

FEBRUARY 2015

Hot Topic: AASLD/IDSA Chronic Hepatitis C Guidance Updates

During the 4th quarter of 2014, there were multiple rulings by the Food and Drug Administration (FDA) that brought about new therapies for the treatment of chronic hepatitis C and new indications for previously approved medications. These treatment innovations represent a significant shift in the way hepatitis C can and should be managed. Responding to the addition of the new treatment options, the joint guidelines from the American Association for Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) have updated their standard of care recommendations for initial treatment with revisions being made as recently as January 26, 2015. For treatment-naïve patients with genotype 1a, ledipasvir/sofosbuvir (Harvoni®), paritaprevir/ritonavir/ombitasvir/dasabuvir (Viekira Pak®) + ribavirin, and simeprevir (Olysio®) + sofosbuvir (Sovaldi®) are all recommended as first-line therapies with similar efficacy. For treatment-naïve patients with genotype 1b, the same therapies are recommended as first-line with the distinction that the addition of ribavirin to paritaprevir/ritonavir/ombitasvir/dasabuvir is only recommended for patients with cirrhosis. The recommendation for treatment-naïve patients with genotypes 2 or 3 continues to be sofosbuvir + ribavirin for 12 and 24 weeks, respectively. For treatment-naïve patients with genotype 4, ledipasvir/sofosbuvir, paritaprevir/ritonavir/ombitasvir/dasabuvir + ribavirin, and sofosbuvir + ribavirin, though off-label, are all recommended as first-line initial therapies with similar efficacy.

Significant revisions have also been made to the retreatment section of the guidelines. For genotype 1 patients without cirrhosis in whom prior pegylated interferon + ribavirin therapy has failed, ledipasvir/sofosbuvir for 12 weeks, paritaprevir/ritonavir/ombitasvir/dasabuvir (+ ribavirin for genotype 1a) for 12 weeks, and sofosbuvir + simeprevir ± ribavirin for 12 weeks, are all recommended with similar efficacy. For genotype 1 patients with compensated cirrhosis in whom prior pegylated interferon + ribavirin therapy has failed, ledipasvir/sofosbuvir for 24 weeks, ledipasvir/sofosbuvir + ribavirin for 12 weeks, paritaprevir/ritonavir/ombitasvir/dasabuvir + ribavirin for 12 weeks (genotype 1b) or 24 weeks (genotype 1a), and sofosbuvir + simeprevir ± ribavirin for 24 weeks are all recommended regimens.

Revisions have been made to virtually every section of the guidelines due to the impact of the newly approved FDA therapies. Significant recommendation changes include those related to the treatment of patients with HCV/HIV coinfections, patients with decompensated cirrhosis, and patients with recurrent HCV infection after receiving a liver transplant. The guidance also includes updated information related to drug interactions that are a concern with these newly approved treatments. In addition, the guidance now addresses mixed genotype infections. Since data on use of the direct-acting agents is lacking, awaiting the availability of a pangenotypic regimen may be considered. When treatment is needed, the prescribed antiviral regimen should maximize efficacy against each genotype present. For further details, you are encouraged to access the full recommendations available at: <http://hcvguidelines.org/>

Centers for Disease Control and Prevention (CDC) Health Update: Use of Influenza Antivirals

Influenza activity is high across the U.S. this season, with most states reporting widespread activity, with influenza A (H3N2) viruses most common. Historically, H3N2-predominant

