

Heed this warning! Don't miss important computer alerts

PROBLEM: Although pharmacists enter prescriptions into the pharmacy computer, in many community pharmacy settings, pharmacy technicians or pharmacy interns perform this function. In these circumstances, a pharmacist later verifies that the prescription has been entered correctly. Simultaneously, he or she is assuring the appropriateness of the medication and verifying that the proper drug and dose has been prepared. The verification process is typically accomplished by comparing the prescription, pharmacy label, and the final product. In many locations, bar-code scanning is employed to increase accuracy. As long as the original prescription is included in the verification process, this may seem to be a perfectly acceptable way to verify technician or pharmacy intern order entry and preparation of medications. However, one glaring safety concern still exists with this process: the checking pharmacists may not know about alerts that may have been displayed during the order-entry process. The pharmacist may be unknowingly allowing the computer, and subsequently, the technician to perform the required drug utilization review. As a result, important drug interactions, allergies, duplicate therapies, excessive or subtherapeutic doses, or other identified contraindications may be missed.

While bypassing certain alerts can be clinically appropriate, the technician is not in a position to make this clinical decision, and as such, important warnings sometimes are inappropriately overridden. Bypassing alerts appears to be a rather common practice, especially if the significance of the alert is not valued by the viewer of the information. The alert systems used during order entry are designed to be quite sensitive so users do not miss any critical information. This sensitivity comes at a cost: frequent 'false' alarms—or warnings that may not be clinically significant. Pharmacists can usually cite many examples of these false alarms. Besides being a nuisance, frequent false alarms can lead to alert fatigue and complacency—or the 'cry wolf' syndrome.¹ Individual quirks in some pharmacy systems also contribute to missed alerts—conditions that should have given rise to an alert but did not. Thus, general annoyance and mistrust of the alert system is one reason why it may seem acceptable

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Safety Briefs

■ **Scanning inconsistencies.** Last month we reported dispensing errors could occur with **BYETTA** (exenatide), a medication to improve glucose control in adults with type 2 diabetes, because the manufacturer and product codes in the NDC numbers for both pen injectors are the same. This similarity in NDC numbers increases the risk that manual checks of the



NDC number may not catch product mix-ups. Byetta is supplied as a

sterile solution for subcutaneous injection containing 250 mcg/mL of exenatide in a 5 mcg per dose prefilled pen (NDC 66780-210-07), and in a 10 mcg per dose prefilled pen (NDC 66780-210-08). ISMP has learned of another problem related to the products' NDC numbers. The last two digits may not be read by some bar-code scanners used during the dispensing process in some facilities, particularly community pharmacy settings. As a result, the wrong size pen has been dispensed. Once again, we've notified the FDA and the manufacturer to request distinctly different product code portions of the NDC number for each size of Byetta pen.

■ **Humira Pen and HumaPen. HUMAPEN**

MEMOIR is a reusable pen device that was launched by Lilly for use only with **HUMALOG** (insulin lispro injection [rDNA origin]) 3 mL insulin cartridges. The pen records the date, time, and amount of the last 16 doses of insulin a patient has administered with the device. The ability to record doses and times of meals can help patients and physicians who are developing a diabetes treatment plan that requires an accurate recording of mealtime doses. Don't confuse this new product with **HUMIRA PEN** (adalimumab), which is indicated in immune-related disorders such as moderate to severe rheumatoid arthritis in adults, psoriatic arthritis, ankylosing spondylitis, and moderate to severe Crohn's disease. Humira is also approved for adults who have lost response to or are unable to tolerate infliximab. Both brand names look and sound

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to some to not worry about the alerts that technicians or pharmacy interns may bypass.

SAFE PRACTICE RECOMMENDATIONS: The problems described above are twofold: false alarms with pharmacy computer alert systems and the pharmacist's inability to view and assess alerts that may have been bypassed by other staff during order entry and drug utilization review. While there are no silver bullets that can solve either problem quickly and effectively, a few suggestions are offered below to improve upon the valuable but imperfect alert systems.

Optimize sensitivity of alert system. The most direct way to curtail false alarms is to optimize the sensitivity of the alert system.¹ For example, some pharmacy systems allow users to choose the level of drug-drug interaction alerts (e.g., level 1-3) that will appear during order entry. While the existing level system is not perfect, it offers some relief from false, low significance alarms. *However, keep in mind that reduced alert sensitivity leads to tradeoffs between false alerts and missed alerts.*

Identify priority alerts. Another option is to identify conditions that signal the most serious potential adverse drug events, and use the list to optimize and customize computer alerts. For example, there is a relatively small, finite group of drug interactions that are clinically important from a pharmacodynamic or pharmacokinetic standpoint. Several health professionals have published lists of these priority conditions, which can be used to target customized drug-drug interaction alerts, or to serve as a resource for pharmacists who are checking orders (see table).^{2,3} You can also

Examples of drugs with potentially serious drug-drug interactions**
cyclosporine
lithium
monoamine oxidase inhibitors (MAOIs)
protease inhibitors
selective serotonin reuptake inhibitors (SSRIs)
warfarin

**Source: Drug Interaction Tip Sheet by Francis J. DeRoos, MD, from *Internal Medicine News*.²

identify priority alerts by reviewing previous pharmacy interventions regarding drug-drug interactions, allergies, duplicate therapy, and so on, to learn the conditions that truly warranted a call to the prescriber and changes in drug therapy. Likewise, encourage clinicians to report encounters of invalid warnings so they can be altered or removed from the pharmacy computer system.

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nearly identical. Matching the prescribed medication's indication to the patient's condition will help point out any errors in interpreting prescriptions for these products with look-alike names.

■ **Promotional Advil sample.** An ISMP pharmacist recently received a sample of **ADVIL PM** (ibuprofen and diphenhydramine) in his Sunday newspaper. Enclosed in the sample is one coupon and one packet containing two tablets, each containing ibuprofen 200 mg and diphenhydramine citrate 38 mg. Disturbingly, a large notation near the packet (see photo) encourages the recipient to "Try Now" which, if followed, the patient would take 76 mg of diphenhydramine citrate

(equivalent to 50 mg diphenhydramine hydrochloride). The sample card displays warnings about drowsiness and against driving in small type in the Drug Facts label on the back of the card. Even smaller type is used on the packet itself. More disturbing is that this



unsecured sample could easily end up in the hands of a child or an elderly patient in whom diphenhydramine can increase the risk of falls. Distributing medications through newspaper circulation is dangerous and negates any possibility of pharmacist or prescriber review. Also, patient education and drug recalls are made more difficult. We encourage manufacturers to recognize the safety risks associated with this type of distribution and to avoid distributing samples via the newspaper or direct mail. We have asked both the manufacturer and the newspaper to stop this practice.

■ **Reported adverse events increased nearly 3-fold.**

An ISMP study published September 10 in *Archives of Internal Medicine* (Moore T, et al. Serious adverse drug events reported to the Food and Drug Administration, 1998-2005. *Arch Intern Med.* 2007; 167:1752-1759) showed that the number of reported serious adverse drug events increased 2.6-fold, from 34,966 in 1998 to 89,842 in 2005. The number of fatal adverse drug events increased 2.7-fold during the same time period, from

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Require pharmacist review of high-priority alerts. Once high-priority alerts have been identified, it should be impossible for order-entry technicians or pharmacy interns to bypass these. Instead, these orders should remain in a queue for release by a pharmacist after viewing and responding to the associated problem. If a pharmacist eventually bypasses a high-priority alert, require documentation of the reason so it can be used for improvement activities.

Alerts printed along with labels. Some order-entry systems have the ability to print out any significant alerts on a label along with the other product labels that are produced. This way, the pharmacist will be able to view the bypassed alerts when checking the final product before dispensing.

Print a daily report of bypassed alerts. Most computer systems will allow users to print out a daily report of bypassed alerts for a pharmacist to review. Review can take place during the nighttime hours in some locations, or there

may be other recognized periods when workload is lower, staffing is better, or a pharmacist is scheduled for this purpose. This is much more achievable if the reports are organized first by priority alerts that have been bypassed. Otherwise, the length of the report may prohibit review and follow up. The process for follow up with problematic prescriptions would also need to be described, especially if the review occurs at night. While retrospective review of bypassed alerts is not optimal and should not replace prospective drug utilization review, many drug-drug interactions are unlikely to harm patients until at least a few days after concurrent administration, so there is often time to take action before harm occurs. The same may not be true for some duplicate therapy, allergies, and dosing errors, but harm could be mitigated if the problem is discovered quickly.

References: 1) Wogalter MS, ed. Handbook of Warnings. Lawrence Erlbaum Associates: Mahwah, NJ; 2006. 2) Splete H. Medical history holds clues to drug interactions. *Internal Med News*, 2005;38(22):42. 3) Hansten PD, Horn JR. The top 100 drug interactions: a guide to patient management, 2006 edition. American College of Clinical Pharmacy: Boston, MA; 2006.

Your Reports at Work!

Daytrana voluntary market withdrawal. Earlier this month, Shire Pharmaceuticals announced a voluntary market withdrawal of a limited portion of **DAYTRANA** (methylphenidate transdermal system) due to the difficulty patients and caregivers were having removing the release liner of some patches. Packages with an expiration date of March 31, 2009 or earlier as well as packages with lot numbers 2563511, 2563611, and 2570411 are impacted by this voluntary market withdrawal. In our June 2007 issue, we reported steps parents have been taking to keep the patches affixed to their children's skin (e.g., refrigerating patches, using bandages to tape patches to the skin). Shire expects remaining Daytrana patches, which are not subject to the market withdrawal, to offer patients and caregivers improved ease of use when peeling the release liner off the patch. The more recent patches have been manufactured using an enhanced process. Please inform your patients about this withdrawal. Encourage patients to continue to report any problems they are having with Daytrana. Other than patient satisfaction surveys, Shire is relying on voluntary reports to monitor the efficacy of the enhanced manufacturing process. Unfortunately, we've learned that Shire has not proactively conducted usability testing with actual patients and practitioners to identify potential problems. Patients and their caregivers who have questions regarding Daytrana patches should call Shire customer service at 1-800-828-2088, option 1.

