

This series brings you up-to-date information about medication safety issues and strategies to prevent medication errors. It draws on Australian incidents and US experience, including (with permission) material from ISMP Medication Safety Alert! a bulletin published by the US Institute for Safe Medication Practices <www.ismp.org>. This series is coordinated via the Committee of Specialty Practice in Medication Safety (Chair, Rosemary Burke, Director of Pharmacy, Concord Hospital, NSW). Australian incidents are collated and editorial recommendations made by Penny Thornton (Pharmacy Services Manager, The Children's Hospital, NSW; <pennyt2@chw.edu.au>).

US SAFETY BRIEFS

Revatio=sildenafil=Viagra

A female patient with pulmonary arterial hypertension (PAH), receiving Tracleer (bosentan) and Revatio (sildenafil) went to the emergency department with ischaemic chest pain and ECG changes. The physician reviewed her drug list but did not know that Revatio was sildenafil or understand its contraindications. The patient was given aspirin and sublingual nitroglycerin and later started on nitroglycerin infusion for continued chest pain and elevated troponin-T. Organic nitrates are contraindicated in any form, at any time, while a patient is taking sildenafil. This contraindication is echoed in product monographs for the other phosphodiesterase 5 inhibitors, e.g. Cialis (tadalafil) and Levitra (vardenafil). In this case, the patient experienced no adverse effects or blood pressure changes because an internist recognised the problem and stopped the infusion. Sildenafil is better known as Viagra, a drug approved for the treatment of erectile dysfunction and is typically prescribed in 50 mg doses to be taken 1 to 4 hours before sexual activity. When used to treat PAH, sildenafil is typically prescribed in 20 mg doses to be taken three times daily. Viagra has received widespread professional and direct-to-consumer advertising, including mention of associated contraindications. In this case, if the sildenafil had been prescribed and communicated under the Viagra name, perhaps the physician would have recognised the problem with co-prescribing nitroglycerin. Revatio has the approved indication for treatment of PAH (to improve exercise ability) and Viagra does not. The FDA approved Revatio as the new brand name not because the drug has a new indication but because of the stigma PAH patients might associate with taking Viagra. Dual brand names for a single product are problematic when one of the product names is well established before the new product is launched. Further, patients with PAH frequently have concomitant coronary artery disease, increasing the risk of receiving a nitrate.

Recommendations. FDA often requires companies to analyse whether a dual brand name or two different brand names would be safest for a product marketed for two different indications. If dual brand names are used, manufacturers could clearly warn patients and health professionals on the package label and the package insert that the drug is available under both names. Health professionals can also reduce the risk of errors by conducting a thorough drug history and reviewing drug information if they encounter unfamiliar product names. To help patients avoid taking the same product under different names, health professionals should encourage them to fill their prescriptions at the same pharmacy. Patients with PAH who take Revatio should be encouraged to note on their drug list that it is also marketed as Viagra.

[ISMP Medication Safety Alert! 29 January 2009]

Mobile phones and e-mail could prevent harm.

A patient was accidentally given another patient's drugs and when the pharmacist realised the mistake, he attempted to reach the patient by phone. The patient did not answer and the pharmacist kept trying but did not get through until later that evening. By that time, the patient had already taken Cellcept (mycophenolate mofetil), an immunosuppressant, instead of her new prescription for Zestril (lisinopril) to treat hypertension. Despite of all the communication technology available today, we tend to ask patients only for their home and work phone numbers. Some patients may list their mobile phone number as their home number because they do not have a landline. But we rarely ask patients to provide their mobile phone numbers or e-mail addresses. It makes sense to ask for this information to communicate better with patients in a timely manner.

[ISMP Medication Safety Alert! 29 January 2009]

Lyrica-Lopressor mix-up

A patient with a history of atrial fibrillation was admitted to hospital with an order for Lopressor (metoprolol) 100 mg BID. The doctor's handwriting was poor and the order was misinterpreted and dispensed as Lyrica (pregabalin) 100 mg BID. The patient received three doses of Lyrica and experienced a run of temporally related atrial fibrillation. A nurse then recognised the error. Lyrica is used to treat pain due to nerve damage in patients with diabetes or shingles and is also used to treat pain in people with fibromyalgia. Lyrica is also used to treat certain types of partial onset seizures. The patient had none of these conditions. Hospitals may want to add a computer alert about this newly reported look-alike drug name pair. Matching the drug's indication to the patient's health condition is the best way to avoid confusion between products with look-alike names.



