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ISMP An ECRI Affiliate

Community/Ambulatory Care

ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Quadruple the number of prescribed Stivarga bottles dispensed to a patient

PROBLEM: A patient was prescribed a reduced dose of the antineoplastic agent **STIVARGA** (regorafenib) 40 mg tablets with directions to "Take 3 tablets (120 mg) by mouth daily for 21 days on followed by 7 days off." The prescriber wrote for a quantity of 63 tablets (or 3 bottles of 21 tablets each). The manufacturer, Bayer HealthCare Pharmaceuticals, packages the 21-count bottles in cartons containing 4 bottles. The specialty pharmacy accidentally dispensed 3 cartons (or 12 bottles) of Stivarga 40 mg, enough medication to cover 4 months of treatment. The error was identified the following day when a pharmacy technician was unable to locate sufficient inventory to fill another patient's prescription despite the electronic inventory system indicating the medication was in stock. The patient's caregiver was contacted and counseled on proper dosing.

Contributing Factors

Analysis of this and previously reported events identified several factors that may contribute to these types of errors:

- Originally, Stivarga was only supplied in cartons containing 3 bottles (28 tablets per bottle). Following reports (www.ismp.org/node/18122) of dosing errors in patients who required reduced daily dosing (e.g., 120 mg [3 tablets] instead of the usual dose of 160 mg [4 tablets]), Bayer began supplying the medication in 21-count bottles, with 4 bottles per carton (**Figure 1**). While a 21-count bottle provides a week of the 120 mg daily dosing, the carton of 4 bottles supplies more medication than is needed for a month of therapy. Therefore, pharmacies must open the cartons to dispense only 3 bottles for a month's supply. Bottles are not available for individual purchase.

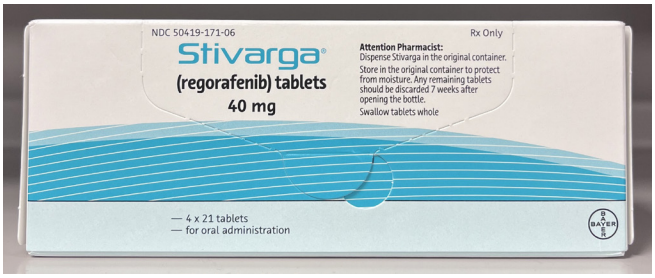

Figure 1. This Stivarga carton supplies 4 bottles, each containing 21 tablets, to accommodate the reduced dosing regimen of 120 mg or 3 tablets daily.

- Stivarga 40 mg tablets are required to be kept in the manufacturer's original bottle during both storage and administration. This means that pharmacies cannot open bottles and count the exact number of tablets to accommodate the prescribed dosing each month regardless of the bottle sizes they have in stock.

- Unique "outer" national drug codes (NDCs) have been assigned to the cartons that are different from the NDCs (i.e., "inner" NDC) assigned to the individual bottles. As the manufacturer's sellable units of the medication are the carton presentations, pharmacies' electronic inventory systems may be configured to only recognize the carton NDC to order the medication from wholesalers, and to maintain and reconcile electronic inventory counts, as was the case in the error described earlier.

- As full implementation and enforcement (later in 2024) of the Drug Supply Chain Security Act (DSCSA) approaches, more manufacturers are printing two-dimensional (2D) barcodes on containers, and more pharmacies are relying on 2D barcodes during dispensing to verify the correct medication has been selected and to record the product's lot number and expiration date.

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Desiccant capsule mistaken for tablet. An elderly patient with poor eyesight had decreased feeling in one of their hands after having a stroke. He was recently diagnosed with an infection and given a prescription for the antibiotic amoxicillin and clavulanate potassium, which was dispensed in the original manufacturer bottle. When it was time to take a dose of the medication, the patient accidentally picked up and swallowed the desiccant capsule that was included in the manufacturer's bottle and choked.

