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News

Alabama State Board of Pharmacy

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Partial Filling of Schedule II Prescriptions

The Alabama State Board of Pharmacy has written about Schedule II partial fills within the past year, but continues to receive questions about this topic. There is also discussion in a number of areas about limiting the number of days of medication that can be dispensed. The Board has no plans to limit the amount of opioids that can be dispensed, but other regulators and payors are looking into the effectiveness of the policy. The Board's concern is about the pharmacist being put into a role of policing prescribers, plus managing the conversations with patients, caregivers, and prescribers.

The old policy about partial fills for Schedule II prescriptions may be found in Drug Enforcement Administration regulations, **§1306.13 Partial filling of prescriptions.**

> The partial filling of a prescription for a controlled substance listed in Schedule II is permissible if the pharmacist is unable to supply the full quantity called for in a written or emergency oral prescription and he makes a notation of the quantity supplied on the face of the written prescription, written record of the emergency oral prescription, or in the electronic prescription record. The remaining portion of the prescription may be filled within 72 hours of the first partial filling; however, if the remaining portion is not or cannot be filled within the 72-hour period, the pharmacist shall notify the prescribing individual practitioner. No further quantity may be supplied beyond 72 hours without a new prescription.

The most recent regulation concerning partial fills is found in federal regulations under the **Comprehensive Addiction and Rehabilitation Act, Section 702.**

> (Sec. 702) This bill amends the Controlled Substances Act to allow a pharmacist to partially fill a prescription for a schedule II controlled substance (such as an opioid) if: (1) such partial fills are not prohibited by state law, (2) a partial fill is requested by the patient or prescribing practitioner, and (3) the total quantity dispensed in partial fillings does not exceed the quantity prescribed.

Please note that partial fills for phoned-in emergency prescriptions must be filled within 72 hours.

The Board will support pharmacies in the use of this law. There must be methods in place to ensure there are not increased opportunities for diversion. Payors will develop methods to reimburse for partial fillings.

Protecting Patients in Pain – The Morphine Milligram Equivalent

By Aaron Beckner, 2018 PharmD Candidate, Samford University McWhorter School of Pharmacy

The persisting opioid crisis in the United States has led to an enhanced focus by the health care community on the guideline-appropriate management of prescription opiates. One specific part of the Centers for Disease Control and Prevention (CDC) guideline recommendations concerning the prescribing and management of opiates that many health care professionals can personally utilize involves the evaluation of a patient's total daily dosage of opioids in relation to the recommended limits on morphine milligram equivalents (MMEs). MME per day is defined by CDC as "the amount of morphine an opioid dose is equal to when prescribed, often used as a gauge of the abuse and overdose potential of the amount of opioid that is being given at a particular time."

CDC recommends that clinicians initiate opioids at the lowest effective dosage. It is also recommended to use caution when prescribing at any dosage, to carefully reassess evidence of risks versus benefits for each individual patient when considering increasing the dose to greater than or equal to 50 MMEs per day, and to either avoid or carefully justify increasing a dosage to greater than or equal to 90 MMEs per day. As a patient's opioid dosage increases, so does his or her risk for overdose and death, as well as the factor by which it increases. According to CDC, dosages between 50 and 100 MMEs per day increase the risk for opioid overdose by factors of 1.9 to 4.6 when compared with dosages from one to 20 MMEs per day, while dosages more than 100 MMEs per day are associated with increased risks of overdose by factors of two to 8.9 times the risk at one to 20 MMEs per day.

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FDA Draft Guidance Addresses Delayed Enforcement of DSCSA Requirements for Product Identifiers

Food and Drug Administration (FDA) issued a draft guidance for industry that informs manufacturers and other supply chain stakeholders that although manufacturers are to begin including a product identifier on prescription drug packages and cases on November 27, 2017, FDA is delaying enforcement of those requirements until November 2018 to provide manufacturers additional time and avoid supply disruptions. The compliance policy outlined in the June 2017 draft guidance, *Product Identifier Requirements Under the Drug Supply Chain Security Act – Compliance Policy,* applies solely to products without a product identifier that are introduced into commerce by a manufacturer between November 27, 2017, and November 26, 2018. While manufacturers work to meet product identifier requirements, they must comply with other Drug Supply Chain Security Act (DSCSA) requirements. The draft guidance can be accessed from FDA's website at *www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/ucm565358.htm.*

Amount of Prescribed Opioids Remains High, Reports CDC

The amount of opioids prescribed remains approximately three times as high as in 1999, despite reductions in each year after 2010 through 2015. Centers for Disease Control and Prevention (CDC) researchers analyzed retail prescription data to assess opioid prescribing in the United States from 2006 to 2015 and county-level prescribing patterns in 2010 and 2015. According to a CDC report, results of the study showed higher amounts of opioids were prescribed in counties that had a greater percentage of non-Hispanic white residents, a higher prevalence of diabetes and arthritis, micropolitan status (ie, town/city; nonmetro), and higher unemployment and Medicaid enrollment rates. The researchers conclude that health care providers should carefully weigh the benefits and risks when prescribing opioids outside of end-of-life care, follow evidence-based guidelines (eg, CDC's *Guideline for Prescribing Opioids for Chronic Pain*), and consider non-opioid therapy for chronic pain treatment.

