PATIENT INFORMATION:
Gonorrhea

Gonorrhea is an infection caused by the bacteria Neisseria gonorrhoeae (N. gonorrhoeae). Around 700,000 new cases are diagnosed each year in the United States. Gonorrhea is the second most common sexually transmitted disease (STD) that is caused by bacteria. Gonorrhea is transmitted from person to person by genital, oral, or anal sex. Infants can get gonorrhea from their infected mother during birth.

**Symptoms of Gonorrhea**

**NOTE: symptoms do not always occur soon enough to prevent transmission to another person.**

In Men:
- Infection of the penis can lead to penile discharge, abnormal urination, and pain and burning during urination.
- Infection of the anus can cause rectal discharge, bleeding, and pain.
- Infection of the mouth can cause fever, sore throat, and swelling of the lymph glands in the neck.

In Women:
- Symptoms may not be present until other complications like pelvic inflammatory disease (PID) occur.
- Abnormal discharge from the vagina.
- Lower abdominal pain.
- Pain during intercourse and urination.
- Vaginal burning and itching.
- Inability to become pregnant or having a premature birth.

**Complications of Gonorrhea**
- Chlamydia and other STDs.
- PID causes scarring of the female reproductive system leading to infertility or pregnancies with complications.
- Pregnant women can spread the infection to the infant at birth. Infants born to infected mothers are at risk of eye infections that can result in blindness.
- Gonorrhea can spread to other parts of the body causing arthritis and conjunctivitis.

**Diagnosis of Gonorrhea**
Samples of discharge from the urethra, cervix, throat, or rectum of a person with suspected gonorrhea infection are tested for the presence of bacteria. Testing of urine samples are performed if no discharge is available.

Individuals at higher risks of infection who need testing include those who have:
- A history of previous gonorrhea infection
- Another type of STD
- A new or numerous sex partners
- Unprotected sex
- A history of exchanging sex for money

People who test positive for gonorrhea should also be tested for syphilis, HIV, and chlamydia.

**Prevention of Gonorrhea**
- Use barrier protection (e.g. condoms) during intercourse.
- Abstain from sexual intercourse.
- Maintain a monogamous relationship where both sex partners only have intercourse with each other.

**Treatment of Gonorrhea**
Gonorrhea is treated and cured with antibiotics. Treatment should start as soon as possible to prevent damage to reproductive organs. Persons infected with gonorrhea are also at high risk for chlamydia infection. All persons infected with gonorrhea receive treatment for chlamydia. Sex partners of people diagnosed with gonorrhea should also be treated. Sexual contact should be avoided during treatment for gonorrhea and until all gonorrhea symptoms are gone.

**Follow-up after Gonorrhea Treatment**
If a person diagnosed with gonorrhea is treated with the recommended antibiotics and symptoms are gone, no further follow-up is needed. But if symptoms continue after treatment, the person should be tested for resistant gonorrhea.
- Most treatment failures result from reinfection because the sex partner was not treated.

By Chris Koerner, PharmD Candidate

References on Page 5
Vorapaxar is a new antiplatelet medication approved for combination therapy with clopidogrel and/or aspirin for the secondary prevention of myocardial infarction (MI) or peripheral artery disease (PAD). Approved May 8, 2014, vorapaxar is the first of a new class of medications called protease activated receptor 1 (PAR-1) antagonists. PAR-1 antagonists block thrombin from activating platelet aggregation and therefore reduce the risk of thrombotic cardiovascular events. Clinical trials suggest a modest reduction in the risk of MI, stroke, and cardiovascular death in patients with a history of MI or PAD when vorapaxar is used in combination with clopidogrel or aspirin. However, clinical trials also discovered a significant increase in moderate to severe bleeding including intracranial hemorrhage (ICH).\(^1,2\)

Vorapaxar has a long elimination half-life of 7-11 days, and steady state concentrations are reached in 21 days.\(^{1}\) After discontinuation, vorapaxar continues to affect platelets for up to 4 weeks. No reversal agent is currently available in the case of bleeding to stop the effects of vorapaxar.\(^1\)

Approval of vorapaxar was based on two large randomized, placebo-controlled clinical trials (TRACER and TRA2P). The TRACER trial had negative results and reported an increased risk of ICH with vorapaxar. Therefore, patients with a history of stroke were withdrawn in year 2 of the TRA2P trial.\(^3,4\)

