BRACE FOR FLU SEASON as COVID-19 Pandemic Persists
Indication
SHINGRIX is a vaccine indicated for prevention of herpes zoster (shingles) in adults aged 50 years and older. SHINGRIX is not indicated for prevention of primary varicella infection (chickenpox).

Important Safety Information
• SHINGRIX is contraindicated in anyone with a history of a severe allergic reaction (eg, anaphylaxis) to any component of the vaccine or after a previous dose of SHINGRIX.
• Review immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions. Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of SHINGRIX.
• Solicited local adverse reactions in subjects aged 50 years and older were pain (78.0%), redness (38.1%), and swelling (25.9%).
• Solicited general adverse reactions in subjects aged 50 years and older were myalgia (44.7%), fatigue (44.5%), headache (37.7%), shivering (26.8%), fever (20.5%), and gastrointestinal symptoms (17.3%).

References:
Talk to patients about possible adverse reactions
Discuss the most common adverse reactions observed in clinical trials. These include pain, redness, and swelling at the injection site, myalgia, fatigue, headache, shivering, fever, and gastrointestinal symptoms.1

Remind patients to get the 2nd dose 2-6 months after the first1
The efficacy results of SHINGRIX were demonstrated in clinical trials when administered as a 2-dose series.2 Ask patients to visit SHINGRIXreminder.com to sign up for reminder calls, emails, or texts.

Review the “What to Expect” pamphlet
Share the key facts patients should know when getting vaccinated with SHINGRIX. There are two ways for you to view: from a tablet or laptop, download and print copies by going to SHINGRIXguide.com; or use your phone to scan the QR code.*

Concomitant administration with influenza vaccine
In an open-label clinical study, subjects 50 years and older received 1 dose each of SHINGRIX and FLUARIX QUADRIVALENT (Influenza Vaccine) (QIV) at Month 0 and 1 dose of SHINGRIX at Month 2 (n=413), or 1 dose of QIV at Month 0 and 1 dose of SHINGRIX at Months 2 and 4 (n=415). There was no evidence for interference in the immune response to any of the antigens contained in SHINGRIX or the coadministered vaccine.

Important Safety Information (cont’d)
• SHINGRIX was not studied in pregnant or lactating women, and it is unknown if it is excreted in human milk. Therefore, it cannot be established whether there is vaccine-associated risk with SHINGRIX in pregnant women or if there are effects on breastfed infants or milk production/excretion
• Vaccination with SHINGRIX may not result in protection of all vaccine recipients

Please see Brief Summary of Prescribing Information for SHINGRIX on the following pages.

References: 1. Prescribing Information for SHINGRIX.

You can access more resources at seeSHINGRIXpharm.com

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SGXJRNA190004 June 2019
Produced in USA.
SHINGRIX (Zoster Vaccine Recombinant, Adjuvanted)

The following is a brief summary only; see full prescribing information for complete product information.

1 INDICATIONS AND USAGE

SHINGRIX is a vaccine indicated for prevention of herpes zoster (shingles) in adults aged 50 years and older.

Limitations of Use:

SHINGRIX is not indicated for prevention of primary varicella infection (chickenpox).

2 DOSAGE AND ADMINISTRATION

2.2 Administration Instructions

For intramuscular injection only.

After reconstitution, administer SHINGRIX immediately or store refrigerated between 2°C and 8°C (36°F and 46°F) and use within 6 hours. Discard reconstituted vaccine if not used within 6 hours.

2.3 Dose and Schedule

Two doses (0.5 mL each) administered intramuscularly according to the following schedule: A first dose at Month 0 followed by a second dose administered anytime between 2 and 6 months later.

The following is a brief summary only; see full prescribing information.

2.4 CONTRAINDICATIONS

Do not administer SHINGRIX to anyone with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine or after a previous dose of SHINGRIX [see Description (11) of full prescribing information].

5 WARNINGS AND PRECAUTIONS

5.1 Preventing and Managing Allergic Vaccine Reactions

Prior to administration, the healthcare provider should review the immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions. Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of SHINGRIX.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice. There is the possibility that broad use of SHINGRIX could reveal adverse reactions not observed in clinical trials.

Overall, 17,041 adults aged 50 years and older received at least 1 dose of SHINGRIX in 17 clinical studies.

The safety of SHINGRIX was evaluated by pooling data from 2 placebo-controlled clinical studies (Studies 1 and 2) involving 29,305 subjects aged 50 years and older who received at least 1 dose of SHINGRIX (n = 14,645) or saline placebo (n = 14,660) administered according to a 0- and 2-month schedule. At the time of vaccination, the mean age of the population was 69 years; 7,296 (24.9%) subjects were aged 50 to 59 years, 4,468 (15.3%) subjects were aged 60 to 69 years, and 17,531 (59.8%) subjects were aged 70 years and older. Both studies were conducted in North America, Latin America, Europe, Asia, and Australia. In the overall population, the majority of subjects were white (74.3%), followed by Asian (18.3%), black (1.4%), and other racial/ethnic groups (6.0%); 58% were female.

6.2 Solicited Adverse Events

In Studies 1 and 2, data on solicited local and general adverse events were collected using standardized diary cards for 7 days following each vaccine dose or placebo (i.e., day of vaccination and the next 6 days) in a subset of subjects (n = 4,886 receiving SHINGRIX, n = 4,881 receiving placebo with at least 1 documented dose). Across both studies, the percentages of subjects aged 50 years and older reporting each

solicited local adverse reaction and each solicited general adverse event following administration of SHINGRIX (both doses combined) were pain (78.0%), redness (38.1%), and swelling (25.9%); and myalgia (44.7%), fatigue (44.5%), headache (37.7%), shivering (26.8%), fever (20.5%), and gastrointestinal symptoms (17.3%), respectively.

The reported frequencies of specific solicited local adverse reactions and general adverse events (overall per subject), by age group, from the 2 studies are presented in Table 1.

Table 1. Percentage of Subjects with Solicited Local Adverse Reactions and General Adverse Events within 7 Days of Vaccination in Adults Aged 50 to 59 Years, 60 to 69 Years, and 70 Years and Older* (Total Vaccinated Cohort with 7-Day Diary Card)

<table>
<thead>
<tr>
<th>Local Adverse Reactions</th>
<th>Aged 50 - 59 Years</th>
<th>Aged 60 - 69 Years</th>
<th>Aged ≥70 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SHINGRIX %</td>
<td>Placebo %</td>
<td>SHINGRIX %</td>
</tr>
<tr>
<td>Pain</td>
<td>88.4</td>
<td>14.4</td>
<td>82.8</td>
</tr>
<tr>
<td>Pain, Grade 3</td>
<td>10.3</td>
<td>0.5</td>
<td>6.9</td>
</tr>
<tr>
<td>Redness</td>
<td>38.7</td>
<td>1.2</td>
<td>38.4</td>
</tr>
<tr>
<td>Redness, &gt;100 mm</td>
<td>2.8</td>
<td>0.0</td>
<td>2.6</td>
</tr>
<tr>
<td>Swelling</td>
<td>30.5</td>
<td>0.8</td>
<td>26.5</td>
</tr>
<tr>
<td>Swelling, &gt;100 mm</td>
<td>1.1</td>
<td>0.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Myalgia</td>
<td>56.9</td>
<td>15.2</td>
<td>49.0</td>
</tr>
<tr>
<td>Myalgia, Grade 3</td>
<td>8.9</td>
<td>0.9</td>
<td>5.3</td>
</tr>
<tr>
<td>Fatigue</td>
<td>57.0</td>
<td>19.8</td>
<td>45.7</td>
</tr>
<tr>
<td>Fatigue, Grade 3</td>
<td>8.5</td>
<td>1.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Headache</td>
<td>50.6</td>
<td>21.6</td>
<td>39.6</td>
</tr>
<tr>
<td>Headache, Grade 3</td>
<td>6.0</td>
<td>1.7</td>
<td>3.7</td>
</tr>
<tr>
<td>Shivering</td>
<td>35.8</td>
<td>7.4</td>
<td>30.3</td>
</tr>
<tr>
<td>Shivering, Grade 3</td>
<td>6.8</td>
<td>0.2</td>
<td>4.5</td>
</tr>
<tr>
<td>Fever</td>
<td>27.8</td>
<td>3.0</td>
<td>23.9</td>
</tr>
<tr>
<td>Fever, Grade 3</td>
<td>0.4</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>GI</td>
<td>24.3</td>
<td>10.7</td>
<td>16.7</td>
</tr>
<tr>
<td>GI, Grade 3</td>
<td>2.1</td>
<td>0.7</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Total vaccinated cohort for safety included all subjects with at least 1 documented dose (n).

7 Days included day of vaccination and the subsequent 6 days.

Data for subjects aged 50 to 59 years and 60 to 69 years are based on Study 1. Data for subjects 70 years and older are based on pooled data from Study 1: NCT01165177 and Study 2: NCT01165229.

Placebo was a saline solution.

Grade 3 pain: Defined as significant pain at rest; prevents normal everyday activities.

Grade 3 myalgia, fatigue, headache, shivering, GI: Defined as preventing normal activity.

Fever defined as ≥37.5°C/99.5°F for oral, axillary, or tympanic route, or ≥38°C/100.4°F for rectal route; Grade 3 fever defined as >39.0°C/102.2°F.

GI = Gastrointestinal symptoms including nausea, vomiting, diarrhea, and/or abdominal pain.

The incidence of solicited local and general symptoms was lower in subjects aged 70 years and older compared with those aged 50 to 69 years.

The majority of solicited local adverse reactions and general adverse events seen with SHINGRIX had a median duration of 2 to 3 days.

(continued on next page)
There were no differences in the proportions of subjects reporting any or Grade 3 solicited local reactions between Dose 1 and Dose 2. Headache and shivering were reported more frequently by subjects after Dose 2 (28.2% and 21.4%, respectively) compared with Dose 1 (24.4% and 13.8%, respectively). Grade 3 solicited general adverse events (headache, shivering, myalgia, and fatigue) were reported more frequently by subjects after Dose 2 (2.3%, 3.1%, 3.6%, and 3.5%, respectively) compared with Dose 1 (1.4%, 1.4%, 2.3%, and 2.4%, respectively).

**Unsolicited Adverse Events**

Unsolicited adverse events that occurred within 30 days following each vaccination (Day 0 to 29) were recorded on a diary card by all subjects. In the 2 studies, unsolicited adverse events occurring within 30 days of vaccination were reported in 50.5% and 32.0% of subjects who received SHINGRIX (n = 14,645) and placebo (n = 14,660), respectively (Total Vaccinated Cohort). Unsolicited adverse events that occurred in ≥1% of recipients of SHINGRIX and at a rate at least 1.5-fold higher than placebo included chills (3.5% versus 0.2%), injection site pruritus (2.2% versus 0.2%), malaise (1.7% versus 0.3%), arthralgia (1.7% versus 1.2%), nausea (1.4% versus 0.5%), and dizziness (1.2% versus 0.8%).

Gout (including gouty arthritis) was reported by 0.18% (n = 27) versus 0.05% (n = 8) of subjects who received SHINGRIX and placebo, respectively, within 30 days of vaccination; available information is insufficient to determine a causal relationship with SHINGRIX.

**Serious Adverse Events (SAEs)**

In the 2 studies, SAEs were reported at similar rates in subjects who received SHINGRIX (2.3%) and placebo (2.2%) from the first administered dose up to 30 days post last vaccination. SAEs were reported for 10.1% of subjects who received SHINGRIX and for 10.4% of subjects who received placebo from the first administered dose up to 1 year post last vaccination. One subject (<0.01%) reported lymphadenitis and 1 subject (<0.01%) reported fever greater than 39°C; there was a basis for a causal relationship with SHINGRIX.

Optic ischemic neuropathy was reported in 3 subjects (0.02%) who received SHINGRIX (all within 50 days after vaccination) and 0 subjects who received placebo; available information is insufficient to determine a causal relationship with SHINGRIX.

**Deaths**

From the first administered dose up to 30 days post last vaccination, deaths were reported for 0.04% of subjects who received SHINGRIX and 0.05% of subjects who received placebo in the 2 studies. From the first administered dose up to 1 year post last vaccination, deaths were reported for 0.8% of subjects who received SHINGRIX and for 0.9% of subjects who received placebo. Causes of death among subjects were consistent with those generally reported in adult and elderly populations.

**Potential Immune-Mediated Diseases**

In the 2 studies, new onset potential immune-mediated diseases (pIMDs) or exacerbation of existing pIMDs were reported for 0.6% of subjects who received SHINGRIX and 0.7% of subjects who received placebo from the first administered dose up to 1 year post last vaccination. The most frequently reported pIMDs occurred with comparable frequencies in the group receiving SHINGRIX and the placebo group.

**Dosing Schedule**

In an open-label clinical study, 238 subjects 50 years and older received SHINGRIX as a 0- and 2-month or 0- and 6-month schedule. The safety profile of SHINGRIX was similar when administered according to a 0- and 2-month or 0- and 6-month schedule and was consistent with that observed in Studies 1 and 2.

**6.2 Postmarketing Experience**

The following adverse reactions have been identified during postapproval use of SHINGRIX. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine.

**General Disorders and Administration Site Conditions**

Decreased mobility of the injected arm which may persist for 1 or more weeks.

**Immune System Disorders**

Hypersensitivity reactions, including angioedema, rash, and urticaria.

**7 DRUG INTERACTIONS**

**7.1 Concomitant Vaccine Administration**

For concomitant administration of SHINGRIX with inactivated influenza vaccine [see Clinical Studies (14.5) of full prescribing information].

**7.2 Immunosuppressive Therapies**

Immunosuppressive therapies may reduce the effectiveness of SHINGRIX.

**8 USE IN SPECIFIC POPULATIONS**

**8.1 Pregnancy**

There are no available human data to establish whether there is vaccine-associated risk with SHINGRIX in pregnant women [see Use in Specific Populations (8.1) of full prescribing information].

**8.2 Lactation**

It is not known whether SHINGRIX is excreted in human milk. Data are not available to assess the effects of SHINGRIX on the breastfed infant or on milk production/excretion [see Use in Specific Populations (8.2) of full prescribing information].

**8.5 Geriatric Use**

Of the total number of subjects who received at least 1 dose of SHINGRIX in the 2 efficacy trials (n = 14,645), 2,243 (15.3%) were aged 60 to 69 years, 6,837 (46.7%) were aged 70 to 79 years, and 1,921 (13.1%) were 80 years and older. There were no clinically meaningful differences in efficacy across the age groups or between these subjects and younger subjects [see Clinical Studies (14.1, 14.2, 14.3) of full prescribing information].

The frequencies of solicited local and general adverse events in subjects aged 70 years and older were lower than in younger adults (aged 50 through 69 years) [see Adverse Reactions (6.1)].

**17 PATIENT COUNSELING INFORMATION**

- Inform patients of the potential benefits and risks of immunization with SHINGRIX and of the importance of completing the 2-dose immunization series according to the schedule.
- Inform patients about the potential for adverse reactions that have been temporally associated with administration of SHINGRIX.
- Provide the Vaccine Information Statements, which are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

**Storage:**

Store Vials of Lyophilized eAntigen and Adjuvant Suspension Components refrigerated between 2° and 8°C (36° and 46°F). Protect vials from light. Do not freeze. Discard if the vials have been frozen.

