



ISMP Medication Safety Alert!®

E-mail: isminfo@ismp.org
Hotline: 1 800 FAIL SAF(E)

Community/Ambulatory Care Edition

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Safe practice with the potent once daily opioid Exalgo

On March 1, 2010, FDA approved the Schedule II controlled substance **EXALGO**, a once daily hydromorphone hydrochloride extended-release tablet. Exalgo is indicated for the management of moderate to severe pain in opioid-tolerant patients requiring continuous, around-the-clock opioid analgesia for an extended period of time. **The drug is not indicated for use as an “as needed” analgesic or for the management of acute or postoperative pain.** Exalgo is available in 8, 12, and 16 mg tablet strengths that should be swallowed whole, and not broken, chewed, dissolved, crushed, or injected. Exalgo is contraindicated in patients who are **not** opioid-tolerant or those with impaired pulmonary function, paralytic ileus, or a narrowed or obstructed gastrointestinal tract.

Exalgo will be launched with a Risk Evaluation and Mitigation Strategy (REMS) program, which includes a Medication Guide and educational materials to ensure appropriate patient selection and dosing. The product packaging contains an encased statement “For opioid-tolerant patients only” to emphasize this point. Patients are considered opioid-tolerant if they have been taking at least one of the following for 1 week or longer:

- 8 mg of oral hydromorphone/day
- 25 mg of oral oxymorphone/day
- 30 mg of oral oxycodone/day
- 60 mg of oral morphine/day
- 25 mcg of transdermal fentanyl/hour
- Equianalgesic dose of another opioid.

The product package also highlights the words “Once Daily” to remind dispensing pharmacists of the dosing frequency for this medication.

Dose conversion to Exalgo requires calculation, and guidance is provided in the prescribing information to help ensure safe conversion from other opioids to Exalgo. The starting dose for Exalgo depends on the specific dose of opioid the patient is taking and the calculated total daily dose of oral hydromorphone. Prescribers should refer to the full prescribing information for dosage and instructions for administration.

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Safety Briefs

■ **How did this happen?** A patient’s daughter recently reported to ISMP that the community pharmacy her father used dispensed the antipsychotic **ABILIFY** (aripiprazole) 10 mg to him when he was prescribed **ARICEPT** (donepezil) 10 mg for Alzheimer’s Disease. Although the pharmacy-generated prescription label correctly listed both the patient’s name and Aricept, it was affixed to a manufacturer’s bottle of Abilify (see Figure 1). The mistake was not noticed and the patient took the incorrect medication for several weeks. The patient became increasingly confused, displayed atypical behavior, and frequently fell. He ultimately required admission to an Alzheimer’s unit at a local nursing home. A nurse at the facility intercepted the error



Figure 1. Pharmacy-generated label for Aricept affixed to an Abilify bottle.

because the patient’s medication did not look like the Aricept tablets other patients were taking. The patient eventually improved and returned home. It is unclear exactly how this error occurred; however, it could have been caught. The reporter recommends that pharmacy personnel

review and examine the prescription with the patient or caregiver at the time of pick-up, and we agree. This would increase the likelihood that a mistake is caught before it reaches the patient. The reporter stated that her pharmacist (at a different store than the one her father used) employs this technique and it seems quite effective. In addition, include a product description on the pharmacy-generated label and teach patients and caregivers to compare that description to the actual contents of the vial/bottle. Bar-code scanning during the production stage of the dispensing process could have identified the error as well.

■ **Same name, different drug.** We learned recently that **ZAVESCA**, marketed in the US as miglustat capsules, is also being marketed in other parts of the *cont'd on page 2*

Exalgo (cont'd from page 1)

Physicians may prescribe Exalgo 8 mg tablets as an initial daily dose. The 8 mg strength of Exalgo overlaps with currently marketed hydromorphone immediate-release products. This overlap in strength may contribute to medication errors if inadvertent substitution between the two hydromorphone products occurs. Confusion between the immediate- and extended-release products could result in an overdose, which may lead to serious adverse events such as respiratory depression and death. Confusion between immediate- and extended-release products could also result in an underdose, leading to poor efficacy. To prevent mix-ups and other types of medication errors with Exalgo, consider the safety recommendations provided below.

Prescribers

- To help minimize the risk of confusion between hydromorphone products, include the proprietary name Exalgo on prescriptions, which may provide greater differentiation than simply using the established name alone.
- If the established name is included or used alone, spell out “hydromorphone extended-release” instead of “hydromorphone ER.” Pharmacists may overlook the modifier “ER” and dispense hydromorphone immediate-release tablets instead of the extended-release tablets, resulting in inadequate around-the-clock pain control.
- When prescribing the immediate-release hydromorphone product by the established name, include just “hydromorphone.” Do not attach modifiers such as “IR” for immediate-release. Pharmacists may misinterpret “IR” for “ER,” especially with handwritten orders, and dispense Exalgo in error, resulting in dispensing the wrong formulation.
- Review the patient’s medication history and verify that the patient is opioid-tolerant before prescribing Exalgo.

