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The Breakup: Errors when Altering Oral Solid Dosage Forms

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Abstract

Altering oral solid dosage forms of medications may be required to meet patient-specific doses, help patients who have swallowing issues, or facilitate administration via enteral feeding tubes. However, this step increases the risk of errors and adverse events. Analysts identified 621 events involving altered solid dosage forms of medications in reports submitted to the Pennsylvania Patient Safety Authority, which occurred from January 2006 through September 2017. Nearly three-quarters (73.9%, n = 459) of events were associated with splitting tablets, while crushing tablets (24.3%, n = 151) and opening capsules (1.8%, n = 11) accounted for the remainder. Almost 90% (87.1%; n = 541) of events reached patients, and 28.2% (n = 175) involved high-alert medications. Overdose and extra dose represented the most commonly reported event types associated with splitting medications (71.5%, n = 328 of 459). More than half of events involved older patients (65 years or older; 56.0%, n = 348 of 621), which is consistent with the higher incidence of dysphagia in this population. Potential risk reduction strategies include using technology to provide patient information (e.g., limitations in swallowing) and drug information to providers, limiting oral dosage form alterations to cases in which commercial alternatives are unavailable, dispensing medications in patient-specific doses to minimize preparation on patient care units, and implementing procedures to handle dosage-form alterations and administration via feeding tubes.

Introduction

Although medications commercially available in oral solid dosage forms are suitable for most patients, there are populations and circumstances that require splitting tablets, crushing tablets, or opening capsules. For example, pediatric and geriatric populations may require dosage strengths that are not commercially available. Variable dosing during dose titration or tapering to prevent withdrawal symptoms may also result in the need to split tablets (e.g., for older patients, a 50 mg tablet must be split to administer traZODone 25 mg initially or as a last dose when tapering

antidepressant therapy). Further, tablets are sometimes split to avoid delays in drug administration while awaiting pharmacy delivery. In addition, pharmacies may not carry all of the commercially available strengths for all products.[1-3] There may be times when patients receive medications through a feeding tube or are unable to swallow whole tablets but liquid medication formulations are unavailable.[2]

Inappropriately altering tablets and capsules can result in treatment failure and patient harm. For example, altering enteric-coated (e.g., delayed-release) tablets can result in local irritation, loss of drug stability, and failure of proper absorption. Altering film- and sugar-coated tablets can result in medication instability and unacceptable taste. Some extended-release capsules can be opened, as long as the pellets inside are not damaged, while others should never be opened, to prevent changes in pharmacokinetics and bioavailability.[2,4-6] Altering hazardous drugs (e.g., chemotherapy, drugs posing a risk of reproductive or developmental harm) raises concerns of occupational health and safety for the healthcare provider.[7,8] Relying on personal or coworker experience rather than consulting a pharmacist or administration guidelines, if available, contributes to nonstandard practices and increases the risk of improper medication preparation and administration and drug incompatibilities when administered with enteral feedings.[2,4,5,9-12]

Risks with splitting oral solid dosage forms include missed or misinterpreted administration instructions (e.g., give "1/2") and dose deviations, which may be especially dangerous with drugs that have narrow therapeutic indexes.[2,13,14] (Narrow therapeutic index drugs, such as warfarin and levothyroxine, are medications for which small differences in dose or blood concentration may lead to serious therapeutic failures and/or adverse drug reactions that result in persistent or significant disability or incapacity or are even life threatening.[15])

In 2016, the U.S. Food and Drug Administration (FDA) reported significant dose variations when tablets are split.[16,17] The Veterans Administration National Center for Patient Safety (VA NCPS) looked at reports of splitting medications and found that patients frequently forgot to split tablets, which resulted in overdose and adverse drug events, or healthcare providers chose the wrong formulation for splitting (e.g., extended release).[18] High-alert medications, drugs that bear a heightened risk of causing significant patient harm when used in error,[19] were involved in about one-quarter of events, and about half of those cases mentioned medications that had commercially available strengths that could have been used without alteration.[18]

In addition to inappropriate manipulation of oral solid dosage forms at the point of administration, prescribers and pharmacists have less ability to prevent medication errors when patient information (e.g., presence of a feeding tube) is not readily available and medications are not matched to the patient's conditions.[2,13,18] In a retrospective chart review, Li et al. found that, among patients for whom pharmacists were not informed that they were receiving their medications via feeding tubes, 43% received one or more medications that should not be crushed.[20] Dysphagia, or difficulty swallowing, a common disorder in older patients, is frequently unidentified.[21-23] With aging populations on the rise, the need to identify and address swallowing issues in medication administration becomes increasingly important.[21,24,25]

This article will review medication errors and other events associated with altered oral solid dosage forms, identify the reasons the events took place, encourage the use of best practices when oral dosage forms need to be altered, and propose risk reduction strategies.

Methods

Analysts queried the Pennsylvania Patient Safety Reporting System (PA-PSRS) database for events reported as medication errors and adverse drug reactions in which the free-text data fields (e.g., event description) included variations of and wildcards for the following keywords: open, crush, break, split, cut, pill, tablet, capsule, half, and ½. In addition, analysts queried a convenience sample from the database for all event types in which an analyst had previously identified the event as an alteration of oral solid dosage forms. The search was limited to events that occurred from January 2006 through September 2017.

The search returned 987 events. A total of 366 events were excluded because they described ---—

- Nondrug events (e.g., crush injury).
- Events with other dosage forms (e.g., injectables, patches).
- Events not involving dosage-form modifications (e.g., two tablets instead of one).
- Other unrelated events (e.g., fragmented pills found in an automated dispensing cabinet [ADC]).

Six hundred twenty-one events involved alteration of oral solid dosage forms, meeting the inclusion criteria, and were included in the final analysis.

The medications involved in the reports were provided by the reporting facilities and were standardized by an analyst to generic names specifying modified-release dosage forms (i.e., delayed release, extended release), if applicable. When a medication-name data field was blank, but the name was provided in the event description, an analyst adjusted the medication name field for data analysis. The reporting facility provided the harm scores,[26] which are adapted from the National Coordinating Council for Medication Error Reporting and Prevention (NCC-MERP) harm index[27], as well as facility type, patient care area, patient age, node of medication-use process, event type, event description, and whether students or new nurses were involved.

Reports were categorized into type of dosage form alteration (i.e., crushing, splitting, opening) and routes of administration (i.e., enteral feeding tube, oral) based on analysis of the event description. Event reports were then categorized into two types: dosage forms that can be altered and dosage forms that should not be altered.

The appropriateness of each medication alteration and commercial availability of alternative medication strengths and formulations were evaluated using the web-based electronic drug information resources DailyMed (U.S. National Library of Medicine, Bethesda, MD)[28] and Lexicomp® Online (Wolters Kluwer Clinical Drug Information, Inc., Hudson, OH)[29] as well as the Institute for Safe Medication Practices' (ISMP) Oral Dosage Forms That Should Not Be Crushed 2016 list.[30] When reports specified that the medication should not be crushed but analysts could not find any supporting references, the medication was categorized as "OK to crush" (e.g., raNITIdine).

