PATIENT INFORMATION:
RSV (Respiratory Syncytial Virus)—An Overview

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<th>What is RSV?</th>
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<td>♦ A respiratory virus which affects everyone</td>
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<td>♦ Can cause upper and lower respiratory tract infections</td>
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<td>♦ Usually most severe in children under 2 years old</td>
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<td>♦ Symptoms occur within 4-6 days of infection with the virus</td>
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<td>♦ Diagnosed with a mucus sample swab and antigen detection test</td>
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<th>How is RSV transmitted?</th>
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<td>♦ Direct or indirect contact with nasal or oral secretions of infected patients</td>
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<td>♦ Patients can spread the virus to other people for 3-8 days after infection</td>
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<td>♦ The virus can live on hard surfaces for many hours</td>
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<th>What are the symptoms of RSV?</th>
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<td>♦ Runny nose, sneezing</td>
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<td>♦ Cough, possibly wheezing</td>
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<td>♦ Fever</td>
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<td>♦ Decreased appetite</td>
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<td>♦ Very young children may also have Irritability</td>
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<td>♦ Decreased activity</td>
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<td>♦ Breathing difficulties</td>
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<th>What is the treatment for RSV?</th>
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<td>♦ Fluids like water and electrolyte-replacing fluids</td>
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<td>♦ Tylenol® (acetaminophen) or Advil® (ibuprofen) for fever</td>
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<td>♦ Blowing nose and using a bulb syringe to remove nasal secretions</td>
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<td>♦ Rest</td>
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<td>♦ Medications to open the lungs (bronchodilators) may help</td>
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<td>♦ Supplemental oxygen is necessary in severe cases</td>
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<td>♦ Prevention is used in high-risk infants with Synagis® (palivizumab)</td>
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<th>REFERENCES:</th>
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From: http://www.cdc.gov/rsv/index.html

♦ 25-40 out of 100 patients infected with RSV will get bronchiolitis or pneumonia
♦ 5-20 out of 1000 patients infected with RSV will need hospitalization

*By Amy Eliason, PharmD Candidate*
Currently, 3 sodium glucose co-transporter 2 (SGLT2) inhibitors are approved for the treatment of type 2 diabetes as adjunct therapy to diet and exercise—canagliflozin (Invokana™), dapagliflozin (Farxiga®), and empagliflozin (Jardiance®). Inhibition of SGLT2 in the proximal tubules of the kidneys reduces the renal reabsorption of glucose, increases the urinary excretion of filtered glucose, and therefore, decreases plasma glucose concentrations.1-4 The Table below compares the SGLT2 inhibitors.

The American Association of Clinical Endocrinologists (AACE) considers SGLT2 inhibitors as fourth-line monotherapy agents. AACE recommends using metformin plus GLP-1 receptor agonists, DPP4 inhibitors, or thiazolidinedione first, then trying an SGLT2 inhibitor with metformin.5 The American Diabetes Association (ADA) also recommends using SGLT2 inhibitors after lifestyle medication and metformin.6 The ADA does not specify which order agents should used in beyond metformin as first-line.6

**Advantages of SGLT2 Inhibitors**1-10

- Novel mechanism of action
- 0.4-1.0% ↓ in HbA1c
- Once daily, oral administration
- Low incidence of hypoglycemia
- ↓ in body weight

**Disadvantages of SGLT2 Inhibitors**1-10

- Cannot use in patients with renal insufficiency
- Cannot use in patients who are hypovolemic
- Cannot use in type 1 diabetes
- Hypoglycemia is more common when used as add-on therapy
- Use with caution in patients with hypotension
- More expensive than other options

**Canagliflozin**

Canagliflozin is effective as monotherapy or in combination with metformin, sulfonylurea, insulin, or pioglitazone.1,7 Canagliflozin significantly decreased HbA1c and body weight (-1.8 to -4.7 kg) when used alone or in combination with other anti-diabetic agents.1,7 However, mean LDL-C increased in the canagliflozin groups. The most common adverse events included UTI, genital mycotic infection, and increased urination.5

**Dapagliflozin**

Dapagliflozin is effective as monotherapy and in combination with other anti-diabetic agents.2,8 Dapagliflozin reduced mean HbA1c and body weight from baseline. The most common adverse events were UTI, genital mycotic infection, and nasopharyngitis.5,8

A possible increase in bladder cancer risk has been noted with dapagliflozin.2,8 Ten patients in 22 clinical trials (n=6045) were diagnosed with bladder cancer after treatment with dapagliflozin; only one patient in the placebo groups (n=3512) had bladder cancer. Therefore, dapagliflozin should not be used in patients with active bladder cancer.2,8

