December 2022 ▪ Volume 21 Issue 12

ISMP
An ECRI Affiliate

Community/Ambulatory Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

Packaging changes and clinical decision support needed to help prevent mix-ups between adult and pediatric Biktarvy products

PROBLEM: ISMP has received multiple reports in which an adult patient was ordered and dispensed the pediatric strength of **BIKTARVY** (bictegravir/emtricitabine/tenofovir alafenamide) instead of the adult strength resulting in underdosing. In one case, an adult patient recently diagnosed with human immunodeficiency virus (HIV) was discharged from a hospital with a new prescription for Biktarvy 30 mg/120 mg/15 mg tablet once daily. This dose is appropriate for pediatric patients weighing 14 to less than 25 kg, not an adult. The community pharmacist did not recognize that this was an underdose and dispensed the medication to the patient. The patient's partner, who was prescribed Biktarvy from an HIV clinic, told the patient that the label on the bottle looked different, so they contacted the HIV clinic. It was then discovered that the prescriber ordered the pediatric formulation in error.

The Biktarvy 30 mg/120 mg/15 mg container label does not state that it is a pediatric formulation (or indicate the intended weight range) (**Figure 1**). It is unclear if the hospital or retail pharmacy had a dose range checking alert set up in their computer systems to confirm the correct dose. The practitioners involved in prescribing and dispensing this medication did not specialize in HIV care which could have contributed to the error.

Figure 1. The Biktarvy 30 mg/120 mg/15 mg label (left) does not indicate that this is intended for pediatric patients weighing 14 to less than 25 kg, and the Biktarvy 50 mg/200 mg/25 mg label (right) does not indicate that this is intended for adult and pediatric patients that weigh equal to or greater than 25 kg.

In a second report, a patient with HIV, who had been stable on the correct adult dose of Biktarvy, was prescribed and dispensed the pediatric dose of Biktarvy for multiple months following a hospitalization. Once the error was discovered, laboratory testing was done. The patient's viral load was detectable which was attributed to the prolonged underdosing with the pediatric strength. Additionally, it was noted that the organizations involved in the error did not specialize in HIV management.

In another report, a prescriber ordered the pediatric dose of Biktarvy for an adult patient, and the community pharmacy dispensed it to the patient for eight months before the error was discovered. The health system identifying this error completed an audit and discovered a second adult patient who was also prescribed the pediatric dose.

HIV medications are typically considered specialty medications due to their high cost, advanced patient management requirements, and critical nature of the treat-

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SAFETY briefs

Missing information on OTC liquid acetaminophen risks overdose. It has been more than 4 years since we warned in our April 2018 issue about misleading labels on acetaminophen liquid products sold in locations such as CVS, Walgreens, and Walmart. The problem was that the product labels displayed "500 mg" without a corresponding volume on the principal display panel, which confused patients when trying to determine the right amount of medication to take. It turns out this is still a problem! Two different people recently reported that CVS over-the-counter (OTC) acetaminophen liquid displays the strength as "1000 mg" without the corresponding volume (**Figure 1**). Information about the proper strength (1,000 mg per 30 mL) and dose is found by peeling back the label on the back of the container which reveals the *Drug Facts* label. Not everyone knows how to find this information or even reads the *Drug Facts* label. Without easy and accessible dosing information, a patient or even a healthcare professional may mistakenly assume the full bottle is 1,000 mg. In addition, the accompanying dosing cup only has a marking at 30 mL, which measures 1,000 mg of acetaminophen. If the patient required a different dose, such as 500 mg,

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Figure 1. CVS acetaminophen oral liquid product displays only "1000 mg" on the front label (left). To know how much liquid to measure, the patient must peel back the label on the back of the container (right) and review the *Drug Facts* label.

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ment. In most of the events submitted to ISMP in which the pediatric strength was dispensed instead of the adult dose, reporters indicated non-infectious disease providers, non-HIV specialists, and pharmacies that do not specialize in HIV were involved with the errors. An untrained and inexperienced prescriber and/or pharmacist may not be aware of the different formulations or dosing cutoffs. Thus, the potential lack of experience with this medication may have contributed to these errors.

Biktarvy was the first single-tablet, combination dosage form for HIV to be approved (October 2021) in a pediatric-specific formulation. Single-tablet antiretroviral therapy (ART) formulations have, up until the approval of the Biktarvy pediatric formulation, been associated with one established adult dose for each component, thus emphasis may not have been placed on memorizing doses in community and ambulatory settings, but instead, focused on ensuring accurate identification of the appropriate brand versus generic names. Also, single-tablet ART formulations may contribute to confusion due to the multiple agents included in a formulation and the look- and sound-alike nature of various drug components.