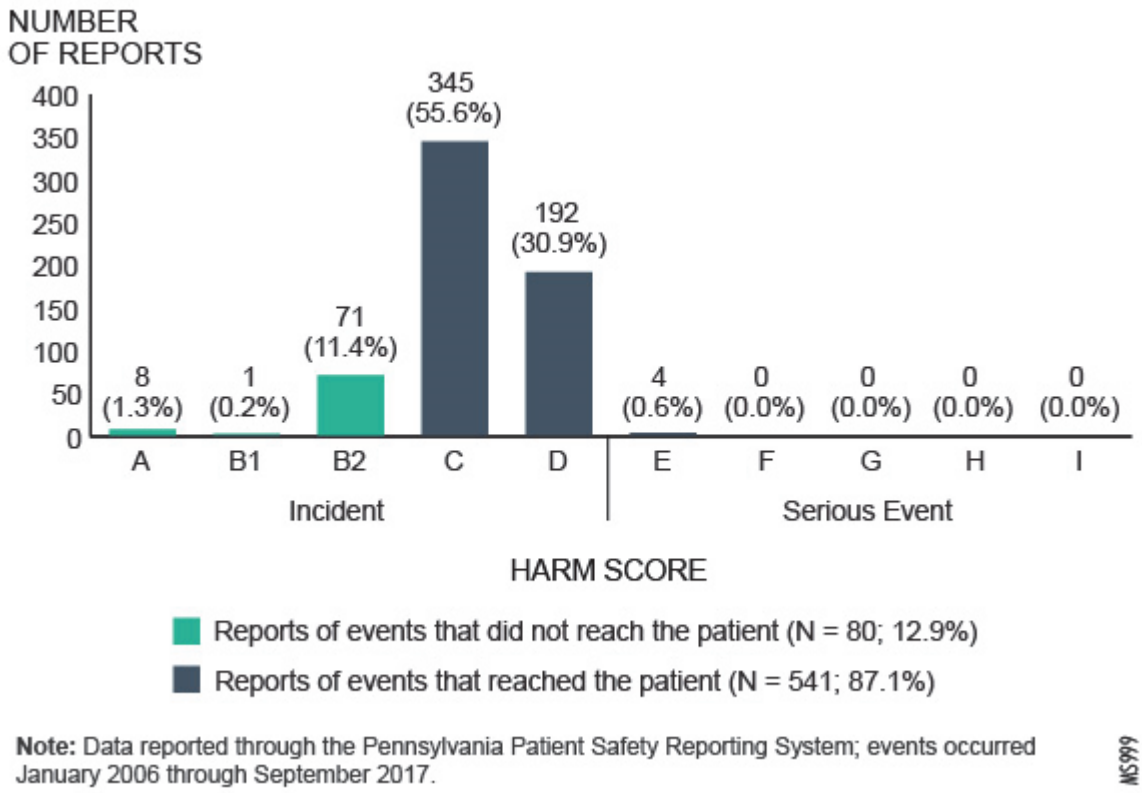
Analysts identified reports involving high-alert medications based on ISMP's lists of high-alert medications in acute care and long-term care settings.[19,31] Analysts identified reports involving hazardous medications based on the list provided by the National Institute for Occupational Safety and Health (NIOSH)[7] and Lexicomp® Online.[29] Analysts identified risk factors and potential prevention strategies based on event descriptions and event recommendations provided by the reporters.

Results

According to reporter-assigned harm scores, 87.1% (n = 541 of 621) of events reached the patient (harm scores C through I; Figure 1). Fewer than 1% (0.6%, n = 4) of the events were marked by reporters as causing patient harm (harm scores E through I). However, there were 14 reports categorized with harm score C or D that described apparent patient harm in the event description. When combined, 2.9% (n = 18) of the reported events were associated with patient harm. Ten reports indicated patients received four times the prescribed dose. One report mentioned that a patient received a 10-fold overdose. Following is the example, reported through PA-PSRS:*

Patient to receive cloNIDine 30 mcg stat. Attending physician entered order for cloNIDine 30 mcg suspension, via oral gastric tube every 8 hours, STAT. In product selection area, chose [100 mcg] tablet form. Pharmacist saw order sentence specifying suspension, but dispensed [3] tablets since that was the product selected in the order. When med dispensed on unit, label on bag read: cloNIDine 30 mcg = 0.3 tabs. All 3 doses for the day were in the bag. Nurse crushed/diluted all 3 tabs and gave them. Error was realized promptly, and the OG [orogastric] tube was aspirated. MD aware. No further interventions or harm. No bp [blood pressure] or VS [vital signs] changes. Per MD, dose given (300 mcg) is within daily limits.

Figure 1. Harm Scores for Events Involving Alteration of Solid Oral Dosage Forms (N = 621)



Note: Data reported through the Pennsylvania Patient Safety Reporting System; events occurred January 2006 through September 2017.

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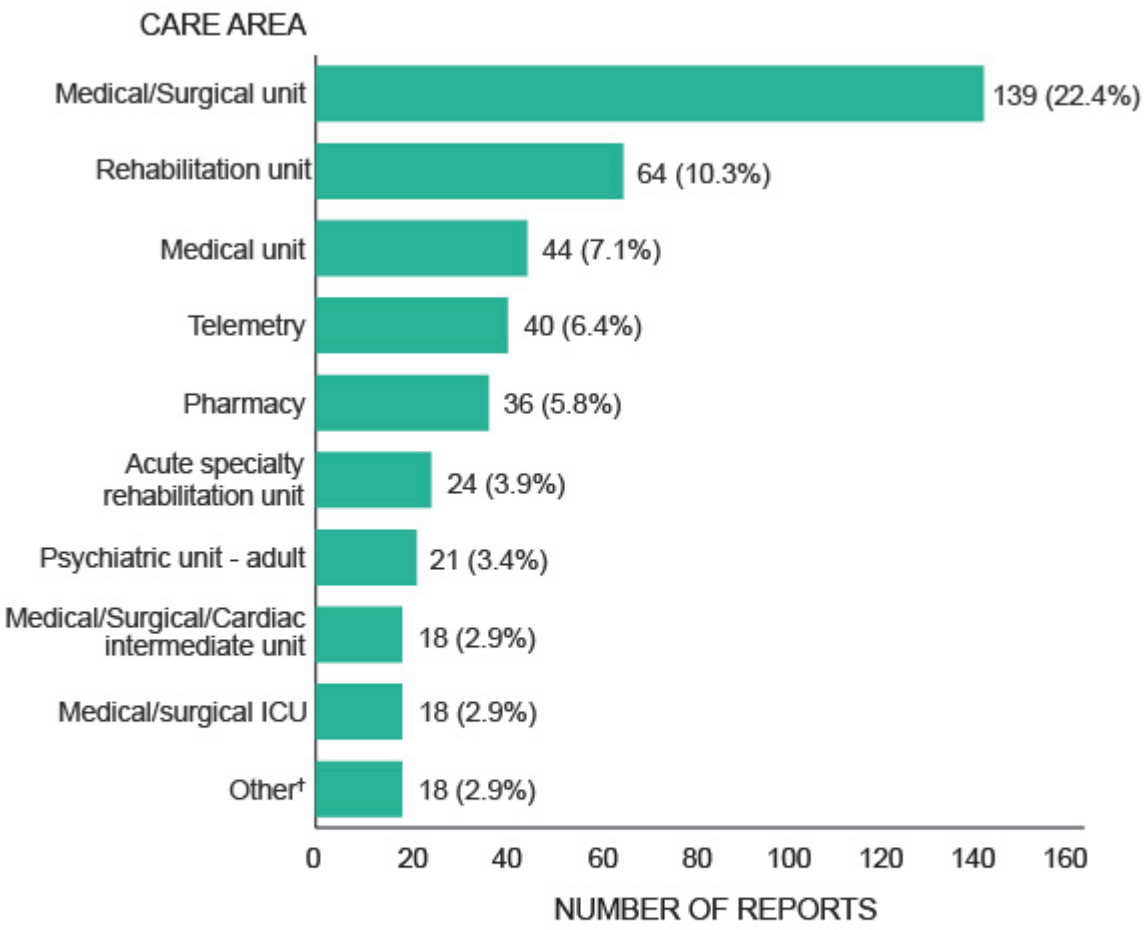
The top facility types identified in event reports were acute care hospitals (75.0%, n = 466 of 621), rehabilitation hospitals (11.9%, n = 74), and long-term acute care hospitals (LTAC; 7.4%, n = 46). Figure 2 shows the most commonly reported patient-care areas, representing 68.0% (n = 422 of 621) of events. More than half of events involved older patients (65 years or older; 56.0%, n = 348), while a minority (4.8%, n = 30) involved pediatric patients (younger than 18 years).