**TRACER Trial**

Vorapaxar added to standard therapy did not significantly reduce cardiovascular events, while significantly increasing bleeding risk.\(^3\) This study randomized 12,944 patients to either vorapaxar or placebo treatment added to standard therapy with aspirin and/or clopidogrel. A 40 mg loading dose followed by a daily 2.5 mg maintenance dose was administered to the vorapaxar group. All patients had a history of an ischemic event within 24 hours of hospitalization. Additionally, patients had one of the following: age >55 years, previous MI, PCI, coronary artery bypass grafting (CABG), diabetes, or PAD.\(^3\)

Vorapaxar and placebo treatment resulted in similar rates of the primary endpoint (death from cardiovascular causes, MI, stroke, recurrent ischemia, or urgent coronary revascularization; 18.5% vs. 19.9%, respectively; HR 0.92; 95% CI, 0.85 to 1.01).\(^3\) Risk of moderate or severe bleeding based on the GUSTO definitions was significantly increased in the vorapaxar group (7.2% vs. 5.2%, respectively; HR 1.35; 95% CI, 1.16 to 1.58). Patients with a history of stroke have an increased risk of ICH, which may have skewed the safety results of this trial.\(^3\)

The rate of moderate or severe GUSTO bleeding was significantly higher in the vorapaxar group (4.2% vs. 2.5%; HR 1.66; 95% CI, 1.43 to 1.93). As noted earlier, patients with a history of stroke were removed from the study after the results from the TRACER trial were published. The risk of bleeding with vorapaxar was higher in patients with a history of stroke (0.8% per year) than in patients without a history of stroke (0.2% per year), so the risk of bleeding should be evaluated prior to starting patients on vorapaxar. Differences in the standard therapy in the patients may have confounded the results and may affect the generalizability of the results. Most patients with a history of MI were on both aspirin and clopidogrel, while clopidogrel was used less often in patients with a history of stroke or PAD.\(^4\)

The risk of moderate to severe bleeding was significantly higher in both clinical studies with vorapaxar compared to placebo. An elevated risk of ICH in patients with a history of stroke was also noted in the studies. Therefore, vorapaxar is not recommended in patients with a history of stroke.\(^1,3,4\)

Vorapaxar is available in 2.08 mg tablets (equivalent to 2.5 mg vorapaxar sulfate) and can be taken with or without food once daily. Vorapaxar is not recommended as monotherapy and should be administered in combination with aspirin and/or clopidogrel. Concomitant use of strong CYP3A4 inducers such as ketoconazole, itraconazole, and erythromycin may increase plasma concentrations of vorapaxar.

---

**Non-Hemorrhagic Adverse Events in TRACER and TRA2P**

<table>
<thead>
<tr>
<th>Event</th>
<th>Vorapaxar (n=19,632)</th>
<th>Placebo (n=19,607)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>982 (5.0%)</td>
<td>783 (4.0%)</td>
</tr>
<tr>
<td>Depression</td>
<td>477 (2.4%)</td>
<td>4.5 (2.1%)</td>
</tr>
<tr>
<td>Rashes, Eruptions, and Exanthemas</td>
<td>439 (2.2%)</td>
<td>395 (2.0%)</td>
</tr>
</tbody>
</table>

Continued on Page 5
**Belsomra® (suvorexant)**

Suvorexant, approved August 13, 2014, is a novel sleeping medication that does not have the same physical dependence issues of traditional insomnia medications such as benzodiazepines.\(^1\),\(^2\) Suvorexant is an orexin inhibitor. Orexin promotes wakefulness.\(^3\) Indicated for use in insomnia, especially difficulties falling asleep or staying asleep, suvorexant is a safe and effective alternative treatment for insomnia.\(^4\)

Suvorexant’s safety and efficacy was confirmed in a one-year, placebo-controlled trial.\(^2\) Seven hundred eighty-one patients were randomly assigned into three groups: 40 mg suvorexant for <65 years old, 30 mg for ≥65 years old, or placebo. Elderly patients received lower doses of suvorexant because of plasma exposure differences seen in earlier clinical trials. After one year, participants either continued suvorexant or switched to placebo for two additional months. Efficacy was assessed using an electronic sleep diary that patients updated every morning. The diary consisted of several subjective measures, such as total sleep time (sTST), time to sleep onset (sTSO), wake after sleep onset, number of awakenings, sleep quality, and how refreshing the sleep was. Clinicians measured efficacy using the clinician and patient global impression of severity. Over the first month, the suvorexant group had significant improvements in sTST (40.9 vs. 17.5 min) and sTSO (-19.2 vs. -10.3 min) compared to placebo.\(^2\) These improvements continued throughout the first year. Subjective measurements of sleep were also improved with suvorexant compared to placebo. These effects diminished when suvorexant was discontinued; however, discontinuation was well tolerated with no significant adverse events between groups. Study limitations include the small sample size, the short duration (no long-term effects known), and lack of objective measurement of quality of life or daytime functioning. The study took place at 106 different centers across America, Australia, Europe, and South Africa so the data should be generalizable.\(^2\)

