**Meeting Basics**

**Registration Desk Hours**
- Sunday: 5:30 a.m. to 8:00 p.m.
- Monday: 5:30 a.m. to 7:30 p.m.
- Tuesday: 9:00 to 5:00 a.m.

**ASH Hypertension Resource Pavilion Hours**
- Sunday: 9:00 a.m. to 12:00 p.m., 5:30 to 6:45 p.m.
- High Tea: 4:45 to 5:45 p.m.
- Monday: 9:00 a.m. to 1:00 p.m., 5:00 to 5:15 p.m.
- High Tea: 4:15 to 5:15 p.m.

**ASH Information / CME Desk**
Visit the ASH Information / CME Desk on the third floor promenade in the registration area for information on ASH programs.

**2010 Annual Scientific Meeting Corporate Sponsors**
The American Society of Hypertension wishes to acknowledge the following corporate sponsors for their generous support of the ASH 25th Annual Scientific Meeting.

Boehringer Ingelheim Pharmaceuticals, Inc.
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**A Look at NYC**

Make the most of your time in the city that never sleeps. Turn to pages 10-11 for dining recommendations and fun facts about New York, New York.

**Hypertension Highlights**

**Biological, sex factors emerging in obesity and hypertension**

*Allyn Mark, MD*

At Hypertension Highlights 2010 by making the distinction between spontaneous physical activity (SPA), such as activities of daily living, and exercise activity—defined as purposeful physical activity for health.

Citing a study where obese individuals spent two hours less per day in SPA than lean individuals, Dr. Mark explained the importance of this observation. “This difference has profound consequences, and accounts for about 350 calories per day difference in these two groups,” he said.

Yet, the implications may extend beyond simple weight control. Studies of the Pima Indians, a population with widespread obesity, showed that 57 percent of variance in SPA was familial and was independent of body fat and weight.

“There are inbred strains of rats that are either genetically prone or genetically resistant to obesity in a high-fat diet. Even before they were fed the high-fat diet, while they were still lean, rats that are genetically prone to obesity had lower activity levels than those that were genetically resistant,” Dr. Mark said. “There appears to be both a genetic and possibly genetic contribution to spontaneous physical activity, both in experimental animals and in humans.”

Against the backdrop of poor long-term compliance in rigorous exercise and dieting in obese individuals, Dr. Mark’s group at Rockefeller University studied oh/oh leptin-deficient mice, whose behavior includes markedly decreased SPA. They were then treated with physiological levels of leptin.

“These studies demonstrate that leptin deficient mice were profoundly hypoactive, and that leptin reconstitution in oh mice produced a rapid increase in activity before weight loss,” Dr. Mark said.

Later in the program, Kathryn Sandberg, PhD, reviewed the role gender plays in blood pressure.

“The prevalence of hypertension increases with age, with men being higher, until the fifties when it switches, and then women have a higher prevalence. So why is this? We think if we understand this we will get some insight into hypertension,” Dr. Sandberg said.

“I’m a basic scientist, and the first question is: Is this sex difference in blood pressure specific to humans? Actually the answer is no,” she said. Male salt-sensitive rats have higher blood pressure than female salt-sensitive rats, and male mice have higher blood pressure than female mice after angiotensin II infusion. Similar effects have been seen in dogs and chickens.

“This sex difference in blood pressure is robust. And it’s across experimental models of hypertension. We see it in humans, and we see it in inducible models of hypertension across species,” Dr. Sandberg said.

Yet, gonadal sex effects are not the only contribution to sex differences in blood pressure. Lowered testosterone levels in castrated men are associated with elevated blood pressure as is elevated testosterone levels in women with polycystic ovary syndrome.

There has been difficulty in separating the expression of the sex chromosomes from the gonadal hormone effect. “But now we have this new animal model called the four core genotype. It is an incredibly powerful model,” she said.

A spontaneous deletion of the Syr gene on a wild type male mouse created an Xy- female. This is an anatomical female with ovaries but also with male chromosomes. “It will add the Syr gene to an autosomal, an Xy- male and create a wild type XX female. The progeny produced includes an XX Syx male. This is an anatomical male (testes) with female chromosomes. “There is, in fact, a sex chromosome effect. We gonadectomized these mice at the six-to-seven-week stage, and then we measured blood pressure after we infused angiotensin II. These were conscious, freely moving mice measured over several days. The XX male, or female, have higher blood pressure than the Xy,” Dr. Sandberg said.

“This suggests that we have unmasked a sex chromosome effect that we couldn’t...”
A Cross-Examination of Contemporary Issues in Hypertension:

Join us for a unique and interactive CME dinner symposium

Monday, May 3, 2010

Registration and Dinner: 7:00 PM - 7:30 PM
Symposium: 7:30 PM - 9:00 PM
Trianon Ballroom, Hilton New York

Today’s Controversy and Consensus

Program Overview
Take part in a “clinician’s courtroom” where 2 faculty “counselors” cross-examine opposing sides of contemporary issues in hypertension. The proceedings will be moderated by the “Judge” who will challenge the counselors to document their statements and consider objections from opposing “Counsel” as well as the audience. The audience plays the part of the jury and will be asked to render a verdict based on the data that are presented.

Chair
George L. Bakris, MD
Professor of Medicine
University of Chicago Medical Center
Chicago, IL

Faculty
Domenic A. Sica, MD
Head, Section of Clinical Pharmacology and Hypertension
Virginia Commonwealth University
Richmond, VA

William B. White, MD
Professor, Department of Medicine
University of Connecticut Health Center
Farmington, CT

Agenda:

Debate #1: Setting treatment goals in hypertension care
Case Study Discussion: Combining blood pressure-lowering agents and emerging treatment options
Debate #2: Using biomarkers to assess risk in hypertension patients

Please join us for what promises to be a unique educational experience and earn 1.5 AMA PRA Category 1 Credits™

Please plan to arrive early to ensure seating

PLEASE REGISTER ON-SITE AT 7:00 PM

Co-sponsored by the American Society of Hypertension, Inc., ASH-Specialist Program Inc., and TCL Institute LLC.

This activity is supported by an educational grant from Tolakki Pharmaceuticals North America, Inc.
Joint session compares guideline differences, similarities

A SH and the European Society of Hypertension (ESH) have a history of cooperation and information sharing that dates back to ASH’s early days in the 1980’s. The relationships between American and European hypertension specialists have grown throughout the years, and today it’s only natural the two societies work together.

As part of the collaborative efforts between these societies, a joint session will take place from 6:00 to 7:30 p.m. tonight, Sunday, May 2, in Beckman Parlor. ASH President Henry R. Black, MD, and ESH President Krzysztof Narkiewicz, MD, PhD, of Gdansk, Poland, will chair the session, “Cornerstones of the European and America Guidelines — Similarities and Differences.”

Dr. Narkiewicz said he hopes this year’s joint session will strengthen the current relationship between ESH and ASH and provide an opportunity to plan for future cooperation.

“We would like to analyze and understand the similarities and differences of the European and American approaches to the diagnosis and treatment of hypertension and cardiovascular disease,” he said. “Secondly, we will compare and discuss the official guidelines that each society has set forth. The ESH will refer to its 2009 publication on the European guidelines, and ASH will likely present elements from the soon-to-be-published JNC 8 guidelines. We hope to find ways to promote these documents in such a way as to increase global awareness of the seriousness of hypertension and cardiovascular disease in the developed and developing worlds.”

The presenters will review the newest body of evidence related to hypertension management and discuss common goals concerning diagnosis and treatment.

Sverre E. Kjeldsen, MD, of Oslo, Norway, will present recent studies assessing the predictive value of organ damage in hypertension. Giuseppe Mancia, MD, of Milan, Italy, will review recent clinical trials focusing on the controversial issue of blood pressure threshold and target values.

We would like to analyze and understand the similarities and differences of the European and America Guidelines — Similarities and Differences,” he said. “Secondly, we will compare and discuss the official guidelines that each society has set forth. The ESH will refer to its 2009 publication on the European guidelines, and ASH will likely present elements from the soon-to-be-published JNC 8 guidelines. We hope to find ways to promote these documents in such a way as to increase global awareness of the seriousness of hypertension and cardiovascular disease in the developed and developing worlds.”

Suzanne Oparil, MD, of Birmingham, Alabama, will summarize growing evidence supporting wider use of combination therapy in hypertension. Finally, George L. Bakris, MD, of Chicago, Illinois, will present recommendations regarding antihypertensive treatment in diabetes and other special clinical conditions.

Session Highlights

“Cornerstones of the European and America Guidelines — Similarities and Differences,” a joint session of the European Society of Hypertension and ASH, will take place from 6:00 to 7:30 p.m. tonight, Sunday, May 2, in Beckman Parlor.