Safe Practice Recommendations: To prevent this type of error, educate prescribers, nurses, and pharmacy staff who may be handling HIV medications on the various dosing regimens and combination therapies. Create weight-based order sentences with dose range checking in the electronic health record (EHR) to guide prescribers to select the correct dose. Pharmacy computer systems should alert and prevent entry of the pediatric formulation for adult patients using patient information such as age and/or weight. If your organization only services adult patients, consider removing the pediatric dose from your preferred drug list. One reporter shared that in their order entry systems they added "pediatric dose" to the drug name for the Biktarvy pediatric product.

ISMP has contacted Gilead, the manufacturer, and recommended they better differentiate the adult and pediatric container labels. This includes investigating the possibility of indicating on the container label the target population for both adult and pediatric products. They will escalate this concern. ISMP has also been contacting drug information vendors to ask them to explore ways to better differentiate the products in their content, including the content embedded in EHR and pharmacy order entry systems. We have also asked them to investigate the potential to include safety messaging about this situation in their referential content.

Methotrexate taken daily after a wrong-drug error

A patient recently reported that they had been inadvertently taking methotrexate 2.5 mg, an antineoplastic and immunosuppressant agent, daily for nearly three months instead of prasugrel 10 mg, an antiplatelet agent, which had been prescribed. A community pharmacy dispensed the incorrect drug after applying the patient's prasugrel prescription label to a manufacturer bottle of methotrexate. The patient experienced worsening adverse effects from when they started taking the methotrexate, including arm and joint pain and hair loss. At the time of the report, the patient was still not feeling well. Thankfully though, it does not appear the patient experienced the serious harm (e.g., stomatitis, serious skin lesions, liver failure, renal failure, myelosuppression, gastrointestinal bleeding, life-threatening pulmonary symptoms, and death) that other patients have suffered when methotrexate has been inadvertently taken daily. Also, the patient did not experience a thrombotic cardiovascular event despite not taking the prescribed prasugrel for three months.

While we do not know the details of how the error occurred, the patient indicated that the methotrexate bottle looked like the prasugrel bottle they routinely received. For example, Mylan uses unique blue colored bottles for their medications (**Figure 1**, page 3) which

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they would not be able to measure this accurately using the cup provided.

In the *Statement of Identity and Strength - Content and Format of Labeling for Human Nonprescription Drug Products Guidance for Industry* (www.ismp.org/ext/1007), the US Food and Drug Administration (FDA) recommends that the strength of the drug product's active ingredient(s) immediately follows the statement of identity (the drug name) on the principal display panel. The lack of clear labeling of the strength (i.e., concentration) is problematic and can result in harm. We have reached out to FDA, as well as CVS, to recommend that the label on the front of the container clearly display the strength of the liquid without requiring the patient to take additional steps.

Critical Truvada stability information not in package insert. Post-exposure prophylaxis (PEP) is used to prevent human immunodeficiency virus (HIV) infection in an HIV-negative person who has had a recent high-risk exposure to HIV. PEP is classified as non-occupational (e.g., sexual contact, injection drug use) or occupational (e.g., needlestick injury). The Centers for Disease Control and Prevention (CDC) recommends a 28-day course of a 3-drug antiretroviral regimen for PEP. The preferred regimen for non-occupational PEP for most patients is **TRUVADA** (emtricitabine and tenofovir disoproxil fumarate) once daily plus, either **ISENTRESS** (raltegravir) twice daily or **TIVICAY** (dolutegravir) once daily (www.ismp.org/ext/1064). For occupational PEP, the preferred regimen for most patients is Truvada once daily and Isentress twice daily (www.ismp.org/ext/1065).

The challenge with this 28-day regimen is that Truvada is only available in bottles containing 30 tablets. Normally, this would not be a problem as the pharmacy would only dispense 28 tablets and keep the remaining tablets in its inventory. However, both the Truvada container label and the package insert (PI) state "Dispense only in original container," and neither provide any stability information about the product once the bottle is opened. So, if the pre-

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may contribute to look-alike similarities. It is also plausible that the pharmacy staff was working on prescriptions for more than one patient at a time, increasing the risk of wrong-drug and wrong-patient errors as manufacturer containers, pharmacy containers, and pharmacy labels could easily be mixed-up. Another possibility is that the methotrexate bottle was on the pharmacy counter after having been pulled in anticipation of using it for a different patient's prescription. What we do know is that despite the patient reporting this event to the pharmacy, they have only received a message stating that a district manager would be in contact.

