ILLINOIS DEPARTMENT OF Healthcare and Family Services
201 South Grand Avenue East
Springfield, Illinois 62763-0002

Bruce Rauner, Governor
Felicia F. Norwood, Director
Telephone: (217) 782-1200
TTY: (800) 526-5812

Drug Utilization Review Board
Meeting Summary
Wednesday, May 20, 2015

The Drug Utilization Review (DUR) Board met on Wednesday, May 20, 2015, at 8:30 a.m. in Conference Room B-16, University of Illinois at Chicago College of Pharmacy, 833 S. Wood Street, Chicago, Illinois.

DUR Board members in attendance: Rachel Caskey, MD, Chairperson; Anitha Nagelli*, PharmD, M.Ed, Vice-chairperson; John E. Tulley, MD; Lori Wilken, PharmD, AE-C.

Illinois Department of Healthcare and Family Services (HFS) Representatives: Donna Clay BSPharm, Prior Authorization, University of Illinois at Chicago (UIC); Sheri Dolan*, BSPharm, HFS Bureau of Professional and Ancillary Health Services (BPAS); Arvind K. Goyal*, MD, Medical Director, Medical Programs, HFS; Dan Lee, PharmD, UIC; Mary Lynn Moody, BSPharm, UIC; Christina Petrykiw, PharmD, CDE, UIC; Linda Schuh*, BSPharm, BPAS; Patricia Steward*, BSPharm, BPAS; Lori Uildriks Pharm D, BCPS, CGP, UIC.

Interested parties: Mark Borkovec, Upsher-Smith Labs; Jennifer Davies, Onyx; Tom Erikson, Bristol Myers Squibb; Chris Gillette, Pfizer; Rebekah Hanson, PharmD, University of Illinois College of Pharmacy; Judy King, MD; Mike Krug, Sunovion; Randi Lewandowski, Teva; Jim McNamara, ViiV Healthcare; Patrick Moty, Supernus; David Skibicki, Pfizer; Keith Stanek, Baxter; Gary Thurnauer, Pfizer.

*Attendance via teleconference

Call to Order. Rachel Caskey, MD, called the meeting to order on May 20, 2015 at 8:34 am.

Agenda, conflict of interest review, and approval of February 18, 2015 meeting minutes. Illinois DUR Board members had no changes to the May 20, 2015 meeting agenda or the February 18, 2015 minutes. Lori Wilken, PharmD, made a motion, seconded by John E. Tulley, MD, and the DUR Board unanimously approved the February 18, 2015 minutes. Rachel Caskey, MD, requested DUR Board members to recuse themselves from discussion if a conflict of interest exists and to update their Conflict of Interest form when conflicts arise.

Department of Healthcare and Family Services, Bureau of Professional and Ancillary Health Services report. Patty Steward, BSPharm, informed members that the new pharmacy benefits management system that will be used for prior authorization claim adjudication and drug utilization review will be live later, not in the summer, as previously announced. Mary Lynn Moody, BSPharm, asked DUR Board members if there was interest in having a demo of the system so members could see what new capabilities the system will provide for us. Rachel Caskey, MD, noted that a demonstration would be helpful to fully understand the new system.

Prospective Drug Utilization Review

Pulmonary arterial hypertension. Dan Lee, PharmD, provided an overview of pulmonary arterial hypertension (PAH), including types of PAH, clinical and hemodynamic features, diagnostic procedures, prognosis, therapy goals, treatment response measures, and treatments. Prior to 1995 therapy incorporated oral anticoagulation, diuretics, calcium channel blockers, and oxygen supplementation. Since 1995 new drug classes of prostacyclin analogues, endothelin antagonists, and phosphodiesterase type 5 (PDE5) inhibitors have lengthened survival of patients with PAH. Current HFS preferred therapies include the endothelin receptor antagonists (ambrisentan [Letairis], bosentan [Tracleer]), PDE5 inhibitors (sildenafil, tadalafil [Adcirca]), and the prostanoid vasodilator epoprostenol (Flolan). The HFS prior authorization criteria for an initial approval of 12 months require Group 1 World Health Organization (WHO) PAH, right-heart catheterization results for mean pulmonary arterial (PA) pressure, PA wedge pressure/PA