6:00 P.M. Assessment of Organ Damage in Hypertension
Sverre E. Kjeldsen, MD, Oslo, Norway

6:22 P.M. Antihypertensive Drug Treatment, Threshold and Target Blood Pressure Values
Giuseppe Mancia, MD, Milan, Italy

6:44 P.M. Combination Treatment in Hypertension
Suzanne Oparil, MD, Birmingham, AL

7:06 P.M. Antihypertensive Treatment in Diabetes and Other Special Clinical Conditions
George L. Bakris, MD, Chicago, IL
Post-trial follow-up offers new insights on study data

Practicing hypertension specialist have more knowledge to inform their long-term treatment strategies for patients with high blood pressure thanks to new data from a follow-up of ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial).

This morning, several experts will present the new data from this follow-up during a symposium titled ‘ALLHAT Long-term Outcomes of Drug Treatment in High CHD Risk Hypertensive Patients.’ The event will take place from 10:00 to 11:30 a.m. today, Sunday, May 2, in the Mercury Ballroom. Moderator Jeffrey A. Cutler, MD, MPH, of the National Institutes of Health’s National Heart, Lung, and Blood Institute, said an overall finding indicated most of the differences between drugs seen in the original trial went away after it ended.

“We think that the treatments of the patients became much more similar, because they were no longer assigned by the trial,” he said. “To some degree, differences were informed by the outcomes of the trial, so it’s not surprising that most of the differences went away. The implications are that the drug-specific advantages of the thiazide-type diuretic disappear as long as that treatment regimen is continued. When there’s a diuretic occurrence as long as that treatment was continued.

The implications are that the thiazide-type diuretic arm was superior in terms of effects on patients, he said. As part of his discussion, Dr. Davis will explain why a post-trial follow-up was conducted and how the data was collected and analyzed.

LONG-TERM OUTCOMES

William C. Cushman, MD, of Memphis, Tennessee, will then present the main results of the follow-up.

“In the follow-up, we looked at the same main outcomes that were studied in the original trial only over a longer period,” Dr. Cutler said. “The original trial was about five years. The total follow-up for the extension phase is eight to 13 years. The main results show that with one exception, none of the outcome differences seen during the trial were seen after the longer follow-up.”

The one exception was the outcome for heart failure, he said. When compared to a calcium channel blocker there was still a slight advantage for the diuretic after a longer follow-up. But if you look at the results both during and after the trial, that was entirely due to the difference during the trial.

Dr. Cutler said it’s also true that in the comparison between the diuretic and the ACE-inhibitor for total cardiovascular events there was an advantage for the diuretic during the trial. But during the post-trial period, it was suggested there’s a slight advantage to the ACE-inhibitor.

“To put all of this in perspective, it’s important to mention a limitation in this study,” Dr. Cutler said. “After the original trial, while we followed people for heart attacks, strokes, and deaths, we didn’t have any further information on what drugs they were taking or what their blood pressures were during this post-trial period. Therefore, the interpretation of these data is a little speculative. What we expect — since the diuretic was the best overall drug during the trial — is that many of the patients who were not on a diuretic during the trial had a diuretic added to whatever drug they had been on during the trial.

“This may help explain why some patients who had originally been on another drug did better after the end of the trial.” Following Dr. Cushman’s discussion of the main results of the follow-up, three more presenters will expand on the results — looking at specific outcomes for heart failure, diabetes, and chronic kidney disease. Linda B. pillar, MD, MPH, of Houston, Texas, will present “Post-incident Heart Failure Mortality in 10 years of Follow-up in ALLHAT.”

Joshua Barzilay, MD, of Tucker, Georgia, will examine “Risk Modification by Diabetes at Baseline and Incident During Randomized Phase of the Trial.”

In addition, Mahboob hooban, MD, of Cleveland, Ohio, will discuss “Cardiovascular and Renal Outcomes in Those with CKD.”

What the Hypertension Specialist Should Know

Back by popular demand, this series will feature presentations on topics important to the hypertension specialist. Following the presentations will be a “Meet the Expert” session on the same topic allowing participants to engage in further dialogue with the speakers.

TODAY’S SCHEDULE

4:00 p.m. — What the Hypertension Specialist Should Know About Peripheral Vascular Disease Kanwar Singh, MD, Farmington, CT

Overview of Vascular Function and Clinical Pharmacology *

West Ballroom

3:00 p.m. — What the Hypertension Specialist Should Know About Pharmacokinetics, Pharmacodynamics and Drug Interaction Domenic A. Sica, MD, Richmond, VA

4:00 p.m. — What the Hypertension Specialist Should Know About Vascular Function Raymond R. Townsend, MD, Philadelphia, PA

POST-TRIAL OVERVIEW

Barry B. Davis, MD, PhD, who is Director of the ALLHAT Coordinating Center, will set the stage by summarizing the original results of the trial, which were reported starting in 2002. As implied above, Dr. Cutler said that among the initial four antihypertensive drug classes that were compared, none of the non-diuretic arms were found to be superior to the thiazide-type diuretic arm (chlorothalidone) for any major outcome. In addition, another key finding from the original results is that for one or more of the major cardiovascular outcomes, the chlorthalidone arm was superior in terms of effects on patients, he said.

As part of his discussion, Dr. Davis will explain why a post-trial follow-up was conducted and how the data was collected and analyzed.

ALLHAT: Long-term Outcomes of Drug Treatment in High CHD Risk Hypertensive Patients” will take place from 10:00 to 11:30 a.m. today, Sunday, May 2, in the Mercury Ballroom.

To attend from Cordoba, Argentina, Maria A. Bendelisky, MD (from left), Mariana A. Cruz, MD, Marcelo Oria, MD, and Fernando Nole mingle during a break in the Hypertension Highlights program Saturday.
Program offers review of key principles, latest information for practicing clinicians

Primary care clinicians looking for the latest strategies and guidelines for evaluating and treating their patients with hypertension will find what they need during the "Hypertension for the Primary Care Clinician" program, which takes place from 7:30 to 11:40 a.m. today, Sunday, May 2, in West Ballroom.

Program moderator Jan N. Basile, MD, who is Chair of the ASH Committee on Education, said the course will be case driven to maximize the educational impact to the clinician in everyday practice.

"This 25th anniversary meeting of ASH is an excellent meeting," he said. "And I think the primary care track will be part of that excellence. And while this program is designated as a primary care track, it will not only be at the level of the primary care physician, but also it will also be appropriate for physician’s assistants and nurse practitioners, who are often involved in the care of those with hypertension. In addition, it will be appropriate for the ASH specialist who often works in the primary care arena and the ASH specialist who works in the subspecialty area."

Throughout the morning, sessions will address some of the key aspects of hypertension, including the measurement of blood pressure.

"It all starts with blood pressure, and if the measurement isn’t accurate, clinicians can may pursue a path that may not be in the patient’s best interest," Dr. Basile said.

**THEME 1**

**Practicing clinician and hypertension specialist** F. Wilford Germino, MD, another organizer of the primary care program and chair of Theme 1 said the day will begin by addressing the common mistakes clinicians make in measuring blood pressure.

"We’re going to demonstrate proper technique," Dr. Germino said. "The majority of blood pressures done in this country and throughout the world are done incorrectly and not according to guidelines. So we felt we should include a refresher to demonstrate how blood pressure should be taken. We will address common errors in blood pressure measurement and how to ensure they will be done properly going forward."

Theme 1 will also review how each type of blood pressure management fits into the decision-making process.

"The attendees will feel confident and comfortable that the data does support the use of some of these other measurements including home and 24-hour ambulatory blood pressures for decision-making in patients with hypertension," Dr. Germino said. "This will be useful for any clinician as these aren’t just concerns in primary care."

**THEME 2**

The second theme will focus on hypertension in the elderly.

"With the recent publication of the Hypertension in the Very Elderly Trial (HYVET), clinicians are continually asking about whether there is a particular age at which we should no longer treating those hypertension, and how to best approach those with isolated systolic hypertension," Dr. Basile said.

This theme will include an in-depth look at these important questions, he said.

Theme 2 will begin with case presentations and then feature a lecture by Steven A. Yarows, MD, on "Isolated Systolic Hypertension." Then Michael Bloch, MD, will present "The Clinical Implications of the HYVET Study."

**THEME 3**

As one of the organizers of Theme 3 — which will focus on resistant hypertension — Samuel J. Mann, MD, said a major concern in the management of hypertension is that many patients are being treated, yet their blood pressures remain uncontrolled.

"Different studies give you a different proportion, but you’re talking about millions of people," he said. "With the medications we have, we should be able to bring patients with hypertension under control in a larger proportion than we currently succeed with."

The purpose of this theme is to convey principles of treatment that can assist the primary care physician — who is the frontline person in managing difficult-to-treat hypertension.

Like all themes as part of the primary care track, this program will be practical and clinically oriented. It will include case presentations and an expert panel and will offer better approaches to using diuretics, strategies for managing patients with hypertension resistant to multiple drugs, and guidelines for when to consider a work-up for secondary hypertension.