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CHAIRMAN’S LETTER

Prepare Your Pharmacy for Flu Season

During this time of year, pharmacies are gearing up for the upcoming influenza season. However, a deadly pandemic continues to circulate the country, spiking in some parts and slowing down in others, but still an ongoing threat to our communities. Pharmacies must brace for an impending influenza season to coincide with the presence of the coronavirus disease 2019 (COVID-19).

Our cover story dives into everything pharmacists need to know for the upcoming flu season, including an overview of currently available flu vaccines and those in the pipeline, as well as considerations for immunizing during a pandemic. Easing the flu burden this year is especially crucial considering COVID’s strain on the health care system. Read on page 8 for more on how to combat flu and COVID-19 from your pharmacy.

The CDC estimates that from October 1, 2019, to April 4, 2020, there were between 410,000 and 740,000 hospitalizations and 24,000 to 62,000 deaths related to influenza in the United States. A total of 185 influenza-associated pediatric deaths were reported to the CDC; generally, approximately 80% occur in those who were not fully vaccinated. Even though the influenza vaccine does not protect against COVID-19, it can help keep patients healthy and prevent hospitalizations during the pandemic. With back-to-school season in full swing, providing education about vaccines is critical.

With further uncertainty surrounding whether schools will reopen for in-person instruction, children who are diagnosed with attention-deficit/hyperactivity disorder (ADHD) may also be facing challenges with the prospect of remote learning. Our story on page 42 discusses how pharmacists can help caregivers navigate ADHD management in this new environment, with conversations around treatment advances and strategies.

In this issue, you’ll also find more expert insights on educating patients about HPV vaccines, diabetes management during the pandemic, and how to protect your pharmacy from cyberattacks. Lastly, this issue presents our new publication design, with streamlined industry-leading content revamped to be more concise, reader-friendly, and easier to navigate. This redesign, coupled with our recently enhanced website, aims to reinforce Drug Topics® position as a leading resource for the practicing pharmacist. Be sure to visit drugtopics.com for more relevant and timely news.

Thank you for reading,
Mike Hennessy Sr,
Chairman and Founder of MJH Life Sciences™

CHIEF EXECUTIVE OFFICER

Mike Hennessy Sr
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BRACE FOR FLU SEASON

Keep up-to-date on flu vaccine options and counseling considerations, especially as coronavirus disease 2019 continues to strike.

By Jennifer Gershman, PharmD, CPh
With influenza season approaching, it is critical to be prepared, because coronavirus disease 2019 (COVID-19) will likely still be circulating throughout the United States. Pharmacists serving on the front lines amid the pandemic also will play an important role in flu vaccine administration and education.

The CDC estimates that from October 1, 2019, to April 4, 2020, there have been 410,000 to 740,000 hospitalizations and 24,000 to 62,000 deaths related to influenza in the United States.† Influenza vaccine efficacy varies and was 39% effective overall during the 2019-2020 season.‡ A total of 185 influenza-associated pediatric deaths were reported to the CDC; approximately 80% occur in those who were not fully vaccinated.§

Promoting flu vaccines is critical to easing the influenza hospital burden, especially because COVID-19 will likely coincide with the upcoming season.© Everyone 6 months and older should receive the current influenza vaccine, which offers the best way to prevent flu and serious complications, including hospitalization and death.¶

Even though the influenza vaccine does not protect against COVID-19, it can help keep patients healthy and prevent hospitalizations during the pandemic.†

Both influenza and COVID-19 are infectious respiratory illnesses, but there are differences between the viruses (Table 1).# Flu symptoms typically include fever, cough, body aches, and fatigue, and patients may also experience vomiting and diarrhea.##

**Influenza Vaccines Available for Upcoming Season**

Vaccine options are similar to the 2019-2020 flu season and include standard-dose quadrivalent, quadrivalent cell-based, and recombinant quadrivalent shots (Table 2).** The live attenuated influenza vaccine nasal spray is also an option.### For adults 65 years and older, 2 new vaccines are available for the 2020-2021 flu season. These include a quadrivalent high-dose vaccine (Fluzone High-Dose Quadrivalent), replacing the trivalent high-dose vaccine, and a quadrivalent adjuvanted vaccine (Fluad Quadrivalent), which is similar to the previous trivalent, with 1 additional influenza B component.## Pharmacists should educate patients to get vaccinated before the end of October to ensure optimal protection and remind them that it takes about 2 weeks after administration for the flu vaccine to become fully effective.###

Additionally, universal influenza vaccines are being investigated to provide long-lasting protection against most or all flu strains. There are currently 2 universal flu vaccines in the pipeline: FLU-v and M-001."))).

**Immunization Counseling Pearls**

Families should be counseled that children 6 months to 8 years of age require 2 doses of the flu vaccine separated by at least 4 weeks if they are receiving it for the first time or previously received just 1 dose.#### Families should ensure that they begin the vaccine process early for their children, especially those being vaccinated for the first time, because full efficacy occurs 2 weeks after administration of the second shot.####

The World Health Organization named vaccine hesitancy as one of the 10 threats to global health in 2019.##### According to a recent survey, approximately 25.8% of parents are hesitant for their children to receive the influenza vaccine.###### These results further emphasize the importance of promoting flu vaccine administration.

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**TABLE 1. DIFFERENTIATING BETWEEN INFLUENZA AND COVID-19**

<table>
<thead>
<tr>
<th>Influenza</th>
<th>COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms:</strong> fever, cough, muscle or body aches, fatigue, sore throat, congestion or runny nose, headache; possibly vomiting and diarrhea</td>
<td><strong>Symptoms:</strong> fever, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea</td>
</tr>
<tr>
<td><strong>Transmission:</strong> person-to-person via respiratory droplets in the air from an infected person coughing, sneezing, or talking</td>
<td><strong>Transmission:</strong> person-to-person via respiratory droplets in the air from an infected person coughing, sneezing, or talking; potential spread through airborne route</td>
</tr>
<tr>
<td><strong>Cause:</strong> several types and strains of influenza viruses</td>
<td><strong>Cause:</strong> SARS-CoV-2</td>
</tr>
<tr>
<td><strong>Vaccine:</strong> available each flu season to prevent infection and reduce risk of serious complications</td>
<td><strong>Vaccine:</strong> none currently available; research under way</td>
</tr>
</tbody>
</table>

---

Atherosclerotic cardiovascular disease (ASCVD), the leading global cause of morbidity and mortality in the United States is largely attributed to a variety of cardiovascular risk factors, including hypertriglyceridemia, elevated low-density lipoprotein cholesterol (LDL-C), insulin resistance, hypertension, and obesity. Coronary heart disease (CHD) is the most common manifestation of cardiovascular disease (CVD), comprising approximately 50% of patients’ first CVD events. Risk factors include a family history of premature ASCVD (men < 55 years old, women < 65 years old), metabolic syndrome (increased body mass index, elevated triglycerides >150 mg/dL, elevated blood pressure), hypercholesterolemia, and chronic kidney disease.

Risk of ASCVD is categorized as low (< 5%), borderline (5%-< 7.5%), intermediate (> 7.5%-< 20%) or high (>20%) over a 10-year period. These risk stratifications can help determine the most appropriate interventions for patients. Those with minimal or borderline ASCVD risk may be eligible for lifestyle modifications, including dietary improvements, physical activity, and smoking cessation if applicable. In addition to lifestyle changes, several therapies are used to lower LDL-C and/or triglyceride levels, but only select agents have demonstrated a significant effect in reducing cardiovascular mortality.

This article reviews the evolving therapeutic landscape for lowering LDL-C and cardiovascular risk, with an emphasis on the role of omega-3 fatty acids.

**THE ROLE OF STATINS IN REDUCING LDL-C**

Cholesterol-lowering statin therapy is frequently used in patients with or without a history of CHD, primarily because their ability to markedly lower LDL-C levels. These reductions in LDL-C levels are generally linearly related to the reductions in atherosclerotic plaques and atherosclerotic events (eg, stroke or myocardial infarction).

Meta analyses suggest that statins reduce major adverse cardiovascular events and all-cause mortality in patients at risk for ASCVD. Additionally, reductions in LDL-C levels associated with the use of statins are generally irrespective of comorbidities, such as diabetes, chronic kidney disease, or previous vascular disease.

The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend moderate or high intensity statins in addition to lifestyle modifications for those at moderate and high risk for recurring cardiovascular events.

**THERAPEUTIC TARGETING OF HYPERTRIGLYCERIDEMIA**

Beyond LDL-cholesterol lowering, therapeutic targeting of triglyceride levels can reduce cardiovascular risk, as triglyceride levels of 150 mg/dL or more are considered a marker of persistent cardiovascular risk despite controlled LDL-C. In high-risk patients, such as those with established cardiovascular disease or diabetes, lowering triglyceride levels, along with decreasing LDL-C levels and raising HDL-C levels, produces trends suggesting reduced cardiovascular mortality. In addition to lifestyle changes, several therapies including ezetimibe, fibrates, and niacin; omega-3 fatty acids have been shown to lower triglyceride and non–HDL-C levels, but only select agents have demonstrated an effect in improving cardiovascular morbidity and mortality.

- When ezetimibe therapy is added to statin or fibrate therapy, decreases in total cholesterol, LDL-C, and triglycerides, as well as increases in HDL-C levels, have been observed; however, the risk of cardiovascular events is only minimally improved and no effect
on cardiovascular mortality has been observed.\(^6\)

- Fibrate therapy has been associated with a 10% relative risk reduction for major cardiovascular events.\(^{17}\)

- Although niacin, in combination with statin therapy, may increase in serum HDL-C levels, it does not reduce cardiovascular mortality or recurrent events in patients with/at high-risk for ASCVD.

- As a class, omega-3 fatty acids (eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA]), have been shown to decrease triglyceride levels. Recent data on EPA/DHA combination regimens generally confer no evidence of a significant effect on cardiovascular disease composite end points or all-cause mortality.\(^{15,16}\)

### THE CARDIOVASCULAR BENEFITS OF OMEGA-3 FATTY ACIDS

Another intervention that has shown efficacy toward lowering triglyceride levels is omega-3 fatty acids, which can be used for patients with high (200-499 mg/dL) or very high (≥ 500 mg/dL) triglyceride levels.\(^8\) Omega-3 fatty acid products are available as prescription or as dietary supplements.\(^{19,20}\) DHA and EPA are the primary long-chain fatty acids components of omega-3 fatty acids.\(^{10}\) The effects of omega-3 fatty acids on LDL-C vary based on the specific long-chain fatty acid (ie, DHA or EPA) component. Findings from a systematic review of head-to-head studies of omega-3 fatty acid products revealed that DHA increased LDL-C by 2.6%, whereas EPA decreased LDL-C by 0.7%.\(^{20}\)

Four FDA-approved omega-3 fatty acid therapies are currently available via prescription in the United States, and all are indicated to decrease triglyceride levels. They include omega-3 acid ethyl esters, omega-3 acid ethyl esters A, omega-carboxylic acids and icosapent ethyl (Table 1).\(^{21-24}\)

Early studies, such as the GISSI-Prevenzione study, demonstrated reductions in cardiovascular events with omega-3 fatty acid supplements;\(^{25}\) however, in the era of statin therapy, these results have generally not been replicated.\(^{26}\) Results from more recent studies have found that EPA/DHA combination products do not confer significant cardiovascular benefits.\(^{15,16}\) For example, the ASCEND trial (NCT00135226) evaluated the use of omega-3 fatty acids in 15,480 patients with type 2 diabetes. Patients were randomized to either 840 mg of omega-3 fatty acids (EPA, 460 mg; DHA, 380 mg) once daily or placebo. Compared with placebo, those in the omega-3 fatty acid group had no significant difference in the risk of serious vascular events.\(^{15}\) Additionally, the VITAL trial (NCT01169259) evaluated the use of vitamin D\(_3\) plus omega-3 fatty acids for the primary prevention of cardiovascular disease and cancer. Overall 25,871 patients were randomized to either vitamin D\(_3\) 2000 IU plus omega-3 fatty acids (EPA, 460 mg; DHA, 380 mg) once daily or placebo. Use of omega-3 fatty acids did not result in a decreased incidence of either cardiovascular events or cancer.\(^{16}\)

Icosapent ethyl, the most recent product in the omega-3 landscape, is indicated as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride levels and established CV disease or diabetes mellitus and 2 or more additional risk

### TABLE 1.
FDA-Approved Prescription Omega-3 Fatty Acid Products\(^{21-24}\)

<table>
<thead>
<tr>
<th>Fatty-acid long-chain components</th>
<th>Omega-3-acid ethyl esters</th>
<th>Omega-3-acid ethyl esters A</th>
<th>Omega-3-carboxylic acids</th>
<th>Icosapent ethyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHA</td>
<td>375 mg</td>
<td>375 mg</td>
<td>Yes; amount not listed</td>
<td>Does not contain</td>
</tr>
<tr>
<td>EPA</td>
<td>465 mg</td>
<td>465 mg</td>
<td>Yes; amount not listed</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

**Indications/limitations of use**

<table>
<thead>
<tr>
<th>Hypertriglyceridemia</th>
<th>Yes</th>
<th>Yes</th>
<th>Yes</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect on cardiovascular risks</td>
<td>Limitation— not determined</td>
<td>Limitation— not determined</td>
<td>Limitation— not determined</td>
<td>Reduces cardiovascular risk beyond cholesterol-lowering therapy in high-risk patients approved for treatment</td>
</tr>
</tbody>
</table>

DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid.
factors for CV disease. It is also indicated as an adjunct to diet to reduce triglyceride levels in adult patients with severe hypertriglyceridemia. Unlike other omega-3 fatty acid formulations that contain DHA and EPA, icosapent ethyl is a purified ethyl ester of EPA.

The approval of icosapent ethyl was based on data from the multicenter, randomized, double-blind REDUCE-IT (Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention) trial (NCT01492361) that demonstrated a reduction of risk of ischemic events, including cardiovascular mortality, in patients receiving icosapent ethyl. Investigators evaluated the use of icosapent ethyl in patients with either (1) established cardiovascular disease or (2) diabetes and other risk factors who had triglyceride levels of 135-499 mg/dL and were currently receiving statin therapy. Overall, 8,179 patients were randomized to statin plus icosapent ethyl 2 g twice daily (n = 4089) or statin plus placebo (n = 4090). The primary end point was a composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina, while the secondary end point was a composite of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke.

After a median of 4.9 years, patients randomized to statin plus icosapent had significantly fewer primary composite (17.2% vs 22%, respectively; P < .001) and secondary composite events (11.2% vs 14.8%, respectively; P < .001) versus those randomized to statin plus placebo. This represented a 25% relative risk reduction in primary composite end point of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina. At a median follow-up of approximately 5 years, the number needed to treat to avoid 1 primary end point was 21.

Because some results from international trials have shown poorer outcomes in patients in the United States, a subgroup analysis of the US-only population (REDUCE-IT USA) was conducted. Primary and secondary composite events were significantly reduced in patients randomized to statin plus icosapent ethyl versus those randomized to statin plus placebo (P = .000001 and P = .00008, respectively). In addition, the US population demonstrated particularly robust risk reductions across a variety of individual and composite end points, including cardiovascular death (P = .007), myocardial infarction (P = .01), stroke (P = .02), and all-cause mortality (P = .004).

