Aldosterone Synthase Inhibitors for the Treatment of Hypertension: Effectiveness and Value

Public Meeting — October 29, 2026

Meeting materials available at: https://icer.org/assessment/hypertension-2026/#timeline

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MIDWEST CEPAC
COMPARATIVE EFFECTIVENESS PUBLIC ADVISORY COUNCIL

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- **Reem Mustafa, MD, MPH, PhD,** Professor of Medicine, Division of Nephrology & Hypertension, The University of Kansas Medical Center
- **Jimi Olaghere**, Sickle Cell Disease Advocate; Entrepreneur, Sugarloaf Capital
- **Kurt Vanden Bosch, PharmD**, System Formulary Lead at St. Luke's Health System
- **Stuart Winston, DO,** Patient Experience Lead Consultant, Trinity Health IHA Medical Group

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Patient Experts

Andrew Bzowyckyj, PharmD, BCPS, Senior Scientific Director, Learning Consultant; National Kidney Foundation

- *Andrew Bzowyckyj is an employee of the National Kidney Foundation. The National Kidney Foundation receives 64% of its annual funding from healthcare companies, including AstraZeneca.*

Brittany Dickerson, Kidney Health Advocate

- *Brittany Dickerson serves as an ambassador and committee member on multiple initiatives for the National Kidney Foundation. She also volunteers with American Kidney Fund, Chronic Disease Coalition, IPRO End Stage Renal Disease Network Program, NephCure, Sharing Hope SC. She receives compensation from Ardelyx as their Kidney Patient Advisory Committee member.*

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Clinical Experts

Jordana (Jordy) Cohen, MD, Associate Professor of Medicine and Epidemiology, University of Pennsylvania

- *Dr. Jordy Cohen has no conflicts to disclose.*

Karol Watson, MD, PhD, Professor of Medicine and Cardiology, David Geffen School of Medicine at UCLA

- *Dr. Karol Watson has served as consultant for Boehringer Ingelheim, Eli Lilly, Merck, Novartis, Novo Nordisk, and Regeneron.*

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ICER Speakers



Sarah K. Emond, MPP
President & CEO



Grace Lin, MD
Evidence Author,
Medical Director for HTA, ICER



David Rind, MD, MSc
Chief Medical Officer



Kangho Suh, PharmD, MS, PhD
Lead Modeler and Assistant Professor,
University of Pittsburgh School of Pharmacy;
University of Washington Modeling Group

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Why are we here today?

“Since my heart attack, I no longer work full time because it’s impossible to manage stress and my high blood pressure. I’ve tried many medications, and they all have had some kind of side effect while not completely lowering my blood pressure. I hope to be on a treatment that is more effective than all the three medicines I’m already on.”

Patient Story from ICER Share Your Story Submissions

Why Are We Here Today?

- What happens the day these treatments receive FDA approval?
- Questions about:
  - What are the risks and benefits?
  - How do new treatments fit into the evolving landscape?
  - What are reasonable prices and costs to patients, the health system, and the government?
  - What lessons are being learned to guide our actions in the future?

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The Impact on Rising Health Care Costs for Everyone

GALLUP®

APRIL 1, 2025

In U.S., Inability to Pay for Care, Medicine Hits New High

Rates among Hispanic, Black adults and those with lower incomes worsen markedly since 2021

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America's small businesses are giving up on health insurance

Employers and workers confront unaffordable premium hikes, with no relief in sight

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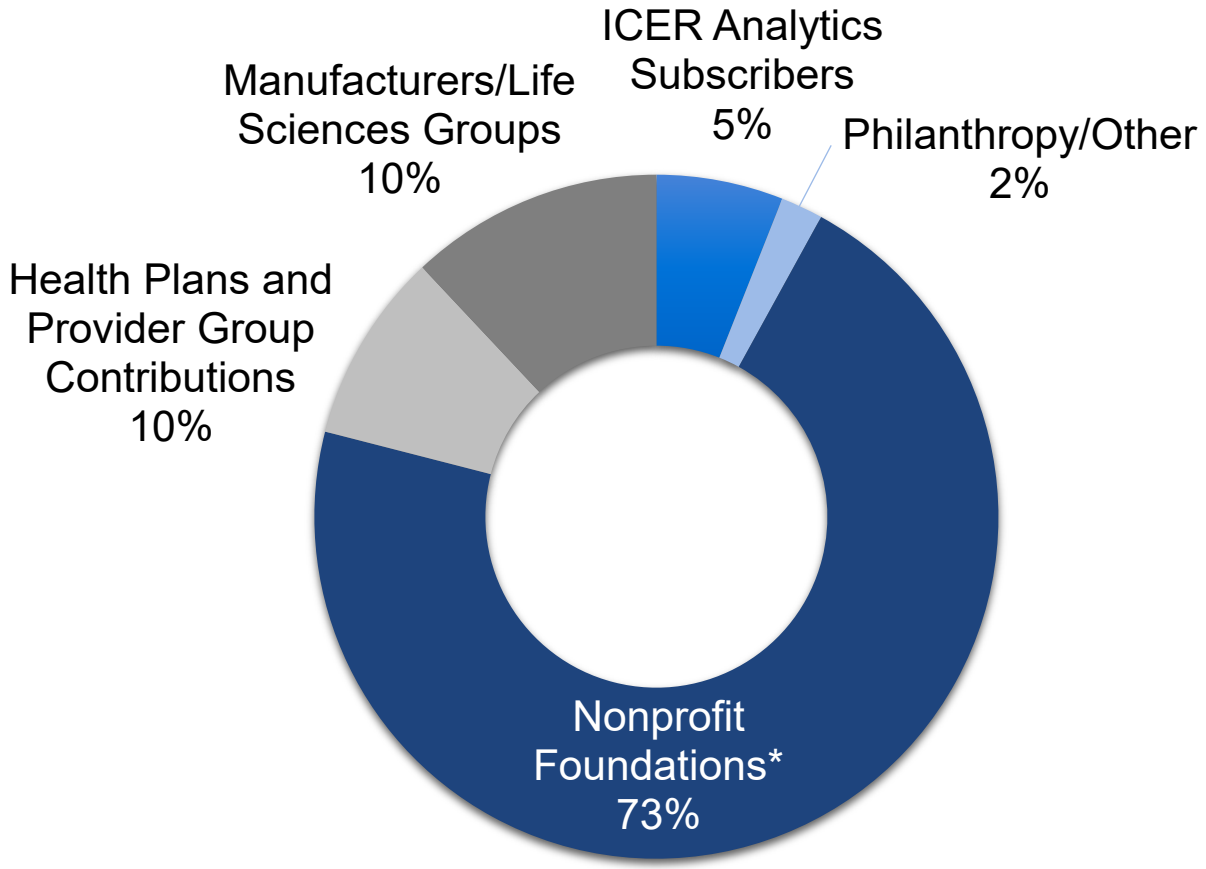
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Organizational Overview



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2026 Funding and Managing COIs



Read our policies to manage potential conflicts of interest: https://icer.org/our-approach/policies/policies-to-manage-conflicts-of-interest/

ICER Policy Summit and non-report activities only

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*ICER received significant funding from Arnold Ventures, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, and the Peterson Center on Healthcare. (represented on our "Sources of Funding" page under "Nonprofit Foundations").

How Was the ICER Report Developed?



