

Community/Ambulatory Care

ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

ISMP updates its list of drug names with tall man (mixed case) letters based on survey results

Several design techniques have been explored for the purpose of differentiating look-alike drug names to prevent medication selection errors. Tall man (mixed case) lettering describes a method for differentiating the unique letter characters of similar drug names known to have been confused with one another. Starting with a generic drug name expressed in lowercase letters, tall man lettering highlights the differences between similar drug names by CAPITALIZING dissimilar letters. Occasionally, brand names, which always start with an UPPERCASE letter, may require the use of tall man letters to differentiate them from other brand or generic names. The use of tall man lettering to accentuate a unique portion of a drug name with UPPERCASE letters, along with other means such as color, **bolding**, or a contrasting background, can draw attention to the dissimilarities between look-alike drug names as well as alert healthcare providers that the drug name can be confused with another drug name.

Since 2008, ISMP has maintained a list of drug names with recommended UPPERCASE and **bolded** tall man letters. The list includes mostly generic-generic drug name pairs or larger groupings, although a few brand-brand or brand-generic name pairs are also included. Periodically, ISMP updates this list; it was last revised in 2016. Each time the list is updated, we analyze reported events from our error databases, survey practitioners on the topic, and conduct an internal review of drug names that would benefit from the application of UPPERCASE and **bolded** tall man lettering. The internal assessment includes an exploration of orthographic similarity; patterns of similarities in dosage, formulation, and use; and the potential for patient harm if the drugs are confused.

Standardization of Tall Man Letters

To promote standardization regarding which letters to present in **bold**/UPPERCASE, ISMP follows a tested methodology whenever possible, called the CD3 rule.¹ The rule suggests working from the left of the drug name first by CAPITALIZING all the characters to the right once two or more dissimilar letters are encountered. Then, working from the right of the word back, returning two or more letters common to both words to lowercase letters. When the rule cannot be applied because there are no common letters on the right side of the word, the methodology suggests CAPITALIZING the central part of the word only. When this rule fails to lead to the best tall man lettering option (e.g., makes names appear too similar or hard to read based on pronunciation), an alternative option is considered. ISMP suggests that the tall man lettering provided by the US Food and Drug Administration (FDA) and ISMP be followed to promote consistency.

ISMP Survey

ISMP conducted a survey between October and December 2022 to help update ISMP's current list of look-alike drug names with tall man (mixed case) letters. We believe healthcare practitioners should be involved in the process of identifying confusing drug names relevant to their respective practice settings, along with reviewing proposed tall man lettering for possible implementation. The CAPITALIZED and **bolded** letters should make the drug names distinguishable from the user's perspective.²

Respondent profile. ISMP extends our sincere appreciation to the 298 respondents who completed our survey on drug names with tall man letters. The respondents were mostly pharmacists (57%),

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SAFETY briefs



⚠️ High Alert Methotrexate multi-dose vial dispensed instead of single-dose vial.

At a specialty pharmacy, a technician was processing a refill for a patient's methotrexate vial for injection, which can be used for non-oncologic indications such as rheumatoid arthritis, psoriasis, or polyarticular juvenile idiopathic arthritis. The technician noticed that the pharmacy had dispensed methotrexate 50 mg/2 mL multi-dose vials with preservative) for the patient the last two months; however, the original prescription was written for the 50 mg/2 mL single-dose vial (preservative-free).

The pharmacy contacted the provider to inform them that the incorrect formulation had been sent previously. The provider confirmed that he wanted the patient to be

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IMPORTANT! Read and utilize the Community/Ambulatory Care Action Agenda

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, selected items from the **September – December 2022** issues of the **ISMP Medication Safety Alert! Community/Ambulatory Care** newsletters have been selected and prepared for you and your staff to stimulate discussion and collaborative action to reduce the risk of medication errors. Each item includes a brief description of the medication safety problem, a few recommendations to reduce the risk of errors, and the issue date to locate additional information.

The **Action Agenda** is available for download as an Excel file (www.ismp.org/node/60453).

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nurses (24%), and pharmacy technicians (12%); however, we also received responses from physicians and other prescribers (2%), and others (e.g., consultant, project manager, respiratory therapist) (5%). The findings from the survey and a discussion of how we updated the FDA and ISMP lists follow.