**Empagliflozin**

Empagliflozin is effective as monotherapy and in combination with other anti-diabetic agents.3,9 Empagliflozin reduced both HbA1c and body weight.9 Patients on empagliflozin also experienced a decrease in blood pressure. Nasopharyngitis, UTI, genital mycotic infections, and dyslipidemia were the most common. One patient taking 10 mg of empagliflozin had a cerebrovascular accident that was deemed related to the drug.9

**By Liz Wolsfelt, PharmD Candidate**

**Comparison of the SGLT2 Inhibitors**

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<tr>
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<th>Efficacy</th>
<th>Dosing</th>
<th>Adverse Events</th>
<th>Comments</th>
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<tr>
<td>Canagliflozin (Invokana™)1,7</td>
<td>↓ HbA1c 0.6-1.0%</td>
<td>Initiate at 100 mg once daily; may increase to 300 mg once daily</td>
<td>UTI, genital mycotic infections, URTI, increased urination, constipation, nausea, dyslipidemia</td>
<td>• Do not use in patients with CrCl &lt; 45 mL/min</td>
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<tr>
<td>Dapagliflozin (Farxiga®)2,8</td>
<td>↓ HbA1c 0.5-0.9%</td>
<td>Initiate at 5 mg once daily; may increase to 10 mg once daily</td>
<td>UTI, genital mycotic infections, nasopharyngitis, increased urination, nausea, dyslipidemia, back pain, constipation</td>
<td>• May be associated with increased risk of bladder cancer</td>
</tr>
<tr>
<td>Empagliflozin (Jardiance®)3,9</td>
<td>↓ HbA1c 0.4-0.8%</td>
<td>Initiate at 10 mg once daily; may increase to 25 mg once daily</td>
<td>UTI, genital mycotic infections, URTI, increased urination, arthralgia, nausea, dyslipidemia</td>
<td>• Possible increased risk of stroke</td>
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HbA1c=hemoglobin A1c; CrCl=creatinine clearance; URTI=upper respiratory tract infection; UTI=urinary tract infection

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Viekira Pak® is a new drug combination package (ombitasvir/paritaprevir/ritonavir 12.5/75/50 mg + dasabuvir 250 mg) for the treatment of chronic hepatitis C genotype 1. It can be given with or without ribavirin and is used for patients with and without cirrhosis. Viekira Pak® offers an advantage over interferon-containing regimens because it has fewer reported side effects. Also, compliance should be increased with the packaging of Viekira Pak® (see picture below).1

A sustained virologic response (SVR) occurred in over 90% of genotype 1a (GT1a) patients treated with Viekira Pak® plus ribavirin (RBV) for 12 weeks in four clinical trials. The patient populations of these trials included treatment naïve groups as well as patients who had previously been treated with peg-interferon and RBV. SVR in all studies of Viekira Pak® was defined as HCV level below the lower limit of quantification 12 weeks after the end of treatment. Viekira Pak® treatment was effective in patients with GT1a or genotype 1b (GT1b) HCV with or without compensated cirrhosis. In some patient populations, Viekira Pak® does not have to be given with RBV, which further decreases the pill burden and improves compliance.1

Due to increased ALT elevations in women taking ethinyl estradiol-containing medications, other forms of contraception should be used when taking Viekira Pak®. Ethinyl estradiol-containing medications may be resumed two weeks after completion of therapy with Viekira Pak®. ALT elevations were similar in subjects taking other estrogens concomitantly with Viekira Pak® and patients who were not taking any estrogens; however, caution is recommended when using these medications together. Viekira Pak® interacts with other medications, so a thorough medication review should be completed prior to starting this therapy.1

Viekira Pak®, like other medications in for hepatitis C, is expensive (~$83,000 for 12 weeks of treatment).2 AbbVie’s assistance program “proCeed – Customer Solutions” helps with patient copays for people with insurance, as well as offering financial assistance for eligible patients.3

By Casey Lauver, PharmD Candidate

REFERENCES:
Avycaz® (ceftazidime/avibactam) is a new cephalosporin/beta-lactamase inhibitor combination product that was approved in February 2015 for the treatment of complicated urinary tract infections, pyelonephritis, and complicated intra-abdominal infections in combination with metronidazole. Ceftazidime/avibactam has activity against extended beta-lactamase producing organisms and provides another avenue for treatment of these resistant organisms.

