FACT SHEET FOR HEALTH CARE PROVIDERS

EMERGENCY USE AUTHORIZATION (EUA) OF FRESENIUS PROPOVEN 2% EMULSION

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, Fresenius Propoven 2% (propofol 20 mg/mL) Emulsion 100 mL, to maintain sedation via continuous infusion in patients greater than 16 years old who require mechanical ventilation in an intensive care unit (ICU) setting.

CAUTION: THERE IS A RISK OF UNINTENTIONAL OVERDOSE WITH THIS UNAPPROVED PRODUCT. Fresenius Propoven 2% Emulsion contains the same active ingredient, propofol, as FDA-approved Diprivan Injectable Emulsion USP 10 mg/mL, but contains double the concentration. BECAUSE OF THIS DIFFERENCE IN CONCENTRATION BETWEEN THIS UNAPPROVED PRODUCT AND THE FDA-APPROVED PRODUCT, THERE IS A RISK OF UNINTENTIONAL OVERDOSE.

NOTE IMPORTANT DIFFERENCES IN FORMULATION AND LABELING BETWEEN THE CURRENT U.S. MARKETED FDA-APPROVED DIPRIVAN INJECTABLE EMULSION, USP 10 MG/ML ® (DIPRIVAN®) PRODUCTS AND FRESENIUS PROPOVEN 2% EMULSION. SEE DETAILS BELOW BEFORE ADMINISTERING FRESENIUS PROPOVEN 2% EMULSION.

Fresenius Propoven 2% Emulsion 100mL is not an FDA-approved drug in the United States. However, FDA has issued an EUA permitting the emergency use of Fresenius Propoven 2% Emulsion during the COVID-19 pandemic.

The scope of the EUA is limited as follows:

- Fresenius Propoven 2% Emulsion will be **used only to maintain sedation via continuous infusion in patients greater than 16 years old** who require mechanical ventilation.
- Fresenius Propoven 2% Emulsion will be administered only by a licensed healthcare provider **in an ICU setting**.
- Fresenius Propoven 2% Emulsion **will NOT be administered to pregnant women**, unless there are no FDA-approved products available to maintain sedation for these patients should they require mechanical ventilation in an ICU setting.
- Fresenius Propoven 2% Emulsion will be used only in accordance with the dosing regimens as detailed in the authorized Fact Sheets.

Product Description

Consistent with the EUA, Fresenius Kabi USA will offer the following presentation of Fresenius Propoven 2% (propofol 20 mg/mL) Emulsion:

Product Name And Description	MCT/LCT Concentration	Source/ Type of Oil	Size
Fresenius Propoven 2% Propofol Emulsion for Continuous Infusion 2,000 mg/100 mL (20 mg/mL)	Medium Chain Triglycerides (MCT) 50 mg/mL Long Chain Triglycerides (LCT) 50 mg/mL	soybean oil, refined; medium-chain triglycerides	100 mL

***NOTE: This propofol 20 mg/mL product contains double the concentration of propofol compared to the FDA-approved and marketed Diprivan (propofol) Injectable Emulsion, USP 10 mg/mL product.**

Fresenius Propoven 2% Emulsion 50 mL is approved in Europe and other international countries. The Fresenius Propoven 2% Emulsion 100mL product will be manufactured by Fresenius Kabi AG in the same FDA inspected facilities as DIPRIVAN® and other Propoven 2% fill sizes.

Key Differences between FDA-approved Diprivan Injectable Emulsion, USP 10 mg/mL Products and Fresenius Propoven 2% (Propofol 20 mg/mL) Emulsion for Continuous Infusion

	Diprivan Injectable Emulsion, USP 10 mg/mL	Fresenius Propoven 2% (propofol 20 mg/mL) Emulsion	What does this mean to you as a healthcare professional?
Concentration	Contains propofol 10 mg/mL	**Contains propofol 20 mg/mL**	**THERE IS A RISK OF UNINTENTIONAL OVERDOSE WITH THIS UNAPPROVED PRODUCT.** Fresenius Propoven 2% (propofol 20 mg/mL) is **DOUBLE THE CONCENTRATION** of US marketed Diprivan 10 mg/mL (Diprivan 1%). Exercise caution and implement steps to ensure dosing calculations, infusion rates and infusion pump settings are accurate. Addition of the new concentration (20 mg/mL) to the drug library of the respective pumps and to electronic health records (EHR) must be implemented.
Indication	General anesthesia, procedural sedation, ICU sedation	**ICU sedation ONLY**	Fresenius Propoven 2% is only **to maintain sedation via continuous infusion in patients greater than 16 years old who require mechanical ventilation in the ICU setting.**
Patient Population	Greater than 3 years old (procedural sedation and general anesthesia) Greater than 16 years old (ICU sedation)	**Greater than 16 years old (ICU sedation)**	Fresenius Propoven 2% is only indicated to maintain sedation via continuous infusion for patients greater than 16 years old who require mechanical ventilation in the ICU setting. Fresenius Propoven 2% should **not be used in pregnant women** unless there are no FDA-approved products available to maintain sedation for these patients who require mechanical ventilation in an ICU setting.
Composition	Contains long-chain triglycerides (LCT)	**Contains a combination of medium-chain triglycerides (MCT)** and long-chain triglycerides (LCT)	Prolonged IV infusion of MCT to pregnant rabbits has been reported in the published literature to increase the **RISK OF NEURAL TUBE DEFECTS**. Because it is not yet clear if there is differential risk for adverse developmental effects with Fresenius Propoven 2% compared to Diprivan 1%, **Fresenius Propoven 2% SHOULD NOT BE USED IN PREGNANT WOMEN unless there are no FDA-approved products**

			available to maintain sedation in these patients who require mechanical ventilation in an ICU setting.
Dosing	See package insert	**Administration rates of 0.3 to 4.0 mg propofol/kg bodyweight/h** have been demonstrated to provide adequate sedation	Infusion rates greater than 4.0 mg propofol/kg bodyweight/h are not recommended due to risk of Propofol Infusion Syndrome. The duration of administration must not exceed 7 days.
Method of administration	Bolus or infusion	**Infusion ONLY**	Fresenius Propoven 2% Emulsion is administered **undiluted** intravenously by continuous infusion. Containers should be shaken before use. If two layers can be seen after shaking the emulsion should not be [illegible]. **Do not admix with other medicinal products.** Co-administration of other medicinal products or fluids added to the Fresenius Propoven 2% Emulsion infusion line must occur close to the cannula site using a Y-piece connector or a three-way valve. Fresenius Propoven 2% Emulsion must not be administered via a microbiological filter.
Other Special Patient Populations	See package insert	**Caution should be taken when treating patients with mitochondrial disease, epilepsy, and disorders of fat metabolism.**	Patients with mitochondrial disease may be susceptible to exacerbations of their disorder when undergoing ICU care. Maintenance of normothermia, provision of carbohydrates and good hydration are recommended for such patients. The early presentations of mitochondrial disease exacerbation and of the 'propofol infusion syndrome' may be similar. Although several studies have demonstrated efficacy in treating status epilepticus, administration of propofol in epileptic patients may also increase the risk of seizure. For these patients, as well as for ARDS/respiratory failure and tetanus patients, sedation maintenance dosages were generally higher than those for other critically ill patient populations. Appropriate care should be applied in patients with disorders of fat metabolism and in other conditions where lipid emulsions must be used cautiously. It is recommended that blood lipid levels should be monitored if propofol is administered to patients

			thought to be at particular risk of fat overload. Administration of propofol should be adjusted appropriately if the monitoring indicates that fat is being inadequately cleared from the body. If the patient is receiving other intravenous lipid concurrently, a reduction in quantity should be made in order to take account of the amount of lipid infused as part of the propofol formulation; 1.0 mL of Fresenius Propoven 2% Emulsion contains approximately 0.1 g of fat.
Drug Interactions	See package insert	Drug interaction with **fentanyl, cyclosporine and valproate**	After administration of fentanyl, the blood level of propofol may be temporarily increased with an increase in the rate of apnea. Leukoencephalopathy has been reported with administration of lipid emulsions as used for Fresenius Propoven 2% Emulsion in patients receiving cyclosporine. A need for lower propofol doses has been observed in patients taking valproate. When used concomitantly, a dose reduction of propofol may be considered.
Presence of antimicrobial retardant	Yes	**NO**	Fresenius Propoven 2% Emulsion does NOT contain an anti-microbial retardant such as ethylenediaminetetraacetic acid (EDTA), sodium metabisulfite, or benzyl alcohol/sodium benzoate. **STRICT ASEPTIC TECHNIQUE MUST ALWAYS BE MAINTAINED DURING HANDLING.** Each vial of Fresenius Propoven 2% Emulsion is intended only for single administration for an individual patient. Vials are **not intended for multiple use.** If propofol is to be aspirated, it must be drawn aseptically into a sterile syringe immediately after breaking the vial seal. Administration must commence without delay. The unused portion of a vial should be discarded immediately after opening. As with any propofol used in IV infusion, **discard all product and infusion lines after 12 hours.**
Contraindications	See package insert	Fresenius Propoven 2% Emulsion should not be used in patients who	Fresenius Propoven 2% Emulsion is contraindicated in patients with a known hypersensitivity to propofol or

		are hypersensitive to peanut or soy.	any of the excipients: Soybean oil; Medium-chain triglycerides; Purified egg phosphatides; Glycerol; Oleic acid; Sodium hydroxide; Water for injections Fresenius Propoven 2% Emulsion should not be used in patients who are hypersensitive to peanut or soy.
Bar code	Unit of use barcode on individual vials	No unit of use barcode	The barcode used on Fresenius Propoven 2% Emulsion may not register accurately on U.S. scanning systems. Institutions should manually input the product into their systems to confirm that barcode systems do not provide incorrect information when the product is scanned. Alternative procedures should be followed to assure that the correct drug product is being used and administered to individual patients.
	For questions regarding Fresenius Propoven 2% Emulsion in the United States, please contact Fresenius Kabi USA Medical Affairs at 1-800-551-7176 Option 3, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail medinfo.USA@fresenius-kabi.com.		

What is an EUA?

The United States FDA has made the Fresenius Propoven 2% Emulsion available to treat patients in an ICU during the COVID-19 pandemic under an emergency access mechanism called an Emergency Use Authorization (EUA). The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

Fresenius Propoven 2% Emulsion made available under an EUA have not undergone the same type of review as an FDA-approved product. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives. Based on the totality of scientific evidence available, it is reasonable to believe that the Fresenius Propoven 2% Emulsion has met certain criteria for safety, performance, and labeling and may be effective to maintain sedation via continuous infusion in patients greater than 16 years old who require mechanical ventilation in an ICU setting.

This EUA for Fresenius Propoven 2% Emulsion is in effect for the duration of the COVID-19 declaration justifying emergency use of the products, unless terminated or revoked (after which the products may no longer be needed). The EUA will end when the declaration is terminated or revoked or when there is a change in the approval status of the product such that an EUA is no longer needed.

This communication and product information is available on the Fresenius Kabi USA website https://www.fresenius-kabi.com/us/pharmaceutical-product-updates as well as the FDA webpage which includes links to patient fact sheet and manufacturer's instructions https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#covidtherapeutics.

Adverse Event Reporting

Report adverse events or quality problems experienced with the use of this product.

Healthcare facilities and prescribing health care providers or their designee receiving Fresenius Propoven 2% Emulsion will track all medication errors associated with the use of and all serious adverse events that are considered to be potentially attributable to Fresenius Propoven 2% Emulsion use and must report these to FDA using one of the following methods:

- Complete and submit a MedWatch form online (www.fda.gov/medwatch/report.htm)
- Complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178) (this form can be found via link above).