Scope of using tall man letters. A majority (94%) of respondents reported that their facility uses tall man letters. Almost three-quarters (74%) consistently use tall man letters for organization-defined drug names in all required contexts (e.g., computer screens for pharmacy and prescribers). Four out of five (80%) respondents use tall man letters in all settings (e.g., pharmacy, surgical suites) and across multihospital and/or multi-clinic settings.

Internal selection of drug names for tall man letters. Fewer than one out of five (18%) respondents use tall man letters for one or more drug names that do NOT comply with the configurations on the **FDA and ISMP Lists of Look-Alike Drug Names with Recommended Tall Man (Mixed Case) Letters**. However, most of the examples provided by respondents were drug names that were NOT on the FDA or ISMP lists. Examples include dox**EP**in (confused with doxycycline), nitro**GLY**cerin and nitro**PRUS**side, and **ALTE**plase and **TENECTE**plase. One respondent notified us that internally selected tall man letters for drug name pairs created confusion because of differences in the tall man letters used in drug information references (which comply with the FDA and ISMP lists). Thus, the organization opted to use the configurations on the FDA and ISMP lists, and to eliminate the use of tall man letters for drug names not included on either list.

Reduction of errors. The vast majority of respondents felt that the use of tall man lettering helped reduce the risk of errors among medications with look-alike names. Specifically, 95% of respondents felt that the use of tall man letters by the pharmaceutical industry on product and carton labels helps to reduce drug selection errors. More compelling is the fact that 87% of survey respondents were able to recall one or more instances when tall man lettering had actually prevented them from prescribing, transcribing, dispensing, or administering the wrong medication. Respondents provided examples of look-alike name pairs involved in these potential events, including hydr**ALAZINE** and hydr**OXY**zine, lev**ETIRA**acetam and lev**FLOX**acin, and **SOLU**-Medrol and **DEPO**-Medrol. Many others reported a personal experience where tall man lettering has helped them avoid errors when selecting drugs during order entry, removing medications from an automated dispensing cabinet (ADC) via override, programming the smart pump using the drug library, and prior to administration when referencing the medication administration record (MAR). Others reported that the use of tall man lettering on preprinted paper order sets helps prevent errors during electronic health record (EHR) downtime when technological safeguards are unavailable.

Several respondents also told us that tall man lettering alerts them to the possibility of a drug mix-up, reminding them to be cautious. They said that tall man letters are an effective alert system that quickly captures their attention and causes them to pause, read the drug name more carefully a second or third time, and make sure the drug is appropriate for the patient. Respondents referred to the tall man letters as a “tool to highlight errors” that helps to “catch your eyes” and “slow down or stop the process” to ensure they have the correct drug and “to prevent confirmation bias” when handling drugs with similar names.

Updated Lists

FDA list. In 2001, FDA initiated the name differentiation project to continually evaluate postmarketing reports of name pair confusion and to determine if tall man lettering should be used to help differentiate similar generic names (www.ismp.org/ext/1072). Since our last update to the lists in 2016, FDA has added three drug name pairs to its list:

- **CIS**platin and **CARBO**platin

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using the single-dose vial. The pharmacy corrected the entered prescription so that the single-dose vial would be dispensed with future refills. The pharmacist informed the patient of the error and confirmed that the patient had been using the multi-dose vial more than once. The pharmacist advised the patient to only use the single-dose vial once and to safely discard the remainder after each dose. The patient verbalized understanding.

When investigating the error, pharmacy staff noted that the dispensing software does not clearly indicate if the methotrexate product is a multi-dose vial or single-dose vial on the data entry or pre-verification screens. Pharmacy staff must click on the product name to see more information and to determine if the NDC is for the single-dose or multi-dose product.

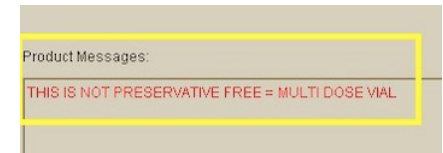


Figure 1. The pharmacy has added a product message to alert the verification pharmacist that the methotrexate vial is a multi-dose vial.

To help prevent this error, the pharmacy added a drug-specific “product message” in the dispensing software (**Figure 1**). This note displays in red text and shows up on the pre-verification screen near the directions. The note informs the pharmacist whether the product selected is a single-dose or multi-dose vial. Assess your dispensing system to determine how the methotrexate single-dose and multi-dose vials are displayed during order entry and verification. Work with your pharmacy system vendor and/or information technology team to update the product name to clearly state the dosage form. Consider adding a note to specify the product differences. Ensure the original prescription is visible, including for subsequent refills, to the verification pharmacist to enable them to check that the correct product has been entered.

