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The University at Buffalo School of Pharmacy and Pharmaceutical Sciences (UB SPPS) Drug Information Newsletter is dedicated to providing timely information relevant to healthcare practitioners in New York. The newsletter supplies information on clinical practice guidelines, medication safety issues, new drug approvals/medications under development, medication shortages, and drug class reviews.

Shingrix®

Olawonuola Abiona, PharmD

The Food and Drug Administration (FDA) recently approved Shingrix®, a new vaccine for the prevention of herpes zoster (shingles).[1] Shingrix® is the preferred vaccine for adults 50 years of age and older to prevent shingles. Shingrix® is the second vaccine approved for the prevention of herpes zoster in patients aged 50 years and older; Zostavax®, a live-attenuated vaccine, was approved by the FDA in 2006.[2]

There are several differences between Zostavax® and Shingrix®, the most notable being that Zostavax® is a live vaccine and Shingrix® is not (see Table 1).[1-3] Because Zostavax® is a live vaccine, it is contraindicated in patients who are pregnant and/or immunocompromised.[2] Another notable difference is that Shingrix® requires storage in the refrigerator, while Zostavax® requires storage in the freezer.[1,2] Additionally, Shingrix® is administered in a 2-dose series while Zostavax® is given in 1 dose.

The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) has approved the 2018 immunization schedule for adults, effective February 2018.[4] In this schedule, the ACIP recommends Shingrix® as the preferred vaccine for adults 50 years of age or older to prevent shingles and its related complications, even in adults who have previously received the Zostavax® vaccine. Two doses should be administered, 2 to 6 months apart.

Table 1. Comparison of vaccines for prevention of herpes zoster.[1-3]

Herpes Zoster Vaccines		
Drug (Manufacturer)	Shingrix® (GSK)	Zostavax® (Merck)
Dosage	0.5 mL IM x 2 doses	0.65 mL SC x 1 dose
Type	Adjuvanted, recombinant subunit	Live-attenuated
Storage	Refrigerator	Freezer
Cost	$280	$223

IM=intramuscular, SC=subcutaneous

Clinical pharmacology

The risk of developing herpes zoster is related to a decline in varicella zoster virus (VZV)-specific immunity and appears to increase with age.[1] Shingrix® works by boosting VZV-specific immune response and protects against the zoster disease. The vaccine consists of 2 components: lyophilized glycoprotein E antigen and the AS01B adjuvant, which are reconstituted for use.

Herpes zoster occurs when latent VZV is reactivated and typically manifests as a vesicular, painful, dermatomal rash.[5,6] A common complication of shingles is postherpetic neuralgia, which can lead to decreased daily activity. Herpes zoster vaccine is indicated for patients 50 years of age or older because the overall incidence is higher in older patients. The overall incidence of herpes zoster is reported anywhere from 2 to 4.6 cases per 1000-person years but increases to 10 to 12.8 per 1000-person years in patients 80 years of age or older.[5] Zostavax® was 51.3% effective against herpes zoster and 66.5% effective against postherpetic neuralgia in participants who were 60 years of age or older.[6]

Dosing and storage

Shingrix® is given intramuscularly after being reconstituted.[1] It should be stored in the refrigerator between 2°C and 8°C (36°F and 46°F) and used within 6 hours after reconstitution. Shingrix® is given in a 2-dose series at month 0 followed by a second dose administered anytime between 2 and 6 months.

Warnings and precautions

Before administering this vaccine, a patient's medical history should be reviewed for possible vaccine sensitivity and previous vaccination adverse reactions.[1] Shingrix® is contraindicated in patients with a history of severe allergic reactions to any component of the vaccine.

Clinical trials

The efficacy and safety of the adjuvant herpes zoster subunit vaccine were evaluated in 2 studies.[5,6] The Zoster Efficacy (ZOE-50) study involved patients aged ≥50 years while the ZOE-70 study included patients aged ≥70 years.

ZOE-50 was a randomized, placebo-controlled, phase 3 trial that took place in 18 countries.[5] The primary objective of this study was to evaluate the efficacy and safety of the Shingrix® (HZ/su) vaccine in adults who were 50 years of age or older. The secondary objective of this study was to determine the efficacy in reducing the incidence of herpes zoster in each age group (50 to 59 years, 60 to 69 years, and ≥70 years) along with HZ/su safety and reactogenicity profiles.