Guidance from patients, clinical experts, manufacturers, and other stakeholders

Evidence analysis in collaboration with the **University of California, San Francisco** and cost-effectiveness modeling in collaboration with the **University of Washington**

- **Andrew Bzowyckyj, PharmD, BCPS, CDCES,** Senior Scientific Director, Learning Consultant, National Kidney Foundation
- **Jordana Cohen, MD, MSCE,** Associate Professor of Medicine and Epidemiology, Perelman School of Medicine, University of Pennsylvania
- **Dhruv S. Kazi, MD, MSc, MS,** Associate Director, Richard A. and Susan F. Smith Center for Outcomes Research, Director, Cardiac Critical Care Unit, Beth Israel Deaconess Medical Center

Structured to support **Midwest CEPAC** voting and policy discussion

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Value Assessment Framework: Long-Term Value for Money



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Agenda (CT)

10:00 AM	Meeting Convened and Opening Remarks
10:20 AM	Presentation of the Clinical Evidence
11:00 AM	Presentation of the Economic Model
11:40 AM	Public Comments and Discussion
12:00 PM	Lunch Break
12:50 PM	CEPAC Deliberation and Vote
1:50 PM	Break
2:00 PM	Policy Roundtable Discussion
3:30 PM	Reflections from CEPAC
4:00 PM	Meeting Adjourned

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Presentation of the Clinical Evidence

Grace A. Lin, MD, MAS

Medical Director, Health Technology Assessment, ICER

Professor of Medicine, University of California, San Francisco

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Key Team Members

Name	Title
Grace A. Lin, MD, MAS	Evidence Author; Medical Director, Health Technology Assessment, ICER; Professor of Medicine, UCSF
Dmitriy Nikitin, MSPH	Senior Research Lead, ICER
Sol Sanchez, BA	Research Assistant, ICER

Disclosures

Financial support provided to GL (through the University of California, San Francisco) from the Institute for Clinical and Economic Review (ICER)

DN, SS have no conflicts to disclose.

GL has received grant funding from the National Institutes of Health/National Institute on Aging, National Human Genome Research Institute, Mt. Zion Health Fund, GRAIL, Inc., California Health Benefits Research Program.

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Hypertension

Disease Background

- Defined as a blood pressure ≥130/80 mm Hg
- Affects almost 120 million people in US (48% of population)
  - Almost 80% not at their blood pressure goal (generally <130/80 mm Hg)
  - More than half of those taking medication are not at their blood pressure goal
  - Black, Hispanic, and Asian Americans are less likely to be at their blood pressure goal compared with White Americans
- Clinical inertia, nonadherence, lack of access to care/insurance contribute to population of people with blood pressure not at goal

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US: United States, mm Hg: millimeters of mercury

Causes of Hypertension

Primary (90-95% of cases)

- Genetic & environmental factors
- Risk factors
  - Age
  - Family history
  - Obesity
  - Diet
  - Race
  - Smoking
  - Diabetes

Secondary (5-10% of cases)

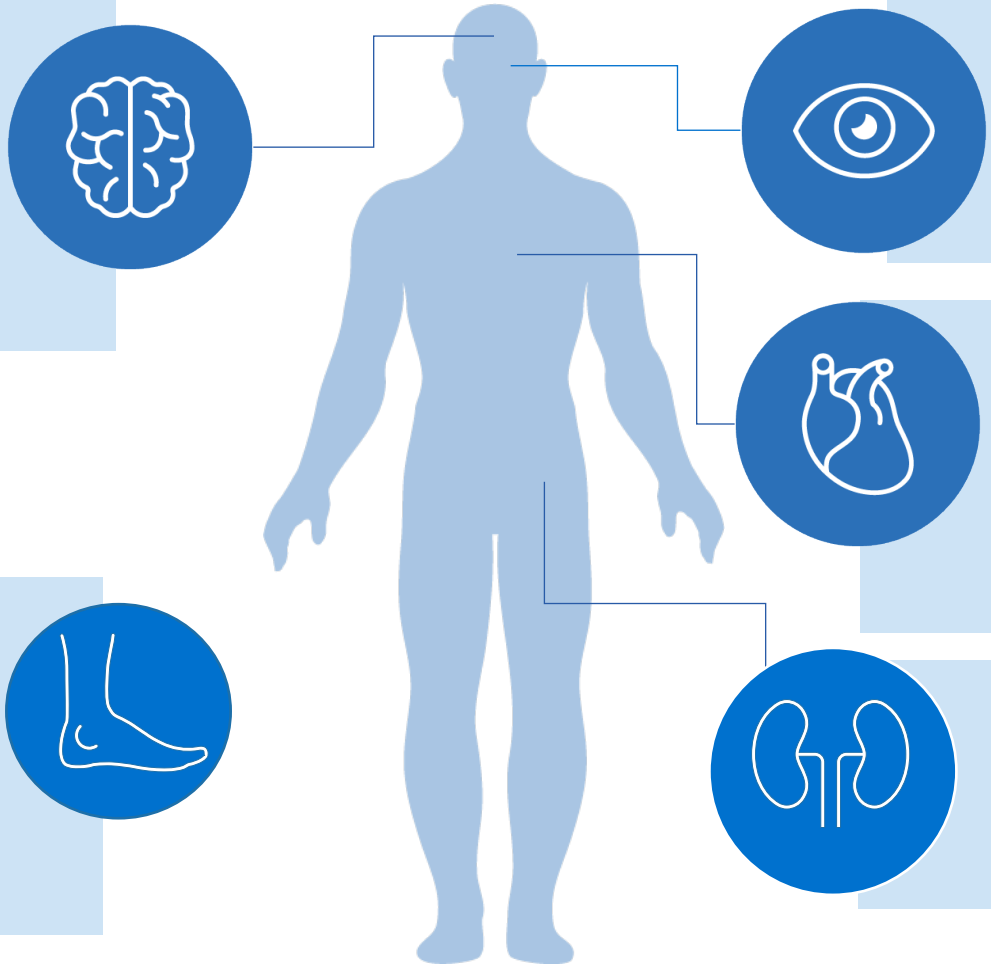
- Kidney Disorders
  - Chronic kidney disease, renal artery stenosis
- Endocrine Disorders
  - Primary aldosteronism, pheochromocytoma
- Cardiovascular Disorders
  - Obstructive sleep apnea, coarctation of aorta
- Medications and Substance Use
  - NSAIDs, stimulants, oral contraceptives, steroids, amphetamines, alcohol, nicotine

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NSAIDs: nonsteroidal anti-inflammatory drugs

Target Organ Damage

Cerebrovascular Disease

Stroke/TIA
Vascular dementia



Eye Disease

Optic neuropathy
Choroidopathy

Cardiovascular Disease

Myocardial infarction
Congestive heart failure
Atrial fibrillation

Peripheral effects

Peripheral arterial disease
Aortic aneurysm/dissection
Erectile dysfunction

Kidney Disease

Chronic kidney disease
End-stage kidney disease

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TIA: transient ischemic attack

Resistant Hypertension

- Defined as a blood pressure ≥130/80 mm Hg while taking 3 or more antihypertensive medications or <130/80 mm Hg while taking 4 or more medications
- More than 10 million adults in the US have resistant hypertension
  - Black Americans have the highest rates of resistant hypertension and the lowest control compared with other racial/ethnic groups in US
- More likely to have a secondary cause of hypertension
  - Primary aldosteronism is the most common secondary cause (~20% of cases)