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5,519 in 1998 to 15,107 in 2005. This increase was four times faster than the total number of outpatient prescriptions dispensed. Although a total of 1,489 drugs were associated with adverse events, a subset of 298, or 20%, were responsible for 87% of the adverse events. Just 51 drugs accounted for a large proportion of the problem; each of these had 500 or more reports per year, and collectively, they accounted for 43.6% of the total adverse event reports. The medications most frequently implicated in deaths included: oxycodone; fentanyl; clozapine; morphine; acetaminophen; methadone; infliximab; interferon beta; and etanercept. The article abstract can be viewed at: <http://archinte.ama-assn.org/cgi/content/short/167/16/1752>.

■ **And the winner is...HYDRomorphone!** Thanks to 1,125 subscribers who responded to our survey about tall man letters for hydromorphone! A majority of respondents felt that the use of tall man letters configured as HYDRomorphone (67%) would prevent more errors than hydromorPHONE (17%). About 17% of respondents felt that tall man letters would make no difference or preferred a different combination of tall man letters than offered in the survey, particularly HYDRomorphONE, HYDRomorphONE, and HYDRomorphOne. We have shared the survey responses with FDA for consideration as they select the official tall man lettering for hydromorphone.

HealthAlerts ▲▲▲▲



FDA and Cephalon have alerted health professionals about deaths stemming from inappropriate patient selection and prescribing of **FENTORA** (fentanyl transmucosal buccal tablets). Fentora is indicated only for the management of breakthrough pain in cancer patients who are already receiving and are tolerant to opioid therapy. Unfortunately, some prescribers have ordered the drug to treat acute pain, such as headaches or back pain, in patients who are not opiate tolerant. At least three deaths attributed to respiratory failure have occurred in patients who received the drug inappropriately. Improper substitution of Fentora for other fentanyl products such as **ACTIQ** (fentanyl transmucosal lozenges) has also contributed to adverse outcomes. Because of the higher bioavailability of fentanyl in the Fentora buccal tablet, mcg-to-mcg substitutions should not be used when converting patients from other oral fentanyl products (including fentanyl Actiq lozenges) to Fentora. Letters were sent to healthcare professionals to emphasize key points regarding appropriate patient selection and proper dosing and administration of Fentora to reduce the risk of respiratory depression. The Public Health Advisory, healthcare information sheet, letters, and the product's Medguide can be viewed at: www.fda.gov/medwatch/safety/2007/safety07.htm#Fentora. As with fentanyl transdermal systems and lozenges, ISMP recommends mandatory pharmacist-patient/caregiver educational encounters when Fentora is dispensed to assure that the patient is opiate tolerant. And always, please remind your patients to keep Fentora stored safely away from children.

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Announcements

■ **ISMP welcomes two new staff.** **Barbara Olson, RNC, MS**, has joined ISMP as the 2007-2008 ISMP Safe Medication Management Fellow. Ms. Olson has an extensive background in perinatal nursing and clinical performance improvement, although she has practiced in a variety of healthcare settings. Ms. Olson received a BSN from Emory University (GA), a MS from Regis University (CO), and is certified in inpatient obstetrical nursing with a certificate of added qualification in electronic fetal monitoring. Ms. Olson will be working closely with ISMP staff and other patient safety organizations during the 12-month fellowship, which is funded through an unrestricted grant from Cardinal Health Foundation.

Stephanie DeGraw, PharmD has joined the staff of our subsidiary Med-E.R.R.S. as a Medication Safety Analyst. She received her Doctor of Pharmacy with a Certificate in Drug Safety from Temple University School of Pharmacy. She brings several years of experience from the community pharmacy setting. In addition, she has worked with ISMP in the past as a reviewer for *ISMP Medication Safety Alert! Community/Ambulatory Care Edition* newsletter. Stephanie also worked with Med-E.R.R.S. as an outside consultant before joining the team full time.

■ **Med-E.R.R.S.** teleconference marks 10 years of service. Our subsidiary, Med-E.R.R.S., is celebrating its 10-year anniversary! The ISMP-owned company provides packaging design consultation to the pharmaceutical industry as well as safety testing of existing package labels and new trademarks. As one of its 10-year anniversary activities, Med-E.R.R.S. will be sponsoring a teleconference for the pharmaceutical industry, **Spotlight on Medication Safety: Designing Safe Packaging and Labels**, to be held on Wednesday, **November 14, 2007**, from 1:30-3:00 p.m., ET. For details, visit: www.med-errs.com.



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