Subjects were included if they did not have a history of herpes zoster, were not previously vaccinated against varicella or herpes zoster and were not immunosuppressed.[5] Participants were randomized and stratified in a 1:1 ratio according to age (50 to 59, 60 to 69, and ≥70 years) and region.

In this study, 15,411 subjects underwent randomization.[5] Baseline demographics were similar in both groups; 71.8% of participants were white, 61.2% were female, and 51.2% were from Europe. Four hundred and eight participants reported suspected herpes zoster, with 244 confirmed cases. Participants were followed for a mean period of 3.2 years. There was an overall incidence of herpes zoster per 1000-person years of 0.3 in the HZ/su group and 9.1 in the placebo group. The overall vaccine efficacy in the HZ/su group was 97.2% (95% confidence interval [CI], 93.7 to 99.0; P<0.001). No significant differences in efficacy were observed among the 3 age groups; the vaccine efficacy for all age groups ranged from 96.6% to 97.9%.

Injection site reactions were evaluated in this study: 84.4% of participants in the HZ/su group and 37.8% of patients in the placebo group reported solicited or unsolicited symptoms within 7 days after vaccination.[5] The most commonly reported injection site reaction was pain (79.1% of the HZ/su group and 11.2% of the placebo group). The most commonly reported systemic reaction was myalgia (46.3% in the HZ/su group and 12.1% in the placebo group). ZOE-50 investigators concluded that the HZ/su vaccine significantly reduced the risk of herpes zoster in patients 50 years of age or older and showed higher efficacy than the Zostavax® vaccine.

ZOE-70 was a randomized, placebo-controlled, phase 3 trial conducted in adults aged ≥70 years in 18 countries.[6] The primary objective was to evaluate the efficacy of HZ/su, as compared with placebo, in reducing the risk of herpes zoster in adults 70 years of age or older. Secondary objectives of this study were to evaluate the vaccine efficacy against postherpetic neuralgia and to evaluate the vaccine reactogenicity and safety. Patients aged ≥70 years were eligible for this study; exclusion criteria included a history of herpes zoster, an immunosuppressive condition, and previous vaccination against varicella or herpes zoster. Participants were randomized to receive HZ/su or placebo in a 1:1 ratio. Subjects were also stratified according to region (Asia and Australia, Europe, Latin America, and North America) and age group (70 to 79 years vs. ≥80 years [in a 3:1 ratio]).

Participants were given 2 doses of HZ/su in the deltoid muscle at months 0 and 2.[6] Participants were followed for at least 30 months after the completion of their vaccination. A total of 14,816 participants were enrolled and underwent randomization; 916 patients were excluded because they did not meet the inclusion criteria. Baseline demographics were well matched; the mean age of patients in both groups was 75.6 years. Approximately 55% of participants were female, 55% were from the European region, and 55% of participants were Caucasian.

There were 432 suspected cases of herpes zoster reported in the ZOE-70 study, and 270 cases were confirmed as herpes zoster.[6] Of the 270 confirmed cases, 87 cases occurred in HZ/su recipients and 345 in placebo recipients, after a mean follow-up period of 3.7 years. The incidence of herpes zoster per 1000 person-years was 0.9 in the HZ/su group and 9.2 in the placebo group, for an overall vaccine efficacy of 89.8% (95% CI, 84.2 to 93.7; P<0.001). The vaccine was 89.1% effective in patients who were 80 years or older and 90% effective in patients who were between the ages of 70 and 79 years.

Postherpetic neuralgia was evaluated and reported in 4 patients in the HZ/su group and 46 patients in the placebo group during a mean follow-up period of 3.8 years.[6] The vaccine effectiveness against postherpetic neuralgia among participants 70 years old or older was 88.8% (95% CI, 68.7 to 97.1%; P<0.001). The cumulative incidence of postherpetic neuralgia was lower in the HZ/su group than in the placebo group.

One thousand and twenty-five participants were stratified and randomized to the reactogenicity subgroup: 512 in the HZ/su group and 513 in the placebo group.[6] Solicited reports of reactions within 7 days after vaccination were recorded. Approximately 79% of participants in the HZ/su group reported reactions versus 29.5% of patients in the placebo group. The most commonly reported reactions in the HZ/su group were pain at the injection site (68.7%) and fatigue (32.9%). Serious adverse events occurred in 16.6% of HZ/su recipients and in 17.5% of placebo recipients, and potential immune-mediated diseases occurred in 1.3% of HZ/su recipients and in 1.4% of placebo recipients.