Figure 1. The correct prasugrel label (right) was inadvertently applied to the manufacturer bottle of methotrexate (left). Medication bottles from Mylan are blue and share label design elements that could contribute to look-alike similarities.

To prevent the type of error described above, it is critical that pharmacy staff generate prescription labels for one patient at a time and then fill that patient's prescription(s) to avoid affixing the wrong label to a bottle of medication intended for another patient. Baskets or trays can be used to keep labeled containers, stock bottles, and documentation for one patient together until final verification. When affixing the pharmacy label to a manufacturer's container, avoid covering critical information, including the drug name and strength. Return unused or partially used medication bottles to the pharmacy shelves as quickly as possible to reduce the potential for wrong-drug errors during production. If you encounter look-alike containers, investigate ordering one of the containers from a different manufacturer.

If not already done, install and use barcode verification during production. Scan each package or container (e.g., bottle, carton) used to fill a prescription, including each manufacturer carton or bottle that may be dispensed to a patient. Have the computer system alert the pharmacist during product verification if barcode scanning was bypassed during production. Standardized processes should be developed to guide the pharmacist's final verification of a medication.

At the point-of-sale, have the patient review the pharmacy labels and contents of each prescription container to check that the medication is correct—even if this requires opening the bag. When a patient reports a potential or actual error, respond to the patient in a timely manner with transparency and honesty. The goal is to correct the error, minimize any harm or negative impact to the patient, and work to regain their trust in the system. To learn more about how pharmacies can plan to respond to patients who report potential or actual errors, please visit: www.ismp.org/node/23867.

Your *Reports* at *Work*

Rotarix reformulated but beware of the cap

We were pleased to see that GSK recently received approval for a ready-to-administer presentation of **ROTARIX** (rotavirus vaccine, live, oral) (**Figure 1**, page 4). The new product will be available in early 2023 (www.ismp.org/ext/1031). Rotarix is administered orally to infants to prevent gastroenteritis caused by rotavirus.

Historically, Rotarix has only been available as a two-component product. The lyophilized vaccine requires reconstitution with the liquid contained in an oral

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scriber orders a PEP regimen with a 28-day supply of Truvada, the pharmacy should open the bottle and dispense only 28 tablets. But how do they dispense these in the original container? And what do they do with the remaining two tablets? How long are the tablets stable once the manufacturer bottle is opened? Of course, if the prescriber writes for a PEP regimen containing a 30-day supply, the pharmacy would be able to dispense the entire, sealed bottle; however, the patient would be taking two extra days of medication, which are not indicated.

A specialty pharmacy recently reported this situation to ISMP. They had received a prescription for Truvada for PEP and could not locate any stability information for the drug once the manufacturer bottle was opened. So, they contacted Gilead Sciences, the drug manufacturer. Gilead informed the pharmacy that they do have additional stability information that is not included in the PI. The manufacturer provided the pharmacy with a "Truvada Storage and Stability" medical information sheet which states that Truvada is stable for a maximum of 6 weeks once the bottle opened, depending on temperature and humidity. This information is currently only available via a direct request to Gilead, so many pharmacies may not be aware of the shortened expiration date for Truvada once the bottle is opened.

We have contacted both Gilead and the US Food and Drug Administration (FDA) to encourage including updated stability and expiration data in the PI as soon as possible. Of course, this will not solve the issue of only having 30-count bottles available. FDA and manufacturers should work together, ideally prior to initial marketing approval, to ensure various packaging and package quantities are available to accommodate variations in dosing as well as support safe dispensing practices in various care settings. For example, the manufacturer, knowing that this product will be used in inpatient as well as outpatient settings, should offer unit dose packaging. This would allow for both safe use in hospitals (rather than dispensing 30-count bottles to patient care areas) and provide flexibility for various dosing regimens (e.g., PEP regimens) in outpa-

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dosing applicator, which looks like a prefilled syringe, using a supplied transfer device (**Figure 2**). However, there have been long-standing issues with practitioners inadvertently omitting reconstitution and using the liquid in the syringe by itself. Or the vaccine was mixed, transferred to a parenteral syringe, and injected. To avoid the need for dilution and to facilitate the correct route of administration, the new, fully liquid formulation is provided in an oral dosing applicator, and the tip does not allow for a needle to be attached (www.ismp.org/ext/1032).

Figure 1. The new Rotarix (GSK) prefilled oral dosing applicator and tip cap.