Figure 2. Ten Most Common Care Areas Associated with Events Involving Alteration of Solid Oral Dosage Forms (N = 621)*



Note: Data reported through the Pennsylvania Patient Safety Reporting System; events occurred January 2006 through September 2017.

ICU, Intensive care unit.

* Percentages in the figure are based on N = 621. The number of reported events (n = 422 of 621) represented in the figure corresponds to the 10 most common care areas associated with events involving alteration of solid oral dosage forms.

† As classified by the reporting facilities.

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High-alert medications, including opioids, hypoglycemic agents, and anticoagulants, were involved in 28.2% (n = 175 of 621) of events. Almost 5% (4.7%, n = 29) of events involved a narrow therapeutic index drug. Hazardous medications were involved in 11.6% (n = 72) of events. Nearly three quarters (73.9%, n = 459) of the events involved splitting of medications. The remainder of the reports involved either crushing a medication (24.3%, n = 151) or opening a capsule (1.8%, n = 11).

Four hundred thirty (69.2%) reports specified that errors took place during the administration node. Students and new nurses were involved in a small number of events (4.2%, n = 26 of 621).

Patients and family members helped identify or prevent errors in five reports (0.8%). However, patients also contributed to a small number of events. Nineteen reports (3.1%) specified a patient as the one altering the solid dosage form. Following is an example of such an event reported through PA-PSRS:

Patient reported to be chewing phenytoin extended-release capsules. Pharmacy made aware. Geriatrics and trauma made aware. Phenytoin free level drawn and medication changed to liquid form.

In two cases, nurses altered OxyCONTIN® (oxyCODONE extended release) per patient's request. Following is an example of such an event reported through PA-PSRS:

Apparently told nurse she crushes her OxyCONTIN for administration as an outpatient. Nurse administered crushed tablet. Patient developed a change in mental status and was given Narcan® [naloxone] X 3.

Splitting Medications

A majority (73.9%, n = 459 of 621) of the events were related to splitting or failure to split medications. Figure 3 shows the medications commonly involved in these events. Overdose and extra dose represented the most commonly reported event types associated with splitting medications (71.5%, n = 328 of 459; Figure 4). Analysts identified that patients were harmed in 1.1% (n = 5 of 459) of reports. High-alert medications were involved in 26.1% (n = 120 of 459) of the reports, almost half (43.3%, n = 52 of 120) of which were long-acting opioids.

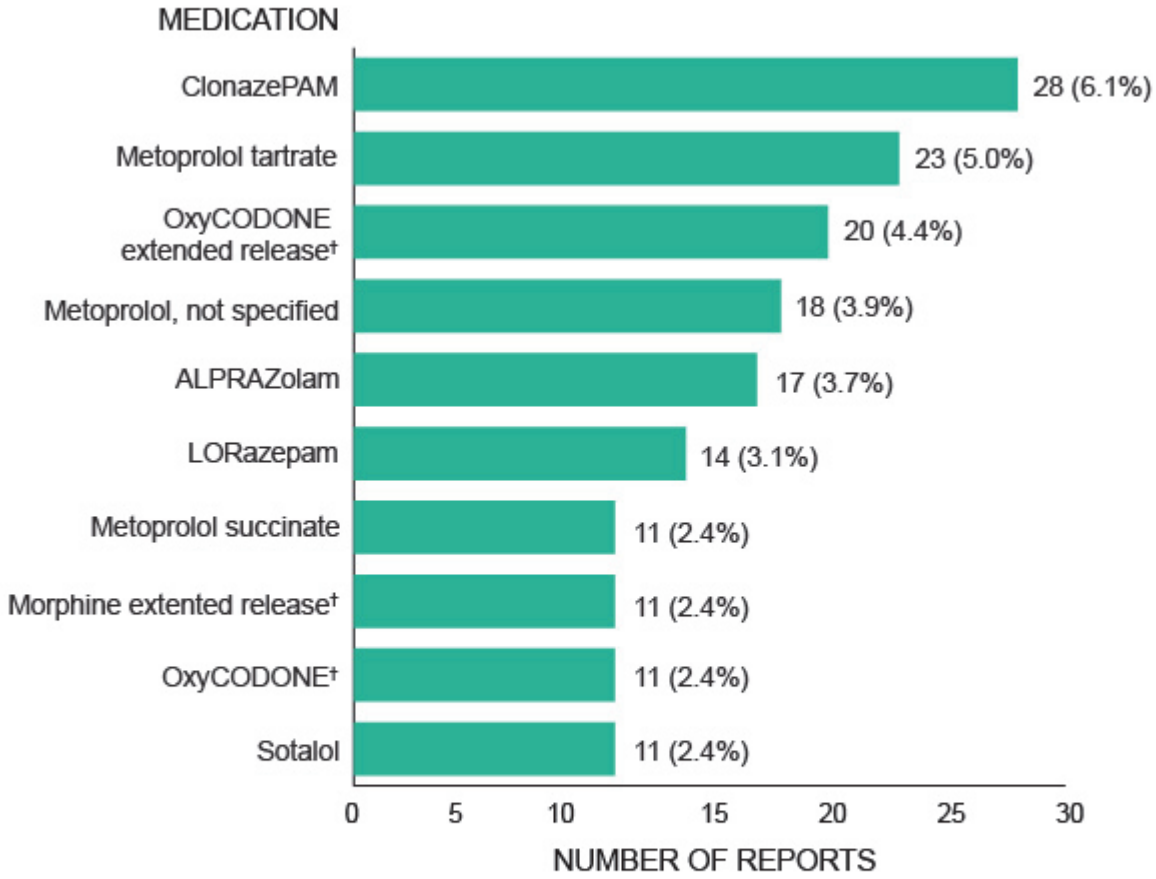
Commercially available products and strengths could have been used without alteration in 31.6% (n = 145 of 459) of the events. Misinterpreting or missing directions to administer ½ tablet was specified in 10.7% (n = 49) of reports and involved all stages of the medication-use process, including medication reconciliation, prescribing, transcribing, and administration stages.