In the overall international population and in the U.S.-only cohort, overall rates of adverse events, and serious adverse events leading to discontinuation did not significantly differ between groups. Icosapent ethyl was generally well tolerated and presented with no

### TABLE 2. Guideline Recommendations for the Use of Icosapent Ethyl for Cardiovascular Risk Reduction

<table>
<thead>
<tr>
<th>Guideline name</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Diabetes Association Standards of Medical Care in Diabetes for 2020</td>
<td>In diabetic patients with ASCVD or other cardiac risk factors that are currently on a statin with controlled LDL-C, but have elevated triglycerides, the guidelines recommend considering icosapent ethyl to reduce cardiovascular risk (level of evidence, A).</td>
</tr>
<tr>
<td>American Association of Clinical Endocrinologists and American College of Endocrinology 2020 Comprehensive Type 2 Diabetes</td>
<td>Within the ASCVD risk factor modification algorithm for dyslipidemia, guidelines recommend icosapent ethyl 4 g per day if triglycerides are elevated (135-499 mg/dL) and the patient maximally tolerates statins.</td>
</tr>
<tr>
<td>American Heart Association 2020 Science Advisory on the Management of Stable Coronary Artery Disease in Patients With Type 2 Diabetes Mellitus</td>
<td>Considered first-line therapy for patients with type 2 diabetes and cardiovascular disease who have elevated triglycerides (&gt;135 mg/dL) despite maximally tolerated statin therapy and lifestyle changes.</td>
</tr>
<tr>
<td>National Lipid Association Scientific Statement on the Use of Icosapent Ethyl</td>
<td>Icosapent ethyl is recommended for ASCVD risk reduction in patients ≥ 45 years with clinical ASCVD (or ≥ 50 years with diabetes mellitus requiring medication plus ≥ 1 additional risk factor) who have fasting triglycerides of 135-499 mg/dL and are receiving high-intensity or maximally tolerated statin therapy (± ezetimibe) (evidence rating, class I; evidence level, B-R).</td>
</tr>
</tbody>
</table>

ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol.
polypharmacy issues when combined with statins. Following the REDUCE-IT findings, numerous guidelines were updated to include recommendations for the use of icosapent ethyl to reduce cardiovascular risks (Table 2).19-30

CONCLUSIONS

With the approval of icosapent ethyl, the role of omega-3 fatty acids in the evolving spectrum of ASCVD management and prevention is expanding. Moreover, the continued research and integration of icosapent ethyl in combination with other approaches could potentially reduce risks of CV events.

References


important role that pharmacists can play in countering vaccine hesitancy and the antivaccination movement. As schools begin to reopen, it is critical to ensure that children are vaccinated against influenza, because pediatric patients are at a high risk of serious complications.

The CDC’s Advisory Committee on Immunization Practices met June 24, 2020, and recommends any approved influenza vaccine for the upcoming flu season, listing certain conditions as contraindications for the live vaccine FluMist nasal spray and providing more information about antiviral drug interactions (Table 2). Individuals at high risk of serious complications from the flu include adults 65 years and older, pregnant women, young children, and individuals with chronic health conditions including asthma, cardiovascular disease, diabetes, HIV/AIDS, and cancer. Most of these are also risk factors for severe COVID-19 complications, making flu vaccination especially critical this season. Pregnant women are at a higher risk of complications from influenza because changes in the immune system, heart, and lungs occur during pregnancy. Results from a recent CDC study revealed that pregnant women may also be at an increased risk of COVID-19 complications including hospitalization, intensive care unit admission, and mechanical ventilation compared with non-pregnant women. Therefore, it is extremely important to get the influenza vaccine during pregnancy for maternal protection and to pass on protective antibodies to the developing baby as the COVID-19 pandemic continues during flu season.

**Flu Vaccine Health and Safety Guidance During COVID-19**

Pharmacists can serve as vaccine champions and promote a safe immunization administration environment. Experts including Anthony S. Fauci, MD, director of the National Institute of Allergy and Infectious Diseases, and Robert R. Redfield, MD, director of the CDC, provided testimony on June 23, 2020, on COVID-19 and the impending flu season. One of the hot topics centered on a new laboratory test, developed by the CDC, that checks for 3 viruses simultaneously: influenza viruses A and B and severe acute respiratory syndrome coronavirus 2, which causes COVID-19. This would enhance public health surveillance and provide an important diagnostic tool for detecting and treating coinfection with influenza and COVID-19, and on June 18, 2020, the CDC requested emergency use authorization (EUA). On July 2, the FDA issued the EUA for the test on July 2, making it the third diagnostic test for detection and differentiation of viruses causing influenza and COVID-19.

**TABLE 2. VACCINE OPTIONS FOR 2020–2021 FLU SEASON**

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>APPROVED AGE GROUPS</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afluria Quadrivalent</td>
<td>6 months and older</td>
<td>Inactivated</td>
</tr>
<tr>
<td>Fluad Quadrivalent</td>
<td>65 years and older</td>
<td>Inactivated, adjuvanted to help promote enhanced immune response</td>
</tr>
<tr>
<td>Fluarix Quadrivalent</td>
<td>6 months and older</td>
<td>Inactivated</td>
</tr>
<tr>
<td>Flublok Quadrivalent</td>
<td>18 years and older</td>
<td>Inactivated recombinant, egg free</td>
</tr>
<tr>
<td>Flueltax Quadrivalent</td>
<td>4 years and older</td>
<td>Inactivated cell-based, egg free</td>
</tr>
<tr>
<td>FluLaval Quadrivalent</td>
<td>6 months and older</td>
<td>Inactivated</td>
</tr>
<tr>
<td>FluMist Quadrivalent</td>
<td>2-49 years</td>
<td>Nasal spray, live vaccine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Certain antivirals may interact with vaccine.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Individuals who should not receive this vaccine: pregnant women; children 2-17 years receiving aspirin medications; immunocompromised patients; children 2-4 years with asthma or history of wheezing in past 12 months; individuals caring for immunocompromised patients; patients with asplenia, cochlear implants, or active cerebrospinal fluid leaks</td>
</tr>
<tr>
<td>Fluzone High-Dose Quadrivalent</td>
<td>65 years and older</td>
<td>Inactivated, contains 4 times the antigen of standard-dose inactivated influenza vaccines</td>
</tr>
<tr>
<td>Fluzone Quadrivalent</td>
<td>6 months and older</td>
<td>Inactivated</td>
</tr>
</tbody>
</table>
Other discussion points included goals for greater influenza vaccine coverage through education and increasing flu vaccines for uninsured, high-risk adults. The CDC awarded $140 million to 64 jurisdictions to enable state health departments to launch an initial scale-up for influenza season, and the funds will also support staffing and preparedness during summer. In an email with Drug Topics®, Natalie E. Azar, MD, assistant professor of rheumatology at NYU Langone and NBC News medical contributor, discussed the concern of flu predisposing patients to COVID-19 complications, such as COVID pneumonia. “Thus, rather than having a direct protective effect from vaccination against influenza, getting the flu shot could indirectly protect folks from a bad outcome from COVID-19,” Azar said.

Although there are no vaccines currently available to directly protect against COVID-19, there are several investigational candidates currently going through clinical trials (Table 3). The CDC recommends that pharmacies and other facilities resume administering routine vaccinations to ensure that communities are protected from vaccine-preventable diseases, and influenza vaccination is emphasized to reduce the overall burden of respiratory illness especially during COVID-19. Specific guidance is provided to protect pharmacists, staff, and patients during vaccine administration. Pharmacies should implement strategies to screen patients for fever and COVID-19 symptoms prior to providing influenza vaccines, and face masks should be worn by pharmacists, staff, and patients. Eye protection should also be considered when administering immunizations. Gloves should be worn and changed between patients, and hands should be washed before and after vaccine administration. There should also be a dedicated space ensuring at least 6 feet between patients in line or waiting areas.

Walgreens recently announced that they resumed immunization services ahead of flu season with additional health and safety measures that follow the updated CDC guidelines. Key measures include requiring all pharmacy team members to wear disposable face masks while administering immunizations. Patients are encouraged to wear a face covering when entering the pharmacy and will be provided with a face mask if they do not have one prior to receiving vaccines. All pharmacy team members administering vaccines will be given plastic face shields for additional protection. At least 6 feet of distance will be maintained between pharmacy areas for completing paperwork and waiting for immunizations. For references, visit drugtopics.com.

**TABLE 3. TOP COVID-19 VACCINE CANDIDATES IN THE PIPELINE**

<table>
<thead>
<tr>
<th>VACCINE NAME</th>
<th>MANUFACTURER/SPONSOR</th>
<th>CLINICAL TRIAL STATUS/ANTICIPATED STUDY DATES</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA-1273</td>
<td>Moderna and NIAID*</td>
<td>Phase 1 study showed vaccine produced immune response in all participants with no serious adverse effects; phase 2 study began enrollment in May and phase 3 trial began July 2020</td>
</tr>
<tr>
<td>AZD1222</td>
<td>AstraZeneca and Oxford University</td>
<td>Interim results from ongoing Phase 1/2 trial showed immune response was generated and no evidence of severe adverse effects; phase 2/3 studies currently underway in UK, Brazil, and South Africa with plans to begin in the US</td>
</tr>
<tr>
<td>Measles vector-based vaccine; vaccine developed using recombinant vesicular stomatitis virus technology (same technology as Ebola virus vaccine Ervebo)</td>
<td>Merck acquired Themis; IAVI and Merck are collaborating</td>
<td>Preclinical development of 2 vaccines; measles vector-based vaccine studies planned to start at the end of 2020</td>
</tr>
<tr>
<td>BNT162b1</td>
<td>Pfizer and BioNTech</td>
<td>Phase 1/2 studies showed positive data with antibody and T cell responses and no serious adverse effects; Phase 2/3 safety and efficacy trial began July 2020</td>
</tr>
<tr>
<td>Ad5</td>
<td>CanSino Biologics</td>
<td>Phase 2 study conducted in China demonstrated immune response and safety; currently planning phase 3 trial</td>
</tr>
<tr>
<td>Ad26.COV2-S, recombinant</td>
<td>Johnson &amp; Johnson</td>
<td>Phase 1/2a first human clinical trial for the investigational vaccine began in July in the U.S. and Belgium</td>
</tr>
</tbody>
</table>

NIAID indicates National Institute of Allergy and Infectious Diseases
Oxford’s COVID-19 Vaccine Induces Strong Immune Responses in Early-Stage Trial

By Gabrielle Ientile, Assistant Editor

An ongoing clinical trial led by Oxford University investigating a potential severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine against the novel coronavirus disease 2019 (COVID-19) reported encouraging early results, according to investigators.

Published in The Lancet, the phase 1/2 COV001 study’s investigators found that a single dose of the AZD1222 vaccine, previously known as ChAdOx1 nCoV-19, prompted effective immune and T cell responses. More specifically, the dose resulted in a 4-fold increase in antibodies for SARS-CoV-2 in 95% of participants 1 month following receiving the vaccine, and all participants showed a T-cell response that remained 2 months after being administered AZD1222.

The phase 1/2 trial, which incorporated 1077 healthy adult participants, correlated the vaccine with strong antibody and T cell immune responses up to day 56 on the trial, which plans to evaluate participants for 364 days. Adding to these interim results, investigators also evaluated a second dose of the vaccine in a sub-group of 10 participants and found an even stronger immune response.

Study Suggests Azithromycin Associated With Heart Death Risk

Azithromycin may be linked to a greater risk of cardiovascular death, according to a recent study.

This retrospective cohort study, published in JAMA Network Open, included 2 large, diverse, community-based integrated care delivery systems that captured encounters and prescriptions from 1998 through 2014.

The study included over 7.8 million antibiotic exposures, including azithromycin and amoxicillin exposures for outpatient use.

The cohort included nearly 3 million patients ranging from 30 to 74 years old who had at least 12 months of health-plan enrollment prior to antibiotic exposure.

The investigators noted that azithromycin was associated with a significantly increased hazard of cardiovascular death but not sudden cardiac death, within 5 days of exposure. However, they did not find any increase risk of cardiovascular death 6 to 10 days after exposure.

They noted similar results in patients within the top decile of cardiovascular risk. Azithromycin was also associated with an increased risk of noncardiovascular death and all-cause mortality within 5 days of exposure.

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• Cross-specialty feedback for multidisciplinary approaches to treatment and guidelines

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Communicating Facts Can Help Boost HPV Vaccination Rates

Pharmacists should counsel patients on how taking steps now can prevent certain cancers later. By Karen Appold

A n estimated 80% of Americans will be infected with human papillomavirus (HPV) at some point. For many people, the infection will clear on its own without causing symptoms; for others, it can cause cancer later in life.1

Community pharmacists are among the most accessible health care professionals; more than 90% of Americans live within 5 miles of a pharmacy, noted Deanna Tran, PharmD, BCACP, an assistant professor of pharmacy practice and science at the University of Maryland School of Pharmacy in Baltimore. These providers interact with customers who are picking up their medications, getting an OTC recommendation, or just passing by while buying something else.

"Through these regular interactions, pharmacists are uniquely positioned to provide education on HPV and HPV vaccines, debunk myths associated with the vaccine, and administer the vaccine at the pharmacy," she said.

Furthermore, young adults, including those in the age group indicated for the vaccine, often seek out convenient health care. Community pharmacists can provide that convenience, Tran said. Pharmacies may be open later than a traditional medical office or clinic practice, and pharmacists can administer vaccines with minimal wait times or without appointments. Community pharmacists can also play a vital role in rural or underserved areas, where a primary care provider may not be as easily visited.

Pharmacists who work in an ambulatory care clinic or in a hospital also can help boost vaccination rates. As medication experts, they often review medications and screen patients for necessary vaccinations, Tran said.

Vital Vaccine Information

HPV vaccination helps prevent new HPV infections. It does not prevent progression of HPV infection to disease, decrease time to clearance of HPV infection, or treat HPV-related disease.

The Advisory Committee on Immunization Practice (ACIP) recommends that the HPV vaccination series be started at age 11 or 12 years, although it can be initiated as early as age 9. Catch-up is recommended for all individuals through age 26 who weren’t adequately vaccinated previously.1

For unvaccinated patients aged 27 to 45 years, vaccination can be considered based on shared clinical decision-making between the provider and patient. "Although transmission is most likely to occur in adolescents and young adults, some people may have specific behavioral or medical risk factors that increase their risk of HPV infection," said Danielle C. Mayer, PharmD, BCACP, an assistant professor in the Department of Pharmacy Practice at Thomas Jefferson University’s Jefferson College of Pharmacy in Philadelphia, Pennsylvania. Currently, HPV vaccines aren’t licensed for use in adults older than 45.

"Vaccine effectiveness is lower in this older age group because these individuals may already be exposed to HPV, so a discussion with a provider would be beneficial," Tran added.

The vaccine is not recommended for pregnant women. If a woman has not been fully vaccinated for HPV, Mayer recommends starting or finishing the series in the postpartum period. The vaccine can be administered to a

Continues on Page 21 >>
$9 FOR A 90-DAY SUPPLY*

For adults on maximally tolerated statins with TG ≥150 mg/dL and established CVD or diabetes and ≥2 CVD risk factors

Add VASCEPA®
(icosapent ethyl) to
a statin for 25% RRR
in at-risk patients¹

Capsule is not actual size.

