Cariprazine (Vraylar®)

Cariprazine is an oral capsule indicated in the treatment of schizophrenia and acute treatment of manic or mixed episodes associated with bipolar I disorder. It is an atypical antipsychotic and a dopamine D3 and D2 receptor partial agonist, with preferential binding to D3 receptors. This is thought to be beneficial in treating both positive and negative symptoms, mood, and cognitive impairment in schizophrenia. The common adverse effects, warning, and precautions are similar to other atypical antipsychotics and include metabolic changes, extrapyramidal symptoms, and has drug interactions with strong CYP3A4 inhibitors and inducers. Other atypical antipsychotics on formulary are olanzapine, risperidone, quetiapine, and aripiprazole.

Umeclidinium and vilanterol dry powder inhaler (Anoro Ellipta®)

Umeclidinium/vilanterol is indicated in the treatment of COPD, including chronic bronchitis and/or emphysema. It is a once daily maintenance medication available as a combination LAMA/LABA which is the recommendation and standard of care for COPD treatment as per the 2017 GOLD Guidelines. It is contraindicated in patients who have severe hypersensitivity to milk proteins and may interact with strong CYP3A4 inhibitors. Common adverse effects include pharyngitis, sinusitis, and lower respiratory tract infection. This is the only formulary combination LAMA/LABA inhalation device at TVH.

Edaravone (Radicava®)

Edaravone is one of the few drugs that have been approved for the treatment of amyotrophic lateral sclerosis (ALS). It is a free radical scavenger, however, the mechanism of how it treats ALS is unknown. Edaravone is an intravenous infusion given over 60 minutes according to a cycle treatment schedule, which is restricted to Luckow Pavilion.

Intrapleural alteplase + dornase alfa (TPA/Activase® and DNase/Pulmozyme®)

The off-label intrapleural use of these two drugs has been approved by the Pharmacy and Therapeutics Committee at The Valley Hospital for patients with pleural infection/effusion. Alteplase is a fibrinolytic that is typically administered intravenously, but has been shown to help break down fibrin in the pleural space when administered intrapleurally via chest tube. Dornase alfa is a mucolytic that is typically administered via nebulizer in cystic fibrosis patients. When given intrapleurally following alteplase administration, these medications have been shown to synergistically decrease pleural fluid viscosity and aid with drainage in the setting of pleural infection. This off-label intrapleural combination is restricted to pulmonology and thoracic surgery.

Smoflipid®: A new lipid emulsion for parenteral nutrition

by Jason Voss, BS, MBA, PharmD Candidate 2018

Parenteral nutrition (PN) is administered intravenously when a patient cannot achieve adequate nutrition orally or enterally. Typically, PN provides the three macronutrients: protein (via amino acid solutions), carbohydrates (via dextrose solution) and fats (via soybean oil emulsion lipids). The brand name products of soybean lipid emulsions available in the United States are Intralipid® (Fresenius Kabi/Baxter Pharmaceuticals) and Nutrallipid® (IBraun Medical, Inc.). At TVH, Intralipid® is on formulary.

Smoflipid® is a new intravenous lipid product that was approved by the FDA in 2016 for use in adults as an intravenous source of calories and essential fatty acids for parenteral nutrition. Manufactured by Fresenius Kabi, Smoflipid® is the first and only four-oil lipid emulsion in the United States, as it combines soybean oil, medium-chain triglycerides (MCTs), olive oil, and fish oil. At TVH, Smoflipid® is restricted to the NICU.

Because Smoflipid combines four different oils, the lipid emulsion conveys the unique benefits of each oil:

- **Soybean oil** provides essential fatty acids
- **Medium-chain triglycerides** provide a readily usable energy source
- **Olive oil** provides omega-9, monounsaturated fatty acids, and some essential fatty acids
- **Fish oil** provides EPA and DHA, which are conditionally essential fatty acids, and omega-3.

Intralipid®, also manufactured by Fresenius Kabi, uses only soybean oil to provide fatty acids, and is therefore more pro-inflammatory. Smoflipid®, which is comprised of 30% soybean oil, may have fewer pro-inflammatory properties.

Intralipid® and Smoflipid® share many common considerations, some of which are that both products:

- require administration with a 1.2-micron filter
- may be infused via central or peripheral vein
- provide essential fatty acids
- have a Black Box Warning for “death in preterm infants”

For differences between the lipid emulsions, please see Table 1. Smoflipid® has been widely studied in neonates, pediatrics, children and adolescents. For dosing information, please refer to the package inserts or your pharmacist.
Question: Can gabapentin be used for management of acute pain?