ENFit patient resource guide. The Global Enteral Device Supplier Association (GEDSA) continued on page 3 — **SAFETY** briefs >

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- mig**AL**astat and mig**LU**stat
- tra**ZO**done and tra**MAD**ol

Two of these name pairs were already on the ISMP list: **CIS**platin and **CARBO**platin, and tra**ZO**done and tra**MAD**ol. Also, aceto**HEXAMIDE**, sulfi**SOXAZOLE**, and **TOLBUT**amide have been discontinued and are not marketed in the United States. However, FDA does not want to remove these names from its list because the names might still be listed in electronic drug information sources. Also, unless a drug is removed from the market for reasons of safety or efficacy, the drug could still be marketed at a later date.

Table 1. Drug names tested for possible addition to the *ISMP List of Look-Alike Drug Names with Recommended Tall Man Letters*

Drug Names	Aware of Confusion? (%)	Add to List? (%)
py RI Dostigmine and PHYS ostigmine	49	91
cyclo PHOS phamide (confused with cyclo SPORINE and cyclo SERINE , already on FDA list)	50	83
dro PER idol and dro NAB inol	37	82
lina GLI ptin and lina CLO tide	27	79
le NALID omide and le FLUN omide	21	79
hydroxy UREA (confused with hydr OXY zine, already on FDA list)	43	77
dex AMETH asone and dexmede TOMID ine	44	75
DESMO pressin and VASO pressin	44	71
NIZ atidine and nita ZOX anide	21	68
metho TREX ate (confused with met OL azone, meth IMA zole, and methazol AMIDE , already on ISMP list)	31	63

ISMP list. In the 2022 survey, we asked for feedback on 10 potential new drug name pairs or single drug names that may be confused with another drug name pair already on the list. Of these, 75% or more of the respondents felt that seven of these should be added to the ISMP list of drug names with tall man letters (**Table 1**). For these seven drug names or pairs, we evaluated the potential for overlap among indications, frequency of administration, storage, drug formulation, and available strengths, along with the potential for harm if a mix-up occurred. We also searched our error-reporting databases to see how often we received reports of mix-ups with a similar-looking drug name. Based on this assessment, the following drug names were added to the ISMP list of drug names with tall man letters:

- cyclo**PHOS**phamide (confused with cyclo**SPORINE** and cyclo**SERINE**, already on FDA list)
- dro**PER**idol and dro**NAB**inol
- dex**AMETH**asone and dexmede**TOMID**ine
- py**RI**Dostigmine and **PHYS**ostigmine

Many respondents shared their thoughts regarding other drug names that were not tested in the survey. We reviewed each suggestion while considering all risk factors and the need to keep the list short enough to avoid diluting the effectiveness of tall man letters. Overuse of tall man letters may reduce effectiveness, as names would no longer appear novel.² More than 30 name pairs with tall man letters were suggested (many brand names, which we hesitate to include without FDA approval). There were drug name pairs or single drug names that may be confused with other drug names already on the list that were closely associated with a high risk of harm if a mix-up were to occur, therefore, the following were added to the ISMP list:

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has created an ENFit guide for patients and caregivers (<https://stayconnected.org/pharmaguide/>). Patients and caregivers can use this resource to identify appropriate ENFit products (e.g., syringes, bottle adaptors) to safeguard administration of oral and enteral medications. Patients can then source the products themselves or communicate their needs to their pharmacy, home infusion, or durable medical equipment (DME) provider. Please share this resource with patients.

Worth repeating...



Ensure medications are properly reconstituted

We have published several cases of medications dispensed to patients before they were reconstituted, particularly unmixed antibiotics (February 2007, February 2008, February 2013, June 2015, and May 2017). Most of the cases involved pediatric patients who received overdoses of antibiotics when their parents administered the drug powder to their children. Unfortunately, we continue to receive reports of this type of error.

In a recent case, the pharmacy dispensed amoxicillin and clavulanate potassium for oral suspension as a powder. The toddler's parent did not know it was supposed to be mixed by the pharmacy, so they read the package insert and tried to follow the directions to mix a dose of the medication. The parent did not mix the medication correctly, in part because they made mistakes trying to convert mg to teaspoonful. The child vomited after the parent administered the first dose of the antibiotic.