Additionally, the researchers conclude that state and local jurisdictions can use these findings along with prescription drug monitoring program (PDMP) data to identify prescribing patterns that place patients at risk for opioid use disorder and overdose and to target interventions with prescribers based on opioid prescribing guidelines. The July 7, 2017 *Morbidity and Mortality Weekly Report,* "Vital Signs: Changes in Opioid Prescribing in the United States, 2006–2015," can be accessed on the CDC website at *www.cdc.gov/mmwr/index.html* in the Weekly Report section.

AMA Opioid Task Force Encourages Co-Prescribing Naloxone to At-Risk Patients

The American Medical Association (AMA) Opioid Task Force encourages physicians to consider co-prescribing naloxone when it is clinically appropriate to do so. The AMA Opioid Task Force offers several questions for determining whether to co-prescribe naloxone to a patient or a patient's family member or close friend, which may be found in the August 2017 document, "AMA Opioid Task Force naloxone recommendations," available on the AMA opioid microsite at *https://www.end-opioid-epidemic.org.*

The Naloxone section of the AMA opioid microsite also offers physicians multiple resources on co-prescribing naloxone in their practice and community. To help end the opioid epidemic, the AMA Opioid Task Force made several recommendations for physicians, including registering and using state PDMPs, training and education on evidence-based treatment, and promoting safe storage and disposal of opioids and medications.

Opioid Addiction Medications Should Not Be Withheld From Patients Taking Benzodiazepines or CNS Depressants

Opioid addiction medications – buprenorphine and methadone – should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system (CNS), advises FDA. The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction usually outweighs these risks. Careful medication management by health care providers can reduce these risks, notes a safety alert. FDA is requiring this information to be added to the buprenorphine and methadone drug labels along with detailed recommendations for

minimizing the use of medication-assisted treatment drugs and benzodiazepines together.

Health care providers should take several actions and precautions and should develop a treatment plan when buprenorphine or methadone is used in combination with benzodiazepines or other CNS depressants. Additional information may be found in an FDA Drug Safety Communication announcement at *www.fda.gov/Drugs/DrugSafety/ucm575307.htm.*

New Study Shows Substantial Variation in the Availability of Pharmacies Across the Country

Despite the rising number of US pharmacies from 2007 to 2015, the availability of pharmacies varied significantly across local areas, indicates a new study. The study, *The availability of pharmacies in the United States: 2007–2015,* found that the number of community pharmacies increased 6.3% from 63,752 to 67,753 between 2007 and 2015. Although the number of pharmacies per capita remained at 2.11 per 10,000 individuals between 2007 and 2015, the researchers found substantial variation across counties. "Some counties have 13 pharmacies per capita, while others have none," said Dima Qato, lead study author and assistant professor of pharmacy systems, outcomes and policy, in a University of Illinois at Chicago (UIC) news release.

In 2015, counties in the highest quintile had nearly three-fold more pharmacies than those in the lowest quintile. Counties in the lowest quintile are located in the Pacific West, Southwest, and Great Lakes regions, while counties with the highest tend to be located in the Northeast, Southeast, Northern Appalachia, and Plains states. The researchers conclude that future programs and policies should address the availability of pharmacies and ensure that pharmacy characteristics, including accommodations such as multilingual staffing and home delivery, align with local population needs.

To view the study, visit *https://doi.org/10.1371/journal.pone.0183172.* The UIC news release is available at *https://today.uic.edu/access-to-pharmacies-limited-to-some-patients.*

Consent Decree Entered Against Outsourcing Facility Isomeric Pharmacy Solutions

Under a consent decree of permanent injunction entered in August 2017, Isomeric Pharmacy Solutions of Salt Lake City, UT, its owners, and chief operating officer are prohibited from manufacturing, processing, packing, holding, or distributing drugs until they comply with the Federal Food, Drug, and Cosmetic Act (FD&C Act) and its regulations, in addition to other requirements. Isomeric manufactured and distributed purportedly sterile drug products, including injectable and ophthalmic drugs, that were adulterated because the drugs were made under insanitary conditions and in violation of current good manufacturing practice requirements under the FD&C Act, according to the complaint for permanent injunction. The complaint also alleges that Isomeric manufactured and distributed unapproved drugs and drugs that were misbranded because their labeling did not bear adequate directions for use. Isomeric initially registered as an outsourcing facility in July 2015 and reregistered in December 2015 and January 2017. Additional information is available in an FDA news release at *www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm570130.htm.*

FDA Issues Warning on Alcohol Pads or Benzalkonium Chloride Antiseptic Towelettes Made by Foshan

In September 2017, FDA alerted health care providers and patients to not use alcohol pads or benzalkonium chloride antiseptic towelettes made by Foshan Flying Medical Products Co, Ltd, located in China, due to lack of sterility assurance and other quality issues. These products are distributed by Total Resources International, of Walnut, CA, and Simple Diagnostics, Inc, of Williston Park, NY. The use of these alcohol pads and antiseptic towelettes could cause infections.