Pharmacists and Nurses

- Verify the prescribed hydromorphone product with the order or prescription. Exalgo is dosed once daily while the usual dosing frequency for immediate-release hydromorphone is every 4 to 6 hours as needed.
- Verify opioid tolerance by asking the patient for his/her medication history and checking the patient’s pharmacy profile and medication administration record. Build alerts into the pharmacy computer system to remind the pharmacist to verify opioid tolerance.
- Counsel patients to take Exalgo once daily, to swallow the tablets whole without chewing or crushing them, and to

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world with the active ingredient escitalopram, which is **LEXAPRO** in the US. Miglustat is primarily used in the treatment of mild-to-moderate type 1 Gaucher disease when enzyme replacement therapy is not a therapeutic option. Escitalopram is a selective serotonin reuptake inhibitor used for depression and anxiety disorders. In 2005, ISMP noted a problem where some FDA-approved products have the same brand names as foreign drug products with completely different ingredients. FDA later published a Public Health Advisory noting that 105 US brand names are dangerously close to foreign brand names used for different products, and that patients who fill prescriptions abroad may get the wrong drugs. When patients travel overseas, FDA and ISMP suggest carrying an adequate supply of medications, as well as a list of the medications noting both generic and brand drug names. Those needing a temporary supply while overseas should confirm that the correct drug has been dispensed (by verifying the generic name/active ingredients of the dispensed product) since brand-name products may contain different active ingredients in different countries.

■ **Mandatory counseling when dispensing insulin pens.** A diabetes educator reported that a patient presented with a “mysterious” loss of control of her blood glucose. The patient had recently switched to using a **NOVOLOG MIX 70/30 FLEXPEN** (insulin aspart protamine suspension and insulin aspart injection, [rDNA origin]). In speaking with the patient, the diabetes educator discovered the patient did not know how to use the pen correctly despite having read the directions. The patient was able to measure her dose but was not pushing down on the button/plunger nor was she holding the pen in place (with the needle in the injection site) for at least 6 seconds. Once the diabetes educator worked with the patient to correct her technique, the patient required less insulin to control her blood sugar. The diabetes educator suggests that prescribers teach patients how to use the pen rather than expect the patient to learn it from the literature. We recommend that pharmacists provide patient education using the “teach-back” method too. Educational material on how to use the various insulin pens is available from the manufacturers that make them.

■ **Report bad advertising.** FDA’s Division of Drug Marketing, Advertising, and Communication (DDMAC) launched its **Bad Ad Program** (www.fda.gov/badad) on cont'd on page 3



Exalgo (cont'd from page 2)

avoid alcohol while taking this medication. Also advise patients to inform their healthcare provider if Exalgo does not provide adequate pain control.

- Verify patient understanding about how to take the tablets at home by asking open-ended questions.
- Advise patients to read the Medication Guide and call their healthcare provider if they have any questions.
- Instruct patients to check the appearance of each Exalgo tablet before taking it to ensure it matches the product description or image when this information is provided on the pharmacy-generated label or in the pharmacy leaflet.

FDA Advise-ERR was provided by the FDA Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis, in cooperation with ISMP.

Editor's note: ISMP urges clinicians to ensure Exalgo is prescribed, dispensed, and administered only to opioid-tolerant patients with chronic pain, not acute pain.

Safety Briefs (cont'd from page 2)

May 11 with a dual purpose: 1) to educate healthcare providers about the steps FDA is taking to prevent misleading or inaccurate promotion of prescription drugs by drug companies; and 2) to request help from healthcare providers in identifying and reporting these activities. Pharmaceutical companies spend up to three times more on advertising directly to healthcare professionals than consumers. Such “detailing” occurs primarily in medical offices, hospitals, and at medical meetings. Informative and responsible promotional efforts can provide professionals with valuable information about the latest drug therapies. However, information that may affect prescribing decisions must be accurate and balanced. You can report misleading prescription drug promotion by calling (877) RX-DDMAC (877-793-3622) or emailing the incident to BadAd@fda.gov. If you are unsure about what constitutes misleading promotion, please call DDMAC at (301) 796-1200.

Your Reports at Work!