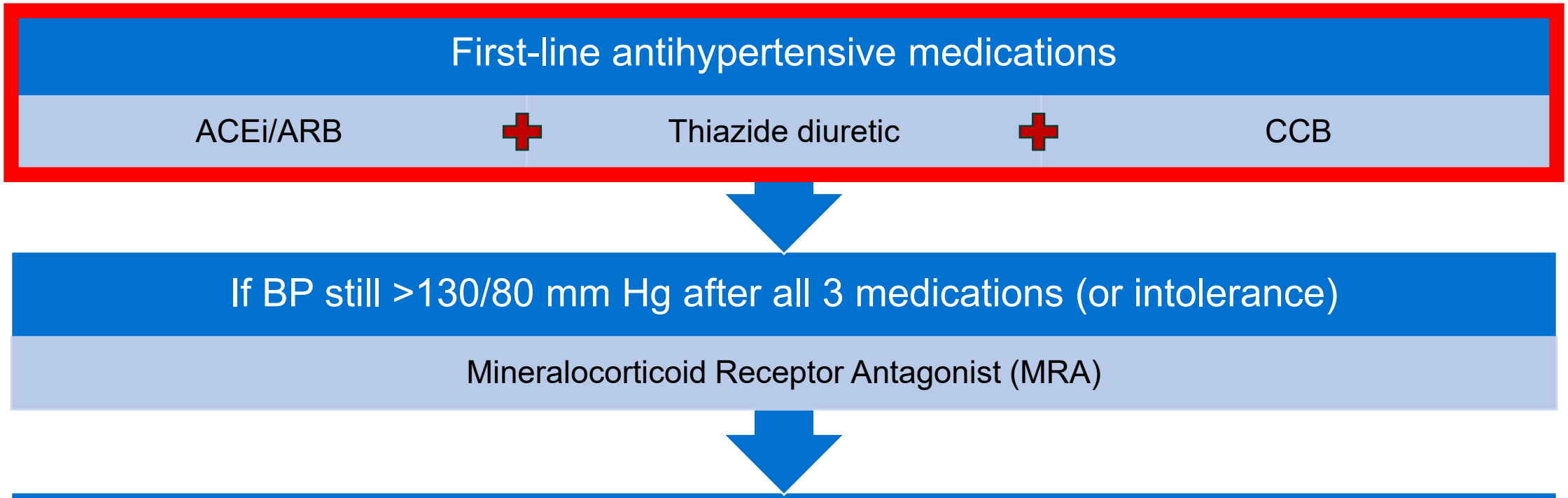
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Standard of Care and Management

- For most people, blood pressure goal is <130/80 mm Hg
- Lowering blood pressure decreases risk of target organ damage
  - e.g., CV events, stroke, heart failure, kidney disease
- Lifestyle changes (e.g., DASH diet, physical activity, decreased alcohol intake, weight loss) are recommended for everyone
  - Each intervention can lead to blood pressure lowering of 2-10 mm Hg
- Medication initiation depends on cardiovascular risk
  - Higher risk = start antihypertensive medications at lower blood pressure threshold

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CV: cardiovascular, DASH: Dietary Approaches to Stop Hypertension, mm Hg: millimeters of mercury

Standard of Care and Management

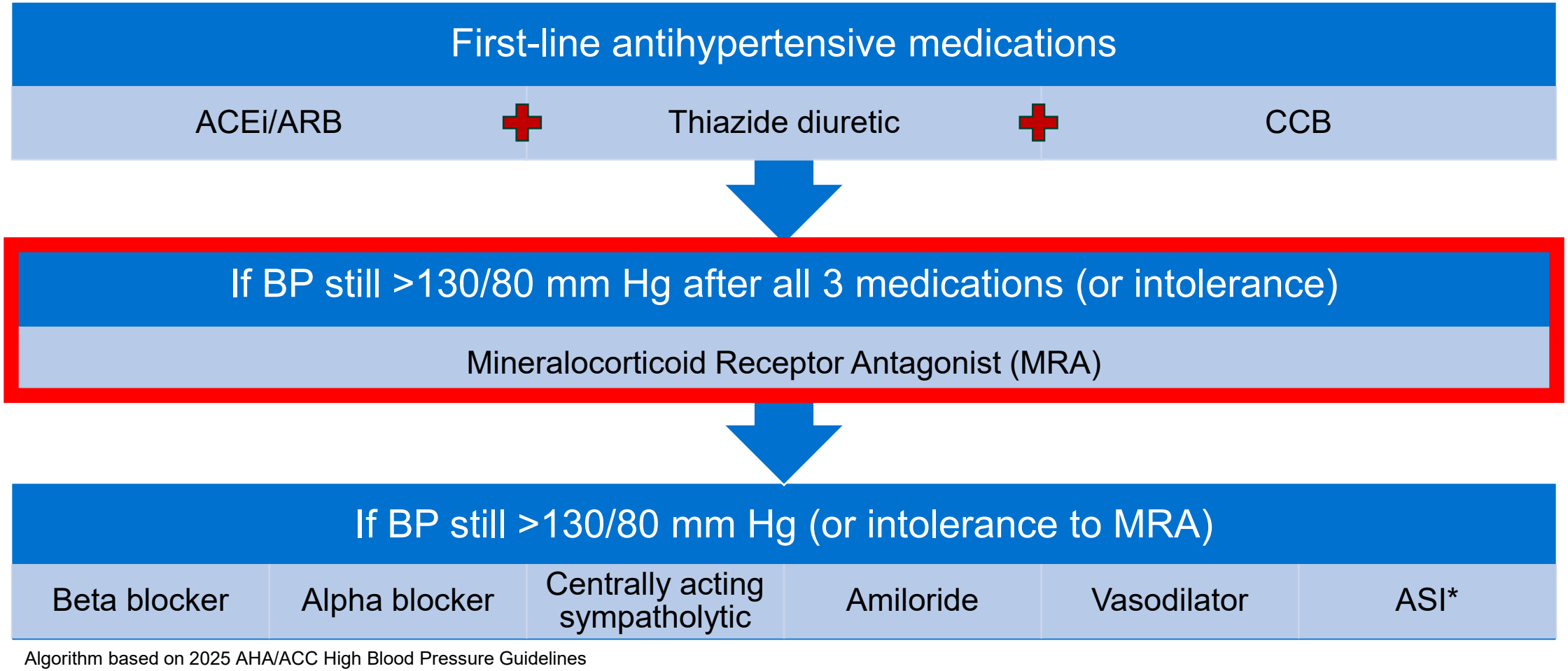


Algorithm based on 2025 AHA/ACC High Blood Pressure Guidelines
*2026 ACC Expert Consensus Decision Pathway

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ACEi: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, ASI: aldosterone synthase inhibitor, BP: blood pressure, CCB: calcium channel blocker, mm Hg: millimeters of mercury