These study findings showed that vaccine efficacy against herpes zoster was similar in all age groups; the findings were consistent with the results of ZOE-50.[5,6] In contrast, the efficacy of Zostavax® was found to decline with increasing age; the efficacy was 70% in adults aged 50 to 59 years, 64% in adults aged 60 to 69 years, 41% in adults aged 70 to 79 years, and 18% in adults aged ≥80 years.[6,7]

In conclusion, ZOE-70 showed that the HZ/su vaccine reduced the risk of herpes zoster and postherpetic neuralgia among adults aged ≥70 years, without substantial safety concerns.[6]

ZOE-50 and ZOE-70 were conducted in an identical manner to provide a more robust assessment of vaccine efficacy against herpes zoster.[5,6] The pooled analysis showed very similar results among the participants in each individual study. Vaccine efficacy against herpes zoster in the pooled analysis was 91.3% among participants 70 to 79 years of age and 91.4% among participant's ≥80 years of age, which indicated that there was no decline in efficacy with age.

Summary

Shingrix® is a newly approved vaccine for prevention of herpes zoster.[1] The CDC ACIP recommends Shingrix® as the preferred vaccine for adults 50 years of age or older to prevent shingles and its related complications, even in adults who have previously received the Zostavax® vaccine.[1,4] Current data show that Shingrix® is safe and effective and can be injected at the same time as other vaccines such as the influenza vaccine.[1] Shingrix® is expected to cost about $280 for the 2 doses and is likely to be covered by most insurance companies.[3]

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Ingestible Drug Sensors: A Look at Abilify Mycite®

Amanda Zelinski, PharmD

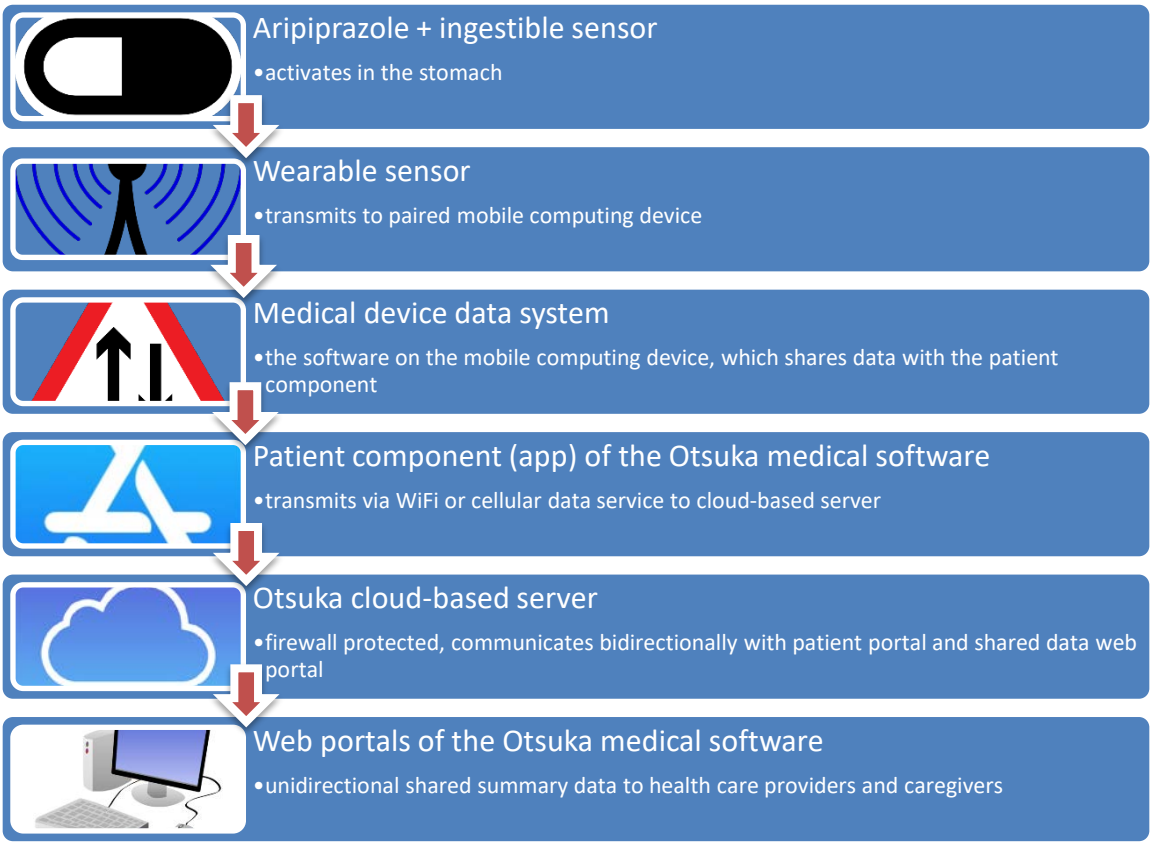
The Food and Drug Administration (FDA) has approved a new formulation of aripiprazole under the trade name Abilify Mycite®.[1] This unique tablet is imbedded with an Ingestible Event Marker (IEM), which has the ability to track drug ingestion.[2] The IEM communicates with a sensor worn by the patient (Mycite® Patch) which transmits data to a smartphone application (Mycite® App). The patient can then choose to authorize individuals to access these data on a web-based portal (see Figure 1).