In our February 2009 issue, we reported on cases of accidental ingestion of **Benadryl Extra Strength Itch Stopping Gel** (diphenhydrAMINE), some of which led to serious adverse reactions requiring emergency treatment or hospitalization. This topical Benadryl product is intended “For Skin Use Only.” Between 2001 and 2009, 121 cases of ingestion of Benadryl Extra Strength Itch Relief Gel were reported to the manufacturer. Of these cases, 7 resulted in patients requiring treatment in the emergency room, hospitalization, or admission to the intensive care unit. Other reported adverse events included hallucinations, unconsciousness, sleepiness, difficulty walking and speaking, and dizziness.

In response to reports, Johnson & Johnson, in cooperation with FDA, are making changes to the graphics and information displayed on the front of the product container to reduce the risk of consumers mistakenly ingesting the

medication. More information about this hazardous condition and the planned changes, with images, can be found on the FDA Web site at www.ismp.org/sc?k=ucm211395.

Reports like these should remind all of us about the importance of advising patients to always read the container and drug facts labels that are affixed to over-the-counter products. If they are unsure how the product is to be used, they should be encouraged to ask the pharmacist. “Shelf Talkers” in OTC areas encouraging patients to ask for a pharmacist if they have questions may help in this effort. Pharmacies and others who stock Benadryl Itch Stopping Gel should keep this product separate from products that are supposed to be swallowed. We also recommend that stores selling this product take the extra step to label shelves about the product being for application to the skin only. Otherwise consider not stocking this product at all until the updated product reaches the market.

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ISMP is a Federally Certified Patient Safety Organization, providing legal protection and confidentiality for submitted patient safety data and error reports. ISMP is also an FDA MEDWATCH partner. Call 1-800-FAIL-SAF(E) to report medication errors to the ISMP Medication Errors Reporting Program (MERP) or report online at www.ismp.org. Unless noted, published errors were received through the MERP. ISMP guarantees confidentiality and security of information received and respects reporters' wishes as to the level of detail included in publications. Editors: Michael J. Gaunt, PharmD; Michael R. Cohen, RPh, MS, ScD; Judy Smetzer, RN, BSN, FISMP. Institute for Safe Medication Practices, 200 Lakeside Drive, Suite 200, Horsham, PA 19044. Tel: 215-947-7797; Fax: 215-914-1492; EMAIL: community@ismp.org. This is a peer-reviewed publication.



One of the most important ways to prevent medication errors is to learn about problems that have occurred in other organizations and to use that information to prevent similar problems at your practice site. To promote such a process, the following selected agenda items have been prepared for you and your staff to stimulate discussion and collaborative action to reduce the risk of medication errors. These agenda topics appeared in the *ISMP Medication Safety Alert! Community/Ambulatory Care Edition* between January 2010 and April 2010. Each item includes a brief description of the medication safety problem, recommendations to reduce the risk of errors, and the issue to locate additional information. To learn how to use the ISMP Ambulatory Care Action Agenda at your practice site, visit www.ismp.org/newsletters/ambulatory/How_To_Use_AA.asp.

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
03/10	FDA issued an alert about the possibility of serious side effects if consumers mistakenly use MAALOX TOTAL RELIEF , which contains bismuth subsalicylate, instead of using other Maalox products that contain magnesium and aluminum hydroxides. The FDA received 5 reports of harmful errors in patients unknowingly taking the bismuth subsalicylate product.	Novartis has agreed to change the name of Maalox Total Relief to one that does not include the word "Maalox." Until that time (expected September 2010), counsel patients regarding the difference between these two products. Post an alert near these products advising patients to consult with a pharmacist prior to purchasing one of the products.			
Order by metric weight, not volume					
01/10	In most cases, it is unacceptable to express doses in terms of volume alone as dosing errors can occur. For example, the brand product Fer-In-Sol (ferrous sulfate) contains 40% less elemental iron per mL than generics. If Fer-In-Sol is prescribed in terms of mL and generic substitution occurs, the patient would receive nearly twice as much iron as intended.	Healthcare providers should specify the dose in mg and alert patients and parents when multiple concentrations are available.			
Middle four digits of NDC numbers strike again, almost					
03/10	ISMP continues to receive error reports about different manufacturers using identical or very similar product codes, the middle four digits of an NDC number. This practice has caused product mix-ups in hospital outpatient pharmacies and community pharmacies.	When manually verifying product selection, compare the entire NDC number on the manufacturer's product label with the NDC number printed on the pharmacy-generated label. Bar-code scanning during the production stage of the dispensing process can identify when the wrong product is selected from the shelf.			
New risk assessment tool from ISMP					
01/10	<i>Improving Medication Safety in Community Pharmacy: Assessing Risk and Opportunities for Change</i> is a risk assessment tool designed to help community pharmacy personnel proactively identify medication safety risks and implement system improvements.	The community pharmacy team should proactively read the manual, use it for reference when evaluating an error, and incorporate it into the pharmacy's continuing quality improvement program. The tool is available at www.ismp.org/communityRx/aroc .			