Drug Information Highlights

- Merck has announced plans to voluntarily discontinue the manufacture and distribution of boceprevir (Victrelis®). Boceprevir is an HCV NS3/4A protease inhibitor for the treatment of genotype 1 chronic HCV infection in adults with compensated liver disease, including cirrhosis, used in combination with injectable peginterferon alfa and oral ribavirin. This decision was based on the decreasing demand for the drug due to availability of alternative therapies. Market withdrawal is due to occur by December 31, 2015. New patients should not be started on boceprevir; however, current therapy with boceprevir should be completed.
- The FDA approved Teva's esomeprazole magnesium delayed-release, the first generic for Nexium® oral capsule, for treatment of conditions due to excess stomach acid, including gastroesophageal reflux disease, in patients one year of age and older. No labeler has received 180-day exclusivity. Several additional generic labelers can receive FDA approval and launch product at any time.
- The FDA approved an expanded indication for spinosad (Natroba®) topical suspension to include the treatment of head lice infestations in patients six months of age and older. Spinosad, a pediculicide, was previously indicated for use in patients four years of age and older.
- The FDA approved an expanded indication for calcipotriene/betamethasone (Taclonex®) topical suspension to include the treatment of plaque psoriasis of the scalp in patients 12 to 17 years of age. It is also approved for the treatment of plaque psoriasis of the scalp and body in patients 18 years and older.
- Ivacaftor (Kalydeco®) received an expanded indication to include the treatment of cystic fibrosis patients six years and older who have the R117H mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Oral ivacaftor is also indicated for the treatment of cystic fibrosis patients six years and older who have one of the following mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R.
- The FDA approved Roxane's ritonavir tablet, first-time generic for Norvir®, a protease inhibitor used with other antiretroviral agents for the treatment of HIV-1 infection. Norvir is also available as capsules and oral solution that do not have generic equivalent products.

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flu seasons have been associated with increased hospitalizations and deaths in the elderly and young children. On January 9, 2015, the CDC issued an official Health Update due to the elevated nationwide influenza activity. Clinicians are reminded that influenza should be on their list of possible diagnoses for ill patients and the use of influenza antiviral drugs as an adjunct to vaccination is important in protecting people from influenza. The CDC advises that all hospitalized, severely ill, and high-risk patients with suspected influenza infection should receive an influenza antiviral medication as soon as possible, without waiting for test results to confirm the diagnosis. Patients at high risk for influenza complications include: children younger than two years; adults aged 65 years and older; persons with chronic pulmonary, cardiovascular, renal, hepatic, hematological, and metabolic disorders, or neurologic and neurodevelopment conditions; persons with immunosuppression, including that caused by medications or by HIV infection; women who are pregnant or postpartum (within two weeks after delivery); persons younger than 19 years of age who are receiving long-term aspirin therapy; American Indians/Alaska Natives; persons who are morbidly obese; and residents of nursing homes and other chronic-care facilities. Antiviral therapy should be started within 48 hours of symptom onset to be most effective; however, some patients may still derive benefit if initiated after this time period. Three prescription neuraminidase inhibitor antiviral medications are FDA-approved and are recommended for use in the U.S. during the 2014-2015 influenza season: oral oseltamivir (Tamiflu®), inhaled zanamivir (Relenza®), and the recently approved injectable peramivir (Rapivab®). Due to high levels of resistance, adamantane antivirals, rimantadine and amantadine, are not currently recommended for treatment or prevention of influenza. Currently, there are no national shortages of any of the neuraminidase inhibitors. Local spot shortages of oseltamivir have been reported due to increased demand for the product; therefore, it may be necessary for patient to contact multiple pharmacies in order to fill a prescription.

Pipeline News: Upcoming Prescription Drug User Fee Acts (PDUFA) Dates

- **Feb. 6, 2015:** Lucentis®; injectable ranibizumab; diabetic retinopathy; Roche.
- **Feb. 12, 2015:** Banzel®; oral rufinamide; pediatric patients with Lennox-Gastaut syndrome; Eisai/Novartis.
- **Feb. 2015:** empagliflozin/linagliptin; oral SGLT-2 inhibitor/DPP-4 inhibitor; type 2 diabetes; Boehringer Ingelheim/Eli Lilly.
- **Feb. 2015:** ivabradine; oral sinoatrial node funny channels inhibitor; chronic heart disease; Amgen/Servier.
- **Feb. 2015:** Vyvanse®; oral lisdexamfetamine dimesylate; binge eating disorder; Shire.
- **1st Quarter 2015:** ceftazidime/avibactam; intravenous cephalosporin/beta-lactamase inhibitor; complicated intra-abdominal infections and complicated urinary tract infections; Forest/AstraZeneca.
- **1st Quarter 2015:** Zohydro® ER; hydrocodone bitartrate; severe pain; Zogenix/Elan.