**THEME 4**

The morning will conclude with a look at the implications of the ACCORD (Action to Control Cardiovascular Risk in Diabetes) study specifically the impact of the results from the ACCORD blood pressure trial.

"This is a must-see conference," Dr. Basile said. "I urge everyone to participate. If there’s one conference I would want all primary care practitioners to attend throughout the ASH meeting, this is the one. Why? Because it is specifically designed for clinicians in the trenches doing their best to evaluate and control blood pressure in their patients with hypertension."

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**Hypertension for the Primary Care Clinician**

**Blood Pressure Measurement: Which Metric Matters?**

7:30 a.m. — Case Study: Measurement of Blood Pressure

F. Wilford Germino, MD

7:40 a.m. — White Coat and Masked Hypertension: Does It Matter?

Angela L. Brown, MD

8:00 a.m. — 24-Hour Ambulatory and Home Blood Pressure Measurement: How to Use in Clinical Practice

William B. White, MD

8:20 a.m. — Q & A

**Hypertension in the Elderly**

8:30 a.m. — Case Presentation

Steven A. Yarows, MD

8:35 a.m. — Isolated Systolic Hypertension

Samuel Mann, MD

9:05 a.m. — The Clinical Implications of the HYVET Study

Michael Bloch, MD

9:35 a.m. — Q & A

**Resistant Hypertension: Optimizing Drug Therapy**

10:00 a.m. — Differential Diagnosis of Resistant Hypertension: When to Work-Up for Secondary Hypertension

Samuel Mann, MD

10:10 a.m. — Case Presentations: Panel Discussion

William J. Elliott, MD, PhD; David A. Calhoun, MD; and Stephen C. Tector, MD

**Evidence vs. Guidelines — What Should Be the Goal Blood Pressure in Diabetics: Results of the ACCORD Study**

11:00 a.m. — Results of the ACCORD Blood Pressure Trial

Lucia Kirtland, MD

11:20 a.m. — What These Results Mean to the Primary Care Clinician

Myra Kilenpater, MD

11:50 a.m. — Q & A

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**Continuing Education Credit**

The American Society of Hypertension, Inc., is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The American Society of Hypertension, Inc., designates this educational activity for a maximum of 35.5 AMA PRA Category 1 Credits™. Each physician should claim credit commensurate with the extent of their participation in the activity.
As ASH celebrates its 25th anniversary during the 2010 Annual Scientific Meeting and Exposition, look back at the milestones – both for the Society and the profession – and the leaders we’ve had along the way.

JOHN H. LARAGH, MD
Founding President, 1985

EDWARD G.
BIGLIERI, MD
President 1988-1990

LOUIS TOBIAN, MD
President 1992-1994

JAY N. COHN, MD
President 1990-1992

BARRY M. BRENNER, MD
President 1994-1995

MICHAEL H.
ALDERMAN, MD
President 1996–1998

HARALAMBOS GAVRAS, MD
President 2002-2004

LAWRENCE R.
KRAKOFF, MD
President 1995-1996

MICHAEL A. WEBER, MD
President 1998-2000
NEW YORK, May 2, 2010 — Data unveiled today at the ASH 25th Annual Scientific Meeting and Exposition suggest children and adolescents of parents with hypertension and larger waist and hip circumference should be evaluated for hypertension even if they exhibit normal blood pressure levels in the doctor’s office. Investigators found that these patients exhibited masked hypertension, which occurs when BP levels are normal when measured inside the doctor’s office but increase when measured outside the doctor’s office, when evaluated with ambulatory blood pressure monitoring (ABPM). Masked hypertension is not rare in children and adolescents and implies an increased risk of cardiovascular disease.

“The children found to be hypertensive with ABPM were not even in a pre-hypertensive state in the doctor’s office. Their blood pressure was normal,” said lead author of the study, Claudia Maria Salgado, MD, PhD, adjunct professor, Department of Pediatrics and Hypertension League, Federal University of Goiás, Brazil. “The fact that the blood pressure rates for these patients escalated so significantly is alarming and warrants attention, if additional data confirm these findings.”

A total of 110 children and adolescents (aged 5-15) were included in this prospective study. Of the 110 enrolled, 99 completed the BP evaluation. Participants were evaluated for family BP history, weight, height, body mass index, waist circumference (WC) and hip circumference (HC). Data from 82 subjects who had an office BP lower than the 95th percentile were analyzed. Of these, 70 had normal BP (<50th percentile) and 12 were pre-hypertensive (>90th and <95th percentile). Through ABPM, 10 were diagnosed with masked hypertension. None of those considered pre-hypertensive presented with hypertension in the ambulatory setting. Children of hypertensive parents had more than a four-fold increased risk (p=0.02). Children of hypertensive parents with a WC/HC ≥ 0.9 (abdominal obesity) had a nine-fold increased risk (p=0.02) of having masked hypertension. Age, sex, ethnicity, and excess weight (simple obesity and overweight) had no influence on risk.

Patients were studied in an outpatient clinic specializing in hypertension. Office BP was measured with an OMRON Hem-705CP (4th Task Force). Three measurements were taken on three separate occasions. Ambulatory blood pressure was taken with SPACELABS 90201 equipment with the same size sleeve as used in the office measurement. One measurement was taken every 20 minutes during the period of wakefulness (7:00 a.m. to 10:00 p.m.) and every 30 minutes during the period of sleep (10:00 p.m. to 7:00 a.m.).

The children found to be hypertensive with ABPM were not even in a pre-hypertensive state in the doctor’s office. Their blood pressure was normal. The fact that the blood pressure rates for these patients escalated so significantly is alarming and warrants attention, if additional data confirm these findings.

- Claudia Maria Salgado, MD, PhD

Data suggest need for ambulatory monitoring for children and adolescents of hypertensive patients who appear to have normal blood pressure in the doctor’s office.

Parents’ risk factors key to identifying masked hypertension in their kids

NEW YORK, May 2, 2010 — Data unveiled today at the ASH 25th Annual Scientific Meeting and Exposition suggest children and adolescents of parents with hypertension and larger waist and hip circumference should be evaluated for hypertension even if they exhibit normal blood pressure levels in the doctor’s office. Investigators found that these patients exhibited masked hypertension, which occurs when BP levels are normal when measured inside the doctor’s office but increase when measured outside the doctor’s office, when evaluated with ambulatory blood pressure monitoring (ABPM). Masked hypertension is not rare in children and adolescents and implies an increased risk of cardiovascular disease.

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- Claudia Maria Salgado, MD, PhD
Expert educator to deliver the Marvin Moser Clinical Hypertension Award

Published ASH Position Papers


ASH statement on the Institute of Medicine’s efforts to reduce sodium intake

As reflected by the Institute of Medicine’s recommendation to the Food and Drug Association to set new standards for the amount of sodium in processed and prepared foods, reducing the prevalence and consequences of hypertension is now a public health imperative for policy makers.

The American Society of Hypertension’s position paper, “Dietary Approaches to Lower Blood Pressure,” published in July 2009, advocates for reducing sodium intake, along with several other strategies to control hypertension.

As outlined in the position paper, decades of research has shown that reducing salt intake can prevent hypertension from occurring and reduce cardiovascular events. The paper says “any effective strategy to reduce sodium intake must involve the cooperation of food manufacturers and restaurants, which should progressively reduce the sodium added to foods by 50 percent during the next 10 years, as recommended by the American Medical Association.”

As the voice of hypertension, ASH is committed to working with all stakeholders, including the CDC, FDA, industry partners and healthcare professionals help them implement the Institute of Medicine’s recommendations and build the broad and multifaceted approach necessary to eliminate hypertension and improve the public’s health.

To review the ASH position paper on “Dietary Approaches to Lower Blood Pressure,” visit www.ash-us.org/pub/position_papers.htm.

Celebrated cardiologist to present Irvine Page Award Lecture

Donald Heistad, MD, the Zahn Professor of Cardiology and Professor of Internal Medicine and Pharmacology at the University of Iowa Carver College of Medicine, has been honored with the Irvine Page Award and will present a special lecture during Plenary Session II, which begins at 1:15 p.m. on Monday, May 3, in the East Ballroom. In addition to his teaching post at the University of Iowa Carver College of Medicine, Dr. Heistad is also Deputy Director of the Cardiovascular Center.

Heistad was born in Chicago and received his medical degree from the University of Chicago. He has received international recognition for his studies of hypertension, atherosclerosis, and the cerebrovascular circulation. His research has resulted in almost 500 original papers and reviews.

Dr. Heistad’s research has built the foundation for understanding cerebrovascular adaptive mechanisms and consequences of hypertension. The studies have demonstrated structural changes and endothelial dysfunction in the cerebral circulation during hypertension. His recent studies have clarified mechanisms by which hypertension leads to intracerebral hemorrhage.

