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News & Noteworthy: I-STOP to E-Prescribe

by Sarah Jung, Pharmacy Practice Resident

As of March 27, 2016, all New York State prescriptions for controlled and non-controlled substances were expected to be electronically transmitted to pharmacies. An electronic prescription (unlike written, oral, or faxed prescriptions) is a prescription that is electronically encrypted, signed, and submitted to dispensing pharmacies. Benefits of e-prescribing are convenience, integration in electronic health records, decreased risk of forgery or tampering, enhanced legibility, and faster processing of prescriptions. Some challenges of e-prescribing are alterations in work flow and implementation of new software.

Implementation of electronic prescribing of controlled substances (EPCS) is the second major mandate under the Internet System for Tracking Over-Prescribing (I-STOP) Law signed in 2012 to hinder prescription opioid abuse in New York State. The first major mandate, in practice since August 2013, requires licensed practitioners to review the Prescription Monitoring Program (PMP) registry for a patient's controlled substance utilization of CII through IV substances within the 24 hours prior to prescribing or dispensing controlled drugs, unless the prescriber is providing less than a 5-day supply from the emergency department.

EPCS requires two-factor authentication to prove authorized provider identity and access (e.g., password and electronic signature, biometric identifier, or hard token). As not all electronic systems at University Hospital of Brooklyn (UHB) had been ready for the March deadline, hardcopies of prescriptions for controlled substances (CII - V) generated in HealthBridge have been authorized by a waiver from the Commissioner of Health for UHB patients. Prescriptions for non-controlled drugs are required to be submitted electronically. Individual suites, clinics, and practice groups may have also received waivers for controlled and/or non-controlled substance prescriptions.

See page 3 for more answers to frequently asked questions.

Pharmacy & Therapeutics Committee Updates

by Sarah Jung, Pharmacy Practice Resident

During the first quarter of 2016, several policies and protocols were approved or updated and several changes were made to the hospital formulary.

The committee approved an updated Pain-Agitation-Delirium protocol for the management and assessment of intubated patients in adult intensive care units (ICUs). In addition to changes in first-line pharmacologic choices and a shift to use the Richmond Agitation-Sedation Scale (RASS), the new protocol also provides more guidance on management of delirium. It is currently being piloted in the ICUs.

As a cost-containment measure, the committee also approved guidelines for use and discontinuation of granulocyte-stimulating factor (G-CSF, filgrastim, Neupogen[®]) according to recommendations from the National Comprehensive Cancer Network for prevention of neutropenia associated with intermediate- and high-risk agents and treatment of febrile neutropenia in oncology patients. Pegfilgrastim (Neulasta[®]) will be restricted to outpatient use for prevention of neutropenia in at-risk patients, as well.

Changes to the hospital formulary include addition of Sacubitril/valsartan (Entresto[®]), ivabradine (Corlanor[®]), and filgrastim-sndz (Zarxio[®]) and removal of fluphenazine (Prolixin[®]), thiothixene (Navane[®]), alvimopan (Entereg[®]), and fidoxamicin (Dificid[®]). Levofloxacin (Levaquin[®]) was also approved to replace moxifloxacin (Avelox[®]) and ciprofloxacin (Cipro[®]) as the formulary fluoroquinolone. (Read more about the new drugs for heart failure on page 2.) The crash cart formulary was updated to remove vasopressin (Vasostrict[®]), verapamil, methylprednisolone (Solu-Medrol[®]).

Two New Drugs with New Mechanisms of Action for Heart Failure

New Drug Primer: Ivabradine (Corlanor®)

by Sarah Jung, Pharmacy Practice Resident

Ivabradine is a hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker indicated to reduce worsening heart failure hospitalization in patients with stable, symptomatic chronic heart failure (with left ventricular ejection fraction $\leq 35\%$ and in sinus rhythm with heart rate ≥ 70 beats per minute) who are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use. Blockage of the HCN channel in the sinoatrial node results in reduced heart rate without effects on contractility or ventricular repolarization.

