APP®
A Fresenius Kabi Company

URGENT: PROPOFOL UPDATE

June 19, 2012

Dear Healthcare Professional,

APP® is coordinating with the FDA to increase the availability of propofol products as continuous supply of this essential drug is critical to patient care. Therefore, APP, under an exercise of enforcement discretion by FDA, will *reintroduce* **Fresenius Propoven 1%** (propofol 1%) to the US market. **Fresenius Propoven 1%** (propofol 1%) to be temporarily imported in 2012 is the same anesthesia product that was imported during the 2009 and 2010 propofol drug shortage. **Fresenius Propoven 1%** (propofol 1%) is manufactured in FDA inspected facilities by APP's parent company, Fresenius Kabi AG. All of these facilities are in compliance with FDA manufacturing standards.

At this time, FDA has exercised its enforcement discretion to allow for the importation of **Fresenius Propoven 1%** (propofol 1%) solely by APP during the critical shortage of propofol. Importation or distribution of **Fresenius Propoven 1%** (propofol 1%) vials by any entity other than APP, or its authorized distributors, is outside the scope of FDA's enforcement discretion, and **Fresenius Propoven 1%** (propofol 1%) is not an FDA approved marketed drug in the United States.

Effective immediately, and during this temporary period, APP will offer propofol 1% in the following versions:

	APP DIPRIVAN®	**APP Propofol 1%** (generic DIPRIVAN®)	**Fresenius Propoven 1%** (propofol 1%)
20 mL SD Vial	NDC # 63323-269-20	NDC # 63323-270-25	N/A
20 mL Ampule	N/A	N/A	Product # 831230221
50 mL SD Vial	NDC # 63323-269-50	NDC # 63323-270-50	Product # 4266051
100 mL SD Vial	NDC # 63323-269-65	NDC # 63323-270-65	Product # 4266031

APP's Propofol Injectable Emulsion, USP formulation is identical to DIPRIVAN®

Fresenius Propoven 1% (propofol 1%) contains the same active ingredient, propofol, in the same concentration as APP DIPRIVAN® (propofol 1%). **It is important to note that there are some key differences in the formulation and labeling between the US marketed propofol products and the international Fresenius Propoven 1% (propofol 1%), that you need to be aware of:**

- **Fresenius Propoven 1%** (propofol 1%) contains a combination of long-chain triglycerides (LCT), similar to those found in DIPRIVAN®; however, **Fresenius Propoven 1%** (propofol 1%) also contains medium-chain triglycerides (MCT) that are not present in the DIPRIVAN® formulation. As with DIPRIVAN® and other propofol products, special care should be applied in patients with disorders of fat metabolism, patients receiving Total Parenteral Nutrition (TPN), and in patients with other conditions where lipid emulsions must be used with caution.
- **Fresenius Propoven 1%** (propofol 1%) does **NOT** contain an anti-microbial retardant such as ethylenediaminetetraacetic acid (EDTA), sodium meta-bisulfate, or benzyl alcohol/sodium benzoate.
  - **STRICT ASEPTIC TECHNIQUE MUST ALWAYS BE MAINTAINED DURING HANDLING.**
  - Each vial of **Fresenius Propoven 1%** (propofol 1%) is intended only for single administration for an individual patient. **Vials are not intended for multidose use.**

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- As stated in USP Chapter 797, Pharmaceutical Compounding-Sterile Preparations, the solution content of ampules should be passed through a sterile filter needle to remove any particles. When withdrawing from **Fresenius Propoven 1%** (propofol 1%) 20 mL glass ampules, the use of a 5 micron blunt filter needle is recommended in order to maintain the integrity of the emulsion and reduce the risk of particulate including glass.
- Unused **Fresenius Propoven 1%** (propofol 1%) should be discarded within 6 hours after being drawn up into a syringe.
- The unused portion of a vial or ampule should be discarded immediately after opening.
- As with any propofol 1% used for IV infusion, discard all product and infusion therapy systems after 12 hours.