Following are examples of events involving splitting of medications reported through PA-PSRS:

Digoxin entered incorrectly into [electronic health record] and confirmed as correct. 0.125 mg 1/2 tablet ordered. 0.125 – 1 1/2 tabs entered. The patient received 3x ordered dose for one dose.

Order read glipiZIDE 2.5 mg 1/2 tab. Nurse dispensed 1/2 tablet of a 2.5 mg tablet = 1.25 mg. This order should have been clarified when written. Physician meant 1/2 tablet of a 5 mg tablet = 2.5 mg. order was clarified one hour post med administration.

Figure 3. Ten Most Common Medications Associated with Events Involving Splitting of Solid Oral Dosage Forms (N = 459)*



Note: Data reported through the Pennsylvania Patient Safety Reporting System; events occurred January 2006 through September 2017.

* Percentages in the figure are based on N = 459 medication-associated events involving splitting of solid oral dosage forms. The number of events (n = 164 of 459) represented in the figure corresponds to the 10 most commonly reported medications.

† A high-alert medication.

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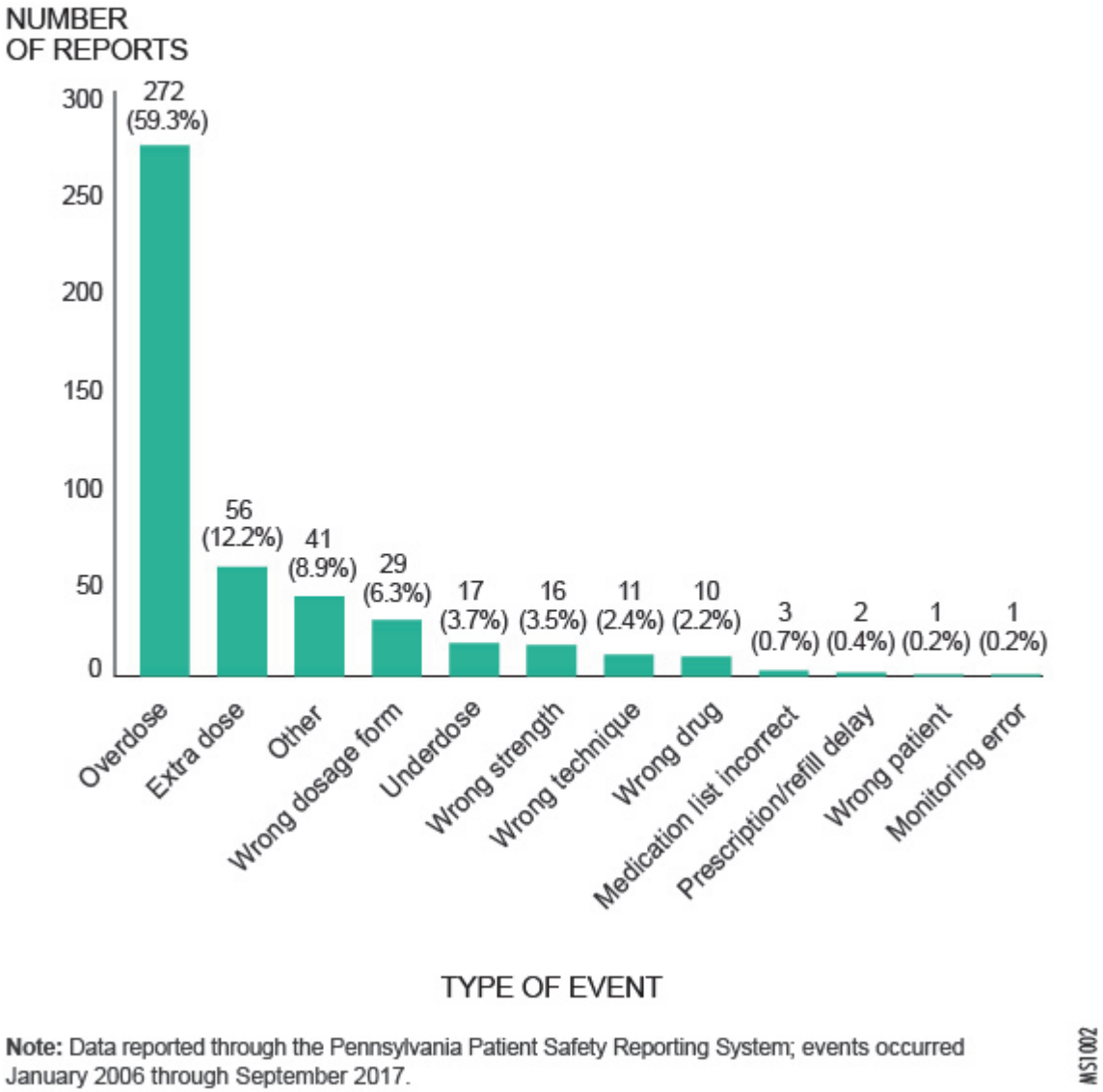
Figure 4. Types of Events Involving Splitting of Solid Oral Dosage Forms (N = 459)



Note: Data reported through the Pennsylvania Patient Safety Reporting System; events occurred January 2006 through September 2017.

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OK to Split

A majority (80.6%, n = 370 of 459) of the events related to splitting medications involved oral dosage forms that can be split but were not when dispensing or administering the patient's specific dose. Almost one in five (17.6%, n = 65 of 370) reports specifically stated that a medication was not dispensed in a split form. In other event descriptions, it was unclear why medications were not available in a patient-specific dose, although a few reported that whole tablets from a supply of previous (discontinued) doses were used. Reporters described in 12.7% (n = 47 of 370) of the events that errors occurred despite use of a barcode medication administration (BCMA) system. In these events, reporters documented the following as factors contributing to practitioners administering more medication (e.g., a whole tablet, two halves of a tablet) than prescribed:

- Medication administration takes place before barcode scanning.
- Practitioners are not looking at the computer screen when a product is scanned.
- Barcode scanners malfunction.

- Practitioners misunderstand the system warnings.
- There is pressure to multitask.
- Distractions occur.

A few events involved medications that can be split, but selection of an inappropriate tablet strength precluded dividing tablets accurately, as seen in the following example:

Patient was ordered warfarin 1.25 mg PO q PM [by mouth, once every night]. When medication was verified in [the pharmacy computer system], the order defaulted to a warfarin 2 mg tablet. [For five days] multiple nurses vended warfarin 2 mg tablets from the automated dispensing machine. In order to achieve the 1.25 mg dose from a 2 mg tablet, 0.63 tab would need to be administered. All doses were charted as given on the MAR [medication administration record] as 1.25 mg. The pharmacy was not contacted by the nursing staff to make any adjustments to the order to obtain the appropriate tablet size (2.5 mg) that could be split in half to achieve the ordered 1.25 mg dose. The patient's INR [international normalized ratio] subsequently rose to a peak of 6.1 [most common target INR ranges, depending on diagnosis, are 2 to 3 and 2.5 to 3.5[32]] and he required PO vitamin K.

Among these 370 reports, prescribed dosage strengths were commercially available in more than one-quarter of cases (26.5%, n = 98).

Do Not Split

Almost one in five events (19.4%, n = 89 of 459) involved medications that should not be split. A few reported events involved the accidental selection of an extended-release product instead of an immediate-release dosage form. Following are examples of errors with medications that should not be split:

Patient ordered MS Contin® [morphine sulfate extended release] 7.5 mg BID [twice a day]. Pharmacy closed. Nurse did override on med [medication] cabinet. 7.5 mg not available. Nurse took 15 mg and cut it in half and administered it. It was an extended-release tablet. Pt required IV naloxone after becoming unarousable. Vitals OK.