Because we continue to receive reports of this same error over and over again, we think reviewing strategies that can help prevent these errors from reaching patients is **Worth repeating**:

- Incorporate technology at the point-of-sale that will alert pharmacy staff that the prescription needs to be reconstituted. Explore options to have the alert be interactive, requiring the staff person to acknowledge that the medication has been reconstituted.

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- **AL**fentanil (confused with **SUF**entanil and fenta**NYL**, already on the ISMP list)
- **BUP**ivacaine and **ROP**ivacaine
- oxy**BUTY**nin (confused with oxy**CODONE**, Oxy**CONTIN**, and oxy**MOR**phone, already on the ISMP list)

ISMP has previously recommended NOT using brand names of drugs that have been discontinued (e.g., Versed); thus, three name pairs were removed from the ISMP list:

- **AVIN**za (discontinued) and **INV**anz
- **SINE**quan (discontinued) and **SERO**quel
- **TREN**tal (discontinued) and **TEG**retol

A notation was also added for a medication that is not currently available in the United States:

- ra**NITI**dine (not available) confused with ri**MANTA**dine

The **FDA and ISMP Lists of Look-Alike Drug Names with Recommended Tall Man (Mixed Case) Letters** has been updated and available on our website (www.ismp.org/node/136).

Ongoing Research

In 2016, ISMP published an up-to-date review of the research, **Tall man letters: A review of the evidence; in Special Edition: Tall Man Lettering; ISMP Updates Its List of Drug Names with Tall Man Letters** (www.ismp.org/node/250). Using tall man letters, alone or with other text enhancements, has been shown to reduce errors due to drug name similarity. However, the evidence is mixed, with some studies showing the method may not be effective. Interestingly, a 2021 meta-analysis (www.ismp.org/ext/1077) that looked at 11 articles representing 20 individual trials, showed a significant reduction in wrong medication selection errors caused by look-alike drug names when using tall man lettering or other forms of text enhancement.

ISMP is currently serving as a co-investigator in a 4-year Northwestern University (Chicago) research project, led by Bruce L. Lambert, PhD, to assess the comparative effectiveness of various methods of tall man lettering, text enhancements, and their ability to reduce errors during drug selection. This research project is being funded through a grant from FDA. We look forward to participating in the research project and learning more about the effectiveness of tall man lettering.

Although there are still questions to be answered, tall man lettering is done at little or no cost, has little or no downside, and is not known to be associated with any potential risk for patient harm. Considering past research showing it may be an effective way to prevent mix-ups, and the overwhelming support for tall man lettering shown by survey respondents, ISMP strongly encourages continued use by FDA, pharmaceutical manufacturers, outsourcers and compounders, hospitals, and other practice locations, while we conduct further research to answer questions about the most effective way to differentiate look-alike drug name pairs.

References

- 1) Gerrett D, Gale AG, Darker IT, Filik R, Purdy KJ. Tall man lettering. Final report of the use of tall man lettering to minimize selection errors of medicine names in computer prescribing and dispensing systems. Loughborough University Enterprises Ltd; 2009.
- 2) ISMP Canada. Principles for the application of tallman lettering in Canada. October 2015. www.ismp.org/ext/1083

> **Worth repeating** continued from page 3

- Add a note or label to the prescription receipt, or use some other distinct visual cue (e.g., brightly colored "Need to mix" card) indicating that the medication needs to be reconstituted prior to dispensing.
- Place the actual product container that requires reconstitution in a separate area (e.g., not with other medications in the will-call area awaiting pick up, not bagged with other prescriptions for the patient). After the product is reconstituted, the product should be given to the pharmacist, along with any other prescriptions, to counsel the patient on how to measure the medication.
- Include specific product descriptions on the prescription label (e.g., orange flavored, white, opaque liquid) that will cue the consumer that they should be receiving an oral, liquid product.
- At the point-of-sale, review with the patient or caregiver the label, storage requirements, route of administration, directions for use, and if the amount of medication will cover the days of therapy. Shake the bottle to demonstrate how to mix the suspension prior to administering. Open the bottle with the patient or caregiver to check that the contents have been reconstituted.
- Ensure that an appropriate metric dosing device, which corresponds to the instructions on the label, is provided with the product.
- Use the teach back method when educating patients. Have the caregiver or patient demonstrate how they will measure and administer the dose to validate learning.

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