Dr. Heistad has received several major research awards, including the Research Achievement Award of the American Heart Association, the Harry Goldblatt Award and Novartis Award from the Council for High Blood Pressure Research of the AHA; the Irving S. Wright Award of the Stroke Council of the AHA; the Merck International Award of the International Society of Hypertension; Distinguished Alumni Award from the University of Chicago, the Carl J. Wiggers Award of the American Physiological Society; and the Eugene M. Landsis Award of the Microcirculatory Society.

He is a member of the Association of American Physicians and the American Society for Clinical Investigation.

Dr. Heistad has given numerous named national and international lectures, including the Abbott Lecture of the American Society of Hypertension. He is recognized internationally as a leading cardiovascular investigator and mentor for biomedical scientists.
The ASH Hypertension Resource Pavilion will be open from 9:00 a.m. to noon and from 3:30 to 6:45 p.m. today, Sunday, May 2. High Tea will take place from 4:45 to 5:45 p.m. The ASH Hypertension Resource Pavilion can be found in Americas Hall on the third floor of the Hilton.

This year, featured in the Resource Pavilion will be the Innovations Theater. See the program book for a schedule of events.
NYC Eats

**AMERICAN**

B.B. King Blues Club & Grill. 243 W. 42nd St., 212-997-5144. The Blues King's Times Square restaurant and club features live performances every night of the week. The menu mirrors the diversity of the Big Apple with a hint of Southern fare and is available during all seated shows. Moderate.

Ben Benson's Steak House. 123 W. 52nd St. (between 6th and 7th Aves.), 212-581-8888. Known for its crab cakes, this raucous and masculine steakhouse has an urban hunting-lodge motif in its assented dining rooms, which are adorned with mounted and bronzed buffalo, lions, bears, and the like. The ester's huge steaks rival those of the city's more famous steakhouses. The T-bone is exceptionally tender and flavorful, as are the broiled veal chops, plump lamb chops, and roast prime rib. Expensive.

Cafe St. Barts. 109 E. 50th St. (at Park Ave.), 212-586-9067. In the warm months, Cafe St. Bart's occupies the tiled terrace of Saint Bartholomew's Church. The handsome church lends to one side, the Waldorf-Astoria is across the street, and midtown's soaring office towers are visible in every direction. The menu offers new American dishes, including New York strips, a grilled lamb sandwich, and pizza. Expensive.

Carnegie Deli. 854 7th Ave. (at 55th St.), 212-757-2245. An only-in-New York experience where portions are colossal, the Carnegie is renowned for its pastrami and corned beef sandwiches, which are home-made and delicously briny, rich but not fatty. Lean, tender beef brisket also should not be missed. Other favorites are the chubby cheese blintzes with sour cream, succulent baked potatoes served with mashed potatoes, Nova Scotia salmon omelet, and stuffed cabbage with sweet and sour sauce. Inexpensive.

Eatery. 798 9th Ave. (at 53rd St.), 212-765-7080. This trendy spot brings mom's Irish restaurant is a boisterous Theater District restaurant serves lunch and dinner daily. Moderate.

**MEXICAN/TAPAS**

Boqueria. 717 Spring St. (between Thompson St. and Wooster St.), 212-343-4255. This SoHo tapas restaurant is known for its unique take on tapas, great presentation, and helpful service. Boqueria doesn't take reservations, but the lively crowd and sangria makes any wait entertaining. Expensive.

El Paso Taqueria. 237 E. 116th (at 3rd Ave.), 212-860-4875. If you're looking for authentic Mexican food, try this East Harlem favorite. Serious taco lovers swear by El Paso Taqueria, which provides a warm, homely backdrop for its hearty, flavorful dishes. Regulars also rave about the made-to-order guacamole and chili rellenos. Moderate.

Manhattan Chili Company. 109 E. 42nd St. (dining concourse at Grand Central Station), 212-682-0442. This lively, colorful, restaurant offers sizzling Southwestern cuisine (as mild or spicy as you like) at comfortable prices. Specialties include a variety of fish sandwiches, and vegetarian options. Inexpensive.

**Italian**

Bar Vetro. 222 E. 58th St. (between 2nd and 3rd Aves.), 212-308-0121. Featuring dynamic cuisine in a sensual atmosphere, Bar Vetro is about a 15-minute walk from Times Square. Meaning "glass" in Italian, vetro refers to the muted green, transparent glass sheet that floats above the bar. The intimate dining room, decorated in cool greens and suffused with warm lavender light, is the perfect complement to the innovative menu, which features tasting dishes known as asga throughout Italy. These unique menu items are served in curved, interlocking dishes, ideal for sharing with the table or sampling as a tasting dinner. Moderate to expensive.

Carmine's Midtown. 200 W. 44th St. (between 8th Ave. and Broadway), 212-221-3800. This traditional Italian restaurant near Times Square is popular among tourists. The enormous portions are sized for three to four people, making Carmine's a great value. All of the garlic-saturated dishes come on strong with robust flavors. Rich sauces make pastas a good bet. Moderate.

John's Pizzeria. 260 W. 44th St. (between 8th Ave. and Broadway), 212-591-7560. The Times Square version of this legendary Greenwich Village pizzaeria bares little resemblance to the original, but the brick-oven pizza carries the torch nobly. The tomato and cheese pies—slices aren't available—are reasonably priced and tasty. Inexpensive.

Trattoria Dopo Teatro. 125 W. 44th St. (between 6th Ave. and Broadway), 212-869-2849. Nestled in the heart of the Theater District, Trattoria Dopo Teatro is a great place to enjoy delicious Italian cuisine before a show. Dine in the restaurant's indoor garden featuring a sky-lit center courtyard with stone waterfall, wine cellar, and grappa library. In addition to a four-course pre-theater menu, the restaur-ant serves lunch and dinner daily. Moderate.

**American**

Island Burgers and Shakes. 766 9th Ave. (between 51st and 52nd streets), 212-307-7934. This small, West Coast-style, french fry-less burger shack has attracted quite a following. The colorful interior features bright orange-and-red tables as well as paintings and mirrors in the shape of surfboards. Both the burgers and grilled chicken breast sandwiches rank among the best in the city. The menu features 63 varieties of each, with everything from basic cheeseburgers to more elaborate concoctions like the Slick Willie (with ham, relish, American cheese, bacon, sour cream, barbecue sauce, and onions). Inexpensive.

Rosie O'Grady's Midtown. 800 7th Ave. (at 53rd St.), 212-582-2975. This spacious Irish restaurant is a boisterous Theater District favorite. While the polished-wood, street-level bar may be jammed with drinkers, there's usually and entirely different scene downstairs. There's a fireplace with sofas and comfy chairs set around it, and a bar off to the side. Moderate.

**Asian**

Jewel of India. 15 W. 44th St. (between 5th and 6th Aves.), 212-869-5544. Although it's located far from the popular corridor of Indian restaurants in the city's East Village, the Jewel of India's menu doesn't disappoint. All of the standard northern Indian staples you'd find downtown are on the menu here and prepared with great care and finesse. The tandoori and chicken tikka are delicately seasoned, while the signature breads are slightly charred and never oily. The curry dishes also stand out. Moderate.

**Heartland Brewery Midtown. 1285 6th Ave. (at 51st St.), 212-582-8244. This casual chain brewery is a safe bet for groups and out-of-towners. Colorful paintings and exposed brick give the space a homey charm. The menu offers the usual pub assortment of nachos, quesadillas, burgers, ribs, and pasta dishes. But the rotating list of beers is the real draw. At any given time there are five house beers to choose from, including a lager, a red ale, and an oatmeal stout, as well as two or three seasonal brews. Moderate.**
Fun facts about the city that never sleeps

WHY IS NEW YORK CITY CALLED THE BIG APPLE?
In the 1920s, a sportswriter for the Morning Telegram named John Fitzgerald overheard stable hands in New Orleans refer to NYC’s racetracks as “the Big Apple.” He named his column “Around the Big Apple.” A decade later, jazz musicians adopted the term to refer to New York City, and especially Harlem, as the jazz capital of the world. There are many apples on the trees of success, they were saying, but when you pick New York City, you pick the big apple.

GETTING AROUND TOWN
Getting around New York City is a breeze, thanks to 3,700 buses, 714 miles of subways, 12,000 taxis and limousines, and countless feeder roads. There are also ferries, helicopters, bicycles, and frequent Amtrak and commuter rail service. And don’t forget your feet! NYC is a walking city — flat and much of it on a grid.

THE STATEN ISLAND FERRY
The Staten Island Ferry is one of the city’s transportation and sightseeing treasures. It’s been a municipal service since 1905, and although it’s primarily a commuter route between Staten Island and lower Manhattan, it’s a glorious, 5.2-mile, 20-minute mini-cruise with great views of the Statue of Liberty, New York Harbor, and lower Manhattan — and it’s free!

WHY ARE NYC CABS YELLOW?
John Hertz, who founded the Yellow Cab Company in 1907, chose yellow because he had read a study conducted by the University of Chicago that indicated it was the easiest color to spot.