Standard of Care and Management

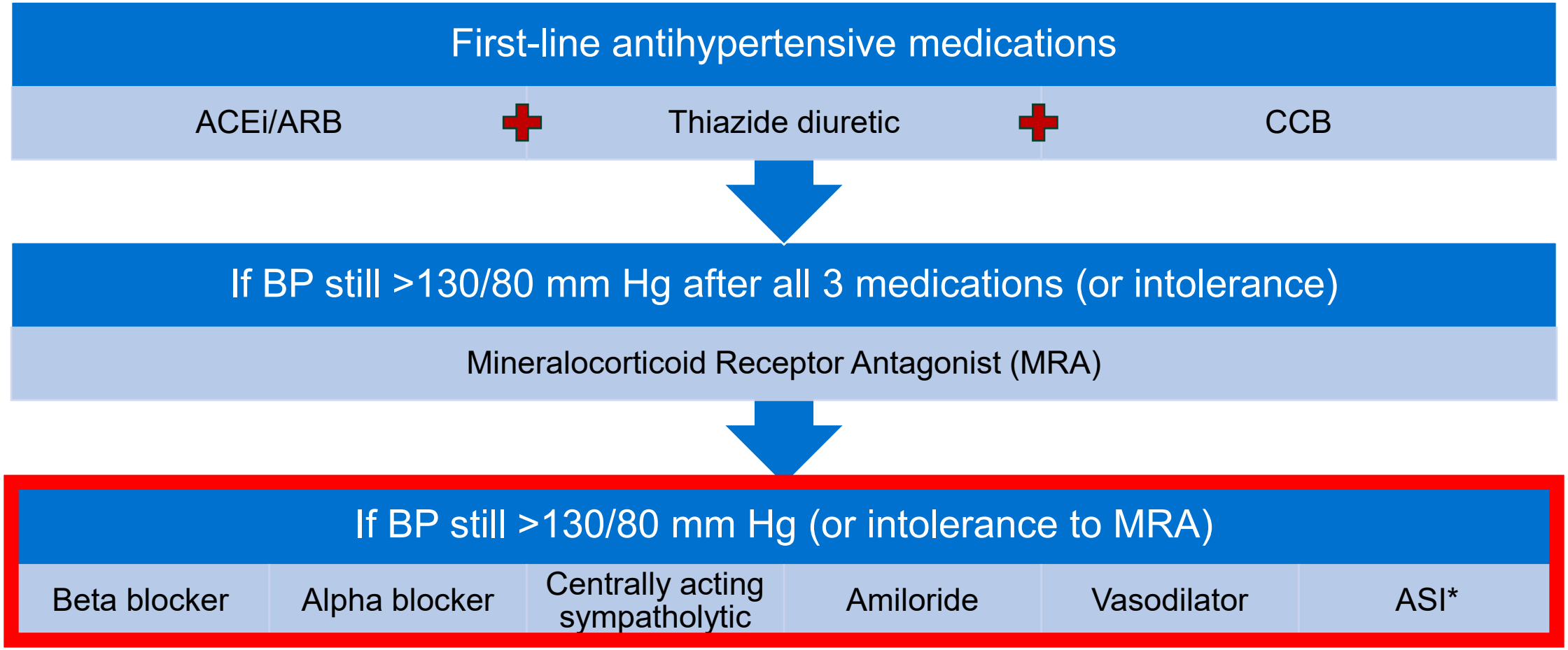


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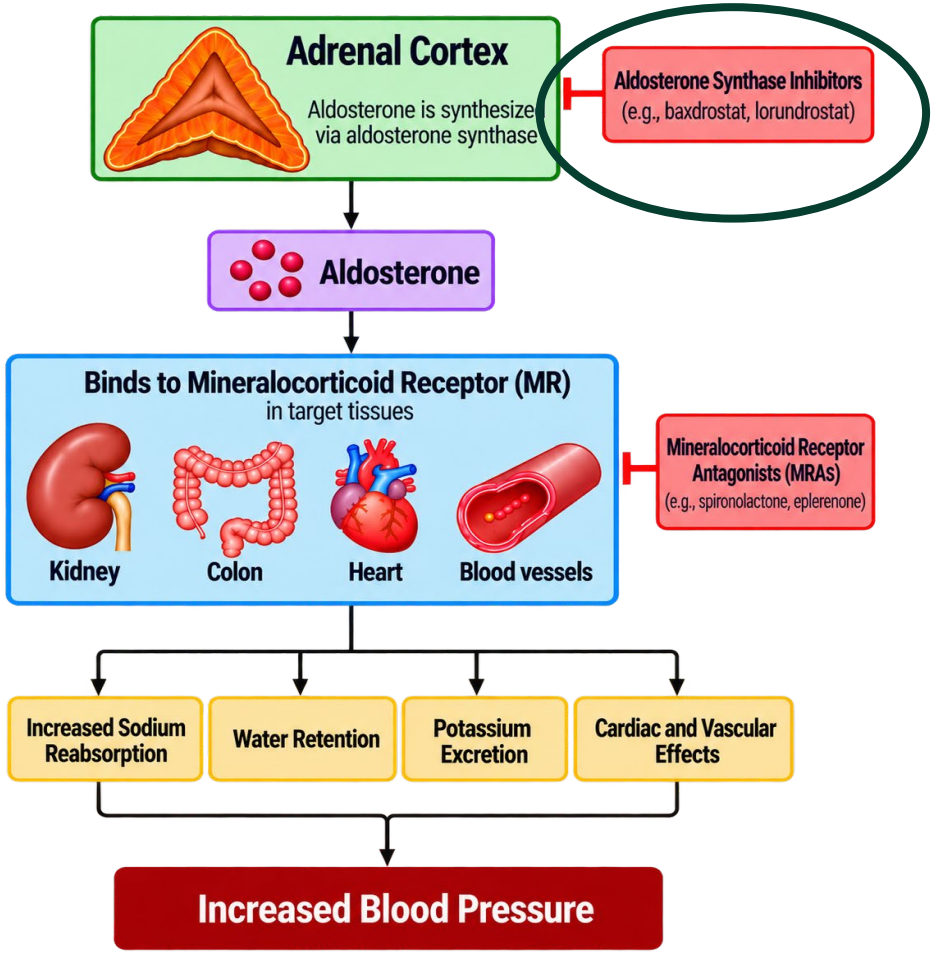
Scope of Review

- Clinical effectiveness of aldosterone synthase inhibitors baxdrostat (BAXFENDY™) and lorundrostat in the following populations:
  - **Population 1:** Blood pressure above goal despite use of ≥3 antihypertensive medications (uncontrolled resistant hypertension)
  - **Population 2:** Blood pressure above goal despite use of two first-line antihypertensive medications and unable to tolerate a third first-line agent
  - **Population 3:** Blood pressure above goal on ≥2 first-line antihypertensive medications and have not yet tried a third first-line agent

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Interventions and Comparators

- Interventions
  - Baxdrostat (BAXFENDY, AstraZeneca) 2 mg daily
  - Lorundrostat (Mineralys Therapeutics) 50 mg daily
- Comparators
  - For Populations 1 and 2: mineralocorticoid receptor antagonists (MRAs) spironolactone and eplerenone; amiloride
  - For Population 3: amlodipine