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Parents' dosing accuracy					
02/10	A study published in <i>Archives of Pediatrics and Adolescent Medicine</i> assessed parents' liquid medication administration errors by dosing device type and the influence of parents' health literacy. The study showed that parents were able to use oral syringes and a dropper to accurately measure the dose more than 90% of the time, but dosing errors were highly prevalent with dosing cups.	Provide patients and their caregivers with an appropriate measuring device to ensure that they can accurately measure doses of medications. Provide patient education using the "teach-back" method to assess understanding.			
Hydrofluorakane (HFA) inhaler maintenance					
02/10	Inhalers are now HFA propelled which makes them taste and feel different. The inhaler's mouthpiece can become blocked or clogged with use. Patients may not realize their inhaler is blocked since, with the new HFA inhalers, they no longer feel the medication during inhalation.	Advise patients to follow the priming, cleaning, and drying instructions specific to their inhaler. Ensure that the patients or caregivers understand how to properly use and maintain their inhaler. This is best accomplished by using the "teach-back" method that includes a repeat demonstration by the user.			
Distribute instructions for oral dispenser					
04/10	Some oral dispensers that accompany some liquid medications (e.g., morphine sulfate concentrated oral solution 100 mg per 5 mL manufactured by Roxane) have a plunger with a pointed end instead of the usual flat end. This design has caused confusion on how to measure liquid oral drugs—from the pointed end of the plunger or from its widest part.	Educate healthcare professionals, patients, and caregivers about the proper use of these syringes. Distribute the "patient instructions for use" found in the product's medication guide when dispensing these types of syringes.			
Drug name mix-up between levetiracetam (KEPPRA) and levocarnitine (CARNITOR)					
02/10	Two pediatric patients received levetiracetam instead of levocarnitine in error. Both medications have the same elixir strength of 100 mg/mL and are dosed similarly in pediatric patients. Fortunately, neither patient was harmed; however, a patient who is seizure free on daily doses of levetiracetam could have a seizure if levocarnitine is given in error.	Use both brand and generic names when prescribing these medications, or the brand names primarily. Consider adding these drugs to your list of look-alike drug names. Require staff to match the prescribed drug with the patient's medical history. Another strategy to prevent this error would be to change the drug name of levocarnitine to L-carnitine.			

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
02/10	A mix-up between sulfADIAZINE and sulfasalazine occurred in a pharmacy but was caught before the medication reached the patient.	Separate storage of the two medications. Additionally, consider placing them in different colored bins. To help alert staff to the possibility of mix-up, share the error and post look-alike/sound-alike labels.	sulfADIAZINE and sulfasalazine look-alike names		
PRIOSEC and PRISTIQ sound-alike names					
04/10	PRISTIQ (desvenlafaxine succinate) was initially heard as PRIOSEC (omeprazole) through the pharmacy voice mail. The sound similarity is stronger when these names are spoken with a foreign accent. Accents can lead to misinterpretation when receiving and transcribing telephone orders. Confirmation bias may also contribute to the mix-up.	Prescribers should always include the indication for the medication on the prescription and when leaving a prescription on the pharmacy's voice mail system.			
2009-2010 trivalent influenza vaccine H1N1 component is not 2009 pandemic strain					
04/10	The 2009-2010 trivalent influenza vaccine includes the A/Brisbane/59/2007 (H1N1) strain but this is not the virus strain responsible for pandemic flu and used for H1N1 monovalent influenza vaccine is A/California/7/2009 (H1N1) . However, some patients were given the 2009-2010 trivalent vaccine instead of the H1N1 2009 pandemic vaccine in error.	Educate healthcare professionals and patients that the 2009-2010 trivalent influenza vaccine does not provide protection against the pandemic H1N1 influenza virus strain. For more information please visit www.cdc.gov/h1n1flu .			
Dangerous abbreviations BIW and TIW					
04/10	An order written for LEUKERAN (chlorambucil) to be given BIW was transcribed by a pharmacist as "twice daily." The error was caught by another pharmacist during verification. Similar errors have occurred with the abbreviation TIW in which patients received the medication three times daily instead of the intended three times a week.	Ban these abbreviations. Remind prescribers that BIW and TIW should never be used in handwritten or electronic prescriptions (BIW and TIW should not be a selection for dose frequency). Write, or have electronic systems print, "twice a week" or "three times a week." Prescribers should indicate the specific days the patient is to take the medication so that the pharmacist can place that information on the patient's prescription label.			