This formulation of aripiprazole is approved for use in adults with schizophrenia or bipolar I disorder, and as adjunctive treatment for major depressive disorder.[2] Patients with these mental illnesses are often poorly

adherent to their medication regimens, with 1 report asserting medication possession ratios (MPRs) ranging from 37%-55%.[3,4] When any patient is non-adherent to his/her medicine regimen, it can result in poor health outcomes and increased healthcare system costs.[5] In the case of mental illness, it can result in a manic episode, violence, or attempted suicide.[6]

Currently there are several methods to measure adherence to medications indirectly or subjectively, including direct patient questioning, tracking of pharmacy refill dates, or electronic devices that capture pill container openings.[7] None of these methods guarantee that the patient physically swallowed the medication. The IEM, developed by Otsuka Pharmaceuticals and Proteus Digital Health, is able to track ingestion with 97% effectiveness.[4]

Figure 1. A brief description of the components of Abilify Mycite®.[2]



The IEM itself is the size of a grain of sand, measuring 300 micrometers tall, and is made of ingredients found in food (including magnesium, copper, ethyl citrate, and cellulose).[8] Safety studies conducted on rats and canines concluded that the IEM successfully passes through the gastrointestinal tract and is excreted in the feces with a similar transit time as food.[9] These studies also observed no safety concerns related to electrical output, which is observed to be 1.85 V.[8]

The IEM's magnesium and copper components activate once exposed to the conductive fluid of the stomach, and the device communicates the time and date of ingestion.[8] Clinical trials revealed the mean latency time from ingestion to signal detection by the wearable sensor was 1.1-1.3 minutes,[4] and Proteus determined that the sensor was able to detect ingestion in persons with a body mass index (BMI) up to 56.8 kg/m^2 during device development.[8] The latency time to upload to the web portal was a mean of 6.2-10.3 minutes, with some results of greater than 30 minutes.[4] Studies did not address the potential for the distance between the subject and the smartphone to affect the latency period.

The primary issue in the usability of this device is the ability of a person with mental illness to apply and remove the wearable sensor and manipulate the smartphone application. An open-label study was conducted to assess usability in 67 patients with stable schizophrenia who were already taking aripiprazole.[10] The participants were given a 3-week training phase followed by a 5-week independent phase to assess their ability to change the wearable sensor once weekly and pair it digitally with the smartphone application. A total of 67 patients started the study and 49 completed the 8-week study period. In the end, 82.1% of trial participants were able to complete the tasks independently or with minimal assistance. As a secondary endpoint, the study analyzed patient adherence for the duration of the study period, expressed as the number of detected ingestions divided by the number of days with >80% data coverage; the mean adherence rate was 73.9%. This is higher than the average MPR for schizophrenic patients which is approximately 58.8%.[11] However, MPR is typically measured over a longer period of time (e.g., 6 months vs. 8 weeks).[12] This study does have other limitations; most significantly, the study cohort is comprised of schizophrenic patients rated as “mildly ill” on the Clinical Global Impression-Severity scale.[11] Patients with mild illness may be more likely to be adherent and more capable of manipulating a wearable sensor and smartphone device compared to patients with more severe disease. Also, the sample size of this study was small. This study, therefore, may not be generalizable to all patients with schizophrenia.

Otsuka Pharmaceuticals expects that Abilify Mycite® tablets, Mycite® patches, and the Mycite® app will be available in the second quarter of 2018; the price for the kit is currently unknown. The original Abilify® tablets are currently $892 per bottle (30-tablet count; wholesale acquisition cost).[13] The practicality of using this new technology in everyday practice is slight, given the complex nature of the components and a high anticipated monthly cost, but it does give health care professionals a look toward the future of medication adherence monitoring.