Cardizem CD® [dilTIAZem] 120 mg was ordered for patient and Pharmacy order was for Cardizem CD 240 mg 1/2 capsule. Patient received several doses before RN contacted the pharmacy concerning splitting a capsule. Medication order was corrected.

For medications that should not be split, high-alert medications were involved in 53.9% (n = 48 of 89) of the reports. Almost half (49.4%, n = 44) of reports of medications that should not be split involved long-acting opioids. Some events, such as the one below, describe the pharmacy entering orders for half tablets for medications that should not be split:

Pharmacy profiled 100 mg oxyCONTIN as 2½ tabs of 40 mg tablets. Staff administered split oxyCONTIN tab to patient.

Among these 89 reports, prescribed dosage strengths were commercially available in more than one-half (52.8%, n = 47) of cases.

Crushing Medications

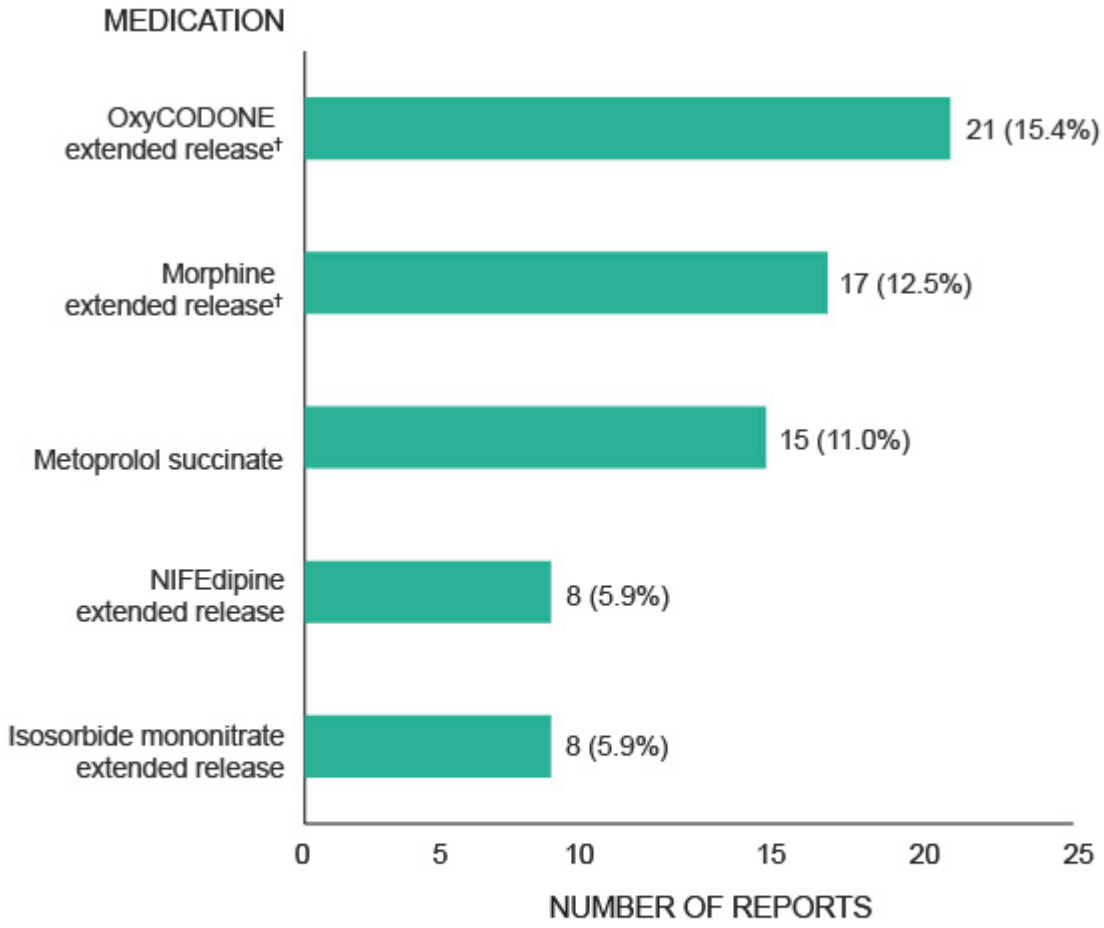
About one-quarter (24.3%, n = 151 of 621) of the overall events were related to crushing medications. Most (90.1%, n = 136 of 151) of these involved medications that should not be crushed. The drugs involved in 50.7% (n = 69 of 136) of medication events in which crushing is contraindicated are listed in Figure 5. Alternative, commercially available products could have been used in the majority (72.8%, n = 99 of 136) of these cases.

Patients were harmed in 8.6% (n = 13 of 151) of reports. Among all events related to crushing medications, almost one in three (31.1%, n = 47 of 151) involved high-alert medications, and a majority of these were long-acting opioids (n = 42). Following are examples of events related to medication crushing reported through PA-PSRS:

OxyCONTIN crushed for oral administration by nurse. Medication is a sustained release med and should not have been crushed. Patient refused medication. Nurse stated she did not know that medication could not be crushed.

Nurse accidently crushed sustained release OxyCONTIN pill with her other meds. No ill effects to patient. Daughter aware.

Figure 5. Five Most Common Medications That Should Not Be Crushed But Were (N = 136)*



Note: Data reported through the Pennsylvania Patient Safety Reporting System; events occurred January 2006 through September 2017.

* Percentages in the figure are based on N = 136. The number of events (n = 69 of 136) represented in the figure corresponds to the five most common medications that should not be crushed but were.

† A high-alert medication.

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Opening Capsules

Events involving opening of capsules to administer the medications were reported the least frequently (1.8%, n = 11 of 621). Most (90.9%, n = 10 of 11) of these involved medication capsules that should not be opened, such as dabigatran and tamsulosin. Commercially available alternatives existed in 27.3% (n = 3 of 11) of the cases. None of the events were associated with harm, but one reporter expressed occupational-hazard concerns with an order for tacrolimus that required opening capsules on the unit.

Enteral Feeding Tube Administration

One hundred thirteen (18.2% of 621) events specifically mentioned an alteration of a solid oral dosage form for administration via an enteral feeding tube. Medications that should not be crushed were involved in 90.3% (n = 102 of 113) of these cases. Although reporters described orders specifying enteral tube administration in the majority of

these cases, 28.3% (n = 32 of 113) of the reports indicated that the prescriber's order directed oral (by mouth) administration. Four cases involved patients in whom enteral tubes were recently placed, but the ordered by-mouth medications were not reviewed for appropriateness of administration via the new route. Following is an example of an error involving an enteral feeding tube reported through PA-PSRS:

Patient admitted with GI [gastrointestinal] bleed, has nasoduodenal tube, was ordered NIFEdipine extended release and [isosorbide mononitrate] to be given oral, nurse crushed both pills and administered through nasoduodenal tube, shortly thereafter, the patient became hypotensive and lethargic, requiring intubation and resuscitation, the patient is stable in the intensive care unit.