[ISMP Medication Safety Alert! 29 January 2009]

U looks like 4

This handwritten order was misread as NovoLog '54 units' instead of the intended '5 units'. Although the word 'units' had been written out, the letter 'u' looked like the number '4' and the remaining part of the word 'nits' was read as 'units'. The mistake was made by three practitioners who either dispensed or administered the drug. The patient received the large dose of insulin and required treatment for severe hypoglycaemia. This error occurred despite the prescriber's avoidance of the abbreviation 'u' for units. Electronic prescribing is one way of reducing the risk of misinterpreting handwritten



orders. Maintaining adequate space between the numerical dose and unit of measure can also increase correct interpretation of the dose. The hospital where this error occurred is considering requiring both a numerical and written number dose (e.g. 5 [five] units) for all handwritten insulin orders, similar to outpatient prescriptions for the quantity of controlled substances (e.g. 30 [thirty]). This order also included an error-prone abbreviation, SQ – subcutaneous should be written out or abbreviated as ‘subcut’.

[ISMP Medication Safety Alert! 15 January 2009]

Australian comment: The NSW TAG abbreviation recommendation is just this – to use ‘subcut’.

USP’s safe practice environment chapter

The United States Pharmacopeia (USP) recently published its proposed new general chapter (1066) on ‘Physical environments that promote safe medication use’. The chapter describes the optimal physical environment needed to promote accurate medication use and how anyone involved in the process can establish a safer workplace. When justified by evidence and expert opinion, standards are provided in five key areas—illumination, interruptions and distractions, sound and noise, physical design and organisation, and medication safety zone.

Illumination. Improper lighting has been a contributing factor in some medication errors. In one case, poor lighting led to the incorrect attachment of tubing to a patient-controlled analgesia unit, causing the drug to run onto the floor. In another case, dicyclomine 10 mg capsules were used to fill a prescription for 20 mg capsules due to poorly lit pharmacy shelves. Numerous studies have shown that proper lighting improves accuracy and efficiency of medication-related tasks. Studies have also found that lighting levels need to be increased for workers older than 45 years and when visual fatigue rises near the end of the work shift. Based on the relationship between lighting and errors, the USP recommends the following:

- use fluorescent cool white deluxe lamps or compact fluorescent lamps;
- use adjustable 50-watt high-intensity task lights in areas where critical tasks are performed, as well as on mobile medication carts, automated dispensing cabinets and in patient rooms for night time administration;
- position all lighting to avoid glare on computer monitors;
- provide magnifying glasses to read labels with very small script;
- clean lighting fixtures routinely (lighting levels can decrease by 25% over 2 years without cleaning);
- ensure illumination levels of around 100 foot candles in areas where critical tasks are performed in the pharmacy and on patient care units; and
- periodically measure lighting using an illuminance meter. Place the meter in key areas with the worker standing in a normal working position. To measure light in medication storage areas, take readings on the top, middle and bottom shelves.

Interruptions and distractions. The MEDMARX data show that distractions are a causative factor in about 45% of medication errors. Co-workers asking for assistance were the most frequent sources of interruptions in one pharmacy study. As individuals have differing

levels of distractability, preventing interruptions and distractions is best accomplished by providing staff with the ability to control their exposure to disturbances. To maximise staff concentration when performing critical tasks, the USP recommends the following:

- minimise the potential for distractions in critical medication use areas; and
- teach workers to avoid interrupting co-workers for non-urgent reasons while they are performing medication-related tasks. Techniques include visual cues (e.g. nurse wearing an orange safety vest when administering medications), physical barriers and checklists to focus and refocus attention.