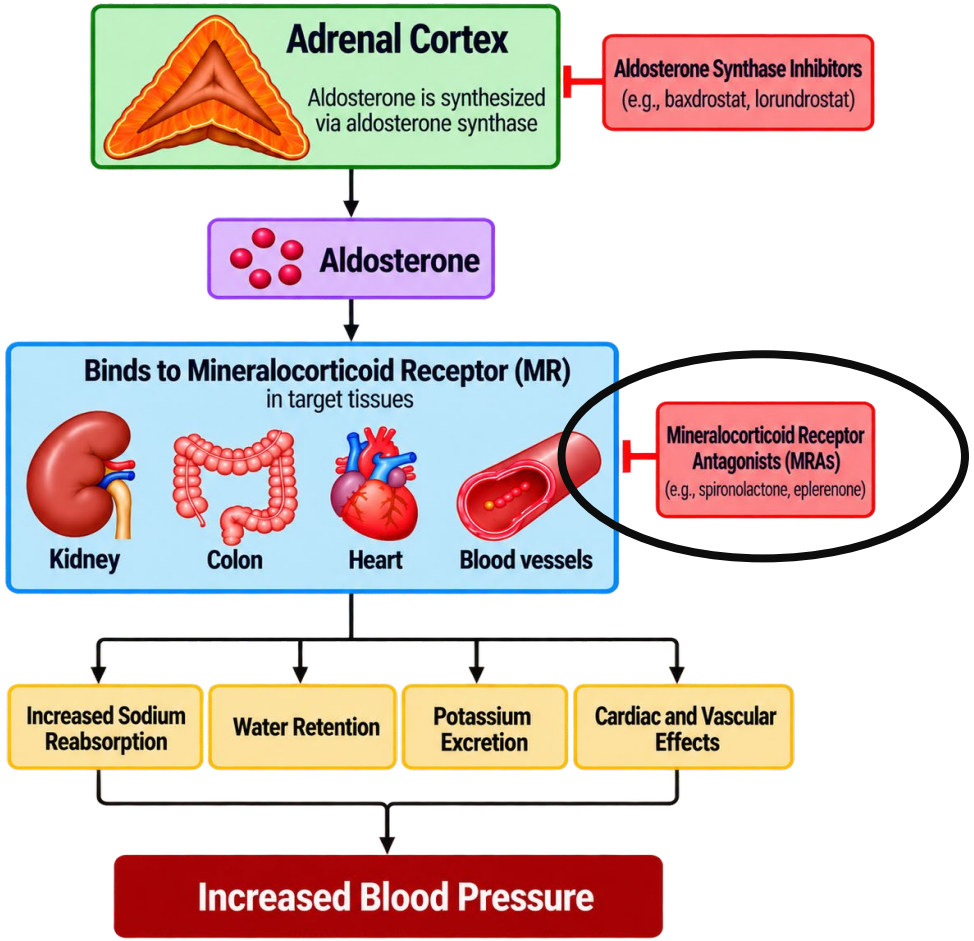


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mg: milligrams

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Outcomes

- Patient-important outcomes
  - Cardiovascular outcomes
  - Kidney outcomes
  - Cognitive outcomes
  - Health-related quality of life
- Surrogate outcomes
  - Mean change in blood pressure
- Safety and tolerability
  - Serious adverse events
  - Electrolyte disturbances, gynecomastia, other treatment-related adverse events

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Insights from Discussions with Patients

- Because hypertension can be asymptomatic, many people are unaware of diagnosis
- Barriers to control of hypertension include:
  - Lack of awareness of dietary impact on hypertension, lack of dietary education
  - Structural and environmental factors – e.g., food deserts, food insecurity – can impede dietary modification
  - Clinical inertia and clinician fear of hyperkalemia and gynecomastia with spironolactone
  - Managing multiple medications, including pill burden and cost

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Clinical Evidence

Key Clinical Trials

Reference	Study	Group	N	Follow-up	# of AHTs (%)	Population(s)
Flack 2025	BaxHTN*	Baxdrostat 2 mg vs. placebo	530	12 weeks	2: 25.2% ≥3: 74.8%	Population 1 Population 3
Azizi 2026	Bax24	Baxdrostat 2 mg vs. placebo	217	12 weeks	≥3: 100%	Population 1
Saxena 2025	Launch-HTN†	Lorundrostat 50 mg vs. placebo	813	12 weeks	2: 39.4% ≥3: 60.6%	Population 1 Population 3

*BaxHTN trial also had baxdrostat 1 mg arm; long-term follow-up data from BaxHTN are available through week 54.
†Launch-HTN trial also had arm with lorundrostat titration from 50 mg to 100 mg based on pre-specified criteria; also has an ongoing open-label extension.

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Population 1 NMA Results: Mean Systolic Blood Pressure Differences (mm Hg)

Baxdrostat					
-0.9 (-5.7, 3.8)	Spironolactone				
-2 (-10.1, 6.2)	-1.1 (-8.9, 6.9)	Lorundrostat			
-2.2 (-9.5, 5.5)	-1.3 (-8.3, 6.3)	-0.2 (-9.8, 9.9)	Eplerenone		
-4.4 (-10.6, 1.8)	-3.5 (-8.4, 1.6)	-2.4 (-11.3, 6.4)	-2.2 (-10.7, 5.8)	Amiloride	
-11 (-14.6, -7.3)	**-10.1 (-13.1, -6.8)**	**-9 (-16.3, -1.7)**	**-8.9 (-15.5, -2.4)**	**-6.6 (-11.5, -1.5)**	Placebo

Note: Data presented as mean SBP (95% CrI).

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CrI: credible interval, mm Hg: millimeters of mercury, NMA: network meta-analysis, SBP: systolic blood pressure

Population 3 NMA Results: Mean Blood Pressure Differences (mm Hg)

Baxdrostat			
-1.5 (-9, 5.7)	Lorundrostat		
-1.8 (-8.6, 4.8)	-0.3 (-4.6, 4.1)	Amlodipine	
-10.1 (-16.6, -3.9)	**-8.6 (-12.4, -4.8)**	**-8.3 (-10.7, -6.2)**	Placebo

Note: Data presented as mean SBP (95% CrI).

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CrI: credible interval, mm Hg: millimeters of mercury, NMA: network meta-analysis, SBP: systolic blood pressure

Limitations of NMA

- Heterogeneity in studies
  - Blood pressure measurement
  - Medication dosages
  - Open-label study (amiloride versus spironolactone)
- Almost all indirect comparisons; only one head-to-head trial

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Cardiovascular and Kidney Outcomes*

Drug	MACE	Stroke	All-cause Mortality	Urine Albumin	ESKD
Baxdrostat†	---	---	---		---
Lorundrostat	---	---	---		---
Spironolactone	---	---	---		No effect
Eplerenone	---	---	---	---	Mixed effect
Amiloride	---	---	---	---	---
Amlodipine				---	

*Data are for HTN population; some drugs may have data in other disease populations

†Baxdrostat (with dapagliflozin) has ongoing cardiovascular and kidney outcome trials (BaxDuo-Pacific, BaxDuo Arctic, Prevent-HF)

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ESKD: end-stage kidney disease,
MACE: major adverse cardiovascular events

Other Patient-Important Outcomes

- No data reported on cognitive outcomes, all-cause mortality, and health-related quality of life for either baxdrostat or lorundrostat

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Harms – Baxdrostat and Lorundrostat

Key Points

- Baxdrostat and lorundrostat both appear well-tolerated with few serious adverse events
- Most common side effects are electrolyte abnormalities such as hyperkalemia or hyponatremia
- Need long-term follow-up to evaluate potential to develop adrenal insufficiency

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Harms – Hyperkalemia

	BAX 1 mg†	BAX 2 mg†	LOR 50 mg‡	SPIR 15-50 mg§	EPL 25-50 mg§
Intervention Arm	6.6	10.2	1.1	17.5	4.8
Placebo Arm	2.5		0.3	7.5	2.6

Note: Hyperkalemia is defined as K >5.5 mmol/L.
†Pooled data from BaxHTN, Bax24, and BrigHTN, as reported in the FDA prescribing information.
‡Pooled data from Launch-HTN and Advance-HTN.
§Data from a systematic review (Vukadinović et al., 2017), limited to trials that defined hyperkalemia as serum potassium >5.5 mmol/L.