WHERE IS MAIN STREET?
There are 6,374.6 miles of streets in New York City, but there’s no Main Street in Manhattan. There is, however, a Main Street in each of the other boroughs (the Bronx, Brooklyn, Queens, and Staten Island) and on Roosevelt Island.

A CITY OF ISLANDS
Manhattan and Staten Island are islands; Queens and Brooklyn are on the western tip of Long Island. So, of New York City’s five boroughs, only the Bronx is part of the mainland. However, there is an island that’s part of the Bronx and yet feels like a New England fishing village: City Island, that’s part of the Bronx and yet feels like a New England fishing village: City Island, that’s part of the Bronx and yet feels like a New England fishing village: City Island, that’s part of the Bronx and yet feels like a New England fishing village: City Island.

A HISTORY OF BUILDINGS
Manhattan and Staten Island are islands; Queens and Brooklyn are on the western tip of Long Island. So, of New York City’s five boroughs, only the Bronx is part of the mainland. However, there is an island that’s part of the Bronx and yet feels like a New England fishing village: City Island, that’s part of the Bronx and yet feels like a New England fishing village: City Island, that’s part of the Bronx and yet feels like a New England fishing village: City Island.

THE BRONX; HOW SWEDISH IT IS
The Bronx was settled in 1639 and is named for the Swedish settler Jonas Bronck. There are more than 60 landmarks and historic districts in the Bronx, including the Edgar Allen Poe Cottage on the Grand Concourse and the stately Van Cortlandt House Museum in Van Cortlandt Park.

THE STATUE OF LIBERTY AND ELLIS ISLAND BY THE NUMBERS
The Lady in the Harbor is 101 feet tall from base to torch and 305 feet tall from pedestal foundation to torch. She has a 35-foot waist and an 8-foot index finger, and she weighs 450,000 pounds. Ellis Island Immigration Station officially opened its doors to the world on Friday, January 1, 1892. From 1892 to 1924, 12 million immigrants entered the United States through Ellis Island.

GIVE MY REGARDS TO WIECHQUAEKECK?
Broadway’s original name was the Wiechquaekek Trail. It was an Algonquin trade route.

WE’LL CROSS THAT BRIDGE WHEN WE COME TO IT
On completion, the Brooklyn Bridge was the world’s longest suspension bridge, the first bridge to be lit using electricity, and the city’s tallest structure. The Verrazano-Narrows Bridge is so long — 4,260 feet — that the towers are a few inches out of parallel to accommodate the curvature of the earth.

23 SKIDOO TO YOU TOO
The triangular shape of the Flatiron Building, an early skyscraper on 23rd Street that is just six feet wide at its apex, produced wind currents that made women’s skirts billow and spurred police to coin the term “23 skidoo” to shoo gawkers from the area.

HERE YOU CAN REALLY SHOP ’TIL YOU DROP
Marcy’s, the world’s largest store, covers 2.1 million square feet of space and stocks more than 500,000 different items.

CENTRAL PARK BY THE NUMBERS
The 843-acre park covers six percent of Manhattan. It has 215 bird species, more than 26,000 trees, 58 miles of scenic paths and nearly 6,000 benches.

LINCOLN CENTER WAS FIRST.
Lincoln Center for the Performing Arts, America’s first performing arts center, held its first performance on September 23, 1962.

AN HISTORIC HOME RUN
Babe Ruth hit the first home run in Yankee Stadium in the first game ever played there.

BEER FOR BREAKFAST ANYONE?
The first public brewery in America was opened in 1635 in the Market Field, which is now the financial district. Colonists loved their beer and often had a mug with their breakfast.

HOME OF THE TICKER-TAPE PARADE
Two hundred ticker-tape parades have taken place in Lower-Broadway’s “Canyon of Heroes.” The first ticker-tape parade celebrated the dedication of the Statue of Liberty in 1886.

THE HIGH COST OF REAL ESTATE
Legend has it that Peter Minuit paid $24 in trinkets to purchase the island of Manhattan from Leni Lenape Indians at Bowling Green.

THE GOLD STANDARD
The vaults of the Federal Reserve Bank on Maiden Lane store more than one-quarter of the world’s gold bullion.

TAKING STOCK OF THE FUTURE
Under the Dutch, Wall Street — where there really was a wall — was the city limit. The New York Stock Exchange began in 1792 when 24 brokers met under a buttonwood tree facing 68 Wall Street. Today, the trading area of the New York Stock Exchange is about two-thirds the size of a football field. It’s the world’s largest exchange, with an annual trading volume of $5.5 trillion.

A REALLY BIG BULL MARKET
A 7,000-pound bronze “Charging Bull” mysteriously appeared one day in 1989 in front of the New York Stock Exchange — the bull is now at Bowling Green.

AND THEN THERE WERE THE PIGS
As late as the 1840s, thousands of pigs roamed Wall Street to consume garbage — an early sanitation system.

AFTER ALL, HOW BIG COULD IT GET?
The northern façade of City Hall was left unfinished when the building was erected in 1803 — no one foresaw that the city would expand beyond Downtown.

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Benicar® (olmesartan medoxomil)/Tablets
II. ADVERSE REACTIONS

1. INDICATIONS AND USAGE

Benicar is indicated for the treatment of hypertension. This fixed dose combination is not to be used as first-line therapy. It is not indicated for the treatment of hypertension in patients with bilateral or unilateral renal artery stenosis. It is contraindicated in patients with bilateral or unilateral renal artery stenosis. It is not indicated for the treatment of hypertension in patients with bilateral or unilateral renal artery stenosis.

2. CLINICAL PHARMACOLOGY

2.1 Mechanism of Action

Olmesartan represents a new class of antihypertensive agents that selectively blocks the angiotensin II receptor.

5. CONTRAINDICATIONS

Benicar is contraindicated in patients who are hypersensitive to any component of this product. It is also contraindicated in patients with bilateral or unilateral renal artery stenosis.

6. DOSAGE AND ADMINISTRATION

6.1 Hypertension

Adult Hypertension

Benicar has been evaluated for safety in more than 3825 patients/treatment subjects, including more than 3275 patients treated for hypertension in controlled clinical trials. Experience included about 1000 patients treated for at least 6 months and more than 525 for at least 1 year. Treatment with Benicar was well tolerated, with an incidence of adverse events similar to that in placebo. Events generally were mild, transient and had no relationship to the dose of Benicar.

The overall frequency of adverse reactions was dose-related. Analysis of gender, age and race groups demonstrated no differences between Benicar and placebo-treated patients. The rate of withdrawals due to adverse events in all trials of Benicar was 2.4% (i.e., 764/3275) of patients treated with Benicar and 2.7% (i.e., 332/12225) of patients treated with placebo. In placebo-controlled trials, the only adverse reaction that occurred in more than 1% of patients treated with Benicar and at a higher incidence versus placebo was dizzi

6.2 Post-Marketing Experience

The following adverse reactions have been reported with Benicar and have been associated with discontinuation of treatment in 1% or more of patients receiving Benicar: glomerulonephritis, aplastic anemia, anaphylactic reaction, angioedema, cerebrovascular accident, drug-induced lupus, erythematous rash, fever, fatal hyperkalemia, Guillain-Barré syndrome, hepatic failure, interstitial nephritis, interstitial pneumonitis, pemphigus, purpura, Stevens-Johnson syndrome, toxic epidermal necrolysis, thrombocytopenia, urticaria, and vasculitis.

6.3 Impaired Renal Function

As a consequence of initiating the renin-angiotensin system, changes in renal function may be anticipated in susceptible individuals treated with Benicar. In patients whose renal function may be impaired, follow up renal function tests should be done periodically. In patients treated with Benicar, serum creatinine increased to 1.5 times the upper limit of normal was observed. Additionally, azotemia and creatinine clearance have been observed in patients treated with Benicar. In clinical trials, elevations of liver enzymes and/or bilirubin were observed infrequently. Five patients had elevations of liver enzymes and/or bilirubin who were observed infrequently. Five patients (0.1%) were assigned to Benicar and one patient (0.2%) was assigned to placebo in clinical trials were withdrawn because of abnormal liver enzymes (transaminases or total bilirubin). Of the five Benicar patients, three had elevated transaminases, and Benicar (0.9%) patients.

6.4 Pediatric Use

Benicar HCT Tablets (olmesartan medoxomil/hydrochlorothiazide)

6.5 ALCHEMISTIC HISTORIES

The following adverse reactions have been reported with Benicar and have been associated with discontinuation of treatment in 1% or more of patients receiving Benicar: glomerulonephritis, aplastic anemia, anaphylactic reaction, angioedema, cerebrovascular accident, drug-induced lupus, erythematous rash, fever, fatal hyperkalemia, Guillain-Barré syndrome, hepatic failure, interstitial nephritis, interstitial pneumonitis, pemphigus, purpura, Stevens-Johnson syndrome, toxic epidermal necrolysis, thrombocytopenia, urticaria, and vasculitis.