FDA Drug Safety Update: Pain Medications During Pregnancy

Prescription and over-the-counter (OTC) medications for the treatment of pain are often used during pregnancy, including non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and opioids. Studies indicate in the U.S. approximately 18-25 percent of pregnancies are exposed to OTC ibuprofen, 65-70 percent of pregnancies are exposed to OTC acetaminophen, and approximately six percent of pregnant women are exposed to opioids. Recent reports have questioned the safety of both OTC and prescription pain medications during pregnancy. As a result, the FDA conducted a review of published studies on the potential risks of the use of pain medications during pregnancy. The studies reviewed examined the following potential risks: prescription NSAIDs and the risk of miscarriage in the first half of pregnancy, opioids and the risk of birth defects of the brain, spine, or spinal cord in babies born to women who took these products during the first trimester of pregnancy, and acetaminophen (OTC and prescription products) and the risk of attention deficit hyperactivity disorder (ADHD) in children born to women who took this medicine at any time during pregnancy. Based on the FDA's evaluation of the studies, they concluded that the weight of evidence is inconclusive regarding a possible connection between NSAID use and miscarriage or regarding a possible connection between acetaminophen use in pregnancy and ADHD in children. Due to the low risk of neural tube defects in the U.S., the FDA concluded that further investigation is needed to determine if an increased risk of neural tube defects is related to opioid exposure in early pregnancy. As a result of this literature review, the FDA's recommendations on how pain medicines are used during pregnancy will remain the same at this time. The use of pain medications in pregnancy should be considered with caution. Health care professionals should continue to follow the recommendations in the drug labels when prescribing pain medicines to pregnant patients.

American Diabetes Association (ADA) Issues 2015 Standards of Medical Care in Diabetes

In January 2015, the ADA issued their Standards of Medical Care in Diabetes. The purpose of these guidelines is to provide clinicians, patients, researchers, payers, and others with components of diabetes care, general treatment goals, and tools to evaluate the quality of care. This replaces the previous ADA Clinical Practice Recommendations, which included the Standards of Medical Care in Diabetes and key ADA position statements. The Standards of Medical Care in Diabetes include evidence-based clinical practice recommendations for screening, diagnostics, and treatment that result in favorable health outcomes for diabetic patients. In the 2015 standards, the ADA now recommends a pre-prandial blood glucose of 80–130 mg/dL, which reflects an increase from the previous recommendation of 70–130 mg/dL. While the target hemoglobin A1c (HbA1c) remains < 7% for most adults, the target HbA1c recommended for all pediatric patients is now < 7.5%. The recommended diastolic blood pressure goal for most patients with diabetes and hypertension was increased from 80 mmHg to 90 mmHg. Additionally, the recommendations for statin treatment and lipid monitoring were updated to coincide with the 2013 American College of Cardiology/American Heart Association guidelines; treatment is now driven primarily by cardiovascular risk rather than low-density lipoprotein cholesterol (LDL-C) level. The majority of recommendations regarding approaches to glycemic treatment remain unchanged; and with the addition of the sodium-glucose cotransporter-2 (SGLT-2) inhibitors to the management algorithm for type 2 diabetes, all of the currently available FDA-approved therapies for type-2 diabetes management are now included in the ADA recommendations. A new section was added to the 2015 Standards pertaining to pregnancy and diabetes, which includes specific recommendations on preconception counseling, medications, blood glucose targets, and monitoring.