Sound and noise. Noise can interfere with effective work performance and pose a health hazard to patients. Hospitals are noisy with studies reporting an average of 45 to 65 dB of noise with peaks between 85 to 90 dB. Noise levels at shift change have been recorded as high as 113 dB, well above the peak levels set by the Environmental Protection Agency (EPA) – 45 dB day/35 dB night and the WHO – 35 dB of background noise in patient rooms. The EPA requires ear protection for workers exposed to sound levels averaging 90 dB. Out of 58 studies reviewed by the USP, 29 showed that noise impaired performance, but seven showed it improved performance. For example, in one of the seven studies, unpredictable but controllable sounds improved prescription filling accuracy, which may indicate that some environmental stimuli are needed to maintain alertness and attention. To maintain a safe level of noise, the USP recommends the following:

- sound levels in medication use areas should be at the level of conversation, 50 dB, slightly higher than the EPA recommendation to ensure critical verbal information can be heard accurately. Total elimination of noise is not feasible or desirable;
- provide a quiet area for staff to use during critical medication-use tasks; and
- reduce noise and other sensory interference by employing activities, tools and design principles such as installing materials that absorb sound. Acoustical engineers can identify additional methods for noise reduction. Periodically measure sound levels in work areas by holding the meter away from the body while standing in a working position and pointing the meter at the source of sound.

Physical design and organisation. The physical design and organisation of the work space can influence the staffs’ ability to use information and perform tasks, for example, the height of counters and drug storage areas can influence visibility. Studies have shown that dispensing errors occur more frequently when medications are stored on cluttered shelves because the items are more difficult to differentiate. The design of the work space can also contribute to poor lighting conditions, distractions and interruptions, high noise levels and unsafe medication safety zones. To reduce the risk of errors, the USP suggests the following:

- keep areas where medications are stored organised and uncluttered, with at least 1 inch between distinct drugs;
- ensure that the height of work counters and supply areas enhance efficiency of tasks and visibility of products; and
- use adjustable fixtures (e.g. task lights, counters) to promote efficiency, visibility and safety.

Medication safety zone. The USP defines a medication safety zone as any critical area where medications are prescribed, transcribed, prepared and administered. Examples include work surfaces in a medication room or counter tops on medication carts, locations where prescribing decisions are made, pharmacies, and patients' bedsides or homes where medications are administered. Medication errors have been linked to the physical design of medication safety zones as well as error-prone methods used within these zones to carry out medication-use activities. The USP recommends that the drug preparation areas are designed so that critical processes are conducted in a manner similar to work in the cockpit of an aeroplane, i.e. the information necessary to make decisions is readily available in a user-friendly format and all together to support fact finding. The information and components within safety zones should be arranged in a manner that promotes correct choices and decreases distractions according to the following principles:

- Importance – place important components in convenient locations (e.g. locate information regarding equipment function and troubleshooting near or on equipment);
- Frequency of use – locate frequently used items in areas where they can be easily found to help prevent workarounds.
- Function – group items that are related to a function together, such as syringes, needles and alcohol swabs.
- Sequence of use – place items in an order that supports the sequence needed to perform the task correctly (e.g. sterile gloves encountered first when opening dressing change kit). Standardise the design of bedside medication administration areas so that information and supplies can be readily located. Standardise medical equipment (e.g. infusion pumps) to reduce mistakes during operation. Employ technologies, such as electronic prescribing, bar-coding and electronic medical records. Use constraints (limit access/use) and forcing functions (design aspect that allows correct performance only) to reduce errors with high-alert medications (e.g. sequester neuromuscular blocking agents in an intubation kit to prevent accidental administration to unventilated patients).

The USP urges health professionals to participate in this important standard setting chapter by providing comments and spreading the word to colleagues <www.usp.org/USPNF/pf/whatsInside.html>.