INDICATIONS AND LIMITATIONS OF USE
• VASCEPA® (icosapent ethyl) is indicated as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥150 mg/dL) and established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease
• VASCEPA is indicated as an adjunct to diet to reduce TG levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia

IMPORTANT SAFETY INFORMATION
• VASCEPA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to VASCEPA or any of its components
• VASCEPA was associated with an increased risk (3% vs 2%) of atrial fibrillation or atrial flutter requiring hospitalization in a double-blind, placebo-controlled trial. The incidence of atrial fibrillation was greater in patients with a previous history of atrial fibrillation or atrial flutter
• It is not known whether patients with allergies to fish and/or shellfish are at an increased risk of an allergic reaction to VASCEPA. Patients with such allergies should discontinue VASCEPA if any reactions occur

The wholesale price of VASCEPA is $330.98 for 120 1g capsules and $387.24 for 240 0.5g capsules. Commercially insured patients can save with the VASCEPA Savings Card. VASCEPA Savings Card may not be used to obtain prescription drugs paid in part by some Federal or State Programs; see vascepahcp.com for more information. There is no generic equivalent for VASCEPA.

With the rise of COVID-19 cases nationwide, the Office for Civil Rights (OCR) has temporarily lifted penalties associated with private telehealth communications between health care providers and their patients. For additional information, please visit the temporarily updated guidelines at hhs.gov/hipaa.
Add the next level of heart protection with VASCEPA

IMPORTANT SAFETY INFORMATION (cont’d)

- VASCEPA was associated with an increased risk (12% vs 10%) of bleeding in a double-blind, placebo-controlled trial. The incidence of bleeding was greater in patients receiving concomitant antithrombotic medications, such as aspirin, clopidogrel or warfarin.

- Common adverse reactions in the cardiovascular outcomes trial (incidence ≥3% and ≥1% more frequent than placebo): musculoskeletal pain (4% vs 3%), peripheral edema (7% vs 5%), constipation (5% vs 4%), gout (4% vs 3%) and atrial fibrillation (5% vs 4%)

- Common adverse reactions in the hypertriglyceridemia trials (incidence ≥1% more frequent than placebo): arthralgia (2% vs 1%) and oropharyngeal pain (1% vs 0.3%)

- Adverse Events, Product Complaints, or Special Situations may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088

- Patients receiving VASCEPA and concomitant anticoagulants and/or anti-platelet agents should be monitored for bleeding

- Patients with allergies should discontinue VASCEPA if any reactions occur

Please see adjacent Brief Summary of full Prescribing Information for VASCEPA or go to www.vascepahcp.com.

RRR=relative risk reduction.
*Offer Restrictions: May not be used to obtain prescription drugs paid in part by Federal or State Programs including Medicare, Medicaid, Medicare Advantage, Medicare Part D, Tricare, VA. Most eligible, insured patients will pay as little as $9 of their copay for either each month or a 90 day fill, with a maximum savings of up to $150 per month or $450 on a 90 day fill. Not for use by residents of VT, nor medical professionals licensed in VT. This offer is not valid for those patients under 18 years of age or patients whose plans do not permit use of a copay card. Void where prohibited by law, taxed, or restricted. Eligible patients include those who participate in commercial insurance, through a healthcare exchange, or pay cash. Offer good through December 31, 2020.

1Cardiovascular events including myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Cardiovascular Outcomes Trial

In a double-blind, randomized, placebo-controlled cardiovascular outcomes trial, 8,179 statin-stabilized patients were randomized to receive VASCEPA or placebo and followed for a median of 4.9 years [see Clinical Studies (14.1)]. The median age at baseline was 64 years, 29% were women, 80% White, 5% Asian, 2% Black, and 4% identified as Hispanic ethnicity. Common adverse reactions (incidence ≥ 5%) on VASCEPA and a ≥ 1% more frequent than placebo included musculoskeletal pain, peripheral edema, constipation, cough, and atrial fibrillation.

Hypertriglyceridemia Trials

In two randomized, double-blind, placebo-controlled trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks, adverse reactions reported with VASCEPA at an incidence ≥ 3% on VASCEPA and ≥ 1% more frequent than placebo based on pooled data included hypertriglyceridemia and cholesterinemia.

6.2 Postmarketing Experience

Additional adverse reactions have been identified after post-approval use of VASCEPA. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

• Diarrhea
• Blood triglycerides increased
• Abdominal discomfort
• Pain in the extremities

7. Drug Interactions

7.1 Increased Bleeding Risk with Anticoagulants and Antiplatelet Agents

Some published studies with omega-3 fatty acids have demonstrated prolongation of bleeding time. The prolongation of bleeding time reported in these studies has not exceeded normal limits and did not produce clinically significant bleeding episodes. Monitor patients receiving VASCEPA and concomitant anticoagulants and/or antiplatelet agents for bleeding.

8. Use in Specific Populations

8.1 Pregnancy

Risk Summary

The available data from published case reports and the pharmacovigilance database on the use of VASCEPA in pregnant women are insufficient to identify a drug-associated risk for major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies in pregnant rats, non-dose-related imbalances for some minor developmental findings were observed with oral administration of icosapent ethyl during organogenesis at exposures that were equivalent to the clinical exposure at the human dose of 4 g/day, based on body surface area comparisons. In a study in pregnant rabbits orally administered icosapent ethyl during organogenesis, there were no clinically relevant adverse developmental effects at exposures that were 5 times the clinical exposure, based on body surface area comparisons (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Consider the following reports in the labeling:

• Atrial Fibrillation or Atrial Flutter (see Warnings and Precautions (5.1))
• Potential for Allergic Reactions in Patients with Fish Allergy (see Warnings and Precautions (5.2))
• Bleeding (see Warnings and Precautions (5.3))

8.2 Lactation

Risk Summary

Published studies have detected omega-3 fatty acids, including EPA, in human milk. Lactating women receiving oral omega-3 fatty acids for supplementation have resulted in higher levels of omega-3 fatty acids in human milk. There are no data on the effects of omega-3 fatty acids in human milk on the breastfed infant or on milk production. The developmental and potential long-term health benefits of breastfeeding should be considered along with the mother’s clinical need for VASCEPA and any potential adverse effects on the breastfed child from VASCEPA or from the underlying maternal condition.

8.3 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.4 Geriatric Use

Of the total number of patients in well-controlled clinical studies of VASCEPA, 45% were 65 years of age and over. No overall differences in safety or effectiveness were observed between these patients and younger groups. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

8.7 Hepatic Impairment

In patients with hepatic impairment, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels should be monitored periodically during therapy with VASCEPA.

17. Patient Counseling Information

Advise the patient to read the FDA-approved patient labeling before starting VASCEPA (Patient Information).

Amarin Pharma, Inc.

9.8.5

Manufactured for:

Amarin Pharmaceuticals Ireland Limited

Bridgewater, NJ USA

Dublin, Ireland

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VAS-02466 01/20

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Distributed by: Manufactured for:

Amarin Pharma, Inc.

Amarin Pharmaceuticals Ireland Limited

Bridgewater, NJ USA

Dublin, Ireland

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VAS-02466 01/20
COUNSELING TIPS
Pharmacists can be key in boosting HPV vaccination rates. According to the CDC, just half of adolescents are up-to-date on HPV vaccination.

When speaking with patients or their caregivers, Deanna Tran, PharmD, BCACP aims to explain what diseases the HPV vaccine can prevent, the importance of completing the entire series for full protection, common adverse effects, and when to seek medical attention.

Some important facts that may help patients understand the vaccine’s importance, Tran said, include the following:

- HPV is the most common sexually transmitted infection affecting both men and women; almost every unvaccinated person who is sexually active will get HPV at some point.
- The HPV vaccine is most commonly associated with preventing cervical cancers but also protects against cancers of the oropharynx, rectum, anus, penis, vagina, and vulva. Because only cervical cancer has a recommended screening test available, screening alone won’t protect an individual from most HPV cancers.
- The recommendation to get the vaccine early in life aims to protect against cancers and diseases caused by HPV long before possible exposure. It doesn’t imply that a child is sexually active or encourage becoming sexually active.
- A child who receives the vaccine earlier, at 9 to 14 years old, needs just 2 doses.
- The vaccine prevents more than 90% of cancers caused by HPV, but it doesn’t protect against all types of HPV or against HIV or other STDs.

Managing Adverse Effects
More than 12 years of monitoring data and research demonstrate that the HPV vaccine is very safe, Tran said. Similar to other vaccines, the HPV vaccine can cause injection site reactions such as pain, redness, or swelling, as well as nausea and headache.

Fainting after receiving any vaccine is more common among adolescents, and dizziness or fainting may be more common with the HPV vaccine. Johnson suggests having patients sit or lie down for 15 minutes of observation after getting the vaccine. Patients may minimize potential pain by relaxing their arm during administration and moving their arm around afterward.

For references, visit drugtopics.com.
With more work being done online, cyber protection in pharmacies is more crucial than ever. Pharmacies bear the responsibility to safeguard both provider- and patient-level information in their workflow, which can be especially challenging with enrollment in patient portals.

"Until recently, the concept of cyber protection has largely taken a back seat to general business operation," said Chase Kassel, government relations manager for Acronis, a Tempe, Arizona–based cloud security provider. "Malicious actors have increasingly been turning their attention to the health care industry, [and] new threats to data security have been emerging."

The internet and use of computer technology are the backbone of pharmacy operations, supporting the role of providing drug therapy oversight to patients, according to Barbara Giacomelli, PharmD, area vice president at McKesson Pharmacy Optimization in Vineland, New Jersey. "Malicious actors have increasingly been turning their attention to the health care industry, and new threats to data security have been emerging."

"A cybersecurity attack not only disrupts pharmacy services but also has the potential to [affect] patient care, increase liability, and [have] a negative financial impact," Giacomelli added. "Cybercrime continues to advance tactics to breach computer systems. It is important to stay ahead of cybercriminals by having the latest computer security software, maintaining backup, and considering regular security scans."

Pharmacy personnel also need to be educated on the importance of cybersecurity and phishing risks. Many techniques can be applied to fortify against cyberattacks and protect customers' data.

"You not only want to keep your customers' trust but you [also] want to ensure that they feel safe leaving their details with you," said Heather Paunet, senior vice president of product and marketing at Untangle, a leader in comprehensive network security for small- to medium businesses. "Since most pharmacies take customer details in order to help with prescriptions, there is a risk for those details to be hacked. Implementing the right security within your pharmacy will ensure that all that data are safe, keeping your customers safe and keeping your business safe from further damage."

In this time of change and uncertainty, best practices can still be adopted to help protect pharmacies against breaches and other cyber threats. Giacomelli's top recommendations include giving employees access only to information required to do their jobs, with individual sign-ons and passwords, and running regular system security scans.

**Beware Phishing Attacks and Ransomware**

One of the biggest threats to pharmacies involves phishing, a type of online scam in which hackers send an email that appears to be legitimate and asks for sensitive information, usually to be provided via a link. The information goes straight to the crooks behind these clever fakes.

Many small businesses, including pharmacies, have seen a huge increase in phishing scams related to coronavirus disease 2019 (COVID-19), mostly through emails that claim to have updates concerning the virus. Employees need to be trained to spot phishing attempts, and use phishing filters with any email service. Pharmacies also must look out for ransomware attacks. These involve...
a form of malware that encrypts a victim’s files, and then the attacker demands a ransom to restore access to the data.

“Ransomware is a major threat we’ve seen in recent years,” Kassel said. “If you have a virus, it’s best to get your computer updated and separated from the internet.” He also noted that staff awareness and training are key to mitigating risk.

“Ironically, staff who are most comfortable with their devices are also the most vulnerable,” he said. “As we’ve transitioned to an environment where people are working from home where they are most comfortable, their awareness is not as heightened, and everyone is more susceptible when comfortable.”

Proper backups and an effective ransomware protection solution are also critical for both protection and continuity of operations. In addition, keep all software updated to help eliminate vulnerabilities, and run anti-malware software to protect against other types of malware.

“Internet of Things (IOT) devices are another major concern in today’s world,” Kassel said. “These can be personal devices, like cell phones and smart speakers, or internet-connected equipment to improve efficiency with specific job functions.” He recommends keeping personal devices off any networks with any business systems and separating systems containing PII and PHI from any necessary IOT devices that are incorporated into the business operations.

To guard against e-commerce dangers, invest in and use antivirus software; run scans frequently and at the end of the day, Brychta suggested. Virus scans should filter out known hazards, especially for pharmacists who receive attachments such as order forms. Keep operating systems updated. “These help safeguard against risks. Having an up-to-date computer best protects you,” he said.

“If you can, I highly suggest using a separate computer to receive orders and using different one to do banking and books. If the order-taking computer gets infected, there is less risk because you aren’t logged into any secure sites like banking. While you’re at it, have separate email addresses for orders and administration.”

Virtual Meeting Platforms
When COVID-19 hit, everyone rushed into working remotely. New tools were pushed, with little training, onto employees, and skipping critical steps to ensure correct operation introduced security risks.

“The most common mistake for virtual meetings is not protecting access with a password,” said Nick Santora, CEO of Curricula. “When you’re scheduling a virtual meeting, you can check a box requiring a password. Always make sure that box is checked. If you invite someone to a meeting with that link directly from the platform, it should automatically populate for a URL with the password to be included in the calendar invitation.”

Most companies with a proprietary code base, such as Skype, WhatsApp, and Slack, tend to be vague about how they manage or store customers’ data. Using those platforms means taking many risks, such as the data being routed out of the country and, in turn, not following data privacy laws such as General Data Protection Regulation, Health Insurance Portability and Accountability Act (HIPAA), and California Consumer Privacy Act.

By integrating patient linking and matching technology and adding the right layers of verification and authentication across workflow and platforms, pharmacies can remain HIPAA compliant and protect critical data such as patient names, birth dates, and prescription information, according to Mark Barwig, executive vice president of Epic Pharmacies, Inc, a network of independently owned pharmacies.

“Multifactor approach [MFA] to security and identity management extensively assesses the risk of both physical and digital identity attributes to enable accurate and timely risk detection and identity decisions,” Barwig said. “The MFA uses at least 2 independent elements, or factors, such as identity document authentication, knowledge-based questions, 1-time passwords, email verification, facial recognition, device analytics, or voice biometrics, to verify patients based on the criticality of transactions.”

As cybercrooks evolve with technology, so should pharmacies and staff. A service that receives regular updates and security fixes can help.

“Familiarize yourself with the available features of the service of your choice,” Santora said. “Subscribe to newsletters, use available training and documentation material, and share it with all users. Audit the effectiveness of your selected safety measures regularly, and take action if things are not working the way they should.”
Expert Discusses the Impact of COVID-19 on Patients With Diabetes

Managing this chronic condition during the current pandemic requires some extra steps beyond general guidelines. By Drug Topics® staff

Patients with diabetes may be particularly concerned about coronavirus disease 2019 (COVID-19) and how it could affect them. Even though COVID-19 is a fairly new disease, with limited conclusive data on the virus, the CDC has asserted that there is definite evidence that those with type 2 diabetes are at increased risk of severe illness from COVID-19. In a video interview with Drug Topics®, Carla Cox, PhD, a registered dietitian and certified diabetes educator, discussed key COVID-19 details and health-protecting measures for individuals with diabetes.