Indications and Dose:

- ◆ To reduce the risk of hospitalization associated with chronic heart failure by reducing heart rate.
- ◆ Recommended starting dose of 5 mg twice daily with food. Titrate or adjust dose after 2 weeks by 2.5 mg to achieve resting heart rate between 50-60 beats per minute. Maximum dose is 7.5 mg twice daily.

Contraindications and Precautions:

- ◆ **Contraindications:** Acute decompensated heart failure, blood pressure $< 90/50$ mmHg, sick sinus syndrome, sinoatrial block, resting heart rate < 60 beats per minute prior to treatment, severe hepatic impairment, concomitant strong CYP3A4 inhibitors (such as azole antifungals, macrolide antibiotics, HIV protease inhibitors, and nefazodone)
- ◆ **Precautions:** Pregnancy (animal reproduction studies suggest fetal harm), atrial fibrillation, bradycardia

Adverse Reactions:

- ◆ Bradycardia (10%), atrial fibrillation (8.3%), luminous phenomena/temporary brightness in the field of vision (2.8%)

Hospital Formulary Restrictions:

- ◆ None

New Drug Primer: Sacubitril/valsartan (Entresto®)

by Sarah Jung, Pharmacy Practice Resident

Sacubitril/valsartan is a neprilysin inhibitor in combination with an angiotensin-II receptor blocker. By inhibiting neprilysin, the degradation of natriuretic peptides is inhibited, which promotes vasodilation, decreased sympathetic drive, and inhibition of aldosterone secretion.

Indications and Dose:

- ◆ To reduce the risk of cardiovascular death and hospitalization in patients with heart failure in place of ACE inhibitor or angiotensin-receptor blocker.
- ◆ **Recommended starting dose** of 49 mg/51 mg twice daily. Double the dose every 2-4 weeks to maintenance dose of 97 mg/103 mg twice daily, as tolerated.
- ◆ **Dose adjustment** recommended in patients with severe renal impairment ($\text{CrCl} < 30$ mL/min) and moderate hepatic impairment (Child-Pugh B).

Contraindications and Precautions:

- ◆ **Contraindications:** Hypersensitivity to sacubitril or valsartan, co-administration with ACE inhibitor or ARB, history of angioedema with ACE inhibitor or ARB, concomitant use with aliskiren in patients with diabetes.
- ◆ **Precautions:** Pregnancy – Discontinue drug as soon as possible to reduce potential risk to fetal renal function

Adverse Reactions:

- ◆ Renal dysfunction (1.7%), hyperkalemia (1.7%), hypotension (1.4%)

Hospital Formulary Restrictions:

- ◆ None

Pharmacy Focus: Electronic Prescribing FAQ's

See a full list at http://www.health.ny.gov/professionals/narcotic/electronic_prescribing/docs/epcs_faqs.pdf

Also see http://www.health.ny.gov/professionals/narcotic/electronic_prescribing/

Can pharmacies reject paper prescriptions?

No, pharmacies are expected to fill prescriptions that meet the rules and regulations of New York State. Paper prescriptions should not be rejected solely on this basis. Pharmacies are not responsible to verify waivers or downtime.

What types of prescriptions are not required to be electronically prescribed for hospital patients?

According to the Bureau of Narcotic Enforcement, prescriptions for durable medical equipment, compounds of 2 or more products to be mixed by the pharmacist, prescriptions with long or complicated instructions for use, non-patient specific prescriptions for an opioid antagonist (naloxone), and prescriptions for research protocols do not require electronic submission.

What can be done if a prescription was sent to a different pharmacy than the one the patient now prefers?

The prescriber may call the pharmacy to cancel the prescription and reverse third-party claims, and then resubmit a new prescription to the new pharmacy. For prescriptions with refills, as long as the prescription was not for a controlled substance, the prescriber/patient may also request the new pharmacy transfer one refill from the old pharmacy to the new pharmacy.

Can prescribers still call in, fax, or write prescriptions for prescriptions that are required for electronic prescribing?