6.6 OVERDOSAGE

The most likely manifestations of overdosage would be hypotension, tachycardia, bradycardia could be encountered if parasympathetic (vagal) stimulation occurs. If hypotensive symptoms occur, initiate supportive treatment. The dialyzability of olmesartan is unknown.

7. STORAGE

Store at 20-25°C (68-77°F) [see USP Controlled Room Temperature].

Manufactured for Daiichi Sankyo, Inc.

Parsippany, New Jersey 07054

Rx Only

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8. BACTERIAL HYPERTENSION EFFECTS

The antihypertensive effect of Benicar was smaller in black patients (usually a low-renin population), as has been seen with ACE inhibitors, beta-blockers and other angiotensin receptor blockers.

8.2 Black Patients

The antihypertensive effect of Benicar was smaller in black patients (usually a low-renin population), as has been seen with ACE inhibitors, beta-blockers and other angiotensin receptor blockers.

9. REPRODUCTIVE TOXICITY

Fetal/Neonatal Morbidity and Mortality

Exposure to olmesartan or hydrochlorothiazide during the second and third trimesters of pregnancy has been associated with oliguria and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. A transient hypotensive response is not a contra-

10. DERMATOLOGIC DISORDERS

Skin and Appendages:

Skin: rashes, pruritus, urticaria, alopecia, petechiae, petechial hemorrhages, ecchymoses, ecchymoses, melanic pigmentation, purpura, purpura, facial edema.

11. LABORATORY TEST FINDINGS

Alopecia, pruritus, urticaria

12. ADVERSE REACTIONS

12.1 Clinical Trials

Because clinical studies are conducted under widely varying conditions, adverse reactions observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.
(olmesartan medoxomil) is 20 mg once daily of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations.

Hypersensitivity Reaction

Hypersensitivity reactions (anaphylaxis, angioedema, anaphylactoid reactions, and urticaria) are rare but have been reported with olmesartan medoxomil. (See CLINICAL PHARMACOLOGY, Post-Marketing Experience.)

Lithium

Lithium should be used with caution in patients with impaired renal function. Lithium is not removed by dialysis and hemodialysis may precipitate lithium toxicity.

Gastrointestinal

Diarrhea has been reported to cause a decrease in colonic motility and to precipitate pseudo-obstruction syndrome. (See Post-Marketing Experience.)

Headache

Headache should be reported to the prescribing physician. The patients should be told that if syncope occurs, BENICAR HCT® should be discontinued until the physician has been consulted.

Information for Patients

Thiazide diuretics are indicated for patients with hypertension. They may also be used in the management of edema associated with mild to moderate hepatic or cardiac decompensation.

Drug Interactions

Other Antihypertensive Drugs – should not generally be given with diuretics. Diuretic agents reduce the renal clearance of most antihypertensive drugs, including ACE inhibitors, angiotensin II antagonists, and calcium channel blockers. (See CLINICAL PHARMACOLOGY, Pharmacokinetics.)

In Stores

Thiazide diuretics may cause intermittent and slight elevation in serum total cholesterol and triglyceride levels.

Thiazide diuretics are indicated in the management of hypertension. When used in combination with olmesartan medoxomil, these drugs produce more lowering of blood pressure than either drug alone.

Hypersensitivity to olmesartan medoxomil, hydrochlorothiazide, or any of the excipients of BENICAR HCT® Tablets (olmesartan medoxomil-hydrochlorothiazide) is an indication for discontinuing the drug.

BENICAR HCT® may be administered with other antihypertensive agents. When initiating concomitant therapy with BENICAR HCT® tablets, blood pressure should be assessed two times a week until stable, then at least once a week thereafter.

When administered concurrently the following drugs may interact with thiazide diuretics:

Corticosteroids, ACTH

Other Antihypertensive Drugs

Cyclosporine

Diuretics

Digoxin

Insulin and oral antidiabetic agents

Non-esterified fatty acids

Lithium generally should not be given with thiazides (see WARNINGS, Hypotension in Volume- or Salt-Depleted Patients). Lithium is not removed by dialysis and hemodialysis may precipitate lithium toxicity.

Thiazides may decrease urinary calcium excretion. Thiazides may cause intermittent and slight elevation in serum total cholesterol and triglyceride levels.

Thiazides appear in human milk. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Other Antihypertensive Drugs

Cyclosporine

Diuretics

Digoxin

Insulin and oral antidiabetic agents

Non-esterified fatty acids

Lithium generally should not be given with thiazides (see WARNINGS, Hypotension in Volume- or Salt-Depleted Patients). Lithium is not removed by dialysis and hemodialysis may precipitate lithium toxicity.
Azor® (amlodipine and olmesartan medoxomil) tablets

USE IN PREGNANCY

When pregnancy is detected, discontinue Azor as soon as possible. When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus (see Warnings and Precautions (5.3)).

1 INDICATIONS AND USAGE

Azor is indicated for the treatment of hypertension, alone or with other antihypertensive agents. Azor may also be used as initial therapy in patients who are likely to need multiple antihypertensive agents to achieve their blood pressure goals.

Patients with moderate or severe hypertension are at relatively high risk for cardiovascular events (such as strokes, heart attacks, and heart failure), kidney failure, and vision problems, so prompt treatment is clinically relevant. The decision to use a combination as initial therapy should be individualized and should be shaped by considerations such as baseline blood pressure, the target goal, and the incremental likelihood of achieving goal with a combination compared to monotherapy. Individual blood pressure goals may vary based upon the patient's risk.

Data from an 8-week, placebo-controlled, parallel-group factorial study (see Clinical Studies (14.1) in the full prescribing information) provide estimates of the probability of reaching a blood pressure goal with Azor compared to amlodipine or olmesartan medoxomil monotherapy. The figures below provide estimates of the likelihood of achieving the targeted systolic or diastolic blood pressure goals with Azor 10/40 mg compared with amlodipine or olmesartan medoxomil monotherapy, based upon baseline systolic or diastolic blood pressure. The curve of each treatment group was estimated by logistic regression modeling from all available data of that treatment group. The right tail of each curve is less reliable because of small numbers of subjects with high baseline blood pressures.

Figure 1: Probability of Achieving Systolic Blood Pressure (SBP) <140 mmHg at Week 8 With LOCF

Figure 2: Probability of Achieving Diastolic Blood Pressure (DBP) <90 mmHg at Week 8 With LOCF

The figures above provide an approximation of the likelihood of reaching a targeted blood pressure goal (e.g., Week 8 SBP <140 mmHg or <130 mmHg or <120 mmHg or <110 mmHg) for the high-dose treatment groups evaluated in the study. Azor 5/20 mg, the lowest dose combination treatment group, increases the probability of reaching blood pressure goal compared with the highest dose monotherapies, amlodipine 10 mg and olmesartan medoxomil 40 mg.

For example, a patient with a baseline blood pressure of 160/100 mmHg has about a 48% likelihood of achieving a goal of <140 mmHg (systolic) and a 51% likelihood of achieving a goal of <90 mmHg (diastolic) on monotherapy with olmesartan medoxomil 40 mg and about a 46% likelihood of achieving a goal of <140 mmHg (systolic) and a 60% likelihood of achieving a goal of <90 mmHg (diastolic) on monotherapy with amlodipine 10 mg. The likelihood of achieving these same goals increases to 63% (systolic) and 71% (diastolic) on Azor 5/20 mg, and to 68% (systolic) and 85% (diastolic) on Azor 10/40 mg.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Fetal/Neonatal Morbidity and Mortality

Olmesartan medoxomil. Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. There have been several dozen cases reported in the world literature of patients who were taking angiotensin converting enzyme inhibitors. When pregnancy is detected, discontinue Azor as soon as possible.

During the second and third trimesters of pregnancy, these drugs have been associated with fetal injury that includes hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Olmesartan medoxomil has also been reported, presumably resulting from decreased fetal renal function; oliguria/diphragmatics in this setting has been associated with fetal limb contractions, craniofacial deformation, and hypoplastic lung development. Prematurity, intratracheal growth retardation, and pustulosis antricusis also have been reported, although it is not clear whether these occurrences were due to exposure to the drug.

These adverse effects do not appear to have resulted from intrauterine drug exposure that has been limited to the first trimester. Mothers whose embryos and fetuses are exposed to an angiotensin II receptor antagonist only during the first trimester should be so informed. Nonetheless, when patients become pregnant, physicians should continue the use of Azor as soon as possible.

Rarely (probably less often than once in every thousand pregnancies), no alternative to a drug acting on the renin-angiotensin system will be found. In these cases, the mothers should be apprised of the potential hazards to their fetuses and serial ultrasound examinations should be performed to assess the intra-amniotic environment.

If oligohydramnios is observed, discontinue Azor unless it is considered life-saving for the mother. Contract stress testing (CST), a non-stress test (NST), or biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury.

Infants with histories of in utero exposure to an angiotensin II receptor antagonist should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. Exchange transfusion or dialysis may be required as means of reversing hypotension and/or substituting for disordered renal function.