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Febuxostat: Safety Update

Ivan Alvarez, PharmD

Gout is the most common form of inflammatory arthritis of adulthood with a self-reported prevalence estimated at 3.9% in adults (approximately 8.3 million people) in the United States (US).[1,2] The prevalence of gout has increased in the past decades and is associated with numerous risk factors including dietary factors, alcohol consumption, metabolic syndrome, hypertension, and obesity.[1] Gout is characterized by elevations of serum uric acid levels that lead to deposition of monosodium urate (MSU) crystals in joints and other tissues.[3] MSU crystal deposition manifests as acute episodic arthritis that can progress to a chronic and disabling destructive arthropathy.

Febuxostat was approved by the US Food and Drug Administration (FDA) in 2009 for the chronic management of hyperuricemia in patients with gout.[4] Similar to allopurinol, febuxostat inhibits xanthine oxidase, which leads to decreased production of serum uric acid.[2] In November 2017, the FDA issued a drug safety communication regarding a potential increase in risk of heart-related death with febuxostat.[5] These findings were based on preliminary results from a safety study comparing febuxostat to allopurinol. In the phase III and long-term clinical extension studies of febuxostat, cardiovascular events and deaths were adjudicated to 1 of the pre-defined endpoints from the Anti-Platelet Trialists' Collaborations (APTC; cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke).[4] In the phase III trials, the incidences of adjudicated APTC events per 100 patient-years of exposure were 0 for placebo (95% confidence interval [CI] 0.00 to 6.16) and for febuxostat 40 mg/d (95% CI 0.00 to 1.08), 1.09 for febuxostat 80 mg/d (95% CI 0.44 to 2.24), and 0.60 for 300 mg/d allopurinol (95% CI 0.16 to 1.53). In the long-term extension studies, the incidences of adjudicated APTC events were 0.97 for febuxostat 80 mg/d (95%CI 0.57 to 1.56) and 0.58 for 300 mg/d allopurinol (95% CI 0.02 to 3.24). Although the differences in rates of cardiovascular events were not statistically significant, the FDA required the manufacturer to conduct an additional safety clinical trial after febuxostat was approved to better understand the cardiovascular risk. The package insert of febuxostat currently carries a warning about increased cardiovascular events when compared to allopurinol based on pre-approval clinical trials.

The safety clinical trial, known as the CArdiovascular safety of febuxostat and allopurinol in patients with gout and cardiovascular comoRbiditiES (CARES), has been completed; however, at this time, full results are not available.[5] The methodology of CARES has been described in a 2012 publication.[6] Adult patients (aged ≥50 years if male or ≥55 years if female) with a diagnosis of gout and history of major cardiovascular or cerebrovascular disease were randomized to receive either febuxostat or allopurinol (1:1) in a double-blind manner. The primary endpoint was time to first occurrence of cardiovascular death, nonfatal heart attack, nonfatal stroke, or unstable angina with urgent coronary revascularization. According to the FDA, over 6,000 patients were included in the trial, and preliminary results have shown that febuxostat did not increase the risk of the composite of cardiovascular events compared to allopurinol.[5] However, analyses of the individual outcomes suggest an increased risk of cardiovascular death and all-cause mortality with febuxostat compared to allopurinol. Per the drug safety communication, the FDA will conduct a comprehensive review once the final data are received and will update the public when more information is available.

In the meantime, the FDA recommends that health care professionals consider this safety information when deciding whether to prescribe febuxostat.[5] Patients are encouraged to discuss any questions or concerns regarding febuxostat with their health care provider. Patients are also advised to not stop taking their medication without first consulting with their health care provider. Health care professionals and patients are

encouraged to report adverse events or side effects related to use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program, available at www.fda.gov/MedWatch/report.

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An Update to Guideline-Directed Management and Therapy of Hypertension

Kara Wilcox, PharmD, MBA

In the United States (US), hypertension is a leading preventable cause of death, second only to cigarette smoking, and is responsible for nearly 1 in 6 deaths in adults.[1] Based on findings from the Framingham Heart Study, conducted in the mid-1900s, scientists were able to correlate elevated blood pressure to an increased risk of cardiovascular complications and death.[2] The first comprehensive guideline for management of hypertension was developed by the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC) in 1977 and has evolved into a series of guidelines to assist in the management of patients with elevated blood pressure. The most recent guideline was released in November of 2017 by the American College of Cardiology (ACC) and the American Heart Association (AHA).[3]