FDA placed all drug products made by Foshan on import alert on May 23, 2017, to stop these products from entering the US. However, FDA is concerned these products might still be in distribution in the US. FDA also sent Foshan a warning letter on August 1, 2017, for violations of current good manufacturing practice regulations. FDA initially contacted Foshan regarding a recall on May 25, 2017, and had several follow-up meetings with the company. Foshan has not taken action to remove its alcohol pads or antiseptic towelettes from the market. The safety alert posted to FDA's website may be found at *www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm574576.htm.*

Pharmacies and health care facilities that have alcohol pads and antiseptic towelettes labeled by Total Resources or Simple Diagnostics should immediately stop using them and discard the products. Adverse events or side effects related to the use of these products may be reported to FDA's MedWatch Safety Information and Adverse Event Reporting Program at *www.fda.gov/MedWatch/report.*

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Checking a patient's MME per day is very simple and can be enlightening and beneficial to the patient's course of care. This can be accomplished using the following three-step process:

1. Determine the total daily amount of each opioid the patient takes per day (including *pro re nata* (ie, as needed) doses).
2. Convert each opiate dose to MMEs. Using an appropriate conversion chart like the one shown below, multiply each total dose by the conversion factor for the patient's opiate(s).
3. Add the MMEs for the patient's opiate(s) together.

Calculating morphine milligram equivalents (MME)

OPIOID (doses in mg/day except where noted)	CONVERSION FACTOR
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.

Example: If a patient is taking 10 mg of oxycodone every six hours as needed for pain, the steps to finding the MMEs per day would be:

1. 10 mg x 4 doses per day = 40 mg (total daily amount)
2. 40 mg (total daily dose) x 1.5 (conversion factor) = 60 MMEs
3. Total MMEs per day for this patient would be 60 MMEs if this is the only opiate the patient is taking. Otherwise, you would add the total MMEs for other opiates together at this step for total MMEs per day.

CDC offers a mobile app titled "CDC Opioid Guideline" that contains useful information concerning the prescribing of opiates, as well as an MME calculator.

Caution is advised when converting from one opioid to another. To help avoid unintentional overdose due to differences in pharmacokinetics and potential for incomplete cross-tolerance, a lower starting dose of the new opioid can be initiated based on the calculated MME information. It is also important to note that methadone has an increasing conversion factor at higher doses.

Recognizing the issues with opioids and educating ourselves on how to best solve the problem allows us to take steps toward better protecting patients from harm. Understanding limitations, benefits, and risks of opioids helps us to acknowledge their role in treating pain. Properly monitoring patient MMEs along with this gained understanding has the potential to improve safety and efficacy in patients who suffer from chronic pain.

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Seeing Eye to Eye With Ophthalmic Compounding

By Anne Marie Thibodeaux, 2018 PharmD Candidate, Samford University McWhorter School of Pharmacy

When caring for patients with ophthalmic conditions, many important factors must be considered regarding pharmacotherapy. Because the eye is a sterile environment, sterile technique and sterile environment are critical when preparing ophthalmic medications, including both active and inactive ingredients. Additionally, the pH of ophthalmic drops should be equivalent to the pH of tear fluid: 7.4. To achieve this, a buffer agent may need to be added to the preparation. This buffer, however, must not cause precipitation or deterioration of the active ingredient. Additional considerations include inherent toxicity of the drug, solubility, stability in an appropriate vehicle, viscosity, and packaging and storage of the finished product.[1]

Compounded ophthalmic preparations may not receive as much attention as compounded pain and hormone creams; however, incidents of infection have occurred due to errors in the ophthalmic compounding process. In 2014, the American Academy of Ophthalmology reported incidents of infection associated with bevacizumab injection in four areas around the country: Los Angeles, CA; Miami, FL; Minneapolis, MN; and Nashville, TN. Food and Drug Administration (FDA) issued a warning to providers to be cognizant of where the drug is compounded and only use drugs secured from reliable pharmacies using aseptic techniques for drug preparation.[2] In the summer of 2011, more than a dozen Miami-area patients developed streptococcal endophthalmitis following injection of contaminated

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Avastin® obtained from a single compounding pharmacy. In early 2012, Franck's Compounding Pharmacy was implicated in an outbreak of more than 30 cases of endophthalmitis associated with the use of two different intravitreal medications.[3] Though manufacturers of FDA-regulated medications and outsourcing facilities are required to report adverse events to FDA, this is not required of compounding pharmacies.[4] This can result in less transparency among the prescriber, compounding pharmacy, and patient.

Published reports from FDA, state agencies, and other organizations consistently show that compounded drugs fail to meet specifications and proper preparation guidelines considerably more than FDA-approved drugs.[4] Patients and health care practitioners need to be aware that compounded drugs are not the same as generic drugs, which are approved by FDA. The risk-benefit ratio of using compounded medications is favorable for patients who require specialized medications that are not commercially available. However, if a patient is an appropriate candidate for an FDA-approved product, using a compounded product instead presents a greater risk compared to perceived benefit.

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