Somnolence is the most common adverse event with suvorexant (7%) and may be more prevalent in women.\(^4\) Somnolence occurs more frequently in the first three months and was the most common reason for dropouts in clinical trials. Headache, upper respiratory infection, dry mouth, abnormal dreams, cough, and dizziness have also been reported (≥ 2%). Serious events are listed in the table below. Cataplexy and deaths have not been reported.\(^4\)

**Precautions with suvorexant use**\(^4\)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Precaution</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS depression</td>
<td>Can affect daytime performance, such as driving.</td>
</tr>
<tr>
<td>Abnormal thinking and behavior</td>
<td>Amnesia, anxiety, hallucinations, sleep-driving, and other complex behaviors have been associated with hypnotic use.</td>
</tr>
<tr>
<td>Worsening of depression/suicide ideation</td>
<td>Dose-dependent increase in suicidal ideation in patients taking suvorexant was noted on patient surveys. Patients should be evaluated immediately if suicidal thoughts or signs appear.</td>
</tr>
<tr>
<td>Compromised respiratory function</td>
<td>Suvorexant has not been studied in severe COPD or severe obstructive sleep apnea.</td>
</tr>
<tr>
<td>Sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy-like symptoms</td>
<td>Inability to move for several minutes during the sleep-wake transition and auditory/visual hallucinations of vivid and disturbing perceptions can occur. Increasing doses can lead to mild cataplexy of leg weakness lasting from seconds to a few minutes, both at night and during the day, and may be associated with a trigger.</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Suvorexant is pregnancy category C.</td>
</tr>
<tr>
<td>Hepatic impairment</td>
<td>Mild or moderate hepatic dysfunction does not require a dose adjustment. Suvorexant use in severe hepatic impairment has not been studied and is not recommended for use in this population.</td>
</tr>
<tr>
<td>Narcolepsy</td>
<td>Suvorexant is contraindicated in patients with narcolepsy.</td>
</tr>
</tbody>
</table>

Suvorexant should be used at the lowest effective dose.\(^4\) The recommended dosage is 10 mg 30 minutes before bed with at least 7 hours before wake up time. If lowest dose is tolerable, but ineffective, then an increase in dose can occur with 20 mg being the max dose. Never take more than one in a night. Food may slow the effects of suvorexant.\(^4\)

Suvorexant does not seem to possess the same physical dependence problems of other insomnia medications, and may be an advantageous alternative for treatment of insomnia.\(^2\),\(^3\) Clinical trials have shown suvorexant to be safe and efficacious for patients with insomnia. Most adverse events were mild, but more serious events have been reported.\(^2\),\(^4\)

*By Caelon Vecchio-Miller, PharmD Candidate*

*References on Page 5*
Head lice, also called pediculosis, are insects that live on people’s heads. Live lice or unhatched eggs, called nits, can be found close to the scalp and on eyebrows or eyelashes. They are easily spread through close contact; however, contact with items such as hats, hairbrushes, or bedding may also spread lice. Head lice infestations are most common among school age children, yet anyone can be at risk. Despite what people commonly believe, lack of personal hygiene and cleanliness does not increase a person’s risk of becoming infested. A diagnosis of a head lice infestation is made when a live louse is identified in a person’s hair or on their scalp.

Symptoms
Itching of the scalp is the most common symptom. Difficulty sleeping is also common since lice are most active at night. However, a person with lice might not experience any symptoms at all.

Prevention
- It is important to avoid head to head contact with others at home, school, or elsewhere.
- Do not share items such as hats, hair brushes, hair clips or other items.
- Items such as hair brushes and clips may be disinfected by leaving them in boiling water for 5-10 minutes.
- Avoid bedding, pillows, or furniture that has been in contact with a person infested with head lice.
- Machine wash and dry items that have been recently used by a person infested with head lice.

Treatment
Both prescription and over-the-counter (OTC) medications are available to treat lice. If live lice are still seen after a full treatment with OTC medicines, it may be necessary to contact your healthcare provider for other options.

