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ISMP Medication Error Report Analysis

Tretinoin Confused With Isotretinoin

Death From Intravenous Nimodipine

Incorrect Medication Names Selected During Order Entry

Reduce *Ambien* Dose in Order Sets

Confusion Between Levothyroxine and Liothyronine

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These medication errors have occurred in health care facilities at least once. They will happen again—perhaps where you work. Through education and alertness of personnel and procedural safeguards, they can be avoided. You should consider publishing accounts of errors in your newsletters and/or presenting them at your inservice training programs.

Your assistance is required to continue this feature. The reports described here were received through the Institute for Safe Medication Practices (ISMP) Medication Errors Reporting Program. Any reports published by ISMP will be anonymous. Comments are also invited; the writers' names will be published if desired. ISMP may be contacted at the address shown below.

Errors, close calls, or hazardous conditions may be reported directly to ISMP through the ISMP Web site (www.ismp.org), by calling 800-FAIL-SAFE, or via e-mail at ismpinfo@ismp.org. ISMP guarantees the confidentiality and security of the information received and respects reporters' wishes as to the level of detail included in publications.

TRETINOIN CONFUSED WITH ISOTRETINOIN

A 14-year-old girl diagnosed with acute promyelocytic leukemia (APL) was started on oral tretinoin (all-*trans* retinoic acid [ATRA]) for induction therapy. APL is a medical emergency with a high rate of mortality, so it is critical to start treatment with tretinoin without delay as soon as the diagnosis is even suspected. The patient was hospitalized during treatment. She suffered from APL differentiation syndrome and pseudotumor cerebri such that doses had to be held and reduced, but she was able to finish the treatment course and achieved complete remission.

The patient was discharged. The following month, she returned to the outpatient infusion center to begin 10 cycles of intravenous (IV) chemotherapy. Tretinoin was to continue on an outpatient basis, along with IV chemotherapy per protocol. Instead of the two 14-day cycles of tretinoin as intended, an oncology clinic nurse enrolled the patient and prescriber in the *iPledge* program and called in a prescription for *Claravis* (isotretinoin [13-*cis* retinoic acid]; other brands include *Amnesteem, Myorisan,* and *Sotret*) to a local pharmacy.

The clinic nurse did not realize that tretinoin and isotretinoin are not the same medication. She was

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probably more familiar with isotretinoin, because it is prescribed more frequently than tretinoin in many pediatric oncology centers. The pharmacist at the local pharmacy did not have access to the patient's clinical information, and the physicians continued to use the abbreviation "ATRA" in their office notes, not noting the generic or brand name of the medication on the patient's profile. Thus, the patient began to take *Claravis* at home, not tretinoin.

When the patient was admitted to the hospital about 4 months later, inpatient chemotherapy orders included tretinoin but requested the use of the patient's home supply. When an inpatient nurse and pharmacist checked the patient's supply, they realized it was isotretinoin and not tretinoin as intended. The patient's physicians were contacted and the family was informed of the error. Fortunately, the patient did not experience any reported adverse effects while taking *Claravis* or lack of disease control while not taking the correct drug. The patient continues to be in remission.

Isotretinoin can be used in chemotherapy treatment protocols and in treating severe recalcitrant nodular acne. There is an unlabeled use in children for neuroblastoma at 160 mg/m^2/day in 2 divided doses. Tretinoin is used almost exclusively for APL. The recommended dose is 45 mg/m^2/day administered as 2 evenly divided doses until complete remission is documented. Therapy should be discontinued 30 days after achievement of complete remission or after 90 days of treatment, whichever occurs first. Both tretinoin and isotretinoin are available in liquid-filled 10 mg capsules, but isotretinoin is also available as 20, 30, and 40 mg capsules. Isotretinoin patients must be enrolled in the *iPledge* program, but tretinoin does not require enrollment into any registry.

This type of medication error that is associated with similar medication names is best prevented during the prescribing process with the use of a well-designed order set for APL, highlighting that tretinoin (and not isotretinoin) should be prescribed. Referring to the drug as all-*trans* retinoic acid rather than tretinoin may also help differentiate it from isotretinoin; however, use of the acronym ATRA alone is discouraged. This error also highlights the importance of requiring that the pharmacist filling this prescription knows the patient's diagnosis and the drug's clinical indication at the time the prescription is filled.

DEATH FROM INTRAVENOUS NIMODIPINE

If your hospital treats stroke patients and you have not yet done so, please establish safety requirements for the administration of nimodipine for prophylaxis against cerebral vasospasm. A woman admitted post subarachnoid hemorrhage was placed on oral nimodipine 60 mg every 4 hours. Due to the disease process, she had a nasogastric tube (NG) inserted. However, the admission orders did not reflect this, and the pharmacy was not aware the drug was being given via the NG tube. A few days later, the drug was inadvertently administered through the patient's central IV line instead of the NG tube. The patient died.

At the hospital where this incident took place, the standard process for nimodipine enteral administration was to first withdraw the liquid contents from the capsule with a syringe and needle. The liquid was then placed into a cup and diluted with a volume of liquid sufficient to administer it through an enteral feeding tube or NG tube. This procedure is potentially dangerous, as there have been several reports in which the drug was drawn into a parenteral syringe and accidentally given IV, resulting in severe hypotension, cardiovascular collapse, and cardiac arrest.