The amoxicillin and clavulanate potassium was a white oval tablet. The desiccant was similar in size and the same color (white) as the medication tablets (**Figure 1**). Since the patient was not able to clearly see or feel the difference between the tablet and the desiccant, it is easy to see how the error happened. Although drug manufacturers state that the desiccants they use are not harmful, patients may choke on them. Also, ingesting the desiccant rather than the medication may result in omitted doses of medication and suboptimal treatment.

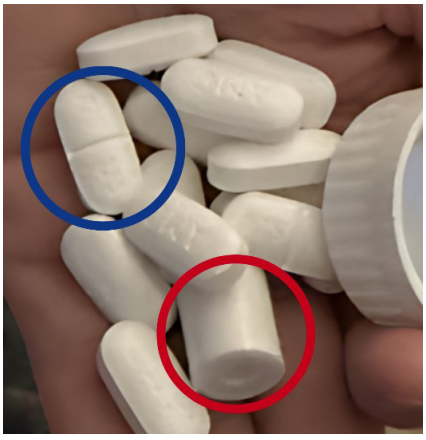

Figure 1. Desiccant (circled in red) is similar in size and color to amoxicillin and clavulanate potassium tablets (circled in blue).

We have previously reported about patients who accidentally ingested desiccant capsules from medication bottles and blister cards. For example, an elderly patient with poor eyesight nearly asphyxiated

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However, as part of the DSCSA, the 2D barcode is only required on the manufacturer's sellable units, which in the case of Stivarga, are the multi-bottle cartons. Only a linear barcode with the inner NDC is printed on the container label on the individual Stivarga bottles (**Figure 2**).

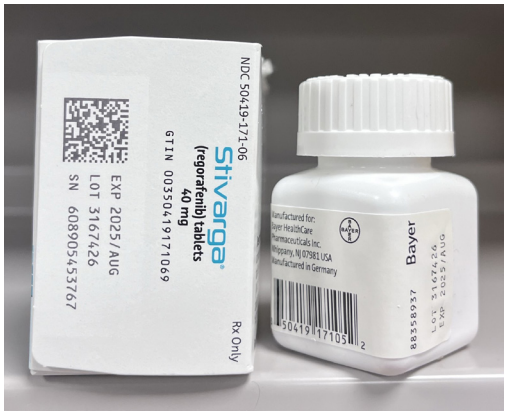

Figure 2. The Stivarga carton (left) contains the carton "outer" NDC and a 2D barcode, which the pharmacy uses during dispensing, while the bottle container label (right) only contains a linear barcode for the "inner" NDC.

- Restricting the pharmacy system to only recognize the carton ("outer") NDC for inventory purposes may have implications on the system's ability to recognize individual bottle ("inner") NDCs during dispensing. For example, the pharmacy, in this case, shared that when the linear barcode on an individual bottle is scanned in their pharmacy dispensing system, an alert fires stating that the wrong NDC has been chosen. To work around this, the pharmacy saves the carton so they can scan the carton's 2D barcode during fulfillment. ISMP is aware of multiple errors that have occurred when pharmacies have scanned barcodes not printed on the immediate medication container (i.e., "proxy" scans). Successful scanning of the carton barcode may also give staff a false sense of security that the correct product/presentation is being dispensed.

- Appropriately, the pharmacy dispensing system printed three pharmacy labels, one for each bottle that should have been dispensed, and required three scans of a manufacturer barcode. However, since the carton's 2D barcode is used during scanning, it is easy for staff to become confused and scan three cartons and apply a pharmacy label to each carton instead of the individual bottles.

- The pharmacy technician who filled the medication order was in training, and the pharmacist was recently hired; neither teammate was familiar with the medication.

Safe Practice Recommendations: Given the current packaging configuration, pharmacies are finding it difficult to identify and implement high-leverage strategies to prevent this type of error without causing significant downstream effects on inventory control and ordering. The pharmacy that shared this recent event has adopted a workflow process in which staff are directed to remove the perforated carton flap upon receipt of the medication before placing it into storage in the specialty pharmacy (**Figure 3**). This process is used to provide a visual reminder that the entire carton should not be dispensed. To reinforce this practice, the pharmacy has adhered large neon-colored stickers to the bin holding Stivarga, reminding staff to open the box upon receipt of the order.