Drug Topics®: We’ve been hearing a lot about how individuals with underlying medical conditions are at a higher risk for severe illness with COVID-19, and a lot of research is being done to understand how the virus is affecting different people. How does COVID-19 affect individuals with diabetes and are there any specific risk factors?

Cox: First of all, it’s important for people with diabetes, particularly those who are well managed, [to understand] that their risk of getting COVID-19 is no greater than anybody else’s. I know a lot of people who are kind of hiding because they’re so worried about getting it. In reality, they’re not at greater risk. So that’s something everyone should know. If you do get COVID-19 and you’re in the population group of over age 60, and you have a comorbid condition, particularly in relationship to diabetes, or if their diabetes has been poorly managed—if they’ve had a lot of variability in their glucose or it’s been chronically elevated for a long time, which some people live with—then they’re at a much higher risk of morbidity and mortality than those who have diabetes and are well managed. Also, many people with diabetes who have had it for a long time, particularly those with type 2 diabetes and obesity and are not, once again, as well managed as one would hope, also have heart disease. That’s a real common side effect, and people who have both high glucose numbers and heart disease are at much higher risk.

Drug Topics®: What are some steps people with diabetes can take to manage their disease and protect themselves from the virus?

Cox: That’s a great question, and I think many of us don’t know the definitive answer. No. 1 is managing their diabetes throughout their lifetime, which is important for a whole host of reasons... (especially because) it’s much more difficult to manage glucose values when sick. If [their glucose] has already been high, it makes them much more susceptible to a progressive problem. Ways to prevent that: First, manage diabetes well; second, do the things that other people are doing, [such as] washing hands when out in public and when returning home. That’s always important for all of us, regardless of COVID-19 or anything else [going around]. We [have flu season] every year, so they need to be doing those things anyway. They should also get a flu [vaccine]. That’s another thing has

“People with diabetes should have plenty of glucose strips available or a second sensor if they’re wearing a continuous glucose monitor, so they’re always able to check their glucose in case they do get sick.”

Carla Cox, PhD

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been proposed, even for COVID-19. Even though it doesn’t affect COVID-19, [it helps prevent] 2 things happening at once. At least that’s my understanding.

Also, don’t be close to people who are sick. If an individual is supposed to go to a family party, and someone is really ill, a good idea is to just call and say, “I think I’m going to go next time, but this time, this is probably not where I need to be.

The other thing is to be prepared. People with diabetes should have plenty of glucose strips available or a second sensor if they’re wearing a continuous glucose monitor, so they’re always able to check their glucose in case they do get sick. They should also have a sick day plan provided by their health care provider.

Drug Topics®: From what you’ve seen, should people with diabetes be at all concerned about possible drug or supply shortages?

Cox: That doesn’t appear to be a problem. The companies have been very up front about saying “We have not had a reduction in our production,” and that goes for both glucose strips and medications. Some of the medications to treat the disease itself may be in short supply, but as far as their diabetes supplies, there does not appear at this time to be a shortage.

Drug Topics®: From your perspective, how well has the health care system in the United States responded to the pandemic? Are providers able to effectively treat patients with COVID-19 who have diabetes now and in the upcoming weeks or months?

Cox: That varies by state and by community. The city of New York, I know, has had some struggles in the past, though they sound like they’re very ready for it now. I have been very impressed with how everyone has come together. Both private and public companies have come together to figure out how we’re going to care for people with diabetes or without diabetes who have COVID-19 and how we are going to work together to try to get rid of this awful scourge that we have right now. I think they’ve done a great job.

The concern has been with people who are hospitalized. Are the necessary glucose checks being done? Are [health care providers] able to oversee people well enough? The advice from the diabetes associations, both the (Association of Diabetes Care and Education Specialists) and the American Diabetes Association, is that patients should be prepared to take care of themselves, actually in the hospital as far as glucose testing. The FDA has allowed personal glucometers to check glucose, which they never used to do, and also continuous glucose monitors, which many people wear. They’re allowing them in hospital care because it’s better for the people caring for patients with diabetes, who can also help take care of themselves a bit while they’re in the hospital. I think they are doing a reasonable job, and the person with diabetes just needs to be up front with their diabetes team: Tell them if they’re getting sick; be tested. If they end up in the hospital, they need to chat with their personal care provider; as well, because some of the oral medications they’re taking may not be appropriate when they have this particular virus.

Editor’s note: This interview transcription has been edited for style and clarity.
The term vasculitis refers to a rare and complex family of diseases that can cause inflammation of the aorta and other arteries, veins, and blood vessels. Vasculitis manifests in many forms, involving different parts of the body and presenting with a diverse range of severity and duration.

Kawasaki disease (KD), a form of vasculitis that is exclusive to children, is known to inflame blood vessels throughout the body, especially those feeding the heart. Currently, the CDC is investigating reports of multisystem inflammatory syndrome associated with coronavirus disease 2019 (COVID-19) in children, which may present with KD-like features. Recent studies suggest that, although rare, KD may be triggered by underlying infections such as COVID-19 or flu. KD produces clinical signs such as prolonged fever; swollen lymph nodes; bloodshot eyes sans drainage; rash; red, cracked lips and tongue; swollen lymph nodes on 1 side of the neck; and a fever of 100.4 °F or more that persists for 5 days or longer. KD typically occurs in children under 5 years of age but can also affect older children.

**The Coronavirus Connection**

The coronavirus family has been suspected of playing a role in the onset of KD for the past 2 decades. In a 2005 study, a group of researchers in Connecticut, identified a novel strain of the disease, human coronavirus New Haven, in the respiratory secretions of 8 of 11 children who had KD versus 1 out of 22 controls. COVID-19 was initially pegged as a disease that primarily affects the respiratory system. However, that changed with news of potential cutaneous involvement in certain populations in Italy in spring 2020, following reports of strange lesions on children’s skin. The results were published in The Lancet in May 2020. The Italian province of Bergamo, which had the highest number of COVID-19 infections and deaths in the Mediterranean country, experienced a 30-fold increase in incidence compared with the monthly incidences recorded during the previous 5 years.

During the month of April, investigators observed an increased incidence of what they referred to as “Kawasaki-like disease.” Between February 18 and April 20, 2020, 10 children (aged 7.5 years [SD, 3.5]) received diagnoses of KD. Children were admitted to the hospital and, on average, presented with fever on day 6 (range, 4 to 8). Half the patients presented with typical manifestations of KD, including cutaneous involvement such as polymorphic rash; hand and feet anomalies such as firm induration, erythema, or both; and nonexudative conjunctivitis. Investigators observed altered appearance of the lips and/or oral cavities of 80% of patients. The remaining 5 patients presented with incomplete forms of KD.

However, truly discerning the connection between COVID-19 or other members of the coronavirus family requires additional study.

**Recognizing KD Cases**

KD manifestations often resolve on their own, and many children recover fully. However, children who fail to receive appropriate medical evaluation and treatment face heart damage and other complications. Because no specific test can diagnose KD, a fever lasting for more than 5 days is often used as an indicator of potential disease. To help determine whether a patient has KD, a physician might run blood and urine tests, an electrocardiogram, and an echocardiogram.

KD has 2 primary treatments: prolonged aspirin therapy initiated every 6 hours and then decreased to once-daily dosing, and intravenous immunoglobulin to curtail swelling in blood vessels.

For references, visit drugtopics.com.
Pharmacy Unions Push for Improvements

Workplace conditions can affect both pharmacist and patient safety. By John Schieszer

High workloads for pharmacists increase the potential for medication errors, and during the current coronavirus disease 2019 (COVID-19) pandemic, the pressures are greater than ever. Unions are taking unprecedented steps to protect pharmacists and their patients. Their focus over the next year will be on making significant and lasting changes to prevent the growing number of obstacles that distract pharmacists from safely dispensing drugs.

In Chicago, permanent changes are occurring. Several years ago, a Chicago Tribune investigation revealed that 52% of 255 Chicago-area pharmacies had failed to warn patients about drug combinations that could cause harm or death. Since then, Teamsters Local 727 has worked with the Illinois legislature to update the state’s pharmacy act to better reflect the issues of working in a retail pharmacy. The union is pushing for mandatory, uninterrupted breaks for pharmacists.

In 2020, Teamsters Local 727 aims to raise standards, improve working conditions, and lift the collective voice of pharmacists and members of Teamsters Local 727. In an email, Teamsters Local 727 told Drug Topics® that the union is advocating for further reforms to the Illinois Pharmacy Practice Act, and, through its 2 seats on the Illinois Pharmaceutical Task Force, this fall it will give recommendations to the state legislature regarding further reforms.

The union supports additional policy reforms, including limiting retail pharmacists’ workdays to 8 hours, requiring that at least 1 pharmacy technician be on duty at all times when a pharmacist is scheduled, and requiring a separate break room to guarantee uninterrupted breaks. In addition, Teamsters Local 727 is asking for a triple-pay penalty for days when a retail employer fails to give a pharmacist the opportunity for an uninterrupted break.

“Retail chains should be held responsible for any failure to allow pharmacists to take uninterrupted breaks. When pharmacists are unable to take breaks, it’s usually due to understaffing in the pharmacy while the duties for pharmacists continue to grow,” Teamsters Local 727 said in the email.

Ilisa Bernstein, PharmD, JD, senior vice president for pharmacy practice and government affairs at the American Pharmacists Association in Washington, DC, said several states have rules governing pharmacist breaks, including the minimum number, based on hours worked, and where they can be taken. “In addition, some employers have begun providing breaks for pharmacists,” Bernstein told Drug Topics® in an email. “Whether by law or policy, employers should provide pharmacists with mandatory, scheduled, uninterrupted meal breaks away from the pharmacy workflow to promote pharmacist well-being and improve patient safety.”

The COVID-19 pandemic has created significant disruptions in pharmacy operations and raised pharmacist safety concerns, according to Bernstein. “Access to appropriate [personal protective equipment (PPE)] and barriers in accordance with CDC guidance, distancing issues, personnel shortages, drug supply disruptions, and more have left pharmacists in a constant state of uncertainty, and they are taking extraordinary measures to ensure consistent delivery of quality patient care,” she said.

States, federal agencies, and employers have taken steps to improve conditions, she said, but as the pandemic evolves, so do pharmacist issues.

“With testing now and immunizations once a vaccine becomes available, community pharmacists could be the centerpiece for helping the country get back to normalcy.” - B. Douglas Hoey, MBA, RPh
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and concerns. For example, she said, although pharmacists welcome the ability to provide COVID-19 testing and a potential vaccine, employers and employees need to collaborate in the workplace to mitigate pharmacy operation and safety concerns.

Veronica Bandy, PharmD, MS, past president of the California Pharmacists Association in Sacramento, said that state laws regarding staff breaks vary. “Breaks for pharmacy personnel are needed to prevent fatigue and allow for time to use the facilities. Adequate staffing, breaks, and safety would be beneficial to be addressed to ensure the ability for pharmacists to provide health care at its highest level,” Bandy told Drug Topics® in an email.

The pandemic has changed the practice of pharmacy. Some pharmacies have placed protective partitions between patients and personnel. Individuals are encouraged to use drive-through or other social distancing methods for prescription pickup. In addition, masks need to be worn, and PPE use and social distancing between staff members must increase. “The California Pharmacists Association has been instrumental in advocating that pharmacists as health care providers have access to face masks and other [PPE]. As with many areas of health care, the practice of pharmacy is adapting on a daily basis as more scientific information becomes available,” Bandy said.

James Broughel, a senior research fellow at the Mercatus Center at George Mason University in Arlington, Virginia, said that in response to the pandemic, many governors expanded pharmacists’ prescribing authority or made it easier for medical professionals licensed in another state to practice. Many states have drive-through COVID-19 testing sites at pharmacy locations; although the extent of these operations varies significantly across states, pharmacists already play a significant role, which is likely to grow over time. “Unions should anticipate that pharmacists are going to be doing a lot of COVID-19 testing and ensure that adequate precautions are taken to ensure the safety of pharmacy staff, as well as customers,” Broughel told Drug Topics®.

Workload Matters

Study results published in 2007 in the journal Medical Care found that high workloads for pharmacists increase the potential for medication errors. In a retrospective study, investigators reviewed data submitted to insurance companies by 672 pharmacies in 18 metropolitan regions. The pharmacies filled an average of 17,948 prescriptions from January to March 2003. The investigators found that factors significantly related to an increased risk of dispensing prescriptions with potential drug-drug interactions included pharmacist workload (odds ratio [OR], 1.03), pharmacy staffing (OR, 1.10), and various technologies, such as sophisticated telephone systems, internet receipt of orders, and refill requests.

The pharmacies employed an average of 1.2 pharmacists for each hour the store was open, and each pharmacist filled an average of 14.1 prescriptions per hour. The risk of dispensing potentially harmful drug combinations increased by 3% for each additional prescription filled per hour. There has been little improvement since the research was done, said study investigator Dan Malone, PhD, RPh, a professor at the University of Utah College of Pharmacy in Salt Lake City. “Working conditions are worse,” Malone told Drug Topics® in an email. “I would suggest that not much has changed.”

Mike DeAngelis, senior director of corporate communications for CVS Health in Woonsocket, Rhode Island, said the company has policies and protocols to help ensure that stores are safe for both employees and patients during the current pandemic. All employees have received protective masks, gloves, hand sanitizer, and cleaning supplies and are required to wear a company-issued mask, their own mask, or a cloth face covering. “We have installed protective panels at our pharmacy counters and front-store checkout stations in all stores. We have hourly protocols in place for cleaning hard surfaces and more frequent cleaning of commonly handled items,” DeAngelis said in an email.

B. Douglas Hoey, MBA, RPh, CEO of the National Community Pharmacists Association in Alexandria, Virginia, said community pharmacies are the safety nets helping their communities during both times of crisis and normal times. In addition, pharmacists now are on the front line in America’s fight against COVID-19, ordering and administering tests. “With testing now and immunizations once a vaccine becomes available, community pharmacists could be the centerpiece for helping the country get back to normalcy,” Hoey told Drug Topics® in an email. How smoothly that goes will depend on the rights and protections afforded pharmacists in retail stores across the nation.

For references, visit drugtopics.com.
Health Crisis Highlights Value of Pharmacy Compounding

Industry insiders share tips for making a successful entry into this crucial field.  

By Keith Loria

In the era of coronavirus disease 2019 (COVID-19), pharmaceutical compounding is as vital as ever. Although compounding has experienced a drop in coverage by shortsighted payers, the events surrounding the COVID-19 pandemic have demonstrated the worth of having ready and capable compounding pharmacies, according to Jesse C. Dresser, Esq, partner at Frier Levitt, a pharmacy law group in New York.

"From mixing hand sanitizer to ensuring a steady supply of [drugs] for patients in dire need, compounding pharmacies have more than proved their worth in the midst of this crisis," he said. "But ultimately, the value and importance of pharmacy compounding in 2020 go far beyond safeguarding against medication shortages and continue to play a vital role in fulfilling unmet medication needs for individual patients and health systems alike."

From nonsterile to sterile compounding, there has never been a greater need for flexibility while maintaining the highest safety standard, with the most robust policies and standard operating procedures to back it up, said AJ Rivosecchi, PharmD, director of clinical solutions at Kit Check.