The 2017 guideline of the ACC and AHA (ACC/AHA) was developed by a Task Force comprised of members from the ACC/AHA and 9 other organizations and is intended as an update to the seventh report of the JNC (JNC 7).[3] While an eighth report of the JNC (JNC 8) was released in 2014, the JNC 8 focused on 3 clinical questions: what is the blood pressure threshold for starting pharmacotherapy, what are the blood pressure goals, and which antihypertensives improve health outcomes.[4] The JNC 8 recommendations were based solely on data from randomized controlled trials (RCTs). The 2017 guideline incorporates new data on various topics, including office-based blood pressure-related risk of cardiovascular disease (CVD), ambulatory blood pressure monitoring, home blood pressure monitoring, and telemedicine.[3] These data are from RCTs as well as registries, non-randomized comparative and observational studies, case series, cohort studies, systematic reviews, and expert opinion. Major changes in recommendations will be discussed in the content below.

Thresholds for hypertension and blood pressure targets

Compared to JNC 7, the 2017 ACC/AHA guideline stratifies blood pressure into fewer categories and recommends more aggressive blood pressure goals.[3,5] Table 1 outlines the new categories of blood pressure in adults.

Table 1. The new categories of blood pressure in adults, per the 2017 ACC/AHA guideline.[3]

BP Category*	SBP (mmHg)		DBP (mmHg)	Treatment	Follow-up
Normal	<120	and	<80	Encourage healthy lifestyle changes to maintain normal BP	Evaluate yearly
Elevated	120-129	and	<80	Recommend healthy lifestyle changes	Reassess in 3-6 months
Clinical hypertension					
Stage 1	130-139	or	80-89	Assess the 10-year risk for CVD or clinical ASCVD using the ASCVD risk calculator • ASCVD risk <10% → start with healthy lifestyle recommendations • ASCVD risk ≥10% or known clinical CVD, diabetes mellitus, or chronic kidney disease → recommend lifestyle changes and BP-lowering medication (1 medication) with goal BP <130/80 mmHg	ASCVD risk → • <10%: reassess in 3-6 months • ≥10%: reassess in 1 month BP goal → • If met after 1 month, reassess in 3-6 months • If not met in 1 month, assess adherence, then consider different medication or titration Continue monthly follow-up until BP control is achieved
Stage 2	≥140	or	≥90	Healthy lifestyle changes and BP-lowering medications (2 medications of different pharmacologic classes) with goal BP <130/80 mmHg	Reassess in 1 month BP goal → • If met after 1 month, reassess in 3-6 months • If not met in 1 month, assess adherence, then consider different medication or titration Continue monthly follow-up until BP control is achieved

ASCVD=atherosclerotic cardiovascular disease, BP=blood pressure, CVD=cardiovascular disease, DBP=diastolic blood pressure, SBP=systolic blood pressure

*Blood pressure is categorized using an average of at least 2 readings obtained on at least 2 occasions. If systolic blood pressure and diastolic blood pressure are in 2 different categories, assign to the higher blood pressure category.

Elimination of prehypertension

The 2017 ACC/AHA guideline eliminates the term "pre-hypertension."[3] This not only simplifies the stratification of blood pressure but arms the practitioner with leverage when encouraging a patient to make lifestyle changes. The term "pre-hypertension" may be misleading, causing patients to believe they have a mild condition and to underestimate the potential consequences. Empowering patients to understand that elevated blood pressure significantly increases their risk for heart attack or stroke when compared to normal blood pressure is vital. The Framingham study reported that men with pre-hypertension were 3.5 times more likely to suffer a heart attack than those with normal blood pressure.[2]

Recent data from the SPRINT study, a landmark trial, impacted the adoption of more aggressive blood pressure goals as this trial demonstrated improvement of major CVD outcomes with more intensive blood pressure control.[3,6] The SPRINT study was an open-label trial that compared the benefits of differing blood pressure targets.[6] Patients aged ≥50 years with a systolic blood pressure of 130 to 180 mmHg and increased risk of cardiovascular events were randomized to a systolic blood pressure target of <120 mmHg (intensive treatment) or <140 mmHg (standard treatment). The participants were evaluated at 3 months and every 3 months thereafter and medications in the intensive-treatment group were adjusted on a monthly basis to target a systolic blood pressure of less than 120 mmHg. Participants in the standard-treatment group were adjusted to a target systolic blood pressure of 130 to 139 mmHg. The primary outcome was a composite of myocardial

infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure, or death from cardiovascular causes.

