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Taligucerase Alfa (Elelyso®)

Taligucerase alpha is a glucocerebrosidase analogue. It is currently indicated to treat Type I Gaucher disease in adults and children four years of age and older. It is administered as an intravenous infusion over 60 to 120 minutes, given every 2 weeks and follows weight based dosing. At TVH, use of taligucerase alpha is restricted to Luckow Pavilion.

Belinostat (Beleopdaq®)

Belinostat is indicated for the treatment of relapsed or refractory peripheral T-Cell lymphoma (PTCL). It is a histone deacetylase inhibitor that is administered as an intravenous infusion over 30 minutes. Belinostat is primarily metabolized by UGT1A1 and may require and initial dose reduction in patients known to be homozygous for the UGT1A1*28 allele. At TVH, use of belinostat is restricted to Luckow Pavilion.

Elotuzumab (Empliciti®)

Elotuzumab is indicated for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three prior therapies. When given for this indication, elotuzumab is used in combination with lenalidomide and dexamethasone. Elotuzumab is a humanized IgG1 immunostimulatory monoclonal antibody that is directed against signaling lymphocytic activation molecule family member 7 (SLAMF7). The SLAMF7 pathway directly activates natural killer cells and mediates antibody-dependent cellular cytotoxicity (ADCC) through the CD16 pathway in myeloma cells. This medication is restricted to Luckow Pavilion.

Daratumumab (Darzalex®)

Daratumumab is indicated for the treatment of multiple myeloma in patients who have received at least three prior lines of therapy including a proteasome inhibitor and/or a immunomodulatory agent. Daratumumab is an IgG1 kappa monoclonal antibody directed against CD38. Patients receiving daratumumab should be screened for blood type prior to the initiation of therapy. At TVH, use of daratumumab is restricted to Luckow Pavilion.

Necitumumab (Portrazza®)

Necitumumab is a monoclonal antibody that is directed against the epidermal growth factor receptor (EGFR). It is indicated as first-line treatment for metastatic squamous non-small cell lung cancer in combination with gemcitabine and cisplatin. It carries a black box warning for cardiopulmonary arrest (occurred in 3% of patients) and hypomagnesemia (occurred in 83% of patients). Necitumumab use is restricted to Luckow Pavilion.

Atezolizumab (Tecentriq®)

Atezolizumab is an anti-PD-L1 monoclonal antibody. It was recently approved by the FDA in May 2016 for the treatment of locally advanced or metastatic urothelial carcinoma in patients who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. At TVH, use of atezolizumab is restricted to Luckow Pavilion.

Epoprostenol sodium (Flolan®)

Epoprostenol sodium is indicated for the treatment of pulmonary arterial hypertension. It is a prostacyclin analog that has 2 major pharmacological actions: direct vasodilation of pulmonary and arterial vascular beds, and inhibition of platelet aggregation. It is an intravenous infusion through a central venous catheter. At The Valley Hospital, this medication is restricted to physicians affiliated with the pulmonary hypertension program.

Rosuvastatin (Crestor®)

Rosuvastatin is an HMG Co-A reductase inhibitor. This drug class is also commonly referred to as “statins.” Rosuvastatin has many indications in adults and children. Most commonly, rosvastatin is used to treat hyperlipidemia, and for risk reduction of MI and stroke. Additional statins on the formulary are simvastatin and atorvastatin.

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Meet the new Pharmacy Residents

Saloni Shah, PharmD, is originally from Rutherford, New Jersey and earned a Doctor of Pharmacy degree in May of 2016 from Philadelphia College of Pharmacy. Saloni is a licensed pharmacist in New Jersey and is currently completing a PGY-1 pharmacy practice residency at The Valley Hospital. She is excited to begin her journey as a pharmacy resident to engage herself in patient care and continue to bring value to the pharmacy profession. Her current interests are in ambulatory care and oncology and would like to pursue a PGY-2 residency in those specialties. Apart from her passion for pharmacy, she enjoys dance, reading, and photography. Her family and friends are indispensable and nothing beats spending quality time with them.

Veronica Feltrin, PharmD, MHS, earned a Doctor of Pharmacy degree and Master of Health Science degree at Fairleigh Dickinson University School of Pharmacy in 2016 as member of the inaugural class. As a licensed pharmacist and PGY1 pharmacy practice resident at The Valley Hospital, she is ready to play a pivotal role as part of a healthcare team and an advocate for the pharmacy profession. Her areas of interest include critical care, emergency medicine, infectious disease, oncology and pediatrics. Upon completion of her residency at The Valley Hospital, Veronica plans on receiving certification as a Board Certified Pharmacotherapy Specialist. Aside from her love of pharmacy and patient care, Veronica enjoys swimming, running and competing in obstacle course races, such as Warrior Dash and Tough Mudder. As for her personal life, she has one younger brother, who serves in the United States Navy, and is a proud mother of her fur baby, a Siberian Husky, named Luna.

**Question:** What are the current recommendations for the administration of metformin in a patient who is to receive contrast media?

**Answer:** Until recently, the recommendations were that metformin should be discontinued prior to any intravascular contrast procedure and held for 48 hours, as stated in the manufacturer’s prescribing information. The justification for this recommendation is that contrast media procedures can decrease renal function, thereby decreasing the clearance of metformin, which can then accumulate and cause lactic acidosis. Symptoms of lactic acidosis include weakness, respiratory depression, somnolence, hypotension, and bradyarrhythmias. Lactic acidosis can be fatal in up to about 50% of cases.¹

In April 2016, the FDA revised these guidelines to expand the use of metformin in patients with reduced renal function. The FDA recommendations related to contrast media and metformin include:²

1. Rather than using serum creatinine levels to assess renal function, the FDA recommends using estimated glomerular filtration rate (eGFR).