We have alerted readers about nimodipine issues, including a 2006 alert (*Hosp Pharm.* 2006;41:500-504). Also in 2006, the US Food and Drug Administration (FDA) asked the manufacturer, Bayer, to add a boxed warning to *Nimotop* (nimodipine) labeling that states: "Do not administer nimotop intravenously or by other parenteral routes. Deaths and serious, life threatening adverse events have occurred when the contents of nimotop capsules have been injected parenterally."

According to a study,[1] nimodipine liquid extracted from capsules, stored in amber oral syringes and placed in light-protected bags, is stable at room temperature for 31 days. The hospital now requires pharmacy preparation of nimodipine oral solution only in oral syringes. In addition, hospital order sets now alert providers to the presence of nasogastric, orogastric, or percutaneous gastrostomy tubes.

INCORRECT MEDICATION NAMES SELECTED DURING ORDER ENTRY

An unfortunate yet common error that occurs during computer order entry is the inadvertent selection of the wrong drug from a drug name search list. For example, a prescriber may intend to enter an order for acetaminophen by typing "aceta," but then accidentally chooses acetazolamide from the search results. In a recent case, that particular error was recognized by the processing pharmacist because the dose and frequency did not seem suitable for acetazolamide. Some of the other drug name pairs that

have led to this kind of error are (1) hydroxychloroquine/hydroxyurea, (2) *Mucomyst* (acetylcysteine)/*Mucinex* (guaifenesin), (3) valacyclovir/valganciclovir, and (4) penicillamine/penicillin.

This type of error occurs because the first portion of the generic or brand names for different medications are identical. When only a few letters of the drug are entered into the search box, the prescriber is often presented with a menu of choices and may quickly choose the medications that appear at the top of the browser. Steps to minimize this selection error include visually enhancing the letter character differences with tall man letters and requiring the prescriber to type as much of the drug name as possible when searching, rather than just a few letters. (Some order entry systems require users to type a certain number of letters before a list appears.)

Prescribers and pharmacists should double-check the choices that are in the order entry browser, become familiar with the usual dosing and frequency of the intended drug, or check references. This process is all the more important as these look-alike medications sometimes have similar strengths, although most have very different indications. Additional safeguards include the requirement for the entry of the intended purpose of drugs with similar indications or an alert for the pharmacist to verify that the indicated use matches the patient's condition. It is often difficult for other caregivers, such as the pharmacist and nurse, to catch a prescribing error or unintended use in the absence of readily available information about the condition for which the drug is being prescribed.

REDUCE AMBIEN DOSE IN ORDER SETS

When reviewing your electronic or preprinted order sets, be sure to keep in mind that the FDA is requiring manufacturers that make zolpidem (*Ambien* and generics) to lower the approved doses of the drug. If the drug is listed on order sets, you should make sure the dose is adjusted accordingly. FDA recently told manufacturers to lower the dose in light of new data showing blood levels in some patients may be high enough the morning after use to impair activities that require alertness, including driving.

FDA has informed the manufacturers that the recommended dose of zolpidem for women should be lowered from 10 mg to 5 mg for immediate-release products and from 12.5 mg to 6.25 mg for the extended-release product, *Ambien CR*. For men, FDA has informed the manufacturers that the labeling should recommend that health care professionals consider prescribing these lower doses (5 mg for immediate-release products and 6.25 mg for extended-release products).

Although most inpatients won't be driving the morning after hospitalization, it is not out of the realm of possibility if the patient is discharged the morning after receiving zolpidem. Complex sleep-related behaviors, such as sleep-walking and sleep-driving (driving while not fully awake and with no memory of the event), have been reported with zolpidem. Central nervous system medications in general can add to or cause confusion, agitation, and delirium. Sleep medications may also increase the risk of a fall, especially in the presence of other risk factors such as advanced age. It seems prudent to heed the label updates for the dosing of this drug.

CONFUSION BETWEEN LEVOTHYROXINE AND LIOTHYRONINE

A child diagnosed with congenital hypothyroidism had been receiving levothyroxine (T4; *Synthroid*) for the first year of life with adjustment of his medication as necessary. At around 14 months, the child had significantly abnormal laboratory values with what appeared to be a central hypothyroidism profile (low TSH, low free T4). It took many months to figure out that the pharmacy was dispensing liothyronine (T3; *Cytomel*) instead of levothyroxine, causing the child to develop a significantly elevated T3 level (>500 ng/dL). Liothyronine is more "potent" than levothyroxine. The pharmacist on duty the day the error was noticed reported that the prescription was written as "L-thyroxine," which apparently was confused as liothyronine (T3).

These 2 drugs are similarly named, and several references warn against confusion. Consider adding an alert detailing the potency difference between these drugs in your order entry system.

REFERENCES

1. Green AE, et al. Stability of nimodipine solution in oral syringes. *Am J Health Syst Pharm.* 2004;61:1493-1496. ■