications.

### *Hepatic Impairment*

In patients with severe hepatic impairment, the dose of Byfavo should be carefully titrated to effect. Depending on the overall status of the patient, lower frequency of supplemental doses may be needed to achieve the level of sedation required for the procedure. All patients should be monitored for sedation-related cardiorespiratory complications.

## Abuse and Dependence

Byfavo is a federally controlled substance (CIV) because it contains remimazolam which has the potential for abuse and physical dependence.

To report SUSPECTED ADVERSE REACTIONS, contact Acacia Pharma at 1-877-357-9237 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

**Please see full [Prescribing Information](#).**

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