❖ **Fresenius Propoven 1%** (propofol 1%) is contraindicated in patients who are allergic to soy or peanut.

❖ The barcode used on **Fresenius Propoven 1%** (propofol 1%) product is an international pharmaceutical manufacturing code and may not be appropriately recognized by scanning systems used in the United States. Institutions should 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 prepared and administered to individual patients.

❖ **Fresenius Propoven 1%** (propofol 1%) product information sheet contains a *patient information leaflet* as part of the international requirement for propofol 1%. For questions regarding **Fresenius Propoven 1%** (propofol 1%) in the United States, please contact APP Vigilance and Medical Affairs at 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail appmedicalinfo@APPpharma.com.

❖ The attached product comparison table highlights the key differences in formulation and labeling between APP DIPRIVAN® and **Fresenius Propoven 1%** (propofol 1%).

Please find attached a copy of the Fresenius Propoven 1% package insert.

To further supplement supply, APP maintains its commitment to expedite the manufacturing of DIPRIVAN® and Propofol to maintain continuous releases on all product presentations. We believe the combination of continuous APP DIPRIVAN® and APP Propofol releases in addition to availability of **Fresenius Propoven 1%** (propofol 1%) will help alleviate a market shortage.

Please evaluate the use of **Fresenius Propoven** (propofol 1%) in your institution and begin placing orders immediately. If your institution desires not to use **Fresenius Propoven** (propofol 1%), you may continue to order APP DIPRIVAN® and/or APP Propofol; APP will reserve some DIPRIVAN® and/or Propofol for those patients where **Fresenius Propoven** (propofol 1%) is contraindicated.

All direct customer orders for propofol products, including APP DIPRIVAN®, APP Propofol, and **Fresenius Propoven** (propofol 1%), will remain on an allocation process. APP will closely monitor the distribution of all propofol products to help manage imbalances in supply. APP will continue to replenish the distribution channel with all propofol products, and encourage customers to check with wholesaler and distributor partners for product availability of APP DIPRIVAN®, APP Propofol, and **Fresenius Propoven** (propofol 1%). Please be aware that **Fresenius Propoven** (propofol 1%) is not returnable and not for resale.

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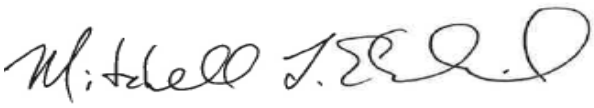
If you have additional questions, please contact Customer Service at 1-888-386-1300, Monday – Friday, between the hours of 7 a.m. and 6 p.m. (CST) or APP Vigilance and Medical Affairs at 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail appmedicalinfo@APPpharma.com. This communication and updated product information is available on the APP web site www.APPpharma.com as well as on the FDA Drug Shortage web site http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm.

To report adverse events among patients administered **Fresenius Propoven 1%** (propofol 1%), please call 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST). Adverse event information may also be reported to FDA's MedWatch Adverse Reporting System either online, by regular mail or by fax:

- Online: www.fda.gov/medwatch/report.htm
- Regular Mail: use postage-paid FDA form 3500 available at: www.fda.gov/MedWatch/getforms.htm
  Mail to MedWatch, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787
- Fax: 1-800-FDA-0178

If you have any questions about the information contained in this letter or the safe and effective use of **Fresenius Propoven 1%** (propofol 1%), please contact our Vigilance and Medical Affairs department at 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail appmedicalinfo@APPpharma.com

Sincerely,



Mitchell L. Ehrlich
Vice President, Quality

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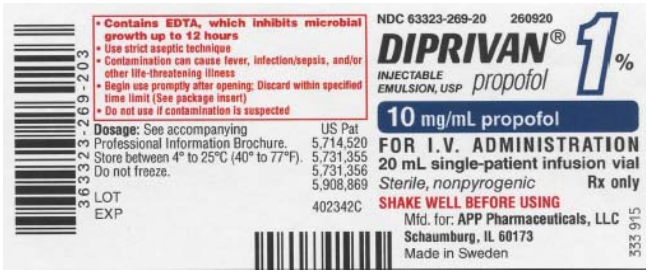
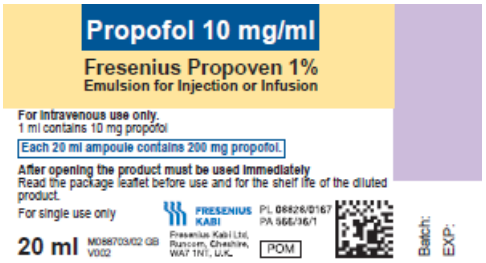
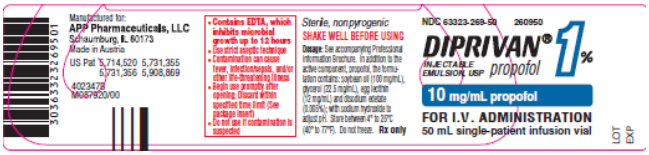
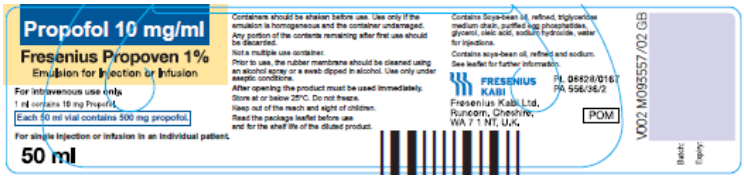
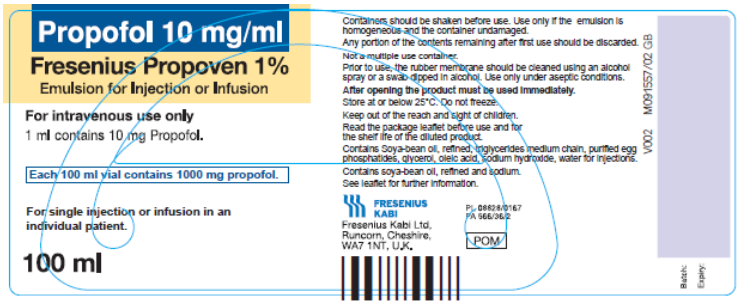
Comparison Table:

APP Label DIPRIVAN® (propofol 1%)	Fresenius Label Propoven 1% (propofol 1%)
	 **Glass Ampule Label**
	
	