Ceftazidime/avibactam has the same mechanism of action as other beta-lactam/beta-lactamase combination products – inhibition of peptidoglycan cross linking in bacterial cell walls. Avibactam alone does not have antimicrobial activity. Avibactam prevents degradation of ceftazidime by beta-lactamases, which prolongs ceftazidime’s duration of action and expands its activity to beta-lactamase-producing organisms. Although ceftazidime/avibactam has activity against resistant organisms, it is not effective against bacteria that are resistant due to overexpression of efflux pumps or decreased membrane permeability.

Ceftazidime-avibactam has demonstrated efficacy against the following organisms (check package insert for complete list):

- **Escherichia coli** (including cephalosporin-resistant organisms)
- **Klebsiella** species (including cephalosporin-resistant organisms)
- **Enterobacter** species
- **Haemophilus influenzae**
- **Moraxella catarrhalis**
- **Pseudomonas aeruginosa** (including ceftazidime- and meropenem-resistant strains)
- Extended spectrum beta-lactamase-producing organisms

In a phase II, randomized, double-blind, controlled trial, clinical response was similar with ceftazidime/avibactam + metronidazole and meropenem monotherapy for patients with complicated intra-abdominal infections. The study included 203 participants who were treated for an average of 6 days. Clinical response rates for the ceftazidime/avibactam + metronidazole and meropenem monotherapy groups were 97.1% and 97.4%, respectively.

A large number of patients in each group had polymicrobial infections, and the most commonly isolated organism was *E. coli*. Overall rates of adverse reactions were similar between groups. Nausea, vomiting, and abdominal pain were more common in the ceftazidime/avibactam + metronidazole group while decreased liver enzymes were more common in the meropenem group. This study was limited by the small number of patients, the large number of *E. coli* isolates, the large number of appendicitis cases, and the patients’ low acute physiological assessment and chronic health evaluation (APACHE II) scores.

Response rates were also similar between ceftazidime/avibactam and imipenem/cilastatin in a phase II, randomized, single-blind study in 135 patients with complicated urinary tract infections ± pyelonephritis. Response rates in patients with urinary tract infections in the ceftazidime/avibactam and imipenem/cilastatin groups were 70.4% and 71.4%, respectively. There was also no difference in response rates for patients with pyelonephritis between the groups (72.2% vs. 73.7%, respectively). The median duration of intravenous therapy for both treatment groups was similar (5 days for ceftazidime/avibactam and 6 days for imipenem/cilastatin).

The ceftazidime/avibactam group had slightly lower adverse event rates than the imipenem/cilastatin group (67.6% vs. 76.1%, respectively). While headache and infusion site reactions were the most commonly reported adverse reactions, the ceftazidime/avibactam patients experienced far fewer infusion site reactions than the imipenem/cilastatin patients (5.9% vs. 22.4%). The most common organism isolated was *E. coli* while *Klebsiella* species were not well represented. This study had several limitations. Only a small number of patients had a positive blood culture which limits extrapolation to patients with urosepsis. All patients with positive blood cultures were infected with *E. coli* and this was a small study so the results may not be generalizable. The doses of ceftazidime/avibactam used in this study were less than those currently recommended by the package insert (500/125 mg every 8 hours vs. 2000/500 mg every 8 hours), which may explain the low response rates reported for some study subgroups.

In clinical trials, ceftazidime/avibactam has generally been well tolerated. Reported adverse reactions include those expected with a broad spectrum beta-lactam antibiotic. Hypersensitivity reactions have been reported, do not use ceftazidime-avibactam in patients with a history of cephalosporin allergies and use with caution in patient with other bet-lactam allergies. There is a risk of *Clostridium difficile*-associated diarrhea and allergic reaction. Ceftazidime/avibactam also carries a risk of seizures due to the ceftazidime component. The risk of seizures is higher in patients with renal failure due to the antibiotic’s extensive renal elimination.

Due to its broad spectrum, ceftazidime/avibactam may be an appropriate choice for patients with suspected or confirmed extended spectrum beta-lactamase-producing organisms or ceftazidime-resistant organisms. Phase III trials with ceftazidime-avibactam have not yet been published and will provide more data about this new antibiotic.

By Emily Kobos, PharmD Candidate

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Avycaz® References (from page 4)


SGLT2 Inhibitors References (from page 2)


Chronic fatigue syndrome (CFS) is a debilitating disorder that can cause severe, unexplained mental and physical exhaustion. People with CFS do not get better with rest, and often the fatigue gets worse with physical or mental exhaustion or stress.