[ISMP Medication Safety Alert! 4 December 2008]

Cotrimoxazole-induced hyperkalaemia

An 86-year-old female was being treated as an outpatient for cellulitis in her left leg caused by methicillin-resistant *Staphylococcus aureus* (MRSA). She was taking two Bactrim DS (sulfamethoxazole 800 mg/trimethoprim 160 mg) tablets twice daily as well as oral lisinopril 20 mg daily for hypertension. Cotrimoxazole is commonly prescribed for urinary tract infections or prophylaxis/treatment of *Pneumocystis jiroveci* pneumonia in immunocompromised patients. Bactrim use has increased because it is active against MRSA infections. The patient had been taking a typical Bactrim dose for MRSA skin infections, according to the *Sanford Guide to Antimicrobial Therapy* (38th edition), but she was admitted to the ICU with ventricular arrhythmia and a

potassium level of 7.9 mEq/L. The first things that come to mind when thinking about the effects of cotrimoxazole are serious skin reactions and crystalluria. However, another and perhaps lesser known adverse effect of concurrent use of Bactrim and lisinopril is hyperkalaemia. The trimethoprim component in Bactrim causes a potassium-sparing effect, much like the potassium-sparing drug amiloride. Trimethoprim blocks sodium channels (particularly amiloride-sensitive sodium channels) in the distal tubule of the nephron. This blockade inhibits potassium secretion into the urine, leading to reabsorption in the blood and possible hyperkalaemia. Prescribers, pharmacists and nurses need to be aware of this adverse effect of the trimethoprim component in Bactrim. Patients at increased risk for cotrimoxazole-induced hyperkalaemia are those on high doses of Bactrim; those with renal impairment, (50% dose reduction is recommended for patients with a creatinine clearance 15 to 30 mL/min); those on other drugs that increase the risk of hyperkalaemia such as angiotensin converting enzyme inhibitors, angiotensin II receptor blockers and potassium-sparing diuretics; those on diets with potassium-rich foods (e.g. tomatoes, raisins, figs, bananas, papayas, pears, cantaloupe, mangoes) or those using potassium salt substitutes. To avoid this reaction, obtain a baseline BUN/creatinine, adjust the dose for patients with renal impairment and periodically monitor potassium levels in at-risk patients and those taking high doses of Bactrim. These recommendations should be included as reminders in pharmacy computer systems and electronic prescribing software.

[ISMP Medication Safety Alert! 4 December 2008]

Alcohol abuse and hand sanitisers

According to a recent letter (Am J Health Syst Pharm 2008; 65: 2203-4), readily available dispensers of alcohol-based hand sanitisers may be too inviting for patients prone to severe alcohol abuse. The authors reported a case in which a hospitalised patient with a known history of ingesting rubbing alcohol and alcohol-containing hand sanitiser and mouthwash was witnessed ingesting Avagard foam hand antiseptic (contains 62% alcohol) from a wall dispenser on two occasions. After the second occurrence, staff removed the hand sanitiser from the wall. The authors pointed out that patients with a history of non-potable alcohol ingestion require careful assessment of abuse patterns in light of the availability of alcohol-based hand sanitisers in hospitals. Their presence increases the risk of alcohol intoxication, falls, and drug interactions. The authors recommended temporary removal of alcohol-based hand sanitisers from wall dispensers when high-risk patients are present.

[ISMP Medication Safety Alert! 4 December 2008]

Misprogramming PCA concentration leads to dosing errors

ISMP has received a small but concerning number of reports of overdoses with patient-controlled analgesia (PCA) as a result of pump programming errors. Although every aspect of the PCA process has the potential for error, ISMP is especially concerned with errors related to programming the concentration of the narcotic. Accidentally entering a higher than actual concentration of narcotic in a PCA pump results in the delivery of a lower dose than prescribed, which can be significant as the patient's pain may not be controlled. If increased

dosing (and thus increased rate of infusion) is prescribed, subsequent changes of the PCA syringe or bag—for which the concentration is then reprogrammed correctly—may result in the delivery of more drug than necessary, risking respiratory depression. At the same time, dosing errors caused by inadvertent programming of a lower-than-actual concentration of a narcotic into the PCA pump may result in the delivery of a higher dose than prescribed. These are the more dangerous errors that have led to adverse drug events, including fatalities. [ISMP Medication Report Analysis. *Hosp Pharm* 2008; 43: 960-4.]