Yes, but only under specific exceptions. Oral, faxed or paper prescriptions will then require timely practitioner notification of the Bureau of Narcotic Enforcement. For each exception to electronic prescribing, the practitioner should email the Bureau of Narcotic Enforcement at erx@health.ny.gov with the required practitioner and patient information as listed at web site http://www.health.ny.gov/professionals/narcotic/electronic_prescribing/practitioner_notification_requirement.htm.

- Within 72 hours of the end of a temporary electrical or technologic failure that prevented electronic prescribing
- Within 48 hours of issue of a prescription to a pharmacy located outside of New York or in situations in which the practitioner deems a delay in obtaining the electronically prescribed substance may adversely affect a patient's medical condition.

Featured
patient-
care
question

Nurses Want To Know ...

Q: I just gave my patient an injection of morphine 4 mg. The physician also wants me to give the morphine controlled-release 60-mg tablet now? Is it too soon for the oral dose?

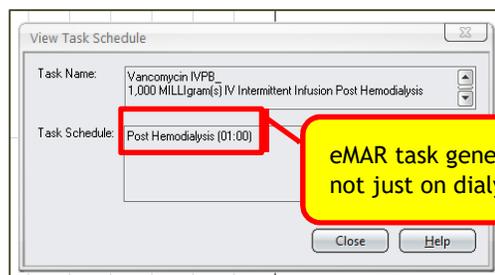
A: No. Whereas injections of opioids start working in as soon as 5-10 minutes and may last 4-5 hours, oral medications take longer to start providing pain relief. In this case, the controlled-release tablet takes 1-2 hours to start working with a peak effect in 3-4 hours for most patients. In contrast, immediate-release medications (such as morphine oral solution or oxycodone immediate-release tablets) usually start working in 30-60 minutes. Longer-acting opioids (e.g., fentanyl patch, methadone for pain) should be administered on a routine schedule to maintain appropriate drug levels for analgesia.

Spotlight on Safety: Renal Dosing Gone Awry

by LilyAnn Jeu, Medication Safety/Internal Medicine Clinical Pharmacist

For medications that require renal dosing, two common strategies for ensuring a safe and effective regimen are reducing the drug amount per dose or increasing the interval (or amount of time) between doses. In patients with end-stage renal disease, hemodialysis may also remove enough medication from the bloodstream that the scheduled dose (or a supplemental dose) may be required after completion of hemodialysis on the dialysis day. Dosing guides and medication orders often include instructions for dialyzable medications to be given "post dialysis," yet for some patients this has been easier said than done.

Several medication incident reports identified patients who received extra doses, either due to erroneous medication orders (e.g., daptomycin ordered the next day despite renal dosing recommendations of one dose every 48 hours) or medication administration schedules that generated tasks on the electronic medication administration record for each day rather than only on dialysis days. On multiple occasions, patients received two or three full doses of vancomycin on consecutive days, despite hemodialysis scheduled on intermittent days two or three times per week.



Some of these errors were detected when drug levels came back unexpectedly high, such as vancomycin pre-dialysis troughs in the 40s or 50s or gentamicin troughs greater than 6 mcg/mL when the usual targets are closer to 20-25 mcg/mL for vancomycin and less than 2 mcg/mL for gentamicin. While renal damage may no longer be a concern for nephrotoxic medications in dialysis patients, prolonged exposure to supratherapeutic levels of any medications may still result in other adverse effects, including ototoxicity or thrombocytopenia. In the patient who received the extra dose of daptomycin, the creatinine kinase level, a marker for muscle injury, reached 568 mcg/L, which is 20-fold higher than the lower limit of normal (30-223 mcg/L).

Clinical Pearls: SGLT2 Inhibitors and Euglycemic DKA

by Sarah Jung, Pharmacy Practice Resident

In 2013, the FDA approved canagliflozin (Invokana[®]) as the first of a new class of oral anti-diabetic medications called sodium-glucose cotransporter-2 (SGLT2) inhibitors as second- or third-line agents for patients with type 2 diabetes mellitus (T2DM).^{1,2} Other drugs in this class include dapagliflozin (Farxiga[®]), empagliflozin (Jardiance[®]), and combination products.

Two years later, the FDA released a warning statement about risk of ketoacidosis.³ In December 2015, an updated warning and change in product labeling were announced based on 73 cases reported between March 2013 and May 2015.⁴ Whereas diabetic ketoacidosis (DKA) has been traditionally diagnosed in patients with glucose levels > 250 mg/dL, "euglycemic DKA" or "DKA with lower-than-anticipated glucose levels" has been observed in patients taking SGLT2 inhibitors at blood glucose levels below 200 mg/dL (even at a blood glucose level of 90 mg/dL).⁵

SGLT2 inhibitors prevent the reabsorption of filtered glucose in the proximal tubules of nephrons, thereby promoting urinary excretion and overall reduction in blood glucose.^{2,6-7} However, lower blood glucose concentrations may also reduce insulin secretion, which may then promote glucagon-mediated lipolysis and subsequent production of ketones from free fatty acids. At the same time, gluconeogenesis from triglycerides and amino acids may also occur. While the ketotic and hyperosmolar state in most DKA presentations leads to anion gap acidosis and severe dehydration with elevated blood glucose levels, the prolonged (> 24-hour) blood-glucose lowering effects of SGLT2 inhibitors may keep blood glucose levels less than 250 mg/dL even in the face of ketosis.^{5,8-9}

Risk factors for DKA with SGLT2 inhibitors include severe illness, reduced insulin doses, history of alcohol intake, and reduced food or fluid intake.⁵ While the incidence has been low (only 0.2 to 0.8 cases per 1000 patient-years in clinical trials with T2DM), awareness and recognition of this potential adverse effect can facilitate prompt diagnosis and treatment.^{5,9}

References:

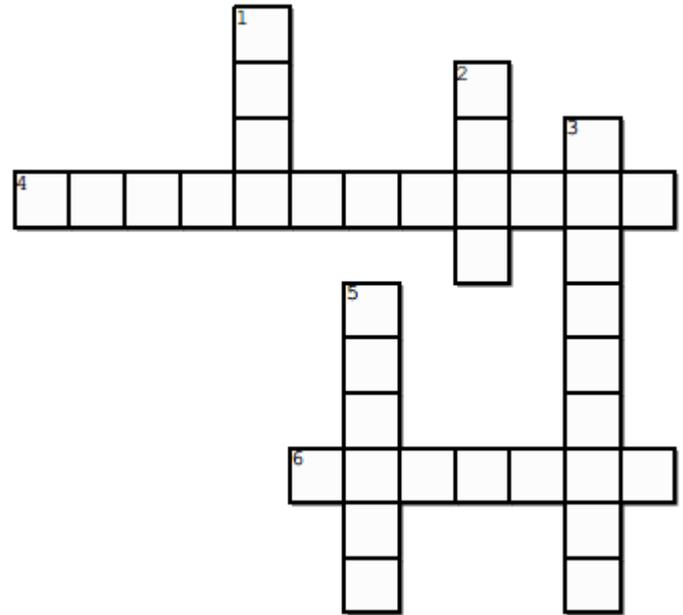
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Answers to Crossword Puzzle:

Across: 4. Hyperkalemia 6. Digoxin
Down: 1. Four 2. ACEi 3. Diuretics 5) Sodium

Crossword Puzzle: Heart Failure

by Sarah Jung, Pharmacy Practice Resident



Across

4. Contraindication for ACE inhibitor use
6. This drug may have symptomatic benefit, but no mortality benefit

Down

1. Number of NYHA classifications for heart failure
2. Class of first-line drugs to reduce cardiomyopathy and decrease mortality
3. Agents used to decrease fluid retention
5. Electrolyte that should be restricted in the diet of heart failure patients



Team Tip of the Day

SMART PUMP INFUSION LIBRARY UPDATE

During the month of April, please upload the latest infusion pump library.

1. Bring pump to Wi-Fi accessible location.
2. Check for Wi-Fi signal.
3. Turn pump OFF, then ON.
4. Select YES for "New patient."
5. Check for Version 19.