Usually the fatigue happens suddenly, and sometimes it occurs after an illness, like a respiratory infection (bronchitis) or mononucleosis (mono) infection. CFS is more common in women, Caucasian populations, and young and middle-age adults. It is not very common in children or the elderly.

 Causes of CFS
There is very little knowledge about why people get chronic fatigue syndrome. Although scientists don’t know exactly what causes CFS, some possibilities are:
- Infections (i.e. Lyme disease)
- Immune system dysfunction
- Low blood pressure (hypotension)
- Stress
- Nutritional deficiency

Symptoms & Diagnosis of CFS
CFS is characterized by severe fatigue that lasts longer than 6 months. Although fatigue is the main symptom, other symptoms may be present, including:
- Headaches
- Difficulty sleeping (insomnia)
- Tender lymph nodes

Diagnosis of CFS can be complicated since there are no tests to determine if the disease is present. Diagnosis is based solely on symptoms and a medical history taken by your healthcare provider.

 Treating CFS
Managing CFS can be very difficult and complex. Unfortunately, there is no cure for CFS, and treatment consists of symptom management and teaching patients how to cope with the disease. Some treatments that may be effective include:
- Cognitive behavioral therapy (CBT)—appointments with a counselor to discuss chronic fatigue syndrome and ways to cope with the disease.
- Maintaining a healthy lifestyle—this means eating a healthy, well-balanced diet and exercising regularly. Exercise can sometimes make CFS worse, but an overall lack of physical activity will also worsen the symptoms. It is important to maintain an active lifestyle with low-intensity exercises.

Other potential treatments:
- Antibiotics—may be used if the patient has an infection, but antibiotics are not effective for the treatment of CFS.
- Sleep-aid medications—often people are unable to sleep due to CFS. This can sometimes be helped with medications.
- Antidepressants—depression is common in people with CFS. There are several effective treatments for depression, and your healthcare provider may start you on something to help you cope better.
- Fibromyalgia treatments—fibromyalgia is very similar to CFS and can also cause pain with no known cause. Your healthcare provider may give you a medication commonly used to treat fibromyalgia.

More Information on CFS
- Always ask your doctor, pharmacist, or other healthcare provider for information on CFS
- www.cdc.gov/cfs

By Liz Wolsfelt, PharmD Candidate

REFERENCES:
PATIENT INFORMATION:
TICKS!!

Ticks are external parasites which live off the blood of other species including mammals, birds, reptiles, and amphibians. In Montana, ticks are most common in the months of March through July and are usually found in thick brushy country with lots of sun exposure. Ticks are associated with the spread of diseases such as Rocky Mountain spotted fever and Lyme disease.

Avoiding Ticks
Reducing exposure to ticks is the primary way to prevent tick-borne illness. The best ways to avoid ticks is to stay on designated trails and avoid brushy areas. Bb bug repellent containing at least 20% DEET will prevent ticks, although protection only lasts for a few hours after the initial application. Permethrin 0.5% can be used to treat clothes and gear and will repel ticks for up to four days after application. Tucking your shirt into your pants and your pants into your socks will make it hard for ticks to get onto your skin. Wearing light color clothing will make it easier to spot ticks.

Tick Check
At the end of every day spent in tick country, you need to perform a tick check. Clothes and gear should be inspected thoroughly for ticks. A shower and a full body tick check with the use of a mirror is recommended. Children should be inspected by an adult. Pets in tick-infested areas should also be checked under their front legs as well as on their neck and ears. Tick checks should be performed daily for 2-3 days after exposure to ticks to make sure nothing goes unnoticed.

How to Remove a Tick
Unfortunately, even with proper precautions, ticks may still find a way to bite. Ticks have an anesthetic in their saliva which numbs the area they bite and lets them attach undetected. The most important thing to remember when removing a tick is to make sure the entire tick is removed. Use a fine-point pair of tweezers, grab the tick as close to the skin where attached as possible, and pull straight out. Squeezing or scratching at the tick is not recommended because part of the tick may break off and still be attached. Once a tick is removed, clean the area with rubbing alcohol or soap and water and allow it to heal.

Signs of Tick-Borne Illness
Symptoms from a tick-borne illness can start while the tick is still attached or up to 30 days after removal. Common symptoms include fever or chills, headache, muscle ache, joint pain, and rash. If you have any of these symptoms during or after a tick bite, you should see a healthcare professional for a full evaluation.

By Hugh Daniels, PharmD Candidate

REFERENCES: