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Safe Practices with Exalgo®

By: Marina Stepanski, Pharm.D.

Background: Exalgo® (Mallinckrodt), an extended-release hydromorphone formulation, was approved by the Food and Drug Administration (FDA) on March 1, 2010 for the treatment of moderate to severe chronic pain in opioid tolerant patients.[1] It is not indicated for the treatment of acute pain or for the management of post-operative pain. Exalgo® contains an osmotic extended release oral delivery system (OROS®) which allows hydromorphone to be delivered at a constant rate over a 24-hour period. This article will highlight safe practices with Exalgo®.

What does opioid tolerant mean? Opioid tolerant is defined as taking at least 60 mg of oral morphine per day, 25 mcg transdermal fentanyl/hour, 30 mg of oral oxycodone/day, 8 mg of oral hydromorphone/day, 25 mg of oral oxymorphone/day or an equianalgesic dose of another opioid, for a week or longer.[1]

What is the OROS® Delayed-Release System? The OROS® "push-pull" technology consists of a bilayer tablet core surrounded by a semipermeable membrane which is permeable to water, but not to drug.[2] The "push layer" of the OROS® system contains a hydrophilic expanding compartment, while the "pull layer" contains active drug and excipients. Water from the gastrointestinal tract flows across the semipermeable membrane causing an osmotic pump to activate in the "push layer". This osmotic pump releases hydromorphone through a small hole in the "pull layer" of the tablet at a consistent rate over a 24-hour period. This technology has been proven to be tamper resistant because the OROS® containing tablet is difficult to crush or extract for injection.[3]

Can Exalgo® be crushed? No, Exalgo® cannot be crushed, chewed, or opened.[1]

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New-trition Update: Novel IV Lipid Emulsion

By: Lindsey Glaze, Pharm.D.

Background: Smoflipid® (Fresenius Kabi) is a new intravenous lipid emulsion indicated for adults as a source of essential fatty acids and calories for parenteral nutrition when enteral nutrition is insufficient or not possible. **Smof**lipid® contains **s**oybean oil, **m**edium-chain triglycerides, **o**live oil, and **f**ish oil.[1] Smoflipid® also contains α-tocopherol, which protects long-chain polyunsaturated fats from peroxidation.[2] It was approved for use by the Food and Drug Administration (FDA) on July 13, 2016, but has been used in Europe since the early 2000s.[3]

What is the difference between Intralipid® and Smoflipid®? Smoflipid® 20% (0.2 grams/mL) lipid injectable emulsion is comprised of 30% soybean oil, 30% medium-chain triglycerides, 25% olive oil, and 15% fish oil. Intralipid® 10% and 20% are comprised of 100% soybean oil.[4] The components of Smoflipid® provide a lower ratio of

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This medication must be swallowed whole. Crushing Exalgo® would cause dose-dumping which could lead to life-threatening adverse events.

Can Exalgo® be taken with food or alcohol? The pharmacokinetic profile of Exalgo® remains unchanged when taken with or without food.[1] Similar effects were seen when different strengths of alcohol were administered with Exalgo®. Although there was an increase in the Cmax, there was no dose dumping seen with Exalgo®.[4] This is important to note since Palladone®, another extended-release hydromorphone formulation, was withdrawn from the market in 2005 due to dose dumping prompted by coadministration with alcohol.[5] Although dose dumping was not seen with Exalgo®, patients should still be told not to drink alcohol with any hydromorphone formulation due to additive central nervous system (CNS) side effects.[1]

Does Exalgo® have a REMS? Yes, Exalgo® is included in the Extended-Release (ER) and Long-Acting (LA) Opioid Analgesic Risk Evaluation and Mitigation Strategies (REMS).[6] The elements of this REMS include a medication guide that is dispensed with each ER/LA opioid and a training FDA guide for healthcare providers who will prescribe these medications.

What is the major safety concern with Exalgo®? Exalgo® is available as 8 mg, 12 mg, 16 mg, and 32 mg oral tablets.[1] Immediate-release hydromorphone is also available as an 8 mg oral tablet. The overlap in strengths can lead to medication errors. To help prevent patients from inadvertently getting the wrong formulation the Institute for Safe Medication Practices (ISMP) has provided some safety recommendations.

- When writing the prescription for a hydromorphone product include the proprietary name
- Spell out extended-release as opposed to writing ER on the prescription
- When writing for immediate-release **do not** attach the IR modifier to the hydromorphone
- Verify the prescribed hydromorphone product dispensed matches the prescription
- Verify that the patient is opioid tolerant by asking the patient about his/her medication history or by checking the patient's profile
- Counsel patients to take Exalgo® once daily as this is not meant for acute pain[7]

What is the best way to convert a patient to Exalgo® from another opioid formulation? In order to convert a patient to Exalgo®, use the information provided in the Exalgo® package insert.[1] The Ohio Pain Initiative (OPI) dosing conversion chart and other opioid conversion charts which include hydromorphone do not provide as accurate and precise dose conversion information. Additionally, when utilizing the conversion ratios in the package insert to calculate a dose for Exalgo®, remember to start at 50% of the calculated dose and titrate upward as needed. It is important to note that the dosage range used in clinical trials for Exalgo® was 8- to 64-mg administered once daily.

What is the Formulary Status of Exalgo®? Exalgo® has been added to the CCHS Formulary restricted to Palliative Medicine and the Department of Hematology and Medical Oncology.

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omega-6 to omega-3 fatty acids compared to Intralipid®. Smoflipid® also contains eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are long-chain polyunsaturated omega-3 fatty acids. Both DHA and EPA are essential fatty acids that are not produced endogenously. The predominant fat in Intralipid® is linoleic acid, which is an essential omega-6 fatty acid.[1]

What patient populations could benefit from the different composition of Smoflipid®? Smoflipid® has been studied and approved for use in adult patients as a safe and efficacious alternative to a standard soybean oil lipid emulsion. Smoflipid® has also been studied in preterm infants.[5,6] The unique composition of Smoflipid® has been reported to be safe and well-tolerated in this neonatal population. Smoflipid® could also be beneficial as it provides a source of essential fatty acids, EPA and DHA, which preterm infants need for growth as well as visual and cognitive development.[5]

What benefits have Smoflipid® shown over traditional soybean oil lipid emulsions (Intralipid®)? One trial evaluated Smoflipid® versus Intralipid® in preterm infants for short-term use.[5] The primary outcome was safety based on changes in serum triglyceride levels from baseline to the end of the trial. The authors also evaluated other laboratory parameters to assess efficacy. After 7 days of treatment with Smoflipid® or Intralipid® both groups had increased serum triglycerides, which remained within normal limits. Patients on Smoflipid® also gained weight at the same rate as Intralipid®. The investigators noted that infants receiving Smoflipid® had significantly decreased total bilirubin levels compared to a significant increase in total bilirubin in the Intralipid® group. This finding suggests Smoflipid® may have a potential benefit in attenuating parenteral nutrition associated cholestasis in newborns.

Can Smoflipid® be administered via 3-in-1 chamber bags along with other parenteral nutrition components? Yes, Smoflipid® can be administered in the same bag (i.e., 3-in-1) with other components of parenteral nutrition if it is mixed in the proper proportions with dextrose and amino acids.[1] To avoid precipitation, dextrose should first be injected in the parenteral container. Next, the amino acid solution should be injected in the container. Last, Smoflipid® can be added to the other components to make a total nutrient admixture (TNA). After each injection, the container should be shaken gently to minimize localized concentration effects. The final product should be shaken gently to distribute all contents evenly. This admixture should be infused soon after preparation or refrigerated under 2° to 8° C until use. Smoflipid® should be infused through DEHP-free tubing with a 1.2 micron in-line filter.

What is the Formulary Status of Smoflipid®? Smoflipid® was added to the Pediatric CCHS Formulary restricted to the Department of Pediatric Gastroenterology. Smoflipid® should be reserved for pediatric patients with short bowel syndrome and/or TPN cholestasis.

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