Permethrin
- Permethrin is one of the drugs of choice used to treat lice.
- After normal shampooing, the product is applied to towel-dried hair and left on for 10 minutes before rinsing off.
- Although permethrin kills active lice, it does not kill unhatched eggs.
- A second application is recommended after 7 to 10 days to ensure complete removal of lice.
- Permethrin is not recommended for use in children under the age of 2 months.
- Permethrin is available OTC and is the active ingredient in the product, Nix®.

Pyrethrins
- Pyrethrins are another drug used to treat lice.
- The application of this product is similar to Nix®; however, they are available in shampoo or mousse formulations.
- Pyrethrins are also only able to kill live lice, not lice eggs.
- A second treatment is recommended in 7 to 10 days to ensure complete removal of lice.
- Products containing pyrethrins should not be used by people with allergies to chrysanthemums.
- The use of pyrethrins is not recommended for patients under the age of 2 years.
- Pyrethrins is available OTC in products such as RID®.

Wet-combing
- Wet-combing is another method to remove lice and might be a good option for very young children or for people who don’t want to use insecticides.
- Wet-combing is much more tedious and time consuming than use of medicated products.
- A fine-toothed comb, called a “nit comb”, is used to comb through the hair to remove the lice and eggs.
- The hair must be wet in order to slow down the lice.
- This process must be repeated multiple times per week for several weeks.

REFERENCES:

By Taryn Moore, PharmD Candidate


**Vorapaxar (from page 2)**

Vorapaxar or inhibitors is contraindicated due to vorapaxar’s elimination through CYP3A4 and CYP2J2. Vorapaxar should be avoided in patients with a history of stroke, transient ischemic attack (TIA), ICH, and patients with active bleeding. Patients with renal or hepatic insufficiencies do not require dosage adjustments according to current knowledge. Dose adjustments based on age or weight are also not supported.1,2

Recently approved, vorapaxar is a PAR-1 antagonist indicated for the prevention of thrombotic events in patients with a history of MI or PAD. Vorapaxar therapy has shown only modest improvement in composite cardiovascular outcomes. Due to significant increase in bleeding risk with minimal improvement in outcomes, risks and benefits should be weighed before initiating vorapaxar.

**REFERENCES:**


MIBG in Heart Failure

AdreView® (Iobenguane I-123; also known as metaiodobenzylguanidine I-123 [MIBG I-123]) is a radiopharmaceutical approved in 2008 for diagnostic imaging of pheochromocytoma and neuroblastoma. In 2013, MIBG I-123 received approval for a new indication—the assessment of mortality risk in patients with congestive heart failure (CHF), a left ventricular ejection fraction <35%, and a New York Heart Association (NYHA) class II or III.1

MIBG is structurally similar to norepinephrine (NE) and undergoes similar uptake by sympathetically innervated tissue. MIBG is carried by NE transporters and accumulates in adrenergically innervated tissue such as the adrenal medulla, liver, spleen, lungs, heart, neuronal crest tumors, and salivary glands. Unlike NE, MIBG has little to no pharmacodynamic effects. Iodine 123 in MIBG I-123 emits gamma radiation observable with gamma-scintigraphy and allows imaging.2

To compensate for a decrease in myocardial function in CHF, the cardiac sympathetic nervous system increases the release of NE. Prolongation of increased sympathetic stimulation of myocardium results in down-regulation of myocardial β-adrenergic receptors. MIBG I-123 allows the visualization and quantification of myocardial β-adrenergic innervation. Quantification and visualization is expressed as the heart to mediastinum (H/M) ratio and is used for risk assessment. An H/M ratio >1.6 is prognostic of low 1- and 2-year mortality risk and <1.6 is prognostic for high 1- and 2-year mortality risk.1,2

MIBG dosing is dependent on age and weight. For patients <16 years of age and weighing <70 kg, the dose should be determined from the weight-based table in the package insert (see table). For cardiac imaging, anterior planar scintigraphy of the chest should be performed 4 hours after drug administration.3

After IV administration, MIBG I-123 rapidly clears from the blood stream and accumulates in adrenergically innervated tissue. Four days after administration, 70-90% of the drug is recovered unchanged in the urine. A metabolite known as Miodohippuric acid and free radioiodine are also recovered in the urine. Renal impairment may decrease elimination of the drug and increase exposure time to radiation, which may also impair the quality of the image. Assessment of renal function on all patients prior to MIBG I-123 administration is recommended. Safety and efficacy dosing in patients with altered renal function are not established.3