"The situation pharmacies find themselves in with unpredictable, ongoing, and pervasive shortages has in many cases taken what may have been a decision on buying finished goods versus compounding based on ability and economics and made it a necessary reality of daily life to maintain standards of care," Rivosecchi said. "Coupling this increased need with the rising regulatory bandwidth being paid to sterile, nonsterile, and hazardous compounding makes pharmacy compounding a top priority in terms of importance for pharmacies around the country."

Understanding Regulations

From FDA-enforced current good manufacturing practices at the manufacturer level down to individual state boards, there is no dearth of regulations in the compounding space.

"The USP [United States Pharmacopeia Convention] chapters 795, 797, and 800 are forefront on the minds of pharmacy leaders," Rivosecchi said. "[USP general chapter] 795 covers nonsterile compounding, 797 covers sterile compounding, and 800 covers hazardous drug handling. This trio of regulations, when taken together, has had the biggest impact on the industry."

Pending revisions to chapters 795 (last updated in 2014) and 797 (last updated in 2008), as well as the official adoption of chapter 800 on December 1, 2019, have guided decisions in the compounding space for the past decade.

Between the proposed revisions and the official version of USP 800, the industry has never before had so much guidance for ensuring both patient and employee safety. Rivosecchi calls that a "real win" for the industry because it will help standardize best practices and prevent bad actors from skirting more lax regulations. However, these mandates are largely unfunded, and good actors, who aim for compliance and maintenance, would benefit from increased funding."

Continues on Page 41 >>
Indication for AirDuo RespiClick/Authorized Generic

AirDuo RespiClick is indicated for the treatment of asthma in patients aged 12 years and older. AirDuo RespiClick is only for patients uncontrolled on an inhaled corticosteroid (ICS) or whose disease severity clearly warrants an ICS/Long-acting beta₂-agonist (LABA).

Important Limitation of Use: AirDuo RespiClick is NOT indicated for the relief of acute bronchospasm.

Important Safety Information for AirDuo RespiClick/Authorized Generic

- **Contraindications:** AirDuo RespiClick is contraindicated in:
  - Primary treatment of status asthmaticus or other acute episodes of asthma requiring intensive measures
  - Patients with known severe hypersensitivity to milk proteins or any ingredients of AirDuo RespiClick

Please see additional Important Safety Information and Brief Summary of Full Prescribing Information on the following pages.
Recommended starting dose: 1 inhalation twice daily\(^1\)-\(^3\)

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<td>Fluticasone propionate + Salmeterol</td>
<td>Fluticasone propionate + Salmeterol</td>
<td>Fluticasone propionate + Salmeterol</td>
</tr>
<tr>
<td>55 mcg + 14 mcg</td>
<td>113 mcg + 14 mcg</td>
<td>232 mcg + 14 mcg</td>
</tr>
<tr>
<td>55 mcg + 14 mcg</td>
<td>113 mcg + 14 mcg</td>
<td>232 mcg + 14 mcg</td>
</tr>
<tr>
<td>100 mcg + 50 mcg</td>
<td>250 mcg + 50 mcg</td>
<td>500 mcg + 50 mcg</td>
</tr>
</tbody>
</table>

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Table is intended to show differences in dosing only and should not be construed to imply safety or efficacy similarities or differences.

**IMPORTANT SAFETY INFORMATION for AirDuo RespiClick/Authorized Generic (continued)**

- **Serious Asthma-Related Events – Hospitalizations, Intubations, Death:** Use of LABA as monotherapy (without ICS) for asthma is associated with an increased risk of asthma-related death. Available data from controlled clinical trials also suggest that use of LABA as monotherapy increases the risk of asthma-related hospitalization in pediatric and adolescent patients. These findings are considered a class effect of LABA monotherapy. When LABA are used in fixed-dose combination with ICS, data from large clinical trials do not show a significant increase in the risk of serious asthma-related events (hospitalizations, intubations, death) compared with ICS alone.

- **Deterioration of Disease and Acute Episodes:** AirDuo RespiClick should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of asthma. AirDuo RespiClick is not indicated for the relief of acute bronchospasm. An inhaled, short-acting beta\(_2\)-agonist, not AirDuo RespiClick, should be used to relieve acute symptoms such as shortness of breath.

- **Excessive Use and Use with Other Long acting Beta\(_2\)-Agonists:** AirDuo RespiClick should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medicines containing LABA, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs. Patients using AirDuo RespiClick should not use another medicine containing a LABA (e.g., salmeterol, formoterol fumarate, arformoterol tartrate, indacaterol) for any reason.

Please see additional Important Safety Information throughout and Brief Summary of Full Prescribing Information on the following pages.
• Local Effects of ICS: Oropharyngeal candidiasis has occurred in patients treated with AirDuo RespiClick. If this occurs, treat with appropriate local or systemic (i.e., oral) antifungal therapy while treatment with AirDuo RespiClick continues, but at times therapy with AirDuo RespiClick may need to be interrupted. Advise the patient to rinse his/her mouth with water without swallowing following inhalation.

• Immunosuppression: Patients who use corticosteroids are at risk for potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex. A more serious or even fatal course of chickenpox or measles may occur in susceptible patients. Use with caution in patients with the above because of the potential for worsening of these infections.

• Transferring Patients from Systemic Corticosteroid Therapy: Particular care is needed for patients who have been transferred from systemically active corticosteroids to ICS because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer from systemic corticosteroids to less systemically available ICS. Taper patients slowly from systemic corticosteroids if transferring to AirDuo RespiClick.

• Hypercorticism and Adrenal Suppression may occur with high doses of ICS, including fluticasone propionate, or at the recommended dose in susceptible individuals. If such changes occur, discontinue AirDuo RespiClick slowly.

• Drug Interactions with Strong Cytochrome P450 3A4 Inhibitors: The use of strong cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., ritonavir, ketoconazole) with AirDuo RespiClick is not recommended because increased systemic corticosteroid and increased cardiovascular adverse effects may occur.

• Paradoxical Bronchospasm and Upper Airway Symptoms: If paradoxical bronchospasm occurs, discontinue AirDuo RespiClick immediately and institute alternative therapy.

• Hypersensitivity Reactions, Including Anaphylaxis: Immediate hypersensitivity reactions (e.g., urticaria, angioedema, rash, bronchospasm, hypotension), including anaphylaxis, may occur after administration of AirDuo RespiClick. Discontinue AirDuo RespiClick if such reactions occur.

• Cardiovascular and Central Nervous System Effects: Salmeterol, a component of AirDuo RespiClick, can produce clinically significant cardiovascular effects in some patients as measured by pulse rate, blood pressure, and/or symptoms. If such effects occur, AirDuo RespiClick may need to be discontinued. AirDuo RespiClick should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

• Reduction in Bone Mineral Density (BMD): Decreases in BMD have been observed with long-term administration of products containing ICS. Patients with major risk factors for decreased bone mineral content, such as prolonged immobilization, family history of osteoporosis, or chronic use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids) should be monitored and treated with established standards of care.

• Effect on Growth: ICS, as well as poorly controlled asthma, may cause a reduction in growth velocity, and the long-term effect on final adult height is unknown. Patients should be maintained on the lowest dose of inhaled corticosteroid that effectively controls their asthma. Monitor growth of pediatric patients.

• Glaucoma and Cataracts: Long-term use of ICS, including fluticasone propionate, a component of AirDuo RespiClick, may increase the risk for cataracts or glaucoma. Regular eye exams should be considered.

• Eosinophilic Conditions and Churg-Strauss Syndrome: Systemic eosinophilic conditions, such as Churg-Strauss syndrome, may occur. Be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy.

• Coexisting Conditions: Use with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, ketoacidosis, and in patients who are unusually responsive to sympathomimetic amines.

• Hypokalemia and Hyperglycemia: Beta-adrenergic agonist medicines may produce significant hypokalemia in some patients, possibly through intracellular shunting, which has the potential to produce adverse cardiovascular effects.

Please see additional Important Safety Information on the previous pages and Brief Summary of Full Prescribing Information on the following pages.
AirDuo RespiClick® (fluticasone propionate and salmeterol) Inhalation Powder:

ASTHMA CONTROL WITH LESS MEDICINE

Not all strengths are depicted above. Additional strengths of AirDuo RespiClick and its authorized generic are 55/14 (fluticasone propionate 55 mcg and salmeterol 14 mcg) and 232/14 (fluticasone propionate 232 mcg and salmeterol 14 mcg).

Total Daily Dose¹⁻³

<table>
<thead>
<tr>
<th></th>
<th>AirDuo RespiClick</th>
<th>Authorized Generic</th>
<th>ADVAIR DISKUS®</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fluticasone propionate + Salmeterol</td>
<td>Fluticasone propionate + Salmeterol</td>
<td>Fluticasone propionate + Salmeterol</td>
</tr>
<tr>
<td>Low</td>
<td>110 mcg + 28 mcg</td>
<td>110 mcg + 28 mcg</td>
<td>200 mcg + 100 mcg</td>
</tr>
<tr>
<td>Medium</td>
<td>226 mcg + 28 mcg</td>
<td>226 mcg + 28 mcg</td>
<td>500 mcg + 100 mcg</td>
</tr>
<tr>
<td>High</td>
<td>464 mcg + 28 mcg</td>
<td>464 mcg + 28 mcg</td>
<td>1000 mcg + 100 mcg</td>
</tr>
</tbody>
</table>

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IMPORTANT SAFETY INFORMATION for AirDuo RespiClick/Authorized Generic (continued)

- Adverse Reactions: Most common adverse reactions (reported in greater than or equal to 3% of patients) include nasopharyngitis, oral candidiasis, headache, cough and back pain

Please see Important Safety Information on the previous pages and Brief Summary of Full Prescribing Information on the following pages.

References

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AIRDUO® RESPICLICK® (fluticasone propionate and salmeterol) inhalation powder

AIRDUO® RESPICLICK did not show a significantly increased risk of a serious asthma-related event compared to ICS based on the prespecified risk margin (2.7), with an estimated hazard ratio of time to first event of 1.29 (95% CI: 0.73, 2.27). Salmeterol Multicenter Asthma Research Trial (SMART)

A 28-week, placebo-controlled, U.S. trial that compared the safety of salmeterol with placebo, each added to usual asthma therapy, showed an increase in asthma-related deaths in subjects receiving salmeterol (13/13,176 in subjects treated with salmeterol versus 3/13,179 in subjects treated with placebo; relative risk: 4.37 (95% CI: 1.25, 15.34)). Use of background ICS was not required in SMART. The increased risk of asthma-related death is considered a class effect of LABA monotherapy.

5.2 Deterioration of Disease and Acute Episodes

AIRDUO RESPICLICK should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of asthma. AIRDUO RESPICLICK has not been studied in subjects with acutely deteriorating asthma. The initiation of AIRDUO RESPICLICK in this setting is not appropriate.

Serious acute respiratory events, including fatalities, have been reported when salmeterol, a component of AIRDUO RESPICLICK, has been initiated in patients with significantly worsening or acutely deteriorating asthma. In most cases, these have occurred in patients with severe asthma (e.g., patients with a history of corticosteroid dependence, low pulmonary function, intubation, mechanical ventilation, frequent hospitalizations, previous life-threatening acute asthma exacerbations) and in some patients with acutely deteriorating asthma, patients with significantly increasing symptoms; increasing need for inhaled, short-acting beta-agonists; decreasing response to usual medications; increasing need for systemic corticosteroids; recent exacerbation (with hospital stay); and patients with asthma-related hospitalizations.

In clinical trials, the development of localised infections of the mouth and pharynx with Candida albicans has occurred in subjects treated with AIRDUO RESPICLICK. When such an infection develops, it should be treated with appropriate local or systemic therapy. If oral thrush develops, treatment with antifungal therapy may be considered.

When beginning treatment with AIRDUO RESPICLICK, patients who have been taking oral or inhaled, short-acting beta-agonists on a regular basis (e.g., 4 times a day) should be instructed to discontinue the regular use of these drugs. Additional beta-agonists should be used as needed for rescue therapy.

5.3 Excessive Use of AIRDUO RESPICLICK and Use with Other Long-Acting Beta-2-Agonists

AIRDUO RESPICLICK should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medications containing LABA, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs. Patients using AIRDUO RESPICLICK should not use another medicine containing a LABA (e.g., albuterol) for treatment of acute symptoms, despite regular twice-daily use of AIRDUO RESPICLICK.

When beginning treatment with AIRDUO RESPICLICK, patients who have been taking oral or inhaled, short-acting beta-agonists on a regular basis (e.g., 4 times a day) should be instructed to discontinue the regular use of these drugs.

5.4 Local Effects of Inhaled Corticosteroids

In clinical trials, the development of localised infections of the mouth and pharynx with Candida albicans has occurred in subjects treated with AIRDUO RESPICLICK. When such an infection develops, it should be treated with appropriate local or systemic therapy. If oral thrush develops, treatment with antifungal therapy may be considered.

5.5 Immunosuppression

Persons who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have more serious or even fatal courses in susceptible adolescents or adults using corticosteroids. In such patients who have not had these diseases or who have not been properly immunized, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If a patient is exposed to chickenpox, prophylaxis with varicella-zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG) may be indicated. If a patient is exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. (See respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered.

Inhaled corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract; systemic fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex.

5.6 Transferring Patients from Systemic Corticosteroid Therapy

If systemic corticosteroids are used, patients who are transferred from systemic active corticosteroids to inhaled corticosteroids because deaths due to adrenal insufficiency have occurred in patients with asthma during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids. After withdrawal from systemic corticosteroids, a number of months are required for recovery of hypothalamic-pituitary-adrenal (HPA) function.
Patients who have been previously maintained on 20 mg or more of prednisone (or its equivalent) may be most susceptible, particularly when their systemic corticosteroids have been almost completely withdrawn. During this period of HPA suppression, patients may exhibit signs and symptoms of adrenal insufficiency when exposed to trauma, surgery, or infection (particularly gastrointestinal), or other conditions associated with severe electrolyte loss. Although AIRDUO RESPICLICK may improve control of asthma symptoms during these episodes, in recommended doses it supplies less than normal physiological amounts of corticosteroid systemically and does not provide the mineralocorticoid activity that is necessary for coping with these emergencies.

During periods of stress or a severe asthmatic attack, patients who have been withdrawn from systemic corticosteroids should be instructed to resume oral corticosteroids (in large doses) immediately and to contact their physician for further instruction. These patients should also be instructed to carry a medical identification warning card indicating that they may need supplemental systemic corticosteroids during periods of stress or a severe asthma attack.

Patients requiring systemic corticosteroids should be weaned slowly from systemic corticosteroid use to AIRDUO RESPICLICK. Lung function (mean forced expiratory volume in 1 second [FEV1], or morning peak expiratory flow [AM PEF]), beta-agonist use, and asthmatic symptoms should be carefully monitored during withdrawal of systemic corticosteroids, some patients may note exacerbation of asthma symptoms during periods of stress.

Tachycardia, tremor, or oral corticosteroids, some patients may note exacerbation of asthma symptoms during periods of stress.

