Continued from page 2….

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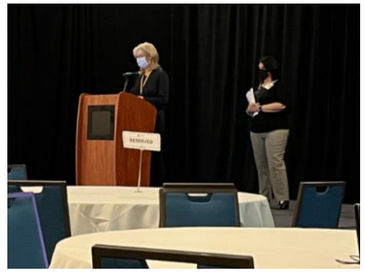
Valley Represented at State Pharmacy Conference

Carlo Lupano, RPh, MBA, FASHP, Maria Leibfried, PharmD, BCNSP, and Katie Ellis, RN, BSN, CWOCN, spoke at the NJ Society of Health-System Pharmacists (NJSHP) in Long Branch, NJ, April 8-9, 2022.



Journal of The Valley Hospital Pharmacy

Pharmacy Focus

Volume 22 Spring

Formulary Update

Bupivacaine liposomal injection (Exparel®)

Liposomal bupivacaine is a long-acting formulation of bupivacaine, a **local anesthetic**. The liposomal component **prolongs the duration of action** for up to 72 hours. It is currently FDA approved for patients age 6 years and older for single-dose infiltration to produce postsurgical analgesia, and in adults as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia. It has been previously approved at Valley for **hemorrhoidectomy, bunionectomy, breast surgery, gynecological procedures, and hernia repairs**. P&T recently expanded use to include the following indications: **thoracotomies, VATS/RATS procedures in patients unable to take NSAIDs/acetaminophen, and in patients with chronic pain syndromes**. This is based upon primary literature that shows it is safe with potentially fewer complications than epidural analgesia, decreased length of stay in pulmonary surgery, and it may decrease pain scores and narcotic usage post-op in thoracotomies.

Tisotumab vedotin-tftv (Tivdak®)

Tisotumab vedotin-tftv is an **antibody drug conjugate** (ADC) that binds to tissue factor on target cells to inhibit the coagulation cascade, which **disrupts tumor growth and metastasis**. It is indicated for the **treatment of recurrent or metastatic cervical cancer with disease progression** on or after chemotherapy. Tisotumab vedotin-tftv caused changes in the corneal epithelium and conjunctiva resulting in changes in vision, including severe vision loss, and corneal ulceration. Conduct an ophthalmic exam at baseline, prior to each dose, and as clinically indicated. Adhere to premedication and required eye care before, during, and after infusion. **Restricted for Luckow ambulatory infusion use only.**

Belantamab mafodotin-blmf (Blenrep®)

Belantamab mafodotin-blmf is an **antibody-drug conjugate** (ADC) directed against B-cell maturation antigen (BCMA), a cell surface protein expressed on multiple myeloma cells but is virtually absent on naïve and memory B cells. It is indicated for the **treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies** including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent. This medication is known to cause changes in the corneal epithelium resulting in changes in vision, including severe vision loss and corneal ulcer, and symptoms, such as blurred vision and dry eyes. **Conduct ophthalmic exams at baseline, prior to each dose, and promptly for worsening symptoms.** Because of the risk of ocular toxicity, **it is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BLENREP REMS. Restricted for Luckow ambulatory infusion use only.**

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Drug Info Corner

Teresa Tran, MBA
PharmD Candidate 2022

Question: Does propofol cause QT prolongation?

Response: The contraction of the heart is the result of ventricular depolarization followed by ventricular repolarization. On an electrocardiogram, the QRS complex represents ventricular depolarization, and the T wave represents ventricular repolarization. The **QT interval measures the time it takes for the heart to repolarize after depolarizing**. When the ion channels do not function properly, there is a **delay in depolarization, and extended repolarization results in a prolonged QT interval**. A QTc (corrected for heart rate) interval greater than 450 milliseconds in males and 470 milliseconds in females is identified as a prolonged QT interval.[1,2] A **prolonged QT interval can lead to life threatening complications** like torsades de pointes, which is a life-threatening ventricular arrhythmia where the ventricles beat faster than the atria.[1]

Risk factors for QT prolongation include:

- age older than 65[1]
- female gender[1]
- medications such as antiarrhythmics, antimicrobials, and antidepressants[2]
- heart rate below 60 bpm[6]
- history of myocardial ischemia[6]
- hypokalemia, hypomagnesemia[1,6]
- subarachnoid hemorrhage[6]
- low ejection fraction[1]

Propofol is an intravenous anesthetic that activates GABA receptors and inhibits the NMDA receptor.[3,4]
Propofol associated QT prolongation is not commonly encountered:

- The propofol (Diprivan®) package insert does not mention QT prolongation.[3]
- Between 2020 and 2021, there have been 54 reports of QT prolongation related to propofol as reported to the FDA.[5]
- A retrospective, observational study measured the incidence of torsades de pointes after propofol exposure in 628,784 patients at Mayo Clinic from August 1998 to November 2015. Of these patients who received propofol, **21 developed torsades de pointes and 17 had at least one additional risk factor** for QT prolongation.[6]

In summary, propofol <u>may</u> cause QT prolongation, especially in patients with other risk factors for QT prolongation. Given the widespread use of propofol for sedation, it should be used cautiously in patients with an increased risk for QT prolongation; these patients may require additional ECG monitoring after propofol administration.