Free radioiodine has the potential for uptake by the thyroid gland, resulting in unwanted nuclear exposure.3 Patients scheduled for MIBG I-123 dosing need to be pretreated with potassium iodide oral solution, Lugol’s solution, or potassium perchlorate at least 1 hour prior to MIBG administration.1

MIBG imaging had the greatest benefit for predicting mortality in patients with CHF, according to a meta-analysis of six studies. The studies included a total of 636 patients and used the H/M ratio. Most (78%) of the patients were male, and the majority had a decreased LVEF (range 7-47%, mean 31.1±12.5%). The patients were followed for 60 months after MIBG diagnosis. Lower H/M ratios and LVEF were associated with higher risk of events for mortality, non-fatal cardiac events, and cardiac transplants, but not dysrhythmias. Additionally, higher NYHA classifications were associated with a higher risk for negative outcomes. Limitations of the meta-analysis include the exclusion of Japanese studies due to the higher H/M values reported in those studies which indicate a difference in measurement techniques. Also, the ADMIRE-HF study were not available when the meta-analysis was performed, but it is likely that the short follow-up in that study would have skewed the meta-analysis results.2

MIBG is effective for predicting negative outcomes in heart failure patients with low LVEF and NYHA classes II and III. MIBG imaging resulting in an H/M ratio <1.6 is associated with poor 1-2 year outcomes.

By Chris Koerner, PharmD Candidate

REFERENCES:

Dosing of MIBG-1231

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 16 years</td>
<td>None clarified</td>
<td>10 mCi</td>
</tr>
<tr>
<td>&lt; 16 years</td>
<td>≥ 70 kg</td>
<td>10 mCi</td>
</tr>
<tr>
<td>&lt; 16 years</td>
<td>&lt; 70 kg</td>
<td>See package insert for recommended dose</td>
</tr>
</tbody>
</table>
PATIENT INFORMATION:
Gout

Gout (sometimes called gouty arthritis) is a form of arthritis that typically affects a single joint in sudden flares. High levels of uric acid can accumulate in the joints and crystallize, causing gout’s painful symptoms. However, not everyone with high uric acid levels develop gout.

Abrupt onset of intense pain, swelling, or redness of the joints occurs at the onset of a gout flare. The big toe is one of the most common joints to be affected by gout attacks. Gout pain can be strong enough to wake you up in the middle of the night with the sensation that your big toe is on fire. Gout flare ups may be separated by long periods without symptoms. However, people are more likely to have a second gout attack within 6-12 months following the first episode.

Gout symptoms:
Gout symptoms present suddenly without warning.
- Severe joint pain
- Typically greatest in the first 12-24 hours
- Resolves within a couple weeks
- Usually in the large toe
- Swelling, redness, and warmth
- Sensitivity to the lightest touch
- Lingering pain
- Gout pain can last from a few days to a few weeks
- Lack of mobility in affected joint
- Lumps caused by uric acid crystals called tophi can form in the elbows, ears, or finger joints

When should you see your healthcare provider?
- Sudden onset of extreme pain in one joint
- Inflamed joints with red skin that are highly sensitive to touch
- High uric acid levels may lead to joint damage even after painful symptoms have disappeared. Your healthcare provider should be seen even after symptoms are gone.

How is gout diagnosed?
- Analysis of joint fluid for uric acid crystals
- Physical exam, medical and family history
- Uric acid levels in the blood or urine

How is gout treated?

Short term treatment
- Rest and ice the joint
- Medications to reduce pain and swelling available by prescription include:
  - Steroids
  - Colchicine
  - Nonsteroidal anti-inflammatory drugs (NSAIDS) *except aspirin
  - Ibuprofen and naproxen are available over-the-counter

Long term treatment/prevention
- Weight loss
- Limit alcohol
- Limit red meat and seafood intake
- Re-evaluate current medications that may increase uric acid levels
- Start medications that can lower uric acid levels

References on Page 5

By Bryan Cooper, PharmD Candidate

Factors you are born with
- Male gender
- Family history
- Genetic conditions

Factors you may be able to change
- Obesity
- Regular to heavy alcohol use
- Diets high in purines from meats and seafood
- Dehydration
- Extreme calorie restriction

Medications that increase uric acid levels
- Daily aspirin or niacin use
- Diuretic medicines (water pills)
- Chemotherapy
- Medicines that decrease immune activity

What are the risk factors for gout?