No teratogenic effects were observed when olmesartan medoxomil was administered to pregnant rats at oral doses up to 1000 mg/kg/day (240 times the maximum recommended human dose (MRHD) on a mg/m² basis) or pregnant rabbits at oral doses up to 1 mg/kg/day (half the MRHD on a mg/m² basis; higher doses could not be evaluated for effects on fetal development as they were lethal to the dams). In rabs, significant decreases in pup birth weight and weight gain were observed at doses ≥1.5 mg/kg/day, and delays in developmental milestones (delayed separation of ear andural, eruption of lower incisors, appearance of abdominal hair, descent of testes, and separation of eyelids) and dose-dependent increases in the incidence of dilution of the renal pelvis were observed at doses ≥2.8 mg/kg/day. The no observed effect dose for developmental toxicity in rats is 0.3 mg/kg/day, about one-tenth the MRHD of the 40 mg/day.

5.2 Hypotension in Volume- or Salt-Depleted Patients

Olmesartan medoxomil. Symptomatic hypotension may be anticipated after initiation of treatment with olmesartan medoxomil. Patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients (e.g., those being treated with high doses of diuretics) may be particularly vulnerable. Initiate treatment with Azor under close medical supervision. If hypotension does occur, place the patient in the supine position and administered an intravenous infusion of normal saline. A transient hypertensive response is not a contraindication to further treatment, which usually can be continued without difficulty once the blood pressure has stabilized.

5.3 Vasodilation

Amlodipine. Since the vasodilatory attribute attributable to amlodipine is Azor is gradual in onset, acute hypotension has rarely been reported after oral administration. Nonetheless, exercise caution, as with any other peripheral vasodilator, when administering Azor, particularly in patients with severe aortic stenosis.

5.4 Patients with Severe Obstructive Coronary Artery Disease

Patients, particularly those with severe obstructive coronary artery disease, may develop increased frequency, duration, or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.

5.5 Patients with Congestive Heart Failure

Amlodipine. General, calcium channel blockers should be used with caution in patients with heart failure. Amlodipine (5-10 mg per day) has been studied in a placebo-controlled trial of 1153 patients with NYHA Class III or IV heart failure on stable doses of ACE inhibitor, digoxin, and diuretics. Follow-up was at least 6 months, with a mean of about 14 months. There was no overall adverse effect on survival or cardiac morbidity (as defined by life-threatening arrhythmia, acute myocardial infarction, or hospitalization for worsening heart failure). Amlodipine has been compared to placebo in four 8-12 week trials of patients with NYHA class III heart failure, involving a total of 697 patients. In these studies, there was no evidence of worsening of heart failure based on measures of exercise tolerance, NYHA classification, symptoms, or UFE.
5.6 Patients with Impaired Renal Function

Azer. There are no studies on Azor in patients with renal impairment.

Olmesartan medoxomil. Changes in renal function may be anticipated in susceptible individuals treated with olmesartan medoxomil as a consequence of inhibiting the renin-angiotensin-aldosterone system. In patients whose renal function may depend upon the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with angiotensin converting enzyme inhibitors and angiotensin receptor antagonists has been associated with oliguria or progressive azotemia and (rarely) with acute renal failure and/or death. Similar effects may occur in patients treated with Azor because of the olmesartan medoxomil component (See Clinical Pharmacology (12.3) in the full prescribing information).

In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have been reported. There has been no long-term use of olmesartan medoxomil in patients with unilateral or bilateral renal artery stenosis, but similar effects would be expected with olmesartan medoxomil and Azor.

5.7 Patients with Hepatic Impairment

Amlodipine. Since amlodipine is extensively metabolized by the liver and the plasma elimination half-life (t1/2) is 58 hours in patients with severely impaired hepatic function, extreme caution when administering Azer to patients with severe hepatic impairment.

Patients with hepatic impairment have decreased clearance of amlodipine. Starting amlodipine or adding amlodipine to either component of Azor in patients with severe hepatic impairment.

In post-marketing experience, increased blood creatinine levels and hyperkalemia have been reported.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

Azer

The data described below reflect exposure to Azor in more than 1600 patients including more than 1000 patients treated with Azor alone or in combination with other antihypertensive agents.

The adverse event profile obtained from 44 weeksofopen-label combination therapy with amlodipine plus olmesartan medoxomil was similar to that observed during the 8-week, double-blind, placebo-controlled clinical trials with amlodipine plus placebo. The rate of withdrawals due to adverse events in all trials of hypertensive patients was 2.4% (i.e., 79/3278) of patients treated with olmesartan medoxomil and 2.7% (i.e., 20/771) of control patients. In placebo-controlled trials, the only adverse event that occurred in more than 1% of patients treated with olmesartan medoxomil and at a higher incidence in olmesartan medoxomil treated patients vs. placebo was diuresis (3% vs 1%).

6.2 Post-Marketing Experience

The following adverse reactions have been reported in post-marketing experience:

- Body as a Whole: asthenia, anemia
- Gastrointestinal: vomiting
- Musculoskeletal: rhabdomyolysis
- Renal and Urinary: acute renal failure
- Skin and Appendages: alopecia, pruritus, urticaria

7 DRUG INTERACTIONS

7.1 Drug Interactions with Azer

The pharmacokinetics of amlodipine and olmesartan medoxomil are not altered when the drugs are co-administered.

No drug interaction studies have been conducted with Azer and other drugs, although studies have been conducted with the individual amlodipine and olmesartan medoxomil components of Azor, as described below, and no significant drug interactions have been observed.

7.2 Drug Interactions with Amlodipine

In vitro data indicate that amlodipine has no effect on the human plasma protein binding of digoxin, phenytoin, warfarin, and indomethacin.

Effect of Other Agents on Amlodipine

Cimetidine: Co-administration of amlodipine with cimetidine did not alter the pharmacokinetics of amlodipine.

Grapefruit juice: Co-administration of 240 ml of grapefruit juice with a single oral dose of amlodipine 10 mg in 20 healthy volunteers had no significant effect on the pharmacokinetics of amlodipine. Opposite effects were observed in 20 healthy volunteers given 20 mg of Maalox® (antacid): Co-administration of the antacid Maalox® with a single dose of amlodipine had no significant effect on the pharmacokinetics of amlodipine. Atorvastatin: Co-administration of amlodipine with atorvastatin resulted in no significant change in the steady state pharmacokinetic parameters of atorvastatin.

Diagnosis: Co-administration of amlodipine with digoxin did not change serum digoxin levels or renal clearance in normal volunteers. Ethanol: (alcohol): Single and multiple 10 mg doses of amlodipine had no significant effect on the pharmacokinetics of ethanol.

Warfarin: Co-administration of amlodipine with warfarin did not change the warfarin protrombin response time.

In clinical trials, amlodipine has been safely administered with thiazide diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, digoxin, warfarin, non-steroidal anti-inflammatory drugs, antidepressants, and oral hypoglycemic drugs.

7.3 Drug Interactions with Olmesartan Medoxomil

No significant drug interactions were reported in studies in which olmesartan medoxomil was co-administered with digoxin or warfarin in healthy volunteers.

The bioavailability of olmesartan medoxomil was not significantly altered by the co-administration of antacids (Al(OH)₃/Mg(OH)₂).

Olmesartan medoxomil is not metabolized by the cytochrome P450 3A4 system and has no effects on P450 3A4. Thus, interactions with drugs that inhibit, induce, or are metabolized by those enzymes are not expected.
**8 USE IN SPECIFIC POPULATIONS**

**8.1 Pregnancy**

**Olmesartan medoxomil.** Pregnancy Categories C (first trimester) and D (second and third trimesters). (See Warnings and Precautions (5.1) and Use in Specific Populations (8.1))

**Amlodipine.** No evidence of teratogenicity or other embryo/fetal toxicity was found when pregnant rats and rabbits were treated orally with amlodipine maleate at doses of up to 10 mg amlodipine/kg/day (respectively 10 and 20 times the maximum recommended human dose of 10 mg amlodipine on a mg/m² basis) during their respective periods of major organogenesis. (Calculations based on a patient weight of 60 kg). However, litter size was significantly decreased (by about 50%) and the number of intratranial deaths was significantly increased (about 5-fold) in rats receiving amlodipine maleate at a dose equivalent to 10 mg amlodipine/kg/day for 14 days before mating and throughout mating and gestation. Amlodipine maleate has been shown to prolong both the gestational period and the duration of labor in rats at this dose. There are no adequate and well-controlled studies in pregnant women. Amlodipine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**8.2 Nursing Mothers**

It is not known whether the amlodipine or olmesartan medoxomil components of Azor are excreted in human milk, but olmesartan is secreted at low concentration in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

**8.4 Pediatric Use**

The safety and effectiveness of Azor in pediatric patients have not been established.

**Amlodipine.** The effect of amlodipine on blood pressure in patients less than 6 years of age is not known.

**Olmesartan medoxomil.** Safety and effectiveness of olmesartan medoxomil in pediatric patients have not been established.

**8.6 Hepatic Impairment**

There are no studies of Azor in patients with hepatic insufficiency, but both amlodipine and olmesartan medoxomil show moderate increases in exposure in patients with hepatic impairment. Use caution when administering Azor to patients with severe hepatic impairment.

Patients with hepatic impairment have decreased clearance of amlodipine. Starting amlodipine or adding amlodipine at 2.5 mg in patients with hepatic impairment is recommended. The lowest dose of Azor is 5/20 mg.

**8.7 Renal Impairment**

There are no studies of Azor in patients with renal impairment.

**Amlodipine.** The pharmacokinetics of amlodipine are not significantly influenced by renal impairment. Patients with renal failure may therefore receive the usual initial dose.

**Olmesartan medoxomil.** Patients with renal insufficiency have elevated serum concentrations of olmesartan compared with patients with normal renal function. After repeated dosing, AUC was approximately tripled in patients with severe renal impairment (creatinine clearance <20 mL/min). No initial dosage adjustment is recommended for patients with moderate to marked renal impairment (creatinine clearance <40 mL/min).

**8.8 Black Patients**

Of the total number of subjects in the double-blind clinical study of Azor, 25% (481/1940) were black patients. Azor was effective in treating black patients (usually a low-renin population), and the magnitude of blood pressure reduction in black patients approached that observed for non-black patients.

**10 OVERDOSAGE**

There is no information on overdosage with Azor in humans. Amlodipine. Single oral doses of amlodipine maleate equivalent to 40 mg amlodipine/kg and 100 mg amlodipine/kg in mice and rats, respectively, caused deaths. Single oral amlodipine maleate doses equivalent to 4 or more mg amlodipine/kg or higher in dogs (11 or more times the maximum recommended human dose on a mg/m² basis) caused a marked peripheral vasodilation and hypotension.

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia. In humans, experience with intentional overdosage of amlodipine is limited. If massive overdose should occur, active cardiac and respiratory monitoring should be instigated. Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine) should be considered with attention to circulating volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. As amlodipine is highly protein bound, hemodialysis is not likely to be of benefit.

**Olmesartan medoxomil.** Limited data are available related to overdosage in humans. The most likely manifestations of overdosage would be hypotension and tachycardia; bradyarrhythmias could be encountered if parasympathetic (vagal) stimulation occurs. If symptomatic hypotension should occur, supportive treatment should be initiated. The dialyzability of olmesartan is unknown.

**17 PATIENT COUNSELING INFORMATION**

Physicians should instruct female patients of childbearing age about the consequences of second and third trimester exposure to drugs that act on the renin-angiotensin system and they should be told that these consequences do not appear to have resulted from intrauterine drug exposure that has been limited to the first trimester. These patients should be informed to report pregnancies to their physicians as soon as possible. (See Warnings and Precautions (5.1) and Use in Specific Populations (8.1))
USE IN PREGNANCY
When pregnancy is detected, discontinue AZOR as soon as possible. When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. See WARNINGS AND PRECAUTIONS, Fetal/Neonatal Morbidity and Mortality.

Hypotension in Volume- or Salt-Depleted Patients
In patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients, symptomatic hypotension due particularly to the olmesartan component may occur after initiation of treatment with AZOR. Treatment should start under close medical supervision.

Vasodilation
Since the vasodilation attributable to amlodipine in AZOR is gradual in onset, acute hypotension has rarely been reported after oral administration. Nonetheless, caution, as with any other peripheral vasodilator, should be exercised when administering AZOR, particularly in patients with severe aortic stenosis.

Severe Obstructive Coronary Artery Disease
Patients, particularly those with severe obstructive coronary artery disease, may develop increased frequency, duration, or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase.

Congestive Heart Failure
In general, calcium channel blockers should be used with caution in patients with heart failure.

Impaired Renal Function
In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have been reported. There has been no long-term use of olmesartan medoxomil in patients with unilateral or bilateral renal artery stenosis, but similar effects would be expected with AZOR because of the olmesartan medoxomil component.

Hepatic Impairment
Since amlodipine is extensively metabolized by the liver and the plasma elimination half-life (t1/2) is 56 hours in patients with severely impaired hepatic function, caution should be exercised when administering AZOR to patients with severe hepatic impairment. Initial therapy with AZOR is not recommended in hepatically impaired patients.

Laboratory Tests
There was a greater decrease in hemoglobin and hematocrit in the combination product compared to either component alone.

Adverse Reactions
The only adverse reaction that occurred in greater than or equal to 3% of patients treated with AZOR and more frequently than placebo was edema. The placebo-subtracted incidence was 5.7% (5/20 mg), 6.2% (5/40 mg), 13.3% (10/20 mg), and 11.2% (10/40 mg). The edema incidence for placebo was 12.3%.

Adverse reactions seen at lower rates but at about the same or greater incidence as in patients receiving placebo included hypotension, orthostatic hypotension, rash, pruritus, palpitation, urinary frequency, and nocturia.

In individual clinical trials of amlodipine and olmesartan medoxomil, other commonly reported adverse reactions included headache, dizziness, and flushing.

Geriatric Use
Elderly patients have decreased clearance of amlodipine. Initial therapy with AZOR is not recommended in patients ≥75 years old.

Please see full prescribing information for AZOR.
AZOR is indicated for the treatment of hypertension, alone or with other antihypertensive agents. AZOR is indicated as initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goals. Initial therapy with AZOR is not recommended in patients ≥75 years of age or in hepatically impaired patients.

BENICAR® (olmesartan medoxomil) and BENICAR HCT (olmesartan medoxomil-hydrochlorothiazide) are indicated for the treatment of hypertension. They may be used alone or in combination with other antihypertensive agents. BENICAR HCT is not indicated for initial therapy. Please see inside back cover for important safety information for BENICAR and BENICAR HCT.

For more information, please visit www.AZOR.com

Please see preceding page for important safety information.

Please see brief summary of prescribing information for AZOR, including boxed WARNING regarding avoiding use in Pregnancy.
**WARNING: AVOID USE IN PREGNANCY**

When pregnancy is detected, discontinue BENICAR or BENICAR HCT as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus.

### Hypotension in Volume- or Salt-Depleted Patients

In patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients (eg, those being treated with high doses of diuretics), symptomatic hypotension may occur after initiation of treatment with BENICAR. Treatment should start under close medical supervision. If hypotension does occur, the patient should be placed in the supine position and, if necessary, given an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further treatment, which usually can be continued without difficulty once the blood pressure has stabilized.

### Impaired Renal Function

In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have been reported. There has been no long-term use of olmesartan medoxomil in patients with unilateral or bilateral renal artery stenosis, but similar results may be expected.

### Fetal/Neonatal Morbidity and Mortality

Thiazides cross the placental barrier and appear in cord blood. There is a risk of fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions that have occurred in adults.

### Hepatic Impairment

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

### Hypersensitivity Reaction

Hypersensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma, but are more likely in patients with such a history.

### Systemic Lupus Erythematosus

Thiazide diuretics have been reported to cause exacerbation or activation of systemic lupus erythematosus.

### Lithium Interaction

Lithium generally should not be given with thiazides.

### Adverse events

- The withdrawal rates due to adverse events (AEs) were similar with BENICAR and BENICAR HCT to placebo: BENICAR (2.4% vs 2.7%); BENICAR HCT (2.0% vs 2.0%)
- The incidence of AEs with BENICAR and BENICAR HCT was similar to placebo
  - The only AE that occurred in >1% of patients treated with BENICAR and more frequently than placebo was dizziness (3% vs 1%)
  - AEs reported in >2% of patients taking BENICAR HCT and more frequently than placebo included nausea (3% vs 0%), hyperuricemia (4% vs 2%), dizziness (9% vs 2%), and upper respiratory tract infection (7% vs 0%)

### Dosing and administration

- No initial dosage adjustments are recommended with BENICAR in elderly or in moderate to marked renal impairment/*hepatic dysfunction
  - In patients with possible depletion of intravascular volume (eg, patients on diuretics, particularly with impaired renal function), BENICAR should be initiated under close medical supervision and consideration given to use of a lower starting dose
- For BENICAR HCT, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosage range

*Creatinine clearance <40 mL/min.

Please see full prescribing information for BENICAR and BENICAR HCT.
WARNING: AVOID USE IN PREGNANCY
When pregnancy is detected, discontinue BENICAR or BENICAR HCT as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus.

BENICAR and BENICAR HCT are indicated for the treatment of hypertension. They may be used alone or in combination with other antihypertensive agents. BENICAR HCT is not indicated for initial therapy.

For more information, please visit www.BENICAR.com

Please see preceding page for important safety information.

Please see brief summary of prescribing information for BENICAR and BENICAR HCT, including boxed WARNING regarding avoiding use in Pregnancy.