Answer: Gabapentin is an antiepileptic drug used as adjunctive therapy in the treatment of partial onset seizures in adults and pediatric patients three years and older with epilepsy. It is also indicated for the management of postherpetic neuralgia in adults and pediatric patients three years and older with shingles. While commonly used for chronic neuropathic pain, studies have found that gabapentin may also be effective in management of acute pain and reducing opioid requirements in the postoperative setting.

Gabapentin (1-aminomethyl-cyclohexanecarboxylic acid) is a structural analogue of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) but has no effect on GABA binding, uptake, or metabolism. While the exact mechanism is unknown, the analgesic effect of gabapentin is thought to be from inhibition of voltage-gated calcium channels, which are normally upregulated in nerve injury due to increased pain signal processing. By binding to these calcium channels in membranes of the brain, gabapentin reduces neuronal calcium influx leading to decreased AMPA receptor activation and norepinephrine release, and subsequent suppression of excitatory neurotransmitters. Since surgical intervention is likely to result in nerve injury, this also explains why gabapentin could be effective in managing acute postoperative pain.

References:

Gabapentin is generally well-tolerated with most common side effects being dizziness and somnolence. The efficacy of gabapentin in reducing post-operative pain and opioid consumption as demonstrated in several clinical studies may warrant further investigation of gabapentin use in this setting.
Statins in patients with rhabdomyolysis: to continue or not to continue?
Brianne Traub, PharmD
PGY-1 Resident Pharmacist

Rhabdomyolysis is caused by injury to the muscles which lead to depletion of ATP within the myocytes. When this happens, there is an imbalance between sodium and calcium which results in an increase in calcium within the cell. This influx of calcium causes contraction of muscles and ultimately, the myocyte breaks down. Lysis of the cell releases electrolytes, enzymes such as creatinine kinase, myoglobin and uric acid into the blood stream which contributes to the renal damage (brown urine) that is associated with rhabdomyolysis.¹

Statins inhibit HMG-coenzyme A reductase which has been associated with myalgia and in some cases rhabdomyolysis. This class of medication works by inhibiting the conversion of HMG-CoA to mevalonic acid, however, the exact mechanism of how statins contribute to myositis and rhabdomyolysis is not clear. An article by Huerta-Alardin, et al. reviewed drug-induced rhabdomyolysis and found that it either occurs within 2-3 weeks after therapy initiation, or months to years later when a precipitating event occurs such as illness, fall, or strenuous exercise.² The pravastatin package insert warns that “Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.”³ Therapy can be restarted following improvement in CPK levels.

Statins have been attributed to reduced mortality and cardiovascular risk.⁴ There is often concern over whether to discontinue statin therapy after patients experience adverse events due to those beneficial effects. A study by Zhang, et al. found that of patients who continued receiving statin therapy after an adverse event saw a 10-20% lower incidence of both cardiovascular events and death from any cause.⁴ There have also been studies to determine the benefit of statin therapy in sepsis despite it being a possible cause for rhabdomyolysis. The ASEPSIS trial reported that administering atorvastatin reduced clinical progression of sepsis however, it did not improve mortality.⁵

Overall, it is important to examine risk versus benefit of statin discontinuation in patients who are diagnosed with rhabdomyolysis with an increase in CPK.

References:
References:


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Table 1. Contrasting Intralipid® and Smoflipid®

<table>
<thead>
<tr>
<th></th>
<th>Intralipid®¹</th>
<th>Smoflipid®³</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA indications</strong></td>
<td>All patients needing PN</td>
<td>Adults needing PN</td>
</tr>
<tr>
<td><strong>Oil Sources</strong></td>
<td>100% Soybean Oil</td>
<td>30% Soybean Oil 30% Medium-Chain Triglycerides</td>
</tr>
<tr>
<td><strong>Allergens</strong></td>
<td>Soybean Egg</td>
<td>Soybean Egg Fish Peanut</td>
</tr>
<tr>
<td><strong>Ratio of</strong></td>
<td>7:1</td>
<td>2.5:1</td>
</tr>
<tr>
<td><strong>(pro-inflammatory) Omega-6 to</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>(less pro-inflammatory) Omega-3</strong>⁴</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TVH formulary availability</strong></td>
<td>Not restricted</td>
<td>Restricted to NICU</td>
</tr>
</tbody>
</table>

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**References:**


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TVH Pharmacy Focus – Winter 2017 - 2018 - Page 4 of 6