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BAX: baxdrostat, EPL: eplerenone, FDA: Food and Drug Administration, K: potassium, LOR: lorundrostat, mg: milligram, mmol/L: millimoles per liter, n: number, SPIR: spironolactone

Other Significant Harms

Spironolactone/Eplerenone

- Gynecomastia most frequent with spironolactone (4-6%), lower rates with eplerenone
- Hyperkalemia and hyponatremia were common

Amiloride

- FDA boxed warning for hyperkalemia

Amlodipine

- Peripheral edema (female > male)

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Unpublished Studies

- Long-term data for baxdrostat (BaxHTN 52-week follow-up) shows durability in blood pressure lowering and similar safety profile
- Long-term safety for baxdrostat (BaxHTN, 52-54 weeks):
  - 14% of participants developed hyperkalemia requiring medical intervention
  - 9.5% had severe hyperkalemia (>6.0 mmol/L).

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Controversies and Uncertainties

Key Points

- Lack of data on patient-important outcomes such as CV events and mortality for ASIs
- Lack of head-to-head trials, reliance on indirect comparisons
- Lack of longer-term data, particularly for side effects
- Limited data on subgroups, particularly CKD

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ASIs: aldosterone synthase inhibitors, CKD: chronic kidney disease, CV: cardiovascular

Benefits Beyond Health and Special Ethical Priorities

Key Points

- Unmet need – 70-80% of people with hypertension are not at goal BP
- Non-Hispanic Black Americans have higher prevalence of resistant hypertension and lower rates of reaching blood pressure goals
- Caregiver burden could decrease with fewer CV events and lower rates of kidney disease and dementia

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BP: blood pressure, CV: cardiovascular

Public Comments Received

- Comparators not appropriate given unique mechanism of action of ASIs, low real-world uptake of MRAs.
  - Comparators chosen were consistent with recommendations from clinical guidelines and clinical experts.
- Comparisons to other antihypertensive medications rely on indirect evidence from NMA.
  - We agree and strongly encourage head-to-head randomized controlled trials of ASIs against active comparators to generate definitive comparative data.
- Primary aldosteronism should be highlighted as an important subgroup.
  - No subgroup data on the effect of ASIs in this population, but they were not excluded so trial results are likely relevant; awaiting ongoing studies in this population.

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ASIs: aldosterone synthase inhibitors, MRAs: mineralocorticoid receptor antagonists, NMA: network meta-analysis

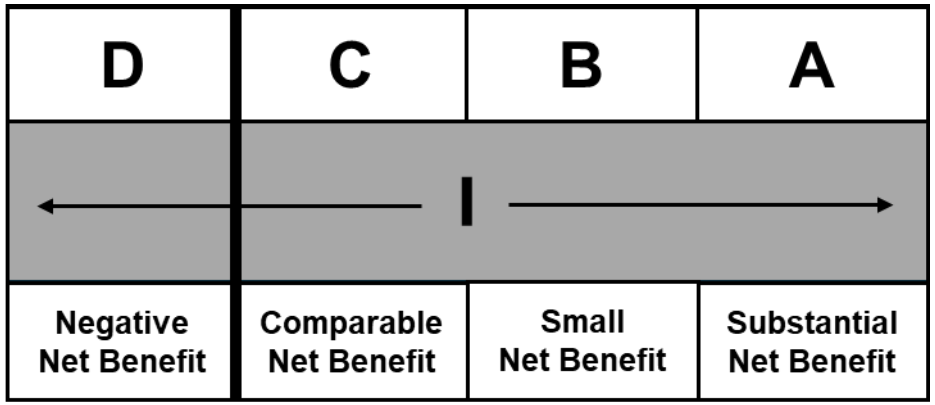
Summary

- Baxdrostat and lorundrostat are similarly effective at lowering blood pressure as MRAs, amiloride, and amlodipine and appear well-tolerated
- No current direct data on cardiovascular or kidney events; emergence of benefit may change evidence ratings
- Clinical inertia is a major barrier to achieving blood pressure goal
- Long-term data on safety and efficacy is needed

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Evidence Ratings of Interventions in People with Uncontrolled Hypertension (Populations 1, 2, and 3)

Baxdrostat *versus* **Lorundrostat**



Insufficient evidence

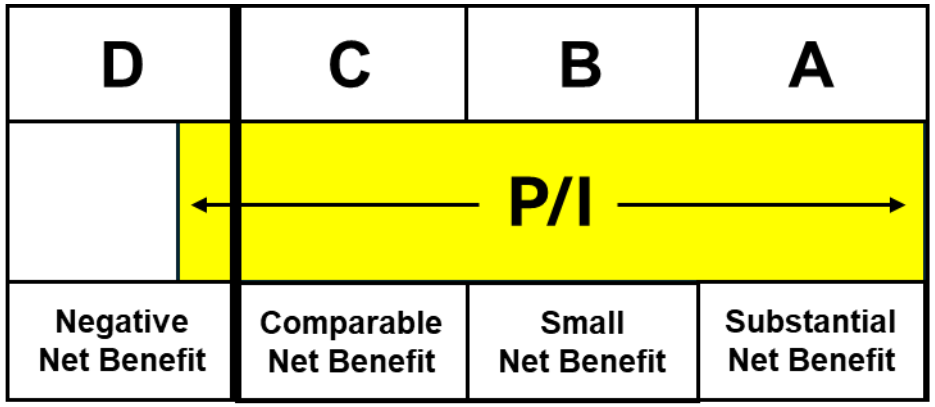
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Evidence Ratings of Interventions in Populations 1 and 2

Baxdrostat
Lorundrostat

each
versus

Spironolactone, Eplerenone, or Amiloride



May be somewhat better, but possibly slightly worse

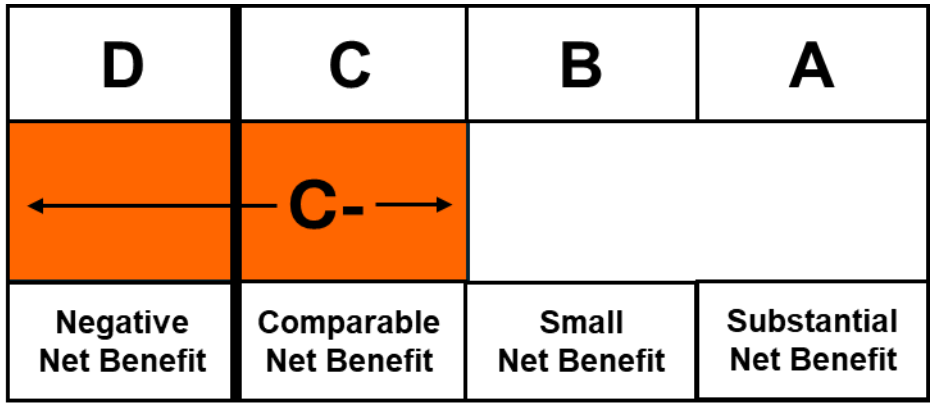
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Evidence Ratings of Interventions in Population 3

Baxdrostat
Lorundrostat

each
versus

Amlodipine



As good at best, possibly worse

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Questions?

Presentation of the Economic Model

Kangho Suh

Assistant Professor, School of Pharmacy, University of Pittsburgh

University of Washington Modeling Group

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Key Team Members

Name	Title
Kangho Suh, PharmD, PhD	Assistant Professor, School of Pharmacy, University of Pittsburgh
Josh Carlson, PhD, MPH	Professor & Graduate Program Director, CHOICE Institute, University of Washington
Marie Phillips, BA	Health Economics Research Assistant, ICER

Disclosures

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KS, JC, and MP have no conflicts to disclose.

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Objective

Uncontrolled Hypertension

To evaluate the lifetime cost-effectiveness of baxdrostat and lorundrostat compared to relevant comparators for the treatment of 1) uncontrolled resistant hypertension and 2) uncontrolled hypertension

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Unmet Need

Condition	Absolute evLY Shortfall	Proportional evLY Shortfall
Hypertension	6.2	33%
Other Example Conditions		
Obesity	6.2	20.4%
Multiple Sclerosis	18.9	52%
Osteoporosis	2.6	19%

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evLY: equal value of life year

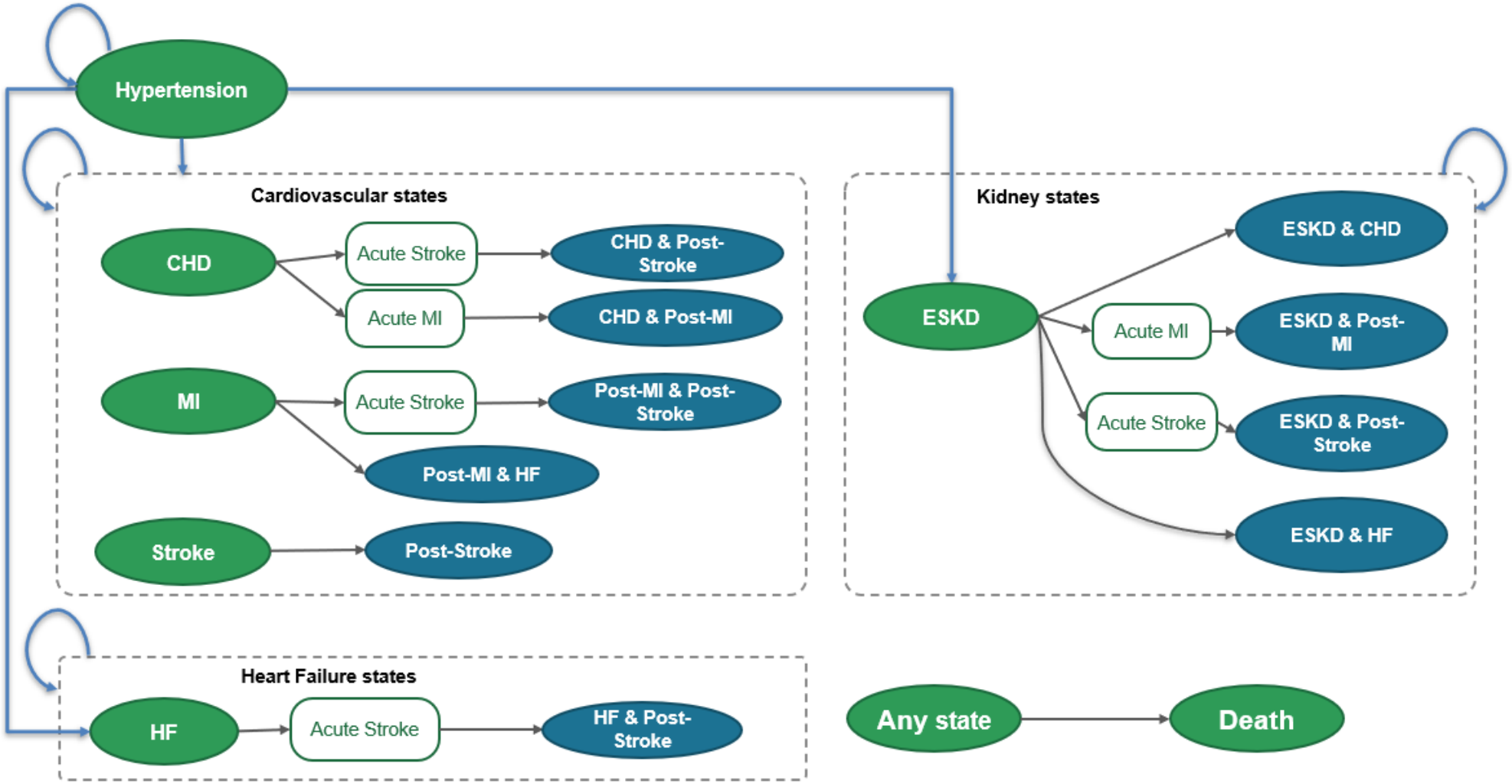
Methods in Brief

Methods Overview

Domain	Approach
Model	Markov model
Setting	United States
Perspective	Health Care Sector Perspective and Modified Societal Perspective
Time Horizon	Lifetime
Discount Rate	3% per year (costs and outcomes)
Cycle Length	3 month
Primary Outcome	Cost per equal value of life years gained (evLY); quality-adjusted life year (QALY) gained; life year gained

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evLY: equal value of life years, QALY: quality-adjusted life years

Model Schematic



Adapted from Geisler et al. 2012 and McFarlane et al. 2025

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CHD: coronary heart disease, ESKD: end stage kidney disease, HF: heart failure, MI: myocardial infarction

Model Characteristics

- Adults with hypertension not at blood pressure goal:
  - Population 1: on ≥3 antihypertensives at maximally tolerated doses (resistant hypertension)
  - Population 2: on two antihypertensives and did not tolerate a third first-line agent
  - The baxdrostat and lorundrostat trials did not include patients exactly like those in Population 2. We assumed treatment effects would be similar to those in Population 1 and developed a single model to inform decisions for both populations.
- Interventions: baxdrostat 2 mg and lorundrostat 50 mg, once daily
- Comparators: spironolactone, eplerenone, and amiloride

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Key Assumptions

Assumption	Rationale
1. **Treatment effect persists while patients remain on therapy**	Consistent with prior models and clinical plausibility. 10 and 20- year durations were tested in scenario analyses.
2. **SBP reduction held constant after trial follow-up period**	Projecting further reductions beyond observed follow-up was not supported by current evidence.
3. **BP returns to baseline immediately upon discontinuation**	Consistent with modeling precedent. Pharmacologic effect ends with discontinuation.
4. **RR reduction per mm Hg SBP lowering does not vary by baseline SBP**	Prior meta-regression found no evidence of effect modification by baseline SBP across any cardiovascular outcome.
5. **CV risk reduction per mm Hg SBP lowering is equivalent across drug classes**	In the absence of head-to-head RCT evidence, differences in cardiovascular outcomes between comparators are assumed to be driven solely by differences in achieved SBP reduction.
6. **Patients who discontinue return to their baseline antihypertensive regimen**	Consistent with modeling precedent and limits the influence of treatment sequence.