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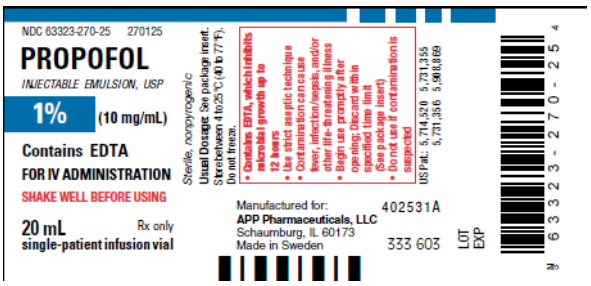
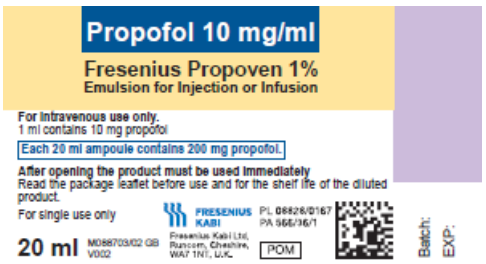
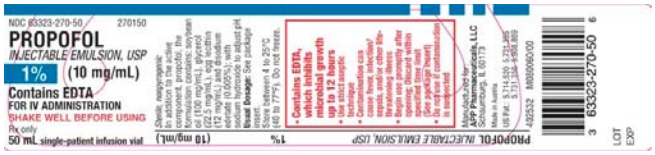
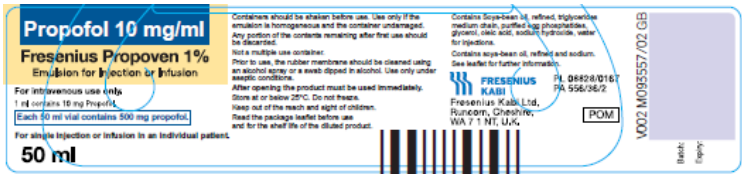
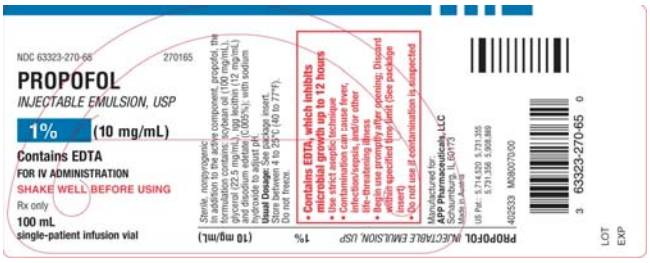
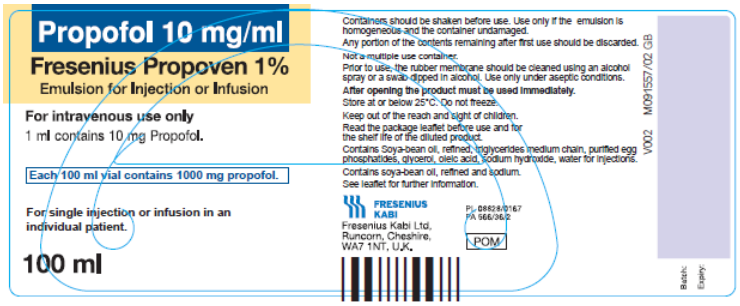
APP Label Propofol 1%	Fresenius Label Propoven 1% (propofol 1%)
	 **Glass Ampule Label**
	
	

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APP DIPRIVAN® and APP Propofol (propofol 1%)	Fresenius Propoven 1% (propofol 1%)	What does this mean to you, as a Healthcare Professional?
Contains ethylenediaminetetraacetic acid (EDTA)	**Does not contain a preservative** such as ethylenediaminetetraacetic acid (EDTA), benzyl alcohol/sodium benzoate, or sodium meta-bisulfate	**Fresenius Propoven 1%** (propofol 1%) **is a single dose vial for administration to a single patient.** **Strict aseptic technique must always be maintained during handling**
Indications and contraindications: see package insert	Indications and contraindications: see package insert **Please note: see package insert on 4.2 method of administration, 4.3 contraindications, and 4.4 special warning and precautions for use**	**Fresenius Propoven 1%** (propofol 1%) may be used for induction of anesthesia in patients above the age of 3 years or for maintenance of anesthesia in patients above the age of 2 months. **Fresenius Propoven 1%** (propofol 1%) is contraindicated in patients who are allergic to soy or peanut.
Contains long-chain triglycerides (LCT)	Contains a combination of medium-chain triglycerides (MCT) plus long-chain triglycerides (LCT)	The presence of MCTs should be taken into consideration when treating patients with disorders of fat metabolism or who are receiving TPN.
Unit of use barcode on individual vials	No unit of use barcode	The barcode used on **Fresenius Propoven 1%** (propofol 1%) may not register accurately on US scanning systems. Other means of confirming the correct drug is being prepared and administered to the correct patient should be utilized.
N/A	Contains a *patient information leaflet*.	For questions regarding **Fresenius Propoven 1%** (propofol 1%) in the United States, please contact APP Vigilance and Medical Affairs at 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail appmedicalinfo@APPpharma.com.
Only available in Single Dose Vials (SDV)	Available in 20 mL glass ampule and 50 mL & 100 mL single dose vials (SDV)	When withdrawing from **Fresenius Propoven 1%** (propofol 1%) 20 mL glass ampules, the use of a 5 micron blunt filter needle is recommended in order to maintain the integrity of the emulsion and reduce the risk of particulate including glass.

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