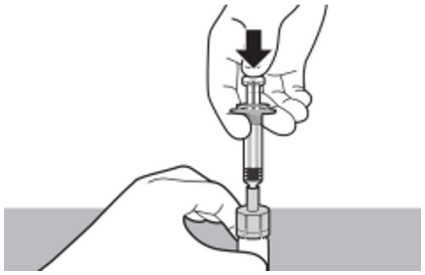

Figure 2. The older two-component Rotarix presentation requires reconstitution of the vial containing the lyophilized vaccine component with the liquid within the dosing applicator.

However, we feel compelled to alert readers that the dosing applicator tip cap could present a choking hazard if used improperly. Practitioners administer the vaccine by placing the oral dosing applicator (which still looks like a prefilled syringe) into the infant's mouth. But there is a protective cap on the tip of the applicator that practitioners must remove before administration. The GSK labeling emphasizes the need to remove the tip cap before administration (**Figure 3**). However, in rare circumstances it is possible that the person administering the vaccine may not be aware of this, which has happened when capped syringes are used for oral medications. Also, leaving the empty dosing applicator or the removed tip cap within reach (e.g., on an examination table) of a baby or child might lead to it being put in their mouth.

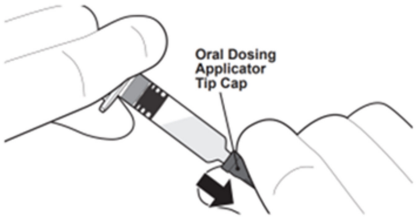

Figure 3. Remove and discard the Rotarix oral dosing applicator tip cap prior to administration.

We are not aware of any such reports with the Rotarix vaccine, but one cannot be too cautious. Years ago, there were cases of asphyxiation after practitioners provided parents with parenteral syringes, which at the time had a tip cap, to measure their child's oral liquid antibiotic dose. Not all parents realized they had to remove the syringe cap before using it. The cap was often loose enough so that the person preparing the dose could draw the oral liquid into the syringe without removing it. Then, when they placed the syringe tip into their child's mouth to administer the dose of medicine, the cap fell off into the child's mouth. As a result, BD eliminated caps from all parenteral syringes. It is interesting to note that Rotarix is available in a squeezable tube in some countries, Canada being one. The manufacturer told us the decision to use the oral applicator presentation in the United States was based on healthcare provider market research, which showed a clear preference for the oral applicator rather than a squeezable tube due to ease of delivery and controlled administration.

If your practice site plans to purchase this product when it becomes available in 2023, ensure vaccinators are aware of this potential choking hazard.

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tient settings. For now, pharmacies should devise a plan for how to handle any extra tablets.

HIGH-ALERT

PDMPs can identify duplicate opioid therapy. An elderly patient in the emergency department (ED) was unable to provide an accurate medication history due to an altered mental status. A pharmacist checked the state's prescription drug monitoring program (PDMP) and found that the patient had been taking multiple opioid medications prescribed by the same pain management provider. The patient had initially been started on **HYDRO**morphone extended release (ER) 16 mg once daily for chronic back pain and hip arthritis, along with **HYDRO**codone 10 mg and acetaminophen 325 mg, one tablet every 8 hours as needed for breakthrough pain. Due to insurance coverage issues, the prescriber intended for the patient to taper off the **HYDRO**morphone ER and transition to morphine ER 60 mg twice daily as this was covered by the patient's insurance. The patient was advised to start with morphine ER 60 mg daily, and then to increase to twice daily if needed, but it is not clear if the patient immediately started with the twice-daily dose. One day prior to the ED visit, the patient had started the newly prescribed morphine ER tablets, and he also picked up a supply of **HYDRO**morphone ER 16 mg tablets.

Prior to prescribing and dispensing an opioid, physicians and pharmacists should confirm whether the patient is opioid-naïve or opioid-tolerant, complete a thorough review of the patient's medication history, and access the state's PDMP to have a full understanding of the controlled substance medications and dosages a patient is taking. Patients should be provided with written instructions and must be counseled when to start and stop opioids, including schedules for tapered doses, and what to do if they experience side effects related to opioid toxicity. Patients who take high doses of opioids should be provided with naloxone, and both the patient and their caregivers/family members should be educated about when and how to use it. Also provide patients with resources about safe drug storage and disposal, including drug take back locations (www.ismp.org/ext/800).