2. Rather than discontinuing metformin for 48 hours when receiving contrast media for all patients, the FDA states that metformin only needs to be discontinued for patients receiving contrast media who have eGFR less than 60 mL/min/1.73m², in patients who have a history of liver disease, alcoholism, or heart failure; or in patients who will be receiving iodinated contrast via intra-arterial administration. After 48 hours have passed, patients can have their eGFR reevaluated to determine if their renal function is stable enough to start using metformin again.

Regardless of contrast media administration, metformin is contraindicated in patients with an eGFR below 30 mL/min/1.73m². For patients whose eGFR falls between 30 and 45 mL/minute/1.73m², starting metformin is not recommended. For patients whose eGFR falls between 30 and 45 mL/minute/1.73m² that are already on metformin, the benefits versus risks of continuing metformin should be assessed.

**References:**


There have been significant changes with opioid prescription medications within the period of a few years. The Food and Drug Administration (FDA) changed the schedule for hydrocodone combination products from CIII to CII, which took place in October 2014.¹ Later in the spring of 2015, the evidence-based Health and Human Services (HHS)-wide opioid initiative kicked off with three priorities:

- Reforming and educating on opioid prescribing practices
- Increasing and expanding the availability of naloxone
- Expanding access to medication-assisted treatment for opioid addiction.²

Additionally, over the past few years, individual states have passed their own legislation designed to expand access to naloxone.³ Abuse and addiction to opioids, particularly prescription opioids, are serious and challenging public health problems according to the HHS.¹ This article will describe the first priority of the HHS initiative to reshape opioid prescribing practices to reduce opioid use disorder/overdose and the evidence supporting the initiative.

The FDA, under the authority of the HHS, has mandated prescription drug labeling changes, specifically updated black box warnings and new safety and warning information.⁴ In March 2016 the FDA introduced new black box warnings for immediate release opioid medications. New safety warnings that will apply to all opioids and will appear in new medication prescribing information package inserts were also introduced in March to further educate on the risks of taking opioids.⁵ This represents the latest action from the evidence-based HHS opioid initiative through actions taken by the FDA.

**Black Box Warnings**

Prescription opioid medications have carried boxed-warnings for life-threatening respiratory depression and accidental ingestion.⁶ In September 2013 the FDA required the addition of two new boxed-warnings to be associated with extended-release and long-acting opioid medications. In March 2016 the FDA expanded these warnings to encompass immediate-release opioid medications as well. The two new warnings are:

- “Serious risk of misuse, abuse, addiction, overdose and death
- Chronic maternal use during pregnancy can result in neonatal opioid withdrawal syndrome (NOWS).”⁵

The addition of the boxed warning for misuse, abuse, addiction, overdose and death is based on data collected by the Centers for Disease Control and Prevention (CDC). The CDC reports that greater than 6 out of every 10 drug-overdose deaths involved an opioid, and the year 2014 recorded the most deaths from drug-overdose than any other year on record.⁷ In May 2012 at the National Institutes of Health workshop, a discussion on the efficacy of opioid medications used in non-cancer pain treatment highlighted concerns about the safety of opioids, especially at high doses, and their risk for misuse and abuse.⁸ This conversation was the beginning of the FDA’s eventual labeling change requirements.

In letters to opioid drug manufacturers, the FDA explained the second box warning for NOWS as a result of alarming data from several studies which document cases of NOWS occurring in newborns of mothers who were dispensed immediate-release opioids.⁹ In addition, between 2000 and 2009 there was an increase in the rates of newborn with NOWS.
from 1.20 to 3.39 occurrences per 1000 births respectively.10

New Safety Warnings

Significant labeling changes for all opioids with updates to product precautions and safety warnings were also put into effect as of March 2016 to include warnings on the following:

- "Risk of serotonin syndrome with concurrent use of antidepressants or migraine medicines"
- "Rare, serious adrenal gland insufficiency associated opioid use"
- "Warning of long-term opioid use being associated with androgen deficiency."

Evidence for two of the three new additional warnings came from the FDA Adverse Event Reporting System (FAERS) computer database. FDA searched the database between January 1, 1969 to June 12, 2013 and identified cases of serotonin syndrome in patients who were taking both opioids and serotonergic drugs. Forty-three events were identified, with the most common culprit opioid being fentanyl, followed by oxycodone, and methadone. The FDA does say that in all events serotonin syndrome did not occur in opioid use alone.

A FAERS search was also conducted to identify adverse event reports of adrenal insufficiency in patients on opioids between the time periods of January 1, 1969 to February 5, 2014. Thirty-seven cases of adrenal insufficiency were found, 27 of them reported opioid monotherapy and the other 10 reported the use of more than one opioid concurrently. Again, fentanyl was at the top of the list, as well as oxycodone, buprenorphine and hydromorphone.

For the third warning of androgen deficiency, the FDA conducted a search of literature regarding opioids being connected with androgen deficiency. Of the 21 references provided, four were published in the 1980’s, the earliest of which is from a 1983 issue of Neuroendocrinology. The remaining 17 references are from more recent publications from a wide variety of journals through the early 2000’s to 2011.11

Expect more opioid updates and changes in labeling in the coming months as the FDA has already announced they are reviewing the literature and searching for evidence of serious outcomes related to drug-drug interactions of opioids taken concurrently with benzodiazepines.5 Additionally, opioid manufactures have ongoing post-marketing studies and clinical trials per the request and direction of the FDA, which have tentative study completion dates of January 2018, which could lead to additional action taking place.8

References