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Pharmacy Residents Present at National Pharmacy Conference

ashp MIDYEAR 2021 Clinical Meeting & Exhibition

Poster title: Appropriateness of oral anticoagulant dosing in patients with stroke and atrial fibrillation in a non-teaching hospital.

Aarezo Riaz, PharmD, PGY1 Community-Based Pharmacy Resident

Institutions that are certified as a **Comprehensive Stroke Center** are required to meet a series of **Standard Quality Measures set by the Joint Commission**. This includes ensuring patients are discharged on antithrombotic therapy, statin medication, and anticoagulation therapy for atrial fibrillation or atrial flutter. Verifying appropriate dosage is not captured as a quality measure. Thus, this retrospective cohort review serves as **a quality improvement initiative** to evaluate the **appropriateness of oral anticoagulant therapy for patients discharged after an ischemic stroke or transient ischemic attack**. A report was generated from the "Get With the Guidelines-Stroke" database to identify patients who were discharged from the hospital between May 1 to July 31, 2021 with an ischemic stroke and atrial fibrillation or atrial flutter. Patients were excluded if they were diagnosed with a hemorrhagic stroke or if they expired prior to discharge. Results showed that the majority of patients were discharged with anticoagulation and appropriate dosage per package insert. Of those who were discharged without anticoagulation, documentation to provide reasoning was provided for 80% of the patients; the most common reason documented was found to be risk of bleeding (including immune thrombocytopenic purpura, hematuria, spontaneous cerebral bleeding, gastrointestinal bleeding, and history of frequent falls). **Our findings suggest that The Valley Hospital is meeting rigorous performance standards**.

Poster title: Evaluation of enoxaparin prophylactic dosing in patients with obesity in a large community hospital.

Jennifer Nacion, PharmD, PGY1 Pharmacy Resident

Enoxaparin is commonly used for thromboprophylaxis of venous thromboembolism (VTE) at a dose of 30 mg subcutaneously every 12 hours or 40 mg subcutaneously once daily in patients with normal renal function. It is presently unclear what the most efficacious dosing strategy is in patients with obesity. Current evidence suggests that **higher doses may be warranted in patients with obesity** given their increased risk of VTE. Dosing strategies in the literature include increased fixed dose regimens such as 40 mg twice daily, 60 mg daily, or 60 mg twice daily, as well as weight-based dosing regimens. Some evidence suggests only increasing dosing for patients with a body mass-index (BMI) ≥ 40 kg/m^2 and further increasing the dose for patients with a BMI ≥ 50 kg/m^2. During our evaluation of prophylactic enoxaparin prescribing practices at our institution, it was discovered that **95% of patients with obesity at Valley currently receive standard prophylactic dosing.** Currently, a committee of pharmacists and physicians is convening to determine the need for an improvement plan.

New drug in our arsenal for managing acute hyperkalemia: PATIROMER

Maria Fatima Iharada, PharmD, Clinical Pharmacy Specialist

Patiromer (Veltassa®, Vifor Pharma, Redwood City, CA) is an oral powder that is to be mixed with water to make an oral suspension. Patiromer **exchanges potassium for calcium in the colon** and **increases fecal potassium excretion**, resulting in **lower serum potassium levels**. Its use has been well established to manage chronic hyperkalemia.[1] Up until recently, little data has been published about the use of patiromer in the management of hyperkalemia in the acute care setting.

On January 26, 2022, *JAMA* published an article entitled "Assessment of Patiromer Monotherapy for Hyperkalemia in an Acute Care Setting." The research article describes a cohort study of 881 patients from Montefiore Medical Center that received oral patiromer for acute, non-life-threatening hyperkalemia (defined as serum K+ 5.0 mEq/L or greater). The authors found patiromer to be associated with a significant reduction in serum potassium levels within the first 6 hours of administration. The study patients had a mean baseline potassium level of 5.6 mEq/L. After one dose of patiromer 8.4 grams, 16.8 grams, or 25.2 grams, the results demonstrated a mean reduction in serum potassium levels was 0.5 mEq/L at 6 hours, 0.46 mEq/L at 6 to 12 hours, and 0.52 mEq/L at 12 hours or greater. Doses of patiromer 16.8 grams or more showed a greater relative reduction in potassium levels than 8.4 grams. A low incidence (0.2%) of hypokalemia was found at 24 hours after administration.[2]

The use of **patiromer may be recommended for patients with acute, non-life-threatening hyperkalemia** in the acute care setting. One dose of patiromer may decrease serum potassium levels by approximately 0.5 mEq/L. In comparison to sodium polystyrene and its risk of intestinal necrosis, the tolerability, safety, and efficacy profile favors patiromer for the treatment of hyperkalemia.

Patiromer is available as 8.4 gram packets and may be dosed up to 25.2 grams/day. The powder must first be reconstituted with soft foods or beverages and other oral medications should not be administered at least 3 hours before or 3 hours after patiromer. Patiromer packets are stored in the refrigerator and may be used up to 3 months at room temperature after refrigerator removal.[1]

Please reach out to your pharmacist with questions!