ISMP 25th Annual Cheers Awards

Walking the Red Carpet with Safety Stars

This month, ISMP celebrated the 25th anniversary of its Cheers Awards, which recognize individuals, organizations, and groups that have demonstrated an extraordinary commitment to advancing the science and study of patient safety. This year's winners were honored at an awards ceremony held on December 6, 2022, in Las Vegas, NV. Please join us in congratulating this impressive group of leaders, who have been true stars and developed innovative best practices and programs to advance patient safety.

Cheers Awards winners

- **Sharp HealthCare**, based in San Diego, CA, was recognized for developing innovative solutions to reduce the risk of patient harm when infusing non-cytotoxic vesicant/irritant medications via peripheral intravenous (IV) lines.
- **Shifa International Hospital**, in Islamabad, Pakistan, was honored for implementing camera-assisted verification for chemotherapy admixture services with limited resources.

George DiDomizio Award winner

The **George DiDomizio Award** was established in 2012 in memory of a late ISMP Board member who advocated for greater cooperation between the medical industry and the broader healthcare community to promote safer drug products.

- **Vitalis**, a pharmaceutical company based in Colombia, was recognized for its dedication to designing safer labels and packages for their medications despite the fact that it is not mandatory at the regulatory level in Latin America. These changes were incorporated into labeling on the medication packaging, ampules, and vials, and today these products are being distributed in several countries, including Colombia, Ecuador, Peru, Chile, Panama, and Costa Rica.

Lifetime Achievement Award winner

The **Lifetime Achievement Award**, which is given in memory of ISMP's late Trustee David Vogel, PharmD, honors individuals who have made ongoing contributions to patient safety throughout their career.

- **Michael R. Cohen, RPh, MS, ScD (hon), DPS (hon), FASHP**, President Emeritus and co-founder of ISMP, was recognized for providing invaluable leadership and service as an unparalleled source of inspiration for so many healthcare practitioners. He has dedicated his career to advocating for medication error prevention.

To read more about the winners and Michael Cohen's keynote address, please visit: www.ismp.org/node/53205.

Thank you

We would like to express our gratitude to all the organizations and individuals who attended and/or supported this year's Cheers Awards. For a list of contributors and winners, please visit: www.ismp.org/node/34185, and for ways you can join us in creating a brighter future for medication safety, please visit: www.ismp.org/support.

ISMP wishes you a happy, safe, and peaceful holiday season, and we look forward to continuing to work together on preventing errors and keeping patients safe in 2023.

Special Announcements

New Targeted Medication Safety Best Practices for Community Pharmacy

Join ISMP on **January 31, 2023**, for a **FREE** webinar to learn about ISMP's soon to be released ***Targeted Medication Safety Best Practices for Community Pharmacy***. This activity is supported by Novartis, Name Creation & Regulatory Strategy, and continuing education (CE) credit is being offered for pharmacists and pharmacy technicians. To register, please visit: www.ismp.org/node/53660.

Become an ISMP Fellow

ISMP will soon be accepting applications for our **Fellowship** programs that will begin in the summer of 2023. For brief descriptions of the Fellowships, candidate qualifications, brochures, and program outlines, visit: www.ismp.org/node/871. More information will be provided early in 2023!

Employment opportunity

ISMP is seeking a full-time pharmacist with at least 5 years of experience in the community and specialty pharmacy practice settings. In addition, 3 years of experience managing performance improvement projects and writing articles and proposals are required. This ***Medication Safety Specialist*** position will support our membership services initiative. For more information and to apply for the position, please visit: www.ismp.org/node/20395.

To subscribe: www.ismp.org/node/126

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ISMP Medication *Safety Alert!* Community/Ambulatory Care (ISSN 1550-6290)

Report medication and vaccine errors to ISMP: Call 1-800-FAIL-SAF(E), or visit www.ismp.org/report-medication-error. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

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Happy Holidays...from the staff, Board of Directors, and Advisory Board at the Institute for Safe Medication Practices (ISMP). We wish you joy, health, and happiness this holiday season!

Special Recognition...

2022 ISMP Medication Safety Alert!® Community/Ambulatory Care Clinical Advisory Board

Production of this peer-reviewed newsletter would not be possible without the assistance of a reliable and talented Clinical Advisory Board. As 2022 nears an end, we want to thank each of the following members of the Clinical Advisory Board for their dedication to making this newsletter a valuable medication safety resource for clinicians.

- **Bryan R. Bailey,** PharmD, MHA, BCPS, FISMP; Landstuhl Regional Medical Center, Germany
- **Brian Barndt,** PharmD; Sam's Club Pharmacy, Temple, PA
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