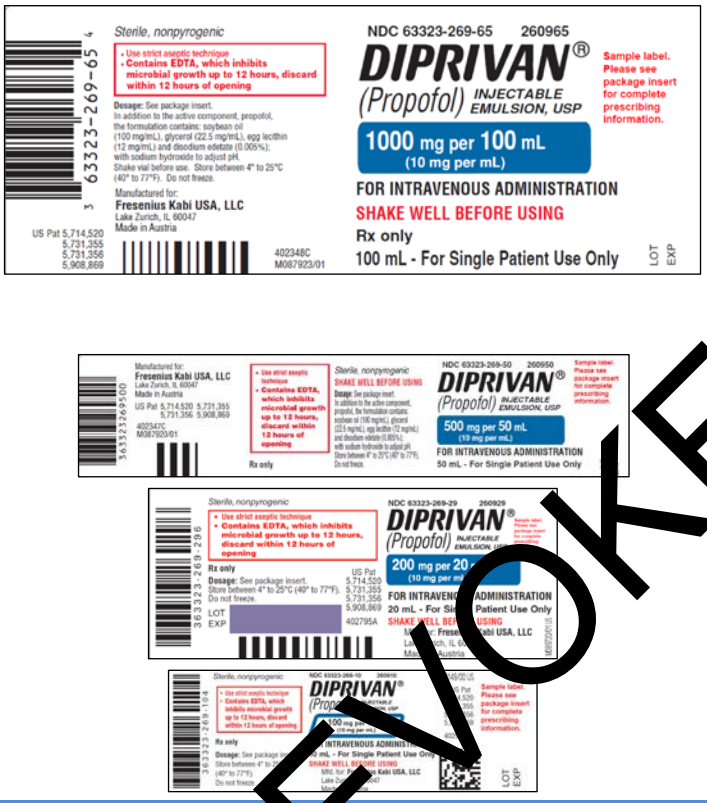
Call 1-800-FDA-1088 for questions. Submitted reports should state, "use of Fresenius Propoven 2% Emulsion was under an EUA" at the beginning of the question "Describe Event" for further analysis.

Fresenius Kabi USA CONTACT NUMBERS: Please use the following contact numbers as appropriate:

Reason To Call	Department	Number
ADE Reporting	Vigilance Department	1-800-551-7176*
Clinical/Technical Info. Or Product Complaint	Medical Affairs Department	
Product Availability & Ordering	Customer Service Department	1-888-386-1300

*Call Fresenius Kabi USA Vigilance or Medical Affairs Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail adverse.events.USA@fresenius-kabi.com or productcomplaint.USA@fresenius-kabi.com.

Comparison Table of FDA-approved Diprivan Injectable Emulsion, USP 10 mg/mL Products and Fresenius Propoven 2% (Propofol 20 mg/mL) Emulsion for Continuous Infusion

Product Name	Diprivan (propofol) Injectable Emulsion, USP	Fresenius Propoven 2% Emulsion for Infusion
Propofol Concentration	10 mg/mL	20 mg/mL
Product Labels		
Active Ingredient	Propofol	Propofol
Excipients	Soybean oil (100 mg/mL) Glycerol (22.5 mg/mL) Egg lecithin (12 mg/mL) Disodium edetate (0.005%) Sodium hydroxide	Soybean oil (50 mg/mL) Medium-chain triglycerides (50 mg/mL) Glycerol (22.5 mg/mL) Purified egg phosphatides (12 mg/mL) Oleic acid (0.4 to 0.8 mg/mL) Sodium hydroxide
Fill Volume	10 mL, 20 mL, 50 mL, 100 mL	100 mL
Duration	Drug holiday after 5 days to replace urine zinc losses	Do Not Administer for more than 7 days
Dilution	Dilution to 2 mg/mL with D5W only	Do Not Dilute
Bolus	Bolus injection permitted	Continuous infusion only
Description	Single Dose Vial for Single Patient Use Only	Single Dose Vial for Single Patient Use Only
Company	Fresenius Kabi USA	Fresenius Kabi AG