Analysis of reports also revealed one case of administering crushed oral medication intravenously while training new staff. Following is the example, reported through PA-PSRS:

Tablet crushed and dissolved in sterile water by preceptor and new staff person. Medication administered via central line instead of gastric tube accidentally.

One report described crushing and administering multiple medications via a feeding tube. Following is the example, reported through PA-PSRS:

Medications spurted out of syringe while giving medications via PEG [percutaneous endoscopic gastrostomy] tube. Since medications were crushed, unsure of which medications patient received and which ones were omitted.

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* The details of the PA-PSRS event narratives in this article have been modified to preserve confidentiality.

Discussion

Data analysis revealed errors with splitting and crushing tablets as well as opening capsules reached patients in 87.1% of reports. Some of the events involved high-alert medications, particularly long-acting opioids, and revealed underutilization of commercially available products that do not require alteration (e.g., oral liquids) or can be altered safely. The prominence of events involving older patients and patients in rehabilitation units is consistent with the higher incidence of dysphagia in this population.[33]

Analysts found that 56.0% of the events involved older adult patients predominantly in acute care, rehabilitation, and LTAC hospitals. Literature suggests that older adults in different healthcare settings are more likely to require dosage-form alteration. This is especially important to remember because in the face of a growing aging population that is more likely to have comorbidities, multiple medications, and be particularly sensitive to toxicities, especially when narrow therapeutic index or high-alert medications are used.[21,24,25] ISMP cautions that lack of or inaccurate patient information—including patient age, presence of an enteral feeding tube, and swallowing issues (e.g., dysphagia, dementia, aspiration risk, Parkinson's disease)—increases risk of errors.[34]

ISMP also cautions that not using commercially available strengths and dosage forms that require no manipulation increases the risk of errors.[4,5,34] Data analysis indicated that commercially available dosage strengths and formulations could have been used without alteration in almost one-third (31.6%) of events involving splitting medications. Commercially available products that require no manipulation or can be altered safely could have been used in the majority (72.8%) of events involving crushing medications and in more than one-quarter (27.3%) of events involving the opening of capsules.

The process of identifying dosage forms that should not be altered should not rely on healthcare practitioner knowledge or memory.[10,12] Hazardous, narrow therapeutic index, and high-alert medications were involved in events. High-alert medications were inappropriately altered in more than one-quarter (28.2%) of cases, including events involving long-acting opioids that can lead to central nervous system (CNS) and respiratory depression. Some reports specifically noted that electronic systems did not warn the user about the risk of altering dosage forms when prescribing, verifying orders in the pharmacy computer system, accessing the MAR, or retrieving medications from an ADC.

Data also showed that even medication names indicating extended release (e.g., NIFEdipine extended release) failed to alert practitioners that the medication should not be crushed. Bassett et al. described the case of a 69-year-old man whose NIFEdipine extended-release 90 mg tablet was crushed and administered through a duodenal tube, resulting in blood pressure 65/44 mm Hg, pulse 80 beats/minute in a ventricularly paced rhythm, and a decreased level of consciousness, requiring pharmacological interventions.[35] The risk is even higher with medication names that do not signal that a drug should not be altered (e.g., OxyCONTIN, MS Contin, Kadian®, Pradaxa®).[4-6,36]

The markings on tablets can also cause confusion about whether a medication should be split. In March 2013, FDA provided guidance to industry that new modified-release products for which the control of drug release can be compromised by tablet splitting should not have a scoring feature;[17] however, there are some older medications that should not be split or crushed but still are scored. In these cases, manufacturers use a scoring feature as part of their tablet identification and imprint system. However, this introduces risk of misinterpretation and inappropriate splitting of the tablet. For example, KlonoPIN 0.5 mg tablets are scored, but the manufacturer states that tablets should be swallowed whole.[37,38] Also, some scored medications can be split but not crushed (e.g., metoprolol succinate).[39,40]

Healthcare practitioners and patients are sometimes faced with information from the manufacturer's product information and the literature that conflicts about whether a product can be altered. In the case of Cymbalta® (DULoxetine), the manufacturer specifies that capsules should be swallowed whole,[41] and FDA states that adverse effects have been reported when patients opened Cymbalta capsules.[42] However, other drug-information resources specify that the medication has been found to be stable for up to two hours after sprinkling the contents of capsule on applesauce or in apple juice, if care is taken to not crush the pellets or damage the enteric coating.[43]

Also, the same medication may be manufactured by different companies that provide different directions for altering the dosage form. For example, most dilTIAZem extended-release products specify that the capsules should not be opened, chewed, or crushed, but this drug under the brand names Taztia XT® and Tiazac® extended release specifies that capsules may be opened.[44-46]

When it comes to safe handling of medications, NIOSH provides information on antineoplastic and other hazardous drugs.[7] Information about handling hazardous drugs may prove even more important with increasing use of oral chemotherapy drugs. Data analysis showed that hazardous medications in NIOSH groups 1, 2, and 3 were involved in 11.6% of events mentioning an alteration of oral solid dosage forms reported through PA-PSRS. Most reporters neither stated concerns about altering hazardous drugs nor mentioned the use of healthcare-provider personal protection measures. This may indicate that these types of employee concerns or potential harm are not captured through PA-PSRS. It may also indicate that staff do not identify certain drugs as hazardous or realize the safety risks of altering them.

Splitting Tablets

Splitting medications was found to be involved in almost three-quarters of the reported events and was most likely to result in extra doses and overdoses. The VA NCPS and VA Patient Safety Centers of Inquiry (VA PSCI) evaluated potential medication problems caused by tablet splitting using their Patient Safety Information System database. They

found a similar risk (66% of adverse pill-splitting events involved patients receiving too high a dose) with this type of oral solid dosage form alteration.[18] The VA analysis also found that the prescribed doses had been commercially available in a form that did not require tablet splitting in more than one-half (51%) of their reported events.[18] Similarly, PA-PSRS data showed that forgetting to split a dose was a common contributing factor to errors and that commercially available alternatives that do not require alteration could have been used in many cases.

Although not explicitly described in the data, the splitting of tablets in place of using commercially available strengths could be associated with pharmacies not carrying certain dosage strengths or use of nonformulary drugs. Some reports indicated that staff remove medications (not patient-specific doses) from night cabinets when a pharmacy is closed or use whole tablets left from a prior dose supply. Because evaluating ADC and night cabinet inventory for adjustment of medication quantity is recommended,[47,48] these data raise the question of whether evaluating prescribing trends might help identify the actual strengths used.

When medications require splitting, information may not be clearly presented and communicated to all healthcare providers throughout the medication use process. Some reporters expressed concern with unclear dosing information on medication orders when strength and ½ tablet directions run together (e.g., does "glipiZIDE 2.5 mg ½ tablet" mean a dose of 2.5 mg or 1.25 mg?). Directions can also be missed if they are placed in the free-text comments or special-instruction fields by prescribers when ordering a medication.

Misinterpretation and miscommunication of doses was observed with medication reconciliation (e.g., patients did not specify that they took only half of a reported tablet strength) and transcribing by a nurse or pharmacist (e.g., half of a tablet was entered as 0.5, ½, 1.5, 1 ½, or 1-2; half tablet was not entered in the order; half tablet did not display on the MAR or ADC screens). Some reports specified that ½ tablet directions were missed or forgotten during administration. Some staff accidently administered the second half of a tablet or split a tablet in half again. These data support prior voiced concerns regarding communicating information about splitting medications.[1,2,13]

Concerns with narrow therapeutic index drugs involved in errors have also been expressed, especially because an FDA study revealed that there is significant dose variation with tablet splitting.[16,17] With narrow therapeutic index medications, even small changes in dose and blood concentrations may lead to serious therapeutic failures or adverse drug events.[15] Accidental extra doses and overdoses increase this risk.