Figure 3. Stivarga cartons (left) containing 4 bottles of 21 tablets each are opened before being placed into storage to help prevent inadvertently dispensing the entire carton. This helps ensure only the appropriate number of individual bottles (right) are dispensed to fill a prescription.

Ideally, the manufacturer should sell Stivarga in individual bottles that include 2D barcodes. By

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when he choked on a desiccant capsule left in his medication bottle. Also, several patients, including two children, ingested the desiccant included in the everolimus blister cards.

We have contacted the US Food and Drug Administration (FDA) and the manufacturer to ask them to explore ways to make desiccants more visually distinct from medication dosage forms. Alert staff about this potential error. When counseling patients, it is critical to let them know that manufacturer bottles may contain desiccants that might look similar to capsules or tablets. Advise patients or caretakers to make sure there is adequate lighting to allow them to read the prescription label and instructions, and to look closely at the medicine before they take it. Using a magnifying glass may also help them read the instructions and inspect their medication.

Only Priorix diluent administered. **PRIORIX** is a measles, mumps, and rubella vaccine manufactured by GSK. It is available in cartons containing 10 single-dose vials of lyophilized antigen component and 10 single-dose prefilled syringes of sterile water diluent. The prefilled diluent syringes have luer tips to accommodate th attachment of needles to reconstitute the vials of lyophilized antigen and to administer the vaccine. Recently, a patient arrived at a clinic for the measles, mumps, and rubella virus vaccine. It was a busy day in the clinic, and when the nurse went to retrieve and prepare the Priorix vaccine, they only removed a syringe of sterile water from the carton, leaving the vial of lyophilized antigen in the carton. They reported they did not see the vial containing the lyophilized antigen as it was "hidden" by the inside flap of the carton. The nurse administered the diluent alone and did not uncover the error until finding an extra vial of lyophilized antigen in the carton a couple of hours later. The patient was contacted and plans to return at a later date to receive the vaccine dose.

We warned practitioners in an October 2023 article, *New error-prone situations after vaccines approved with prefilled*

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doing so, it would support safe pharmacy workflow enabling the practitioner to scan and label each immediate container that is dispensed. For example, individual bottles containing 28 tablets, 21 tablets, or 14 tablets could be marketed to accommodate the 3 indicated weekly dosing regimens, 160 mg daily, 120 mg daily, or 80 mg daily, respectively. If the manufacturer continues to package Stivarga in cartons, they should produce carton and bottle sizes that accommodate the 3 indicated dosing regimens: a carton containing three 28-tablet bottles for 160 mg daily dosing; a carton containing three 21-tablet bottles for 120 mg daily dosing; and a carton containing three 14-tablet bottles for 80 mg daily dosing. ISMP contacted both the US Food and Drug Administration (FDA) and the manufacturer and asked for packaging changes to support safe pharmacy workflow.

LamoTRIgine dispensed with labetalol label

Problem: A patient's daughter recently reported that her parent had been prescribed the beta-blocker labetalol. The prescriber had ordered labetalol 200 mg with instructions to take one tablet by mouth 2 times a day. After taking medication from a bottle recently dispensed by the pharmacy, the patient fell 4 times within a 48-hour period and required a 2-week admission to the hospital. The patient was then transferred to a rehabilitation facility. After 2 weeks at the rehabilitation facility, the patient was discharged home, feeling well and able to engage in some of their normal activities, including shopping and assisting with yard work. However, after two days at home and resuming their home medication regimen, the patient began to exhibit an array of symptoms, including stomach pain, blurred vision, nausea, neck pain, weakness, mood swings, and confusion. The patient was transported to the emergency department (ED) for evaluation. Testing conducted in the ED did not identify any obvious causes of the patient's symptoms. The patient was discharged back home and advised to drink fluids, rest, and follow-up with their primary care provider. However, once the patient was home, the same symptoms continued.