5.9 Paradoxical Bronchospasm and Upper Airway Symptoms

As systemic corticosteroids, a component of AIRDUO RESPICLICK, will often help control asthma symptoms with less suppression of HPA function than therapeutically equivalent oral doses of prednisone. Since fluticasone propionate is absorbed into the circulation and can be systemically active at higher doses, the beneficial effects of AIRDUO RESPICLICK in minimizing HPA dysfunction may be expected only when recommended dosages are not exceeded and individual patients are titrated to the lowest effective dose. A relationship between plasma levels of fluticasone propionate and inhibitory effects on stimulated cortisol production has been shown after 4 weeks of treatment with fluticasone propionate inhalation aerosol. Since individual sensitivity to effects on cortisol production exists, physicians should consider this information when prescribing AIRDUO RESPICLICK.

Because of the possibility of significant systemic absorption of inhaled corticosteroids, patients treated with AIRDUO RESPICLICK should be observed carefully for any evidence of systemic corticosteroid effects. Particular care should be taken in observing patients postoperatively or during periods of stress for evidence of inadequate adrenal response. It is possible that transfer of corticosteroid effects such as hypercorticism and adrenal suppression (including adrenal crisis) may appear in a small number of patients who are sensitive to these effects. If such effects occur, AIRDUO RESPICLICK should be discontinued. If withdrawal of corticosteroids is not possible, patients should consider taking corticosteroids in this clinical setting. Physicians should be alert to eosinophilia, vasculitis, worsening pulmonary symptoms, cardiac complications, and/or neurophytosis in their patients. A causal relationship between fluticasone propionate and these underlying conditions has not been established.

5.10 Hypersensitivity Reactions, Including Anaphylaxis

Inhalation of the fluticasone propionate and salmeterol inhalation powder, including anaphylaxis, may occur after administration of AIRDUO RESPICLICK. There have been reports of anaphylactic reactions in patients with severe milk protein allergy after inhalation of dairy products containing lactose; therefore, patients with severe milk protein allergy should not use AIRDUO RESPICLICK (see Contraindications (4)).

Reactions with other inhaled beta-adrenergic agonists, including inhaled salmeterol, have been reported in patients with a history of asthma and a positive skin test to aspirin or related NSAIDs. In patients with a history of aspirin sensitivity, treatment with inhaled salmeterol should be approached with caution. Patients with a history of aspirin sensitivity may be at increased risk for bronchospasm and other adverse reactions with inhaled beta-adrenergic agonists.

5.11 Cardiovascular and Central Nervous System Effects

Excessive beta-adrenergic stimulation has been associated with seizures, angina, hypertension or hypotension, tachycardia with rates up to 200 beats/min, arrhythmias, nervousness, headache, tremor, palpitation, nausea, dizziness, fatigue, malaise, and insomnia (see Overdosage (10)). Therefore, AIRDUO RESPICLICK, like all products containing sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

6 ADVERSE REACTIONS

Use of LABA may result in the following:

- Serious asthma-related events – hospitalizations, intubations, death (see Warnings and Precautions (5.1))
- Cardiovascular and central nervous system effects (see Warnings and Precautions (5.11))
- Cytotoxic and local corticosteroid use may result in the following:
  - Candida albicans infection (see Warnings and Precautions (5.4))
  - Immunoppression (see Warnings and Precautions (5.5))
- Reduction in bone mineral density (see Warnings and Precautions (5.12))
- Growth effects in pediatrics (see Warnings and Precautions (5.13))
- Glaucoma and cataracts (see Warnings and Precautions (5.14))

In the development of fluticasone propionate, a component of AIRDUO RESPICLICK, the potential for producing ventricular arrhythmias. Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.
AIRDUO® RESPICLICK® (fluticasone propionate and salmeterol) inhalation powder

6.1 Clinical Trials Experience in Asthma

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The clinical trials of AIRDUO RESPICLICK involved 1,364 adolescents and adult patients with persistent symptomatic asthma despite ICS or ICS/LABA therapy, treated twice daily with either placebo; fluticasone propionate 113 mcg or 232 mcg (ARMONAIR RESPICLICK, hereafter referred to as fluticasone propionate MDPI); or AIRDUO RESPICLICK 55 mcg/14 mcg, 113 mcg/14 mcg, or 232 mcg/14 mcg. Sixty percent of patients were female and 80% of patients were white. The average duration of exposure was 82 to 84 days in the fluticasone propionate MDPI and AIRDUO RESPICLICK treatment groups compared with 75 days in the placebo group. Table 2 displays the incidence of most common adverse reactions in pooled Trials 1 and 2.

Table 2: Adverse Reactions with ≥3% Incidence with AIRDUO RESPICLICK, and More Common than Placebo in Subjects with Asthma (Trials 1 and 2)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>AIRDUO RESPICLICK (55 mcg/14 mcg)</th>
<th>Fluticasone Propionate (113 mcg/14 mcg)</th>
<th>Fluticasone Propionate (232 mcg/14 mcg)</th>
<th>AIRDUO RESPICLICK (113 mcg/14 mcg)</th>
<th>AIRDUO RESPICLICK (232 mcg/14 mcg)</th>
<th>Placebo (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>5.4</td>
<td>5.6</td>
<td>4.8</td>
<td>5.6</td>
<td>4.8</td>
<td>4.8</td>
</tr>
<tr>
<td>Oral candidiasis*</td>
<td>3.1</td>
<td>2.9</td>
<td>4.8</td>
<td>3.1</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>Headache</td>
<td>1.6</td>
<td>7.5</td>
<td>4.3</td>
<td>5.8</td>
<td>4.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Cough</td>
<td>1.6</td>
<td>1.8</td>
<td>3.4</td>
<td>2.3</td>
<td>3.7</td>
<td>2.1</td>
</tr>
<tr>
<td>Back pain</td>
<td>0.8</td>
<td>1.3</td>
<td>1.4</td>
<td>0.7</td>
<td>1.4</td>
<td>1.3</td>
</tr>
</tbody>
</table>

* Oral candidiasis includes oropharyngeal candidiasis, oral fungal infection, and oropharyngitis fungal

Other adverse reactions not previously listed (and occurring in ≥3% of patients in three or more patients on AIRDUO RESPICLICK) that were reported more frequently by patients with asthma treated with AIRDUO RESPICLICK compared with patients with placebo include the following:

- Sinusitis, oropharyngeal pain, pharyngitis, dizziness, influenza, rhinitis allergic, nausea, vomiting, abdominal pain, postnasal discharge, abdominal pain/pain, myalgia, pain in extremity, dyspnea, laceration, dermatitis contact, and palpitations.

7 DRUG INTERACTIONS

AIRDUO RESPICLICK has been used concomitantly with other drugs, including short-acting beta-agonists, and inhaled corticosteroids, commonly used in patients with asthma via MDPI, 55 mcg, 113 mcg. No formal drug interaction trials have been performed with AIRDUO RESPICLICK.

7.1 Inhibitors of Cytochrome P450 3A4

Fluticasone propionate and salmeterol, the individual components of AIRDUO RESPICLICK, are substrates of CYP3A4. The use of strong CYP34 inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, ritonavir, lopinavir, and dolutegravir) with AIRDUO RESPICLICK is not recommended because increased systemic corticosteroid and increased cardiovascular adverse effects may occur.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no randomized clinical studies of AIRDUO RESPICLICK or individual components, fluticasone propionate and salmeterol, in pregnancy. There are no clinical considerations with the use of AIRDUO RESPICLICK in pregnant women [see Clinical Considerations]. Animal reproduction studies are available with the combination of fluticasone propionate and salmeterol as well as individual components. In animals, teratogenicity characteristic of corticosteroids, decreased fetal body weight and/or skeletal variations, in rats, mice, and rabbits were observed with subcutaneously administered maternal toxic doses of fluticasone propionate and salmeterol inhalation powder (500 mcg/m2), or fluticasone propionate and salmeterol inhalation powder (500 mcg/m2). The types of adverse reactions were similar to those reported above in placebo controlled studies.

AIRDUO® RESPICLICK® (fluticasone propionate and salmeterol) inhalation powder
Fluticasone Propionate and Salmeterol: In an embryo/fetal development study with pregnant rats that received the combination of fluticasone propionate and oral administration of salmeterol at doses of 0/1000, 100/0, 1000/0, 100/1000, 1000/10,000 mcg/kg/day, fluticasone propionate/salmeterol during the period of organogenesis, findings were generally consistent with the individual monoproducts and there was no exacerbation of expected fetal effects. Omphalocele, increased embryo/fetal deaths, decreased body weight, and skeletal variations were observed in rat fetuses, in the presence of maternal toxicity, when combining fluticasone propionate at a dose approximately 2 times the MRHDID (on a mcg/m² basis at a maternal oral dose of 10,000 mcg/kg/day) and a dose of salmeterol at approximately 3500 times the MRHDID (on a mcg/m² basis at a maternal oral dose of 10,000 mcg/kg/day). The rat test did not exacerbate adverse effect levels. In an embryo/fetal development study with pregnant mice that received the combination of subcutaneous administration of fluticasone propionate and oral administration of salmeterol at doses of 0/1000, 0/10, 100/0, 1000/0, 100/1000, 1000/10,000 mcg/kg/day, the systemic effects of ICS, including AIRDUO RESPICLICK, may cause a reduction in growth velocity in adolescents on any corticosteroid appears to have growth suppression, the possibility that he/she is particularly sensitive to this effect of corticosteroids should be considered. In such patients, the potential effect of fluticasone propionate may cause a reduction in growth velocity in adolescents on any corticosteroid appears to have growth suppression, the possibility that he/she is particularly sensitive to this effect of corticosteroids should be considered. In such patients, the potential effect of prolonged use of AIRDUO RESPICLICK for this indication was supported by evidence from two adequate and well-controlled trials in adolescents 12 years old and older with persistent symptomatic asthma despite treatment with both an ICS and a LABA has been established. Use of AIRDUO RESPICLICK for this indication was supported by evidence from two adequate and well-controlled trials in adolescents 12 years old and older with persistent symptomatic asthma despite treatment with both an ICS and a LABA has been established. Use of AIRDUO RESPICLICK for this indication was supported by evidence from two adequate and well-controlled trials in adolescents 12 years old and older with persistent symptomatic asthma despite treatment with both an ICS and a LABA has been established. 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Use of AIRDUO RESPICLICK for this indication was supported by evidence from two adequate and well-controlled trials in adolescents 12 years old and older with persistent symptomatic asthma despite treatment with both an ICS and a LABA has been established. Use of AIRDUO RESPICLICK for this indication was supported by evidence from two adequate and well-controlled trials in adolescents 12 years old and older with persistent symptomatic asthma despite treatment with both an ICS and a LABA has been established. Use of AIRDUO RESPICLICK for this indication was supported by evidence from two adequate and well-controlled trials in adolescents 12 years old and older with persistent symptomatic asthma despite treatment with both an ICS and a LABA has been established. 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The judicious use of a cardiospecific beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. Cardiac monitoring is recommended in cases of overdosage. Fluticasone propionate Chronic overdosage of fluticasone propionate may result in signs/symptoms of Cushing’s Syndrome (see Warnings and Precautions (5.7)). Inhalation by healthy volunteers of a single dose of 4,000 mcg of fluticasone propionate inhalation powder or single doses of 1,760 and 3,520 mcg of fluticasone propionate CFC inhalation powder has been well tolerated. Fluticasone propionate given by inhalation aerosol at doses of 1,320 mcg twice daily for 7 to 15 days to healthy human volunteers was also well tolerated. Repeat oral doses up to 80 mg daily for 10 days in healthy volunteers and repeat oral doses up to 20 mg daily for 42 days in subjects were well tolerated. Adverse reactions were of mild or moderate severity, and incidences were similar in active and placebo treatment groups.
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Salmeterol
The expected signs and symptoms with overdosage of salmeterol are those of excessive beta-adrenergic stimulation and/or occurrence or exaggeration of any of the signs and symptoms of beta-adrenergic stimulation (e.g., seizures, angina, hypertension or hypotension, tachycardia with rates up to 200 beats/min, arrhythmias, nervousness, headache, tremor, muscle cramps, dry mouth, palpitation, nausea, dizziness, fatigue, malaise, insomnia, hyperglycemia, hypokalemia, metabolic acidosis). Overdosage with salmeterol can lead to clinically significant prolongation of the QTc interval, which can produce ventricular arrhythmias.

As with all inhaled sympathomimetic medicines, cardiac arrest and even death may be associated with an overdose of salmeterol.

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This brief summary is based on the AIRDUO® RESPICLICK® full prescribing information AIRDPI-005.
“Independent ownership is difficult in this time but also has its advantages for those who want to think outside the box.”  

ALMAZ DAWIT, PHARMD

In lieu of promulgating formal regulations, the FDA has opted to issue industry guidance on intended regulatory enforcement. It has taken the FDA several years to “finalize” much of this guidance, Dresser said; at press time, the memorandum of understanding addressing the interstate distribution of compounded medications has not yet been finalized and adopted by states and the FDA.

Finding Success

Industry insiders noted that success in compounding involves understanding the landscape and asking key questions: “What does the market need? Where does it need it? How do I meet that need efficiently to allow me to comply with all relevant regulations?”

“To answer those questions, you must consider what’s already commercially available; what the FDA has deemed appropriate for compounding due to shortages; what is the cost of your materials, labor, and maintaining compliance; and, ultimately, where is the balance that makes all these things an attractive target and leads to success,” Rivosecchi said. “The demand is clearly there, so that much is known—the true key to being successful in this space, whether in a hospital or in a commercial application, is identifying what demand you can meet safely and efficiently.”

According to Dawit, success lies in the ability to meet the specific needs of patients who can pay cash for tailored medications and in being innovative and targeted when selecting products. She also noted the importance of visibility to practitioners who support patients whose needs are not met by typical retail pharmacy. Dawit listed 3 crucial steps toward success: (1) Institute robust procedures that ensure compliance with all applicable forms of regulation. (2) Identify a workable business model in the wake of coverage restrictions. (3) Avoid common legal and regulatory pitfalls.

Entering the Field

Pharmacists who want to get involved in compounding should learn from their peers, according to Rivosecchi. “Whatever your focus will be—sterile, nonsterile, or hazardous—go find people who are doing it well and leverage their best practices and learnings,” he said. “No one will have a turnkey solution for you, but everyone in the field is doing something well, and being a true student of the competition can help you identify how to effectively enter this field in a manner that works for your focus.”

Dresser agrees: “There are many experienced consultants—clinical, business, and legal—who can help guide new pharmacies through this industry,” he said. “Taking proactive steps can help mitigate some of the known challenges, such as aggressive and heavy-handed [pharmacy benefit manager] and payer audits.”

Eager pharmacists need to study demographics and be able to educate local practitioners on what compounding involves, noted Dawit. “Compound- ing pharmacy allows me to help patients who have specific needs and are overall wanting to improve their health, not just treat a condition,” she said. “I like spending time getting to know my patients, and it is rewarding to be able to solve problems that are not addressed by big-box pharmacies. Independent ownership is difficult in this time but also has its advantages for those who want to think outside the box.”

For references, visit drugtopics.com.
Attention-deficit/hyperactivity disorder (ADHD) treatment options for children continue to evolve. This year, however, caregivers may face a new challenge: finding the best treatment strategy for their child during a pandemic. "It's pretty clear that the pandemic has created unprecedented challenges at every level of society, particularly health care," said John Beckner, RPh, senior director of strategic initiatives at the National Community Pharmacists Association (NCPA).

The coronavirus disease 2019 (COVID-19) pandemic has created significant challenges for all children and their families, but those obstacles may be "considerably greater" for those with ADHD, Beckner said, with some students facing virtual classrooms or less access to their regular physicians.

Lea S. Eiland, PharmD, BCPS, BCPPS, FASHP, FPPA, a clinical professor and associate department head of the Department of Pharmacy Practice at Auburn University Harrison School of Pharmacy in Alabama, said parents and health care providers need to consider the child's unique needs and struggles when determining the best care plan.

The good news, she said, is that the ADHD drug market provides multiple options in type of medication, dosage formulation, and dosage requirements. As the market grows, pharmacists can help patients get optimal results from customized regimens.

**Treatment Advances**

Drug treatment options for ADHD fall into 2 categories: stimulants and non-stimulants.

According to Eiland, stimulants continue to be the first-line drug class recommended for both adults and children with ADHD.

With this drug class, which includes amphetamines and methylphenidates, pharmacokinetics and dosage formulations greatly affect the medication's distribution in the body and its efficacy, according to Eiland. "You're seeing, I would say even in the last several years, additional products that are marketed that have longer efficacy with a 1-time dose, and we're still continuing to see that," she said.

Most ADHD medications require dosing in the morning, but in 2019, Jornay PM arrived on the market, signaling the first FDA-approved stimulant designed for evening dosing. The methylphenidate product is taken at night but isn't released in the body until morning, which helps reduce the severity of symptoms early in the day.

Earlier this year, it seemed another drug to treat ADHD could soon enter the market, but in May, Sunovion Pharmaceuticals Inc announced it was withdrawing its new drug application for dasotraline, a dopamine and nor epinephrine reuptake inhibitor. The drug had also been studied for treating binge eating disorder (BED).

"[Although] Sunovion considers dasotraline to be a promising, novel treatment for BED and ADHD, we believe that further clinical studies would be needed to support a regulatory approval for dasotraline in these indications," the drugmaker said in a statement announcing the decision.

The company said it did not plan to pursue further development of the drug at this time.

Sunovion seems to have hit the brakes on dasotraline, but Vallon Pharmaceuticals Inc recently announced positive data from a pilot study of Abuse Deterrent Amphetamine Immediate Release (ADAIR).

"Results from this pilot study suggest that Vallon's investigational immediate-release stimulant, ADAIR, may demonstrate less abuse potential than standard dextroamphetamine when manipulated and misused intranasally," Timothy Whitaker, MD, a board-certified psychiatrist and Vallon's chief medical officer, said in a statement.

If the drug continues to jump approval hurdles, it would be the first intranasal product for ADHD, Eiland said.
Overall, most of the chemical entities in clinical trials focus on the adult ADHD population rather than the pediatric setting. However, in some pediatric studies, investigators are looking into the neurobehavioral effect of drug holidays—stopping medication for a brief period of time, such as during summer break or weekends—or examining the effects of certain behavioral therapy interventions, Eiland said.

**Ways Pharmacists Can Help**

As more drug formulations and options enter the market, Eiland said, the key to determining the best strategy often requires looking at the child’s own needs.

“Do they wake up with symptoms? Do they wake up and it’s hard to get them dressed, get them to school, get them to day care? Or is it that you can get them up, but they have a harder time focusing during school, during the lunch hour, afternoon hours or evenings when they come home? And so we can actually select a stimulant product that works best based on when the child needs the most control for symptoms,” she said.

Pharmacists on a health care team can talk with physicians about individual drug options, the medications’ release in the body, and even the “vast pharmacokinetic difference” between a tablet, capsule, and liquid suspension form of the drug, Eiland said.

Community pharmacists can also play a valuable role by counseling a patient or caregiver on how to administer the medication and what adverse events to watch out for, Eiland said. Pharmacists should also alert the patient’s physician if a patient is struggling with a particular dosage form or there might be an adherence concern.

**New Challenges From COVID-19**

As a result of the ongoing global pandemic, visits to primary care physicians and specialists are down, Beckner said, which suggests that children with ADHD and parents may not get the 1-on-1 time with the physician they had in the past.

As more accessible health care providers, pharmacists can lend a hand by answering patient questions, counseling patients and their caregivers even during refills to identify possible concerns, and helping parents navigate dosage timing.

Children adjusting to new daily schedules may be spending much more time at home than they did in the past. “Behavioral parenting strategies are taking on an even greater role as a supplement to medications,” Beckner said. Some children may head back to the classroom; others may continue with virtual learning. Parents will need to consider individual needs to decide whether a new schedule requires changes to dosage timing or when a child learning from home seems to struggle the most with symptoms.

“There are some students that thrive in the virtual setting, and there are some students that struggle in the virtual setting, and we’re just learning that. That’s going to be something to try to figure out,” Eiland said.

Parents who opt for a medication holiday during summer break may also need to decide whether they want their child to resume medication during virtual learning.

In each case, experts say, pharmacists can help caregivers and children navigate the possible changes ahead. “It’s just talking with them, inquiring...checking on adherence, checking on administration, and checking on [adverse drug reactions],” Eiland said. 

For references, visit drugtopics.com.

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**Novel Behavioral Therapy Option Comes to Market**

A game-based digital therapeutic device aims to improve attention function in children with attention-deficit/hyperactivity disorder (ADHD).

The FDA announced in June that it is permitting the marketing of EndeavorRx. The game, which is targeted toward pediatric patients aged 8 to 12 years, requires a prescription and is designed to improve attention functioning through computer-based testing.

“The EndeavorRx device offers a nondon drug option for improving symptoms associated with ADHD in children and is an important example of the growing field of digital therapy and digital therapeutics,” Jeffrey Shuren, MD, JD, director of the FDA’s Center for Devices and Radiological Health, said in the announcement.

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“It’s pretty clear that the pandemic has created unprecedented challenges at every level of society, particularly health care.”

—John Beckner, RPh
Managing Drug Diversion Amid Pandemic

The COVID-19 crisis poses unique challenges for managing controlled substances in hospitals.

By Gabrielle Ientile, Assistant Editor

A webinar offered by Becton, Dickinson and Company (BD), experts focused on provider collaboration in managing drug diversion amid the novel coronavirus disease 2019 (COVID-19) pandemic.

Presenters from BD—W. Perry Flowers, MS, RPh, vice president of medical affairs, enterprise medication management; Kelly Robke, MBA, MS, RN, vice president of thought leadership, medical affairs; and Doina Dumitru, PharmD, MBA, FASHP, senior director of medical affairs—emphasized that cross-clinical collaborative effort, including collaboration with pharmacists, needs to be part of the solution to drug diversion.

Robke explained that the pressures of the pandemic exacerbate what the presenters referred to as “health care’s hidden pandemic,” in which injured, stressed, or overworked health care workers are vulnerable to substance disorder.

The primary stress drivers in hospitals include short staffing (74%), emotional demands (67%), long hours (60%), and patient volume (60%).

Robke identified factors aggravated by the pandemic; for example, as hospitals experience decreases in available staff, many nurses are taking care of more patients than they usually do.

Opioid misuse can occur when health care workers use readily available drugs to “relieve” occupation-related pain, including that from strenuous work and long hours on your feet, as well as stress. “We hear frequently and consistently stories of stress [related to] the crisis and are aware that many clinicians are faced with a substantial amount of burdens outside of [those] typical of care delivery,” Robke said during the webinar.

According to Robke, effective strategies for minimizing drug diversion include as follows:

• formal training,
• roundtables and informal peer discussion,
• comprehensive surveillance programs,
• more accurate data, and
• access to a rehabilitation pathway.

Current developments could facilitate opioid misuse, according to Dumitru: “As the COVID-19 pandemic has evolved, the impact on health care capacity has created surges in the key medication management areas that have challenged providers in ways unseen before.”

Dumitru explained that rapid deployment of drugs in hospitals—through relaxing or deferring of normal controlled substances processes to accommodate surging needs in new locations—presents an opportunity for diversion. “With the opioid crisis still deeply affecting our country, statistics tell us that diversion will happen in these search settings, potentially with greater frequency than in regular care settings. This makes managing controlled substances an even more challenging operational process than usual, especially if new areas have more access that provides new opportunities in the context of different security procedures,” she said.

With the pandemic bringing in a surge of patients and, subsequently, more variety of narcotics available on the floor, hospitals need to implement collaborative strategies.

“Nursing needs to play a role and really respect the role that [pharmacists] have in the cross-clinical collaborative effort in being a part of the solution,” Robke said. “The most predominant step… is to be partners with our pharmacy colleagues, with our IT [information technology] and informatics colleagues, not only so that we act together…to allow us to comply with standardized workflows that I mentioned previously around medication, but we also need to assume our leadership responsibilities here as patient care leaders.”

For references, visit drugtopics.com.
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To “Buy American” Generic Drugs, Pharmacists Must Be Adequately Reimbursed

After logging over 166,000 miles on her 2011 Toyota RAV4, my wife, Denise, decided she needed a new car. All 3 kids are out of college and have their own homes, so we decided it was time for her to treat herself. She settled on a bright blue 2020 Honda CR-V. Despite being a Japanese model, the 2020 Honda CR-V is also manufactured in North American plants, in Marysville and East Liberty, Ohio; Greensburg, Indiana; and Ontario, Canada. I wish we could say the same about the drugs we dispense in our pharmacies; instead of a foreign brand made in America, we have American brands made in foreign countries.

A lot of noise has been made the past 6 months about buying our medical supplies; namely, personal protective equipment and pharmaceuticals. So much of our drug supply—especially generics, which account for the majority of what we community pharmacists dispense daily—is manufactured in foreign countries. Since the 1990s, US companies have increasingly imported pharmaceutical products from India and China, where ingredients are cheaper and manufacturing is subject to fewer regulations and significantly less FDA oversight. Because of this, the United States relies heavily on India and China for our generics, which I routinely dispense.

“Buy American” is shouted from the rooftops. I’m all for it too; however, the question becomes “Why do we pharmacists buy generics from these manufacturers?” The answer is pure and simple: It is the cost. There are no reasonably priced alternatives, given the ridiculously low level of payment from many of the insurance companies and managed care organizations (MCOs).

Recently, while working “on the bench,” I paid particular attention to the reimbursement levels for very common drugs. One MCO reimbursed 79 cents for a 30-day prescription of lisinopril 20 mg. According to the 2020 Cost of Dispensing Study, it costs $12.40 for a pharmacist to dispense a prescription.1 How much longer can independent pharmacists sustain such reimbursements? That is why we dispense generics that originate from China and India.

In Blair County, Pennsylvania, where I have spent my professional career, we’ve seen 14 independent pharmacies close in the past 10 years. As I said in a column in September 2019, quoting Dr Martin Luther King Jr, “We must learn to live together as brothers or perish together as fools.” The demise of the independent pharmacies is the canary in the coal mine, warning that more and more job opportunities for pharmacists are at risk.

I am all for buying American and bringing as much manufacturing of the medical necessities as possible to our shores so that we are no longer at the mercy of the overseas governments. We have the ability to manufacture all our medical supplies, including generic drugs. For that to become a reality, the government, which spent $325 billion in 2015 on drugs, must ensure proper reimbursement for these American-made generic drugs. Pharmacists need to be reimbursed adequately for every prescription dispensed with a reasonable fee for service.

Direct and indirect remuneration fees need to go away immediately. The pricing schemes of average wholesale price, wholesale acquisition cost, national average drug acquisition cost, and Affordable Care Act–weighted-average manufacturer price must fall into line to reflect exactly what pharmacies pay for these drugs. Because we are getting poorly reimbursed for the cheap overseas generics, we need reassurance that when we are mandated to buy American generics, which I’m sure will be slightly more expensive, we will not take any more of a financial hit.

Denise loves her new car, and the Honda dealer does not have to worry about clawing back on the check we wrote. Isn’t that supposed to be how a business transaction works?

Peter A. Kreckel, RPh, practices community pharmacy in Altoona, Pennsylvania.

For references, visit drugtopics.com.
Opicapone Can Help Treat Patients Experiencing “Off” Episodes With Parkinson Disease

Nirali S. Khusal, PharmD and Kevin W. Chamberlin, PharmD, FASCP

 levodopa/carbidopa is currently the gold standard for controlling motor symptoms associated with Parkinson disease. For patients taking this medication, symptoms such as tremor, difficulty walking, and initiating movement can return throughout the day as the levodopa wears off. On April 24, 2020, the FDA approved opicapone (Ongentys; Neurocrine Biosciences) as an adjunctive treatment for patients with Parkinson disease who experience these “off” episodes.1

Levodopa is peripherally metabolized by catechol-O-methyltransferase (COMT). Opicapone, a selective and reversible COMT inhibitor, aims to prevent this metabolism in the blood and increase the duration of levodopa activity by allowing greater availability across the blood-brain barrier. Evidence suggests that levodopa shortens these episodes compared with entacapone, a treatment already available on the market, with no new safety concerns observed.2

Efficacy

Two randomized, multicenter, double-blind, 12-week trials were conducted in 522 patients taking levodopa/carbidopa who had inadequate control of their symptoms. Trial 1 took place at 104 sites in European countries; trial 2, at 69 sites across Europe and Asia. Opicapone 50 mg was given to 265 patients, and the remaining 275 received a placebo. The primary end point was the change in mean absolute off-time. The secondary end point was on-time without troublesome dyskinesia. Patients kept 24-hour diaries, and efficacy was measured by recorded change in hours from baseline off-time.3,4

Patients who were treated with opicapone demonstrated a significant decrease in mean off-time compared with those who received placebo. Of note, most patients were white; therefore, efficacy among different races cannot be determined.3

Safety

The most reported adverse effect (AE) of opicapone was dyskinesia, which occurred in 20% of patients receiving treatment. This was the most common reason for discontinuation of therapy. Other common AEs defined as at least 4% incidence and greater than placebo include constipation, increased blood creatinine levels, syncope, and weight loss.2 Serious AEs may include decreased blood pressure and fainting, somnolence during normal activity, uncontrolled movements, abnormalities in impulse control, and changes in heart rate and blood pressure when taken with nonselective monoamine oxidase (MAO) inhibitors.3 The occurrence of AEs was similar between men and women, as well as between patients above and below age 65 years.4

Dosing and Administration

Opicapone is available as hard gelatin capsules in 25-mg and 50-mg doses. The current dosing recommendation is one 50-mg oral capsule taken every 24 hours, at bedtime, in addition to levodopa/carbidopa. If a dose is missed, the subsequent dose should be taken at the scheduled time the following day. Do not double doses. For patients with moderate hepatic impairment (Child-Pugh class B), the recommended dose is 25 mg at bedtime. Patients with severe hepatic impairment (class C) should avoid use because there are no studies evaluating this population. Use with nonselective MAO inhibitors is contraindicated.3,4

Patients should be informed not to eat at least 1 hour prior and 1 hour after taking opicapone, because food decreases the mean peak plasma concentration by 62% and mean overall plasma exposure by 31%.3

Nirali S. Khusal, PharmD is a PGY-1 pharmacy resident at University of Connecticut (UConn) John Dempsey Hospital at UConn Health in Farmington.

Kevin W. Chamberlin, PharmD, FASCP, is university director of pharmacy residency programs at UConn Health.

For references, visit drugtopics.com
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