occlusion pressure, and pulmonary vascular resistance; documentation of trial of calcium channel blockers if a therapeutic option based on acute vasodilator response; and for pediatrics a requirement for prescribers to address safety risks of PDE5 inhibitors based on the 2013 Food and Drug Administration (FDA) warning. If a client meets criteria, preference is given for approval of preferred agents. Requests for non-preferred agents are reviewed on a case-by-case basis. Lori Wilken, PharmD, noted that some clinic patients who had sarcoid-related PAH had a difficult time getting PAH agents approved. Dan Lee, PharmD, noted that these clients would fit the WHO Group 5 PAH category that does not need targeted PAH therapy, but does need underlying treatment of the condition that has caused the PAH. Rebekah Hanson, PharmD, noted that some clinic patients are not candidates for a central line or have connective-tissue diseases that impact manual dexterity and ability to program or use a pump for intravenous administration. Patient proximity to a PAH Center of Excellence is also considered. Medications that need to be redosed frequently based on short half-lives may not be options in patients who need to travel far for medical visits. Desired subcutaneous therapy is started in the hospital and the prior authorization process is initiated at the same time to help ensure that patients will have medication at discharge into the outpatient setting. It is unclear to providers when the non-preferred agents that have dosage forms that may be better for these patients may be approved. Dan Lee, PharmD, explained that the prior authorization staff is well aware of urgency of getting these requests approved, since a disruption in therapy can potentially be life-threatening. Requests are adjudicated within 24 hours of receipt, with a major problem being insufficient information provided with the initial request. Priority is given to making sure the patient's underlying disease and hypertension are being treated appropriately first. Patients with scleroderma and systemic lupus erythematosus are reviewed case-by-case to facilitate assessment of risk versus benefit of therapies. Maximal provision of clinical and practical patient information with the requests streamlines the adjudication process. Dr. Goyal, MD, asked about information that was required for initial and renewal requests as well as the effectiveness and costs of therapies. Dan Lee, PharmD, reiterated the information required for the initial request and noted that for renewal requests, medication adherence, all medications being used for PAH, the underlying PAH cause, and clinical notes confirming benefit of therapy were considered. Medication adherence may be better for medications supplied by and monitored by specialty pharmacy providers. Overall the medications for PAH have decreased disease progression and hospitalizations, and if therapy is started and continued, life expectancy may be doubled. When patients cycle starting and stopping therapies, prognosis may be poor. Cost details could be provided by Springfield staff. The DUR Board members unanimously approved the criteria.

Pulmonary fibrosis. Christina Petrykiw, PharmD, provided an overview of pulmonary fibrosis and highlighted impact on survival of treatments. Initial and renewal approval criteria for the use of pirfenidone and nintedanib in the treatment of idiopathic pulmonary fibrosis were reviewed. If initial criteria are met, approval is for 6 months. If renewal criteria are met for subsequent requests, a 6-month approval is also given. Of the 10 requests received as of May 6, 2015, all had been denied. Denial reasons included current smoking status, Forced Vital Capacity out of range for medication requested, change in insurance coverage (including moving to managed care), and not providing clinical data. The DUR Board members discussed criteria related to current smoking status. The potential role of current smoking cessation therapy and use of the cotinine test were addressed. Published clinical data are not available for patients with mild to moderate pulmonary fibrosis and for smokers with pulmonary fibrosis. Patients who were smoking were excluded in clinical studies. Dr. Caskey noted that pill burden and adverse effect of diarrhea with pirfenidone therapy have been concerns. The DUR Board members noted that x-ray confirmation of pulmonary fibrosis diagnosis is no longer done in clinical practice, thus should not be required. A 12-month vs 6-month review of smoking status and use of a 12-month approval were discussed. Dr. Caskey called for a vote and DUR Board members unanimously approved the criteria without the requirement for a confirmatory chest x-ray.

Kalydeco. Lori Uldricks, PharmD notified DUR Board members that the Kalydeco criteria approved October 2014 were updated with FDA newly approved age indications and dosage forms. The updated criteria are posted on the Prior Authorization Website.

Retrospective Drug Utilization Review

Methadone for pain. Christina Petrykiw, PharmD, provided an overview of methadone use in pain management. Currently oral methadone, which has FDA-approved indications for moderate to severe pain or severe pain that requires long-term daily 24-hour opioid analgesic therapy, does not require prior authorization. Methadone's long duration of action and elimination half-life of up to 130 hours with chronic dosing is a safety concern due to drug accumulation. Analgesic effect wears off before methadone is eliminated from the body. Toxicity is increased if

patients take more doses for therapeutic effect before the drug is eliminated. Adverse reactions associated with methadone therapy include respiratory depression that can last up 59 hours as well as cardiac effects such as QT prolongation and Torsades de Pointes. Methadone carries a black-box warning about increased risk of opioid addiction, abuse, or misuse that may cause overdose and death. Providers must pay close attention when starting methadone therapy, converting from or to methadone from other narcotic therapies, and during dose titration. Although methadone represents approximately 2 percent of all opioids prescribed in the United States, it is implicated in at least 16,500 unintentional overdose deaths. This is greater than expected based on the number of prescriptions filled. The American Academy of Pain Medicine notes that evidence does not support methadone's preferred analgesic status on drug lists or formularies. The Academy recommends that methadone have non-preferred status unless provider education about appropriate use is provided. Methadone remains a Drug Enforcement Agency C-II narcotic that requires a new prescription with each fill. Sales of high dose methadone (40 mg) are limited to hospitals and facilities authorized for detoxification and maintenance treatment of opioid addiction. The Centers for Disease Control and Prevention note that methadone is not a drug of choice for treating chronic pain, should not be used for mild or acute pain, and is not appropriate to use on a "as needed" or PRN basis. The Food and Drug Administration issued Public Advisories and Black box warnings for methadone and changed the approved dosing interval from every 4-6 hours to every 8-12 hours. A Government Accounting Office report highlighted increasing deaths due to methadone used for pain management. Methadone has been on the Medicaid Preferred Drug List in at least 31 states, including Illinois. Many states are working to remove methadone from their Medicaid Preferred Drug Lists or instituting criteria for prior authorization. Currently the preferred long-acting narcotics on the HFS Preferred Drug List include fentanyl patches, extended-release oral morphine sulfate tablets, and oral methadone tablets. Non-preferred long-acting narcotics include sustained-release oxymorphone and oxycodone formulations. In state fiscal year 2014, HFS paid approximately 4,000 claims for methadone, while at least 160,000 claims were paid for hydrocodone. The DUR Board members discussed the use of methadone in pain management and the related safety concerns. The DUR Board members unanimously voted to recommend to the Drug and Therapeutics Committee to remove methadone from the HFS Preferred Drug List. Prior Authorization would then be required for methadone. This would allow an opportunity to educate prescribers about appropriate prescribing and help monitor patient safety.

Concomitant use of narcotics and benzodiazepines. Christina Petrykiw, PharmD, provided an overview of concomitant use of narcotics with benzodiazepines. In patients who abuse opiates, a report from the National Association of Medicaid Directors notes that 75% of the patients use benzodiazepines concomitantly. Methadone users have noted that benzodiazepines enhance the opiate effect of euphoria, with diazepam frequently preferred. Benzodiazepines have also been used to decrease opiate withdrawal effects. There has been an increase in benzodiazepine and opiate prescriptions alone and in combination from primary care clinics and Emergency Rooms. Often therapy is started by two different prescribers and both agents are continued by a new provider. There is an increased risk of overdose if both agents are used compared with benzodiazepine use alone. At least 50% of all overdoses include an opiate and a benzodiazepine. Benzodiazepines have been implicated in up to 80% of methadone-related fatal overdoses and in 30% of fatal opiate overdoses. Both drug classes cause respiratory depression. Benzodiazepines may also lower the threshold for respiratory depression and increase opiate levels based on shared metabolic pathways. Benzodiazepines used with methadone can worsen short-term, working memory. Most narcotic treatment centers do not allow benzodiazepine therapy due to potential for addiction and thus use hydroxyzine preferably for treating anxiety. State Medicaid agencies manage concomitant use by requiring prior authorization for methadone if the client is taking a benzodiazepine, requiring prior authorization for the benzodiazepine if the client is taking an opioid or Suboxone, instituting a DUR edit once patients fill 4 CNS depressant classes that can include benzodiazepines and opioids, or only allowing 4 controlled substances in 30 days. Managed Care Organizations have used fills of these combinations to flag clients for potential lock-in status restricting them to one physician and pharmacy. A review of HFS prescription claims for January to March 2015 found approximately 29,000 claims for benzodiazepines and almost 85,000 claims for narcotics. About 1,700 clients were filling a benzodiazepine and a narcotic in the same month. In clients who filled both drug classes in the same month, the most frequently filled narcotics were hydrocodone- or oxycodone-containing products and the most frequently filled benzodiazepines were alprazolam and diazepam. The DUR Board members discussed whether the number of patients getting both products was lower than expected because providers are receiving faxes regarding long-term therapy with benzodiazepines or pain medications, or in the case of Prior Authorization for Suboxone, which excludes patients taking benzodiazepines, whether patients are paying out of pocket for these products. Dr. Caskey suggested an edit that would not allow filling of both medications together, which Anitha Nagelli, PharmD agreed with. Suggestions were made to educate providers about appropriate diagnoses and to track usage via the Illinois Prescription Monitoring Program (ILPMP). It

was unclear whether requiring prior authorization will make a difference in usage. Potentially better approaches than a hard edit or prior authorization were discussed to help decrease patients arguing to get their medicines. Anitha Nagelli, PharmD and Lori Wilken, PharmD suggested that acutely patients may need both agents. Mary Lynn Moody, BSPharm, noted that provider and patient education is an issue. Busy providers often do not have time to check ILPMP. Regularly checking ILPMP may require a change in routine medical practice. The new adjudication computer system may be able to help implement an edit that would stop the concomitant filling of both agents after an acute period. Currently during the adjudication process for Suboxone requests, ILPMP is checked for benzodiazepine use. The DUR Board members suggested determining whether prescribing of both agents was mainly by a few medical providers. Education can then be targeted to these prescribers. Mary Lynn Moody, BSPharm, will check with the new computer system provider whether an alert can be set that can be used as an educational intervention for providers. Anitha Nagalli, PharmD, mentioned that the MEDI system can push out alerts, but providers then have to look through many messages to find the alert, which is not efficient.

Educational initiatives.

Biosimilars. Christina Petrykiw, PharmD, educated DUR Board members about Biosimilars. The Affordable Care Act created an abbreviated mechanism for approval of biological products that are biosimilar to or interchangeable with an FDA-approved biological reference product. Biosimilar biological products are highly similar to the reference (Brand) product and demonstrate no clinically meaningful differences in safety, purity, or potency. Biologicals that are interchangeable must be biosimilar, have the same clinical and safety results as the reference product in patients, and may be substituted at the pharmacy without intervention from the prescriber. Prescribers need to write the brand or generic name of the biosimilar biological product as it is listed in the FDA Purple book for it to be dispensed. Biosimilars may have fewer indications or routes of administration than the referenced product, thus checking the package insert becomes important. The Centers for Medicare and Medicaid Services requested that DUR programs and Pharmacy and Therapeutics Committees inform physicians and pharmacists about appropriate prescribing and dispensing of biological products, including biosimilars and their interchageability. Education should be provided via newsletters, electronic prescribing messaging, or point-of-sale edits. The first biosimilar approved was filgrastim (Zarxio) in March 2015. It is biosimilar to Neupogen, but not deemed interchangeable. There are at least 140 different active-ingredient entities that are in the biosimilar pipeline that will be approved as biologicals or as drugs. Dr. Caskey inquired whether education was required at the state or federal level. Mary Lynn Moody, BSPharm, noted that this legislation may create drama and prescribers need to be educated what they should do. A HFS process for managing biosimilars, including preferred status of interchangeable biosimilars will need to be determined. The DUR Board members asked whether there was a cost benefit to use of the biosimilar agents. At present, this is unknown since they are not yet on the market. Initially there may be confusion for pharmacies since products may be listed as biosimilars, but may not be interchangeable. Mary Lynn Moody, BSPharm, noted that HFS Web presence must be increased for education and that this may be useful to present at state medical societies or other medical groups. Dr. Caskey agreed that education will be needed.

Public comments

Dr. Judy King asked about the role of DUR in relationship to managed care organizations. Christina Petrykiw, PharmD, mentioned that Managed Care Organizations have their own formularies, Drug and Therapeutics Committees, and should be evaluating drug utilization for appropriateness. Current Fee–For-Service processes are separate from the MCOs. At present the managed care organizations provide some information to HFS regarding drug usage as part of federally-mandated quality initiatives. Improving communication and activities between both groups regarding drug utilization is planned.

Adjournment. Rachel Caskey, MD, adjourned the DUR Board meeting at 10:18 am.

Meeting minutes prepared by Christina A. Petrykiw, PharmD, CDE.

Approved September 23, 2015 by the Illinois Drug Utilization Review Board.