A total of 9,361 subjects were enrolled in the SPRINT study.[6] At 1 year, the mean systolic blood pressure was 121.4 mmHg in the intensive-treatment group and 136.2 mmHg in the standard-treatment group. The investigators noted a statistically significant reduction in the risk of the primary outcome with intensive treatment compared to standard treatment. The primary outcome was confirmed in 243 subjects in the intensive treatment group (1.65% per year) and 319 subjects in the standard treatment group (2.19% per year; hazard ratio [HR] with intensive treatment 0.75, 95% confidence interval [CI] 0.64 to 0.89). The investigators identified a significant reduction in risk of heart failure with intensive treatment compared to standard treatment (HR 0.62, 95% CI 0.45 to 0.84). Significant reductions favoring intensive treatment were also observed in cardiovascular death (HR 0.57, 95% CI 0.38 to 0.85) and in all-cause mortality (HR 0.73, 95% CI 0.60 to 0.90).

Evaluation of cardiovascular risk

This new guideline eliminates the different blood pressure goals and treatment relative to a patients age, which was suggested in the JNC-8 algorithm.[3,4] Instead, the ACC/AHA recommends use of the Pooled Cohort Risk Assessment Equation, available at http://tools.acc.org/ASCVD-Risk-Estimator/, to estimate 10-year risk of atherosclerotic cardiovascular disease (ASCVD).[3] This tool is also recommended to further assess the need for addition of medication to lifestyle changes for management of hypertension. It is important to understand limitations of this tool: it is validated for adults in the US, aged 45 to 79 years, in the absence of concurrent statin therapy. In the 2017 guideline, the ACC/AHA recommends assigning a 10-year ASCVD risk score of greater than 10% to people aged >79 years; therefore, the systolic blood pressure threshold for initiation of antihypertensive therapy in these individuals is 130 mmHg.

Early intervention

In the 2017 guideline, there is an emphasis on non-pharmacologic interventions and a recommendation to encourage healthy lifestyle changes in *all* patients with a systolic blood pressure of 120 mmHg or greater.[3] This emphasis on healthy lifestyle changes, in addition to changes in blood pressure targets, should prompt healthcare providers to focus on early intervention. Although, the JNC-8 encouraged lifestyle changes, the new guideline emphasizes early intervention for all patients to help prevent hypertension and further to prevent CVD.[3,4] Poor diet, lack of physical activity, excessive alcohol consumption, obesity, and excessive sodium intake are frequently observed causes of hypertension and are modifiable risk factors.[3] Patient engagement and patient education are major components of hypertension management and should be encouraged along the continuum of care. The preventative approach outlined within this new guideline addresses hypertension as a population health issue.

Drug therapy

Similar to the previous guideline, the first-line therapy recommendations in this guideline includes thiazide diuretics (with a preference for chlorthalidone due to prolonged half-life), calcium channel blockers (CCBs), angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs).[3] Concurrent use of ACE inhibitors, ARBs, or renin inhibitors is potentially harmful and is not recommended in treatment for adults with hypertension. In black adults with hypertension, and without heart failure or chronic kidney disease, initial antihypertensive treatment should include a thiazide-type diuretic or CCB. The new guideline recommends initiating treatment earlier as stage 2 hypertension is now classified as ≥140/90 mmHg; in contrast, it was classified as systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥100 mmHg in JNC-7.[3,5]

It is important to consider other comorbid conditions when selecting the ideal drug therapy.[3] Similar to previous guidelines, specific recommendations in selecting drug therapy are further discussed within the 2017 guidelines for stable ischemic heart disease, chronic heart failure, heart failure with reduced ejection fraction, heart failure with preserved ejection fraction, acute intracerebral hemorrhage, acute ischemic stroke, atrial fibrillation, chronic kidney disease, kidney transplantation and pregnancy.