Recent FDA Approvals

Generic Name	Trade Name	Description	Applicant	FDA Status
carbidopa/levodopa	Rytary®	The FDA approved carbidopa/levodopa (Rytary) for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide or manganese intoxication. Rytary will be available as 23.75 mg/95 mg, 36.25 mg/145 mg, 48.75 mg/195 mg, and 61.25 mg/245 mg (carbidopa/levodopa) extended-release capsules. The starting dosage is 23.75 mg/95 mg three times daily and can be increased to a maximum of 97.5 mg/390 mg three times daily. Dosages of other carbidopa/levodopa products are not interchangeable with Rytary. The package insert contains instructions on conversion from immediate-release regimens. Carbidopa/levodopa extended-release tablet (Sinemet® CR) is also available as a 1:4 milligram ratio.	Impax	FDA NDA approval 01/07/2015
edoxaban	Savaysa™	The oral factor Xa inhibitor edoxaban (Savaysa) has gained FDA approval to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAf) and to treat deep vein thrombosis (DVT) and pulmonary embolism (PE) following 5–10 days of initial therapy with a parenteral anticoagulant. Boxed warnings advise against use in patients with NVAf and creatinine clearance (CrCl) > 95 mL/min due to reduced efficacy, premature discontinuation and increased risk of ischemia, and risk of spinal/epidural hematoma with neuraxial anesthesia or spinal puncture. The recommended dose for NVAf treatment is 60 mg once daily in patients with CrCl 50-95 mL/min and 30 mg once daily in patients with CrCl 15-50 mL/min. For the treatment of DVT and PE, the recommended dosage for most patients is 60 mg once daily; reduce dose to 30 mg once daily in patients with CrCl 15-50 mL/min, body weight ≤ 60 kg or who use certain P-gp inhibitors. Edoxaban is available as 15 mg, 30 mg, and 60 mg tablets.	Daiichi Sankyo	FDA NDA approval 01/08/2015
carbidopa/levodopa	Duopa™	The FDA approved carbidopa/levodopa (Duopa) for the treatment of motor fluctuations in patients with advanced Parkinson's disease. It is available as an enteral suspension containing 4.63 mg/mL carbidopa and 20 mg/mL levodopa. Duopa is to be administered into the jejunum through a percutaneous endoscopic gastrostomy with jejunal tube (PEG-J) with the CADD®-Legacy 1400 portable infusion pump. Total daily dose should be titrated based on clinical response; maximum recommended daily dose is 2,000 mg of levodopa administered over 16 hours.	Abbvie	FDA NDA approval 01/13/2015
perindopril arginine/amlodipine besylate	Prestalia®	The FDA approved the fixed-dose combination amlodipine besylate/perindopril arginine (Prestalia) for the treatment of hypertension. A boxed warning advises against use in pregnant women. It should also not be used with aliskiren-containing products. Prestalia will be available as perindopril arginine/amlodipine besylate 3.5 mg/2.5 mg and 7 mg/5 mg and 14 mg/10 mg tablets. Starting dose is 3.5 mg/2.5 mg once daily.	Symplmed	FDA NDA approval 01/21/2015
secukinumab	Cosentyx™	Secukinumab (Cosentyx) is the first IL-17A antagonist for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Caution is advised for use in patients with chronic or recurrent infection, including tuberculosis, or active Crohn's disease. Recommended dosage is 300 mg, given as two 150 mg subcutaneous (SC) injections, once weekly for five weeks and 300 mg every four weeks thereafter. Secukinumab will be available as a 150 mg/mL solution in a single-use prefilled pen, prefilled syringe, and a 150 mg lyophilized powder in a single-use vial for reconstitution. Patients may self-administer the prefilled pen or syringe after proper training.	Novartis	FDA NDA approval 01/21/2015
parathyroid hormone	Natpara®	Orphan drug status has been granted to injectable recombinant parathyroid hormone (Natpara) to control hypocalcemia in patients with hypoparathyroidism, a rare disease that leads to kidney damage, kidney stones, cataracts, and calcification of soft tissue. A boxed warning cautions that osteosarcoma has been observed in rat studies with Natpara. Although the risk of osteosarcoma in humans is unknown, Natpara is only recommended for use in patients whose hypocalcemia cannot be controlled with calcium supplementation and active forms of vitamin D, and for whom the potential benefits are considered to outweigh this potential risk. Natpara will be available through a restricted Risk Evaluation and Mitigation Strategy (REMS) program. The recommended starting dose is 50 mcg SC once daily. Dosage is titrated based on calcemic response to a maximum of 100 mcg and minimum of 25 mcg per day. Natpara can be self-administered with proper training. It is available as 25 mcg, 50 mcg, 75 mcg, and 100 mcg multi-dose cartridges for use with the reusable Natpara® Mixing Device, and reusable pen injector, Natpara® Q-Cliq™.	NPS	FDA BLA approval 01/23/2015

References

<https://www.magellanmedicaid.com/news/clinicalalerts.asp>
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