References

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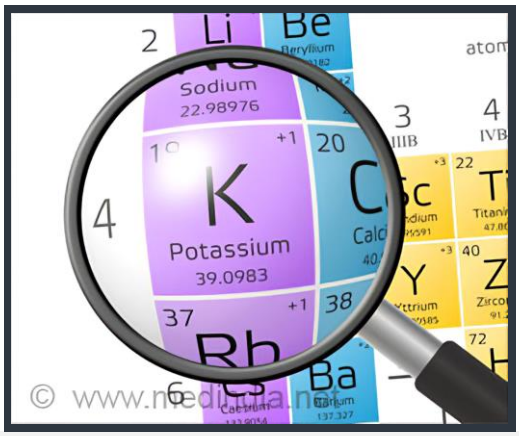

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Asparaginase erwinia chrysanthemi (recombinant)-rywn (RYLAZE®)

Asparaginase erwinia chrysanthemi (recombinant)-rywn is produced by fermentation of a genetically modified bacterium containing *Erwinia chrysanthemi* DNA, allowing it to be more readily available. It shares a **similar mechanism of action to asparaginase Erwinia chrysanthemi, in that it leads to decreased circulating levels of asparagine, resulting in tumor cell death**. Indicated for the treatment of **acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL)** in adult and pediatric patients 1 month or older who have developed hypersensitivity to *E. coli*-derived asparaginase, as a component of a chemotherapeutic regimen**. Restricted for ambulatory infusion use only.**

Tranexamic Acid (Cyklokapron®) for Inhalation

Tranexamic acid (TXA) is an injectable solution that is on formulary for **IV use in acute traumatic injury, orthopedic surgery, and OB**. It is also used **topically for epistaxis and in the operating room during hip/knee arthroplasty**. It is currently added to formulary for off-label **inhalation use.** TXA is an antifibrinolytic agent that reversibly binds to the lysine receptor on plasminogen, inhibiting plasmin formation and preventing clot breakdown. Given the proven efficacy to reduce bleeding in multiple other settings, nebulized tranexamic acid may be used to control volume and duration of bleeding in patients with non-massive hemoptysis. While there is no FDA-approved indication nor general consensus regarding optimal tranexamic doses and route of administration, inhaled tranexamic acid appears to be a reliable option in increasing the resolution of bleeding within 5 days and reducing daily expectorated blood volume. This medication is **restricted to pulmonary and critical care**.

Gemtuzumab ozogamicin (MYLOTARG®)

Gemtuzumab ozogamicin (GO) is an **antibody drug conjugate** that binds to CD33 on target cells. The **antineoplastic activity** is based upon activation of the N-acetyl gamma calicheamicin. N-acetyl gamma calicheamicin induces double-strand DNA breaks causing cell arrest and apoptic cell death. CD33 is a cell surface antigen expressed by myeloid stem cells, myeloblasts, monoblasts, monocytes/macrophages, and mast cells. It is present in more than 80% of patients with acute myeloid leukemia but is absent from pluripotent hematopoietic stem cells. CD33 makes an attractive target due to the widespread expression of CD33 on AML blasts and, in some cases, AML precursors are mainly or entirely CD33 positive. It is indicated for **treatment of newly-diagnosed CD33 positive AML in adults and relapsed or refractory CD33 positive AML in pediatric patients > 2 years and older.** It has been associated with hepatotoxicity, including life-threatening and sometimes fatal hepatic veno-occulusive disease. Assess ALT, AST, total bilirubin and alkaline phosphate prior to each dose. **Restricted for inpatient and ambulatory infusion use only.**

Ustekinumab (STELARA®)

Ustekinumab is a **human immunoglobulin (IgG1) kappa monoclonal antibody.** It exerts its activity by binding to the p40 protein subunit used by both the IL-12 and IL-23 cytokines. These cytokines which occurred naturally are involved in inflammatory and immune responses by activating natural killer cells and CD4+ T-cells. Binding to the p40 protein prevents IL-12 and IL-23 from interacting with the shared cell-surface receptor chain, IL-12Rβ1disrupting mediated signaling and cytokine cascades thus disrupting the inflammatory response. This is an attractive target as the interleukins are associated with the chronic inflammation seen in Crohn's disease. This was approved by The Valley Hospital **for the off-label use of Crohn's treatment of patients 6 years and older.**

Tixagevimab/cilgavimab (Evusheld®)

This is a combination of long acting IgG1 antibodies that are co-packaged and intended to be given in tandem as **pre-prophylaxis exposure to SARs-CoV-19 virus exposure**. Both monoclonal antibodies are responsible for binding to different sites of the COVID19 spike protein-receptor site, blocking viral attachment to the human ACE2 receptor. The product is for patients at least 12 years of age or older and weigh at least 40 Kg (88 pounds) with a history of severe allergy preventing vaccination against COVID19, or moderate to severe immunocompromised status. **This is a one-time dose medication for IM injection.**