ISMP warns that risk can be introduced when a pharmacy fails to dispense patient-specific doses.[34] All the reported events associated with splitting medications required splitting for a patient-specific dose. Almost a fifth of the reports identified the pharmacy's dispensing of whole tablets as a contributing factor to errors. Some also reported a failure of pharmacy labels to specify that a tablet should be split. Reporters described that errors occurred despite BCMA systems in place, highlighting the fact that technology may be unreliable in catching these types of errors.[49]

A few events also indicated concerns with dispensing whole tablets or capsules with label directions to split them unevenly. Some of these included high-alert or narrow therapeutic index drugs, such as the warfarin order, which would have required the nurse to cut tablets to a 0.63-tablet dose.

Crushing Tablets and Opening Capsules

Early identification and communication of a patient's swallowing issue is important. Healthcare practitioners may not always be aware that patients are altering oral solid dosage forms. A survey by Pergolizzi at el. revealed that 80% of patients with chronic pain and dysphagia have never been asked about their ability to swallow medications and 65% did not know that altering dosage forms can result in adverse events and ineffective pain management.[50] Similarly, ISMP received a report of an 83-year old patient dying after chewing his Cardizem CD (dilTIAZem extended release) capsules.[23]

Data submitted through PA-PSRS indicates that patient-initiated dose alterations were not always readily identified. For example, healthcare practitioners did not identify patients who chewed extended-release medications. In other cases, nurses, without first consulting with prescribers or pharmacists, crushed OxyCONTIN (oxyCODONE extended release) based on the patient's report of doing so at home.

Crushing and combining medications for oral administration is another area limited by scant data and guidance. In November 2017, the Centers for Medicare and Medicaid Services (CMS) released a revised version of Appendix PP (Guidance for Surveyors for LTC [Long Term Care] Facilities) in its State Operations Manual.[9] The revision states that best practice is to crush each medication separately and administer each medication separately with food. However, the agency acknowledges that separating crushed medications may not be appropriate for all patients and facilities should implement person-centered approaches for medication administration and ensure appropriate clinicians are consulted for any concerns.[9,51]

Enteral Feeding Tube Administration

Analysts identified a gap in identifying and communicating the presence of a feeding tube among healthcare providers. For example, the oral route of administration was listed in some medication orders for patients with feeding tubes, which can increase the risk that pharmacists dispense unsuitable medications. Lack of guidance on appropriate administration of medications was also mentioned. Similarly, Li et al. found that pharmacists are concerned that they do not always have easy access to information on the actual route of administration for a specific patient and may fail to add "do not crush" directions in order to populate electronic health records and ADC screens.[20]

To address these communication gaps, Li et al. describe a process that optimizes patient safety and improves patient and drug information sharing by using an organization-wide medication review service for patients with feeding tubes.[20] A 600-bed hospital used a publicly available list of medications that should not be crushed to identify medications on the facility's formulary. They then examined their health information technology (IT) platform and ADC systems to make sure they included "do not crush" comments on applicable products. The organization also created an automatic medication substitution list. Additionally, they collaborated with the IT group to create a system that notifies the pharmacist (a generated electronic task list) about patients who have an inserted enteral tube, prompting review of medications and substitutions.[20]

Limitations

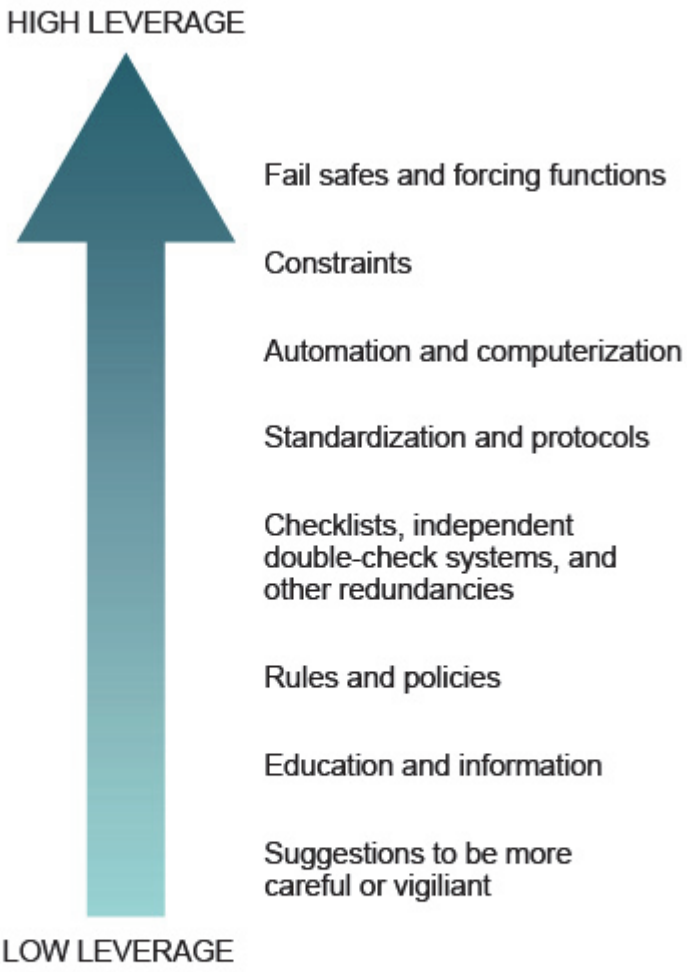
The Authority's analysis of medication errors involving oral solid dosage form alteration is impacted by limitations in the process of reporting information within facilities and through PA-PSRS. The retrieval of reports from the PA-PSRS database is limited by the process of identifying relevant reports, including the use of convenience sampling during ongoing event review.

Risk Reduction Strategies

Organizations and healthcare facilities can strive to identify system-based causes of errors involving the alteration of oral solid dosage forms, keeping in mind that these errors do not occur only during medication administration. Event descriptions support the literature findings that errors involving dosage form alteration originate in all stages of the medication use process, including prescribing and dispensing.[2,18,20] These alteration errors involve a number of key elements of medication use system, such as patient and drug information; communication; drug labeling and packaging; drug storage, stock, standardization, and distribution; environmental factors; staff competency and education; patient education; and quality processes and risk management.[34]

Several reports described implementation of lower-leverage risk reduction strategies,[34] such as double checking by the same person, concentrating on the task at hand, or educating staff. Only two reporters described higher-leverage strategies, such as building in additional redundancies with pharmacist involvement and optimizing use of technology. Educating patients and staff, including students and new employees, is a necessary component of a safety plan but relies on human vigilance to prevent errors. Layering multiple high- and low-leverage strategies is important to reduce the risk of error (Figure 6).

Figure 6. Rank Order of Error Reduction Strategies



Source: ISMP. Medication error prevention "toolbox." Medication Safety Alert! Acute Care Edition. 1999 Jun 2;4(11):1; Cohen MR, Smetzer JL, Tuohy NR, Kilo CM. High-alert medications: safeguarding against errors. Chapter 14. In: Cohen M. Medication errors. 2nd ed. Washington (DC): American Pharmacists Association; 2006.