Near-miss involving cyclophosphamide

An intensive care unit patient was diagnosed with Wegener's granulomatosis and the doctor ordered IV cyclophosphamide 2.2 g daily for 3 days. The pharmacist who reviewed the order checked the patient's medication profile in the pharmacy but could not identify the indication for cyclophosphamide. Furthermore, given the dose of cyclophosphamide that had been ordered, the pharmacist expected an accompanying order for the bladder-protective drug mesna, but there was no order for this drug. The pharmacist contacted the ICU and was advised of the patient's new diagnosis by a nurse. The pharmacist initiated a literature search because she believed that the cyclophosphamide dose for an autoimmune disorder such as Wegener's granulomatosis would be much lower than the prescribed dose. The literature review confirmed the pharmacist's suspicions and she contacted the doctor. The doctor initially affirmed the order as prescribed, but after discussing the matter further and reviewing the information presented by the pharmacist, the doctor realised that he had intended to order a dose of 220 mg. The doctor changed the order and expressed gratitude for the pharmacist's follow-up. The following factors were identified as contributing to this near-miss incident:

- doctor had intended a dose of 4 mg/kg per day x 55 kg (patient's body weight) for a total of 220 mg or 0.22 g. However, when calculating the dose, the physician misread his handwritten note about the weight-based dose. The handwritten note stated '4.0 mg/kg' but the physician misread the amount as '40 mg/kg' and consequently ordered 2.2 g; and
- protocols for cytotoxic drugs used for non-oncology indications were not readily available to either the physician or the pharmacist. (In contrast, when a cytotoxic drug is ordered for an oncology indication, the facility requires that the current protocol be printed from a provincial cancer web site and placed in the patient's chart. These oncology protocols are publicly available and are accessible to all staff.)

Recommendations. Procedures that govern the use of cytotoxic drugs for oncology indications are also applicable when drugs such as cyclophosphamide are used for non-oncology purposes. This near-miss incident exemplifies the value of ensuring that all orders for cytotoxic drugs are reviewed by a pharmacist with the skills for performing such reviews. The following recommendations were developed in collaboration with the reporting facility:

- the drug order specify the therapeutic protocol being used. If a standard protocol is not readily available, require that the prescriber provide, before the cytotoxic drug is prepared, references for the specific

dose and dose schedule that have been prescribed. In addition, a copy of any such reference should be included in the patient's chart, and the information readily available for use by pharmacy and nursing staff;

- all orders for cytotoxic drugs include the relevant patient diagnosis. Given the variety of indications for which cytotoxic drugs can be used and the wide variation in doses and administration schedules, members of the care team need specific diagnostic information to confirm appropriate dose ranges. Admission orders typically include the admission diagnosis, but some comorbidities may not be listed on admission. In addition, conditions diagnosed during the hospital stay may not appear in subsequent orders. Regardless of the indication, require that all orders for cytotoxic drugs include the patient's weight (and height, if the body surface area must be calculated) to allow staff to double-check the dose ordered.
- develop standard protocols for cytotoxic drugs commonly used for non-oncology indications. Ensure that practitioners have ready access to the protocols and other drug information resources. For example, at the hospital where the near miss occurred, the intravenous therapy manual has since been revised to include dosing for cyclophosphamide and other cytotoxic drugs used for non-oncology indications;
- build optimal safeguards into the ordering process for cytotoxic drugs, regardless of indication. Consider incorporating quality checks into pre-printed orders and electronic order entry systems, such as reference dose ranges and dosing schedules, criteria for withholding or reducing the dose (e.g. threshold for absolute neutrophil count), a place to show dose calculations and a clear indication of the days on which the drug is to be given;
- integrate predefined order sets and protocols into computerised prescriber order entry and maximum-dose alerts; and
- avoid use of dangerous dose designations such as trailing zeros. When cytotoxic drugs are ordered for the treatment of cancer, the protocols are readily available, and the drugs are ordered, dispensed and administered by trained health professionals. In addition, the high-alert nature of these drugs is well recognised in oncology practice, and stringent processes, including ensuring availability of the information required to process an order and performing the necessary multiple checks, are routine. Similar system-based safeguards are required for cytotoxic drugs used for non-oncology indications.

[ISMP Canada Safety Bulletin. 30 October 2008]