It was at this point that the patient asked their daughter to check the medication received from the pharmacy. The daughter identified that the antiseizure agent lamo**TRI**gine 200 mg tablets had been dispensed, not the prescribed labetalol. The pharmacy had applied the pharmacy label for labetalol to a manufacturer's bottle of lamo**TRI**gine (**Figure 1**). As a result, the patient had been taking 200 mg of lamo**TRI**gine twice a day, a dose used for patients with epilepsy but which requires titration in order to reduce the risk of severe or potentially fatal cutaneous and other hypersensitivity reactions.

Figure 1. The correct labetalol label was inadvertently applied to the manufacturer bottle of lamo**TRI**gine. The patient took the incorrect medication and suffered repeated adverse events.

Safe Practice Recommendations: While we do not know the details of how this error occurred, there are several strategies that should be implemented to prevent these types of wrong-drug errors. If not already done, install and use barcode verification during dispensing. Scan each package or container used to fill a prescription. If multiple bottles or cartons are required to fill a prescription, work with the pharmacy software vendor to enable scanning of each bottle or carton to ensure all bottles and cartons are the correct medications. Implement a standard workflow process to ensure pharmacy staff generate the prescription label(s) for one patient at a time and then fill that patient's prescription(s) before printing labels for or working on another patient's prescription(s). When affixing the pharmacy label to a manufacturer's container, avoid covering critical information (e.g., the drug name and strength). Have the computer system alert the pharmacist during product verification if barcode scanning was bypassed during filling. 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 and drug container.

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diluent syringes, that diluent syringes meant to reconstitute vaccines such as Priorix could be administered in error. To prevent preparation and administration errors with vaccines that come with prefilled diluent syringes, establish a process to keep vaccines and their corresponding diluents together if storage requirements do not differ. Implement barcode scanning prior to preparing and administering vaccines. Configure the system to require scanning of both the vaccine and corresponding diluent barcodes. Provide vaccine-specific auxiliary labels to facilitate relabeling of the diluent syringe after the vaccine is reconstituted and withdrawn from the vial. Store the labels with the specific vaccine products. Document the national drug code (NDC) number, lot number, and expiration date of each container in the vaccination record or log before administration to confirm appropriate selection or preparation of both components. Documenting the actual administration of the vaccine should always occur after the vaccine is administered.

Ensure correct inhalation product is selected. A pharmacist reported that a medication was entered incorrectly into the pharmacy dispensing system from an electronic prescription. The prescriber had ordered "mometasone 100 mcg-formoterol 5 mcg inhalation"; however, the pharmacy technician entered "mometasone 100 mcg inhalation." Thankfully, a pharmacist intercepted the error while verifying the prescription and corrected the mistake. The correct medication was dispensed to the patient. The pharmacy found that distractions likely contributed to the error. The technician who entered the prescription was completing multiple tasks at one time. This included answering phone calls, assisting patients at the pharmacy counter, and helping to onboard new employees.

To help prevent these types of data entry errors, prescribers should ensure their electronic prescriptions adhere to National Council for Prescription Drug Programs (NCPDP) standards and Surescripts guidelines to best enable pharmacy computer systems to match the prescribed medication to drugs in the pharmacy computer system.

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Worth repeating...

Look-alike Toujeo cartons and pens

A patient was prescribed **TOUJEO MAX SOLOSTAR** (insulin glargine 300 units/mL) prefilled pen to help improve their glycemic control. Toujeo Max SoloStar is available in cartons containing two pen devices, and the patient was supposed to receive three cartons. While the prescription was entered correctly into the pharmacy dispensing system, during fulfillment only two cartons of Toujeo Max SoloStar were retrieved from the refrigerator along with one carton of **TOUJEO SOLOSTAR**. The error was not caught during product verification and both Toujeo Max SoloStar and Toujeo SoloStar pens were dispensed to the patient. The pharmacy discovered the error after finding a discrepancy in the number of Toujeo pen cartons in stock during inventory counts. The pharmacy mentioned that the error was not caught, in part, because the pharmacy dispensing system does not require scanning of each manufacturer container when multiple containers are used to fill a prescription.

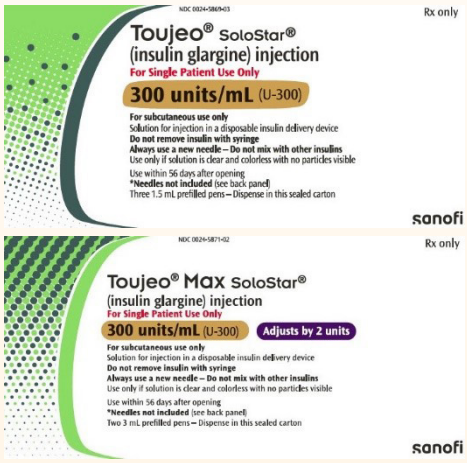

Figure 1. Toujeo SoloStar (top) and Toujeo Max SoloStar (bottom) cartons look similar.

In the March 2019 issue of this newsletter, we alerted readers to the potential for mix-ups between these products due to the look-alike nature of the cartons (**Figure 1**). The overall design of both carton labels overshadows the differentiating characteristics on the Toujeo Max SoloStar packaging (e.g., the word "Max," the phrase "Adjusts by 2 units"). The individual pens also look similar. Toujeo Max SoloStar contains 900 units (3 mL) and measures doses in 2 unit increments up to 160 units per injection while the original pen, Toujeo SoloStar, contains 450 units (1.5 mL) and measures doses in 1 unit increments up to 80 units per injection. If a dispensing error occurs, a patient, especially a visually impaired patient or one who relies on counting dosing dial "clicks" to select the correct dose, may not realize the difference in the dosing increments and inadvertently administer twice as much insulin as intended.

Because of this recent report, we think reviewing strategies that can help prevent these errors is ***Worth* repeating**. Install and use barcode verification during fulfillment. Work with your pharmacy software vendor to enable scanning of each package or container used to fill a prescription. Have the computer system alert the pharmacist during product verification if barcode scanning was bypassed during filling. Develop standardized processes to guide the pharmacist's final verification, including confirmation of the correct medication, using product images within the pharmacy dispensing system when available, and verifying the number of packages being dispensed. Differentiate the product packaging (e.g., highlighting important information on labels). Store these products apart from one another in separate, clearly labeled bins. Provide patient counseling and include a review of the product—especially how to dial the correct dose.

Report medication and vaccine errors to ISMP: Please 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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The pharmacy should also investigate why the pharmacy dispensing system may not automatically match the correct drug and strength (or other information on the prescription) and communicate issues related to the electronic prescription with prescribers and to their pharmacy computer system vendor and/or internal information technology staff. Design pharmacy space and workflow to minimize distractions, especially during data entry, filling, and pharmacist verification. Borrow a concept from the airline industry and create a "sterile cockpit" at each workstation to minimize unnecessary distractions and interruptions. Designate an orientation/staff development leader and safety coaches and provide protected time for onboarding to make sure new hires are competent in the areas and systems in which they are assigned to work. Ideally, those who train new staff should have a reduced workload to accomplish the goals of orientation safely and thoroughly.

Special Announcements

Nominations open for CHEERS AWARDS

Each year, ISMP honors various healthcare disciplines that have demonstrated an exemplary commitment to medication safety through innovative projects with an ISMP **CHEERS AWARD**. Nominations for this year's **CHEERS AWARDS** are now open and will be accepted through **August 2, 2024**. Please refer to the information provided on our website when submitting a nomination. For details, visit: www.ismp.org/node/123.

MSI Workshop for Community, Mail Order, and Specialty Pharmacy

Join us for our ***ISMP Medication Safety Intensive (MSI)*** workshop designed for those working in community, mail order, and specialty pharmacies. Learn how to identify risks before they cause harm and how to use data for continuous improvement. This program will take place on **Friday, September 20** and **Friday, September 27, 2024**, from **7:30 am - 4:30 pm ET**. For more information and to register, please visit: www.ismp.org/node/127.