Note: Items at the top of the list, such as forcing functions, constraints, and automation, are more powerful strategies because they focus on systems. The tools in the middle attempt to fix the system yet rely in some part on human vigilance and memory. Items at the bottom, such as education, are tools that are important but focus on individual performance and therefore are weaker and ineffective when used alone. MS1004

Manufacturers and FDA also have a role in preventing errors. Maintaining up-to-date drug information depends on both groups working together to ensure official prescribing information is updated when new information on altering the dosage form of a drug is available. Timely distribution of updated information to drug-information providers and healthcare practitioners can help them implement or adjust electronic warnings and employ other risk reduction strategies.

To prevent errors, consider the following strategies, based on events reported to the Authority, current guidelines and

literature, and observations from ISMP.

General Strategies

- Limit altering oral solid dosage forms to cases in which commercially available alternatives are unavailable, especially for high-alert and narrow therapeutic index drugs.[3-5,34]
- Do not accept blanket orders to crush or split all medications.[2]
- Remove discontinued dosage forms and strengths from patient care areas.
- Develop guidelines and implement procedures for handling crushing, splitting, and opening of formulary and nonformulary oral solid dosage forms.[2]
- Review the organization's formulary and identify medications and dosage forms that should not be altered.[1,2,20] Consider developing a substitution list for identified medications (e.g., for oral and enteral feeding administration).[20]
- Collaborate with the IT department and system vendors, as follows:
    - Identify ways of alerting practitioners during prescribing, transcribing, verifying, dispensing, and administering (e.g., clinical decision support with order entry, ADC screen, MAR) to medications that should not be altered.
    - Take into consideration the risk of "alert fatigue" when reviewing options.[2,18,20,47]
    - Develop procedures to prevent medication errors during downtimes and technological malfunctions.
- Identify hazardous medications and implement procedures for safe handling (e.g., preparing in the pharmacy under controlled conditions, handling on patient-care units using NIOSH or other resources).[7,8]
- Avoid storing hazardous medications in ADCs.[47]
- Optimize use of profiled ADCs to prevent removal of wrong dosage forms or strengths.[47,48]
- Use barcode scanning to confirm that the medication selected for distribution to the ADC and placed in the ADC matches the medication listed on ADC fill report.[47]
- Minimize distractions during order entry, medication dispensing, ADC stocking, and drug administration.[47,52]
- Increase patient monitoring when switching dosage forms.
- Provide training and periodic competency review for prescribers, pharmacists, nurses, new staff, and students regarding procedures for safe alteration of oral solid dosage forms (i.e., opening of capsules, splitting and crushing of tablets). This should include information on effective use of technology (e.g., computerized prescriber order entry [CPOE] with clinical decision support, pharmacy order entry, electronic MAR, ADC, BCMA).[2,18,20]
- Educate staff to consult pharmacy with all medication-related questions.[1-3]
- During inpatient stays, educate patients on their medication therapy, including medications that should not be altered.[2,23]
- At discharge, provide patients with written and verbal instructions for altering dosage forms and for which medications should not be altered.

  - Provide directions on how to accurately split a tablet as well as use and clean a tablet splitter.
  - Provide instructions on discontinued dosage forms and strengths for medications that may still remain at home.
  - Use the "teach back" method to ensure understanding.[2,3,18,34]

- When a new medication is added to the formulary, perform a proactive risk assessment to evaluate potential risk factors associated with altering of the dosage form and implement risk reduction strategies (e.g., availability of commonly used dosage strengths and alternatives, adding "do not crush" comment).
- Routinely review internal and external error reports related to altering oral solid dosage forms to identify error-prone conditions and implement risk reduction strategies. Ensure staff participating in medication use processes receive this information.[11]
- Ensure sufficient multidisciplinary staffing for evaluation, revision, and implementation of procedures as well as staff education.
- Incorporate prompts or questions into the medication reconciliation process to ask patients whether they split or alter any medication at home for dosing or to facilitate administration.

Splitting Tablets

- Consider analyzing prescribing trends for commonly used doses (including tablet-splitting) and stock ADC and night cabinets with commercially available options whenever possible.[47]
- For cases in which commercial strengths are unavailable, develop a standardized process for orders to provide explicit directions for tablet splitting (e.g., traZODone 50 mg, give half of a tablet [25 mg]) and ensure they appear on medication labels.[1,3,18]
- Perform a proactive risk assessment to ensure doses other than whole tablets are clearly displayed on CPOE, pharmacy, and ADC screens; printed and electronic MARs; and medication labels.
- When splitting is required and appropriate, provide patient-specific doses to patient care units by splitting tablets in the pharmacy.[1-3,34,53]
- If tablet splitting is necessary on a patient care unit, provide clear instructions on medication labels and the MAR.[1,2] Educate nurses to prepare one medication at a time.
- Optimize use of BCMA technology to provide warnings about dosing. Ensure nurses receive initial and ongoing education about the alerting mechanism, what the scanner warnings and sounds indicate, and what to do when scanners malfunction.

Crushing Tablets and Opening Capsules

- Implement a procedure that identifies patients with swallowing issues on admission and with changes in condition (e.g., changing to a soft or pureed diet).[2,23] Collaborate with the IT department and system vendors to identify ways of readily and clearly communicating this information to prescribers and pharmacists.
- Whenever possible, provide ready-to-use doses to minimize mixing, dilution, opening, and crushing medications on patient care units. Provide clear directions if preparation on patient care units is required.[2,34,53]

- Separately prepare and administer extended- and delayed-release capsules that can be opened. Educate patients not to chew contents of these dosage forms.

Enteral Feeding Tube Administration

- Implement a procedure to promptly communicate information about a patient's current or newly inserted feeding tube to better enable pharmacists to conduct a thorough review of the patient's medications, including compatibility of the medications with administration via a feeding tube.[2,20]
- Implement procedures for administering medications through enteral tubes. Include information to guide selection of appropriate dosage forms, preparations of drugs, and administration of each drug separately as recommended by the American Society for Parenteral and Enteral Nutrition (ASPEN) and CMS.[9,10]
- Provide warnings to avoid use of parenteral syringes for enteral administration.[4,5,11]
- Avoid using modified-release dosage forms when administering medications via feeding tubes.[4,5]

Conclusion

Oral solid dosage forms include narrow therapeutic index, hazardous, and high-alert medications, such as long-acting opioids. Opening capsules as well as splitting and crushing tablets that should not be altered can lead to medication errors, increasing the risk of adverse events, such as CNS and respiratory depression. These errors may disproportionately impact vulnerable patient populations with dysphagia in acute care, rehabilitation, and long-term care facilities.

Nearly 9 out of 10 (87.1%) reported events in which pills were split or crushed or capsules were opened reached patients. Of note, nearly three-quarters of reported events associated with splitting medications involved overdose and extra dose. To reduce the risk of errors, healthcare practitioners need up-to-date information on patient swallowing difficulties and the presence of feeding tubes, as well as effective strategies to prevent dangerous drug alterations, including maximizing use of commercially available dosage strengths and formulations. Organizations can implement system-based risk reduction strategies to minimize the occurrence of these medication errors.

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Patient Safety Authority

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