Controversy

The release of the 2017 ACC/AHA guideline has sparked much discussion among practitioners on appropriate blood pressure goals. In fact, there is controversy concerning blood pressure goals and when it is appropriate to begin treatment. As an example, the American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) recently issued a guideline on hypertension in which they recommend initiation of treatment in adults aged 60 years or older with systolic blood pressure persistently at or above 150 mmHg.[7] They further recommend a target systolic blood pressure of <150 mmHg in these patients. In a commentary published in the *British Medical Journal*, it was stated that these recommendations were challenged by the ACC/AHA, who noted that the ACP and AAFP may not have accounted for the extensive body of evidence that supports the benefit of adequate blood pressure control in other patients with hypertension.[8]

Regardless of the standpoint on aggressive blood pressure targets, it is clear that a systematic change to managing blood pressure at the population level is essential.[9] Adoption of intensified thresholds and goals, using a comprehensive approach involving pharmacologic and non-pharmacology therapy, should be considered. System-based approaches are required to address the multi-factorial causes of elevated blood pressure discussed above. Patients along the continuum of care will now require a unified plan of care and goals which involve patient collaboration. Education to promote hypertension self-management in identifying the consequences of poor management are crucial along this continuum of care. Collaboration within healthcare teams can optimize therapy and facilitate achievement of the more aggressive therapeutic goals outlined within the new guideline.

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Authors

Olawonuola Abiona, PharmD
Dr. Abiona received her Doctor of Pharmacy degree from Touro College of Pharmacy in New York City. Prior to that, she received a Bachelor of Science in Biology from Temple University. She completed her PGY-1 residency at Saint Barnabas Medical Center in Livingston, NJ and is currently the PGY-2 ambulatory care pharmacy resident at Lifetime Health Medical Group. Dr. Abiona is actively involved in education and clinical research. Her goal is to become an ambulatory care clinical pharmacist and to make a difference in healthcare, both in America and in her home continent of Africa.

Ivan Alvarez, PharmD
Dr. Alvarez received his Doctor of Pharmacy degree from the University of Rhode Island. He is the current PGY-1 managed care pharmacy resident at BlueCross BlueShield of Western New York. Dr. Alvarez is currently interested in formulary development and management. He would like to pursue a career in managed care after completing his residency program.

Kara Wilcox, PharmD, MBA
Dr. Wilcox received her Doctor of Pharmacy and Master of Business Administration degrees from St. John Fisher. Prior to that, she received a Bachelor of Science in Business Administration from the State University of New York at Fredonia and was involved in social work at The Catholic Charities Archdiocese of Chicago, within the Homelessness Prevention Program. She is currently a PGY-1 community pharmacy resident at Middleport Family Health Center. Her professional interests include transitions of care, chronic disease state management, and project management. Following the completion of her residency program, she plans to continue her career in community and ambulatory care.

Amanda Zelinski, PharmD
Dr. Zelinski received her Doctor of Pharmacy degree from St. John's University. She is currently a PGY-1 community pharmacy resident at Middleport Family Health Center. Dr. Zelinski has several years of experience as a pharmacist in community practice. She is interested in patient care and academia, and she plans to pursue a clinical faculty position after completing her residency program.

Editors

Linda Catanzaro, PharmD
Dr. Catanzaro received her PharmD from the UB SPPS and subsequently completed a specialty residency in HIV informatics. She also developed and directed the UB SPPS PGY-2 drug information residency program. She is currently a Clinical Assistant Professor at the UB SPPS and staffs the New York State Medicaid Drug Information Response Center.

Holly Coe, PharmD
Dr. Coe received her PharmD from the UB SPPS after receiving her BS in Neuroscience from the University of Rochester. She completed PGY-1 and PGY-2 residencies at the UB SPPS specializing in drug information/pharmacoinformatics. She is currently a Clinical Assistant Professor at the UB SPPS and she staffs the New York State Medicaid Drug Information Response Center.

Terry Dunn, PharmD
Dr. Dunn received both her BS in Pharmacy and PharmD from the UB SPPS. She also completed a hospital pharmacy residency at New England Medical Center in Boston. She has had extensive experience as a pharmacist in various settings, including practicing in a traditional role in hospitals as a Clinical Pharmacy Specialist. She has also served as a Science Specialist at a law firm, working with a team of lawyers defending pharmaceutical companies in product liability lawsuits. In addition, she has participated on an FDA contract updating and rewriting drug labels. She is currently a Clinical Assistant Professor at the UB SPPS and Coordinator for the Center for Health Outcomes, Pharmacoinformatics, and Epidemiology (HOPE).

Irene Reilly, PharmD, BCPS
Dr. Reilly received her PharmD from the University of Illinois at Chicago (UIC) College of Pharmacy after receiving her BA in Economics from the University of Chicago. She completed PGY-1 and PGY-2 residencies at the UIC College of Pharmacy, specializing in drug information. She is currently a Clinical Assistant Professor at the UB SPPS and she leads the New York State Medicaid Drug Information Response Center.

Please address any comments or corrections to Dr. Reilly at irenehon@buffalo.edu.