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BP: blood pressure, CV: cardiovascular, mm Hg: millimeters of mercury, RCT: randomized controlled trials, RR: relative risk, SBP: systolic blood pressure

Baseline Transition Probabilities

- Baseline probabilities of moving from hypertension alone to cardiovascular and kidney event states came from published multivariate risk equations used in prior hypertension models[1,2]
  - Stroke, coronary heart disease, and heart failure: Framingham Heart Study equations
  - Myocardial infarction: PROCAM equation
  - End-stage kidney disease: population-based incidence by SBP category matched to the cohort's baseline SBP (3-month probability of 0.14%)[3]
  - Equations apply cohort baseline characteristics (age, sex, baseline SBP, diabetes, lipids), with variables not from the trials taken from the literature

[1]McFarlane et al. J Med Econ 2025; [2]Geisler et al. J Am Coll Cardiol 2012; [3]Kim et al. Sci Rep 2025

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PROCAM: Prospective Cardiovascular Münster, SBP: systolic blood pressure

Repeated CV Events

- Only specific health state combinations were possible based on previous models in resistant and uncontrolled hypertension[1,2]
  - CHD can be followed by MI or stroke, but not ESKD
  - MI can lead to secondary HF
  - ESKD can lead to any other cardiovascular endpoints
- Stroke is a universal secondary event, layered onto any nonfatal state (post MI, HF, ESKD, or CHD)
  - Post-stroke is absorbing as patients can transition only to death
- Hazard ratios of 1.44 (following MI) and 3.4 (ESKD) are applied to baseline transition probabilities to reflect elevated risk of subsequent CV events[3,4]

[1]McFarlane et al. J Med Econ 2025; [2]Geisler et al. J Am Coll Cardiol 2012; [3]Jernberg et al. Eur Heart J 2015; [4]Go et al. NEJM 2004

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CHD: coronary heart disease, CV: cardiovascular, ESKD: end stage kidney disease, HF: heart failure, MI: myocardial infarction

Key Model Inputs: SBP Reduction

Treatment	SBP Reduction vs. Placebo, mm Hg (95% CrI)	Source
Baxdrostat 2 mg	11.0 (7.3, 14.6)	ICER NMA
Lorundrostat 50 mg	9.0 (1.7, 16.4)	ICER NMA
Spironolactone	10.1 (6.7, 13.1)	ICER NMA
Eplerenone	8.8 (2.3, 15.5)	ICER NMA
Amiloride	6.6 (1.4, 11.6)	ICER NMA

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CrI: credible interval, mg: milligrams, mm Hg: millimeters of mercury, NMA: network meta-analysis, SBP: systolic blood pressure

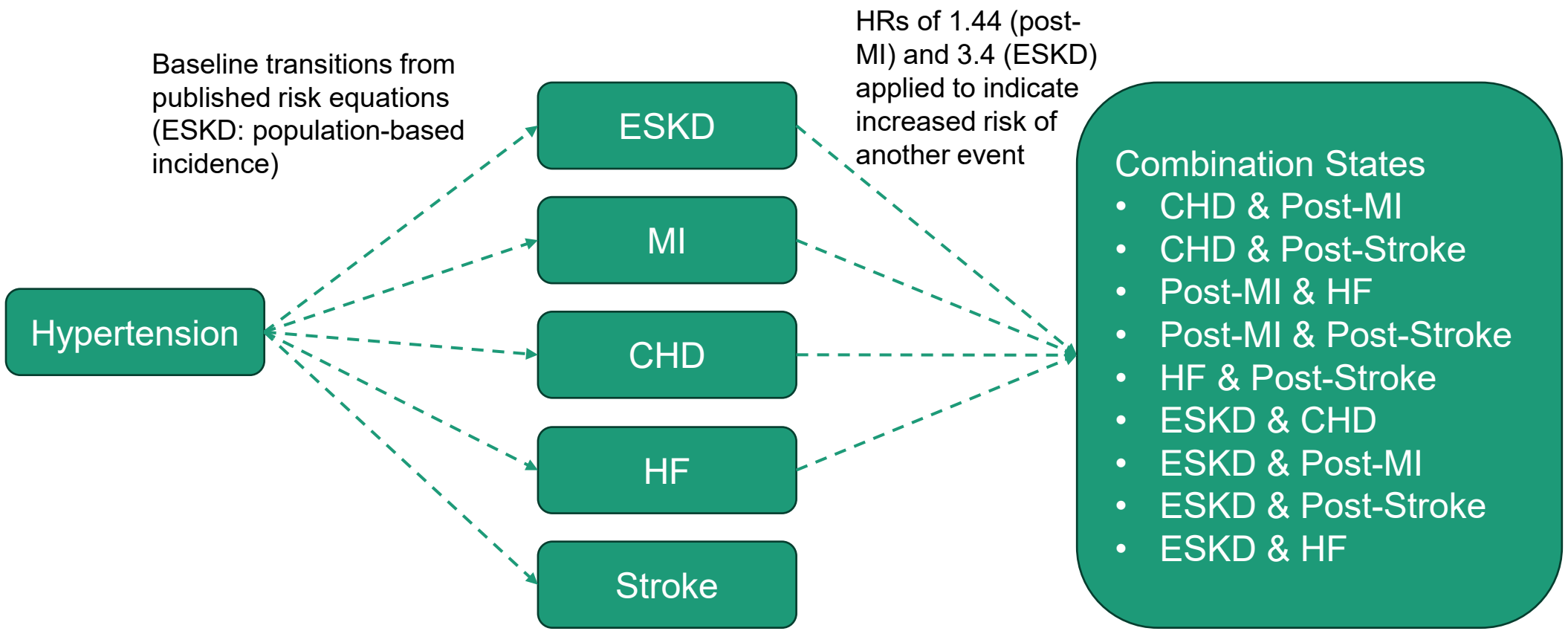
Applying Treatment Effect

- Each treatment's benefit was modeled through its effect on SBP
  - SBP reductions from ICER's NMA were converted into event risk changes using BPLTTC estimates (48 trials, more than 340,000 patients)[1]
  - Event-specific multipliers were applied to baseline transition probabilities to give a treatment-adjusted transition probability per cycle
    - Per 5 mm Hg SBP reduction:[1] stroke HR 0.87 (95% CI: 0.84, 0.91); heart failure HR 0.87 (95% CI: 0.83, 0.92); ischemic heart disease (applied to MI and CHD) HR 0.92 (95% CI: 0.89, 0.95)
    - Per 10 mm Hg SBP reduction:[2] ESKD RR 0.95 (95% CI: 0.84, 1.07)

[1]BPLTTC. Lancet 2021; [2]Ettehad et al. Lancet 2016

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BPLTTC: Blood Pressure Lowering Treatment Trialists' Collaboration, CHD: coronary heart disease, CI: confidence interval, ESKD: end stage kidney disease, HR: hazard ratio,MI: myocardial infarction, NMA: network meta-analysis, RR: relative risk, SBP: systolic blood pressure

Health States and Transitions



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CHD: coronary heart disease, ESKD: end stage kidney disease, HF: heart failure, HR: hazard ratio, MI: myocardial infarction, NMA: network meta-analysis, SBP: systolic blood pressure

Treatment Discontinuation

- First 3-month cycle for baxdrostat and lorundrostat: all-cause discontinuation from the Phase III trials
  - Baxdrostat 2 mg: 45 of 374 patients (13% 3-month probability)
  - Lorundrostat 50 mg: 50 of 541 patients (10% 3-month probability)
- Thereafter, and from the first cycle for comparators: declining persistence curve for calcium channel blockers based on study that observed persistence to antihypertensive drug classes in new users[1]
  - Spironolactone: discontinuation HR of ~1.45 vs. eplerenone for worse tolerability (e.g. gynecomastia), from a heart failure meta-analysis[2]
- Upon discontinuation, patients return to baseline antihypertensive therapy, and SBP returns to baseline and treatment effect ends

[1]Laurell et al. EClinicalMedicine 2026; [2]Elshahat et al. BMC Cardiovasc Disord 2024

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Key Model Inputs: Treatment Costs

Intervention (Dosage)	WAC per Dose	Net Annual Cost	Source
Baxdrostat (2 mg/day)	$30	$10,950	Redbook†
Lorundrostat (50 mg/day)	$30*	$10,950*	Placeholder*
Spironolactone (25–100 mg/day)	$0.12–$0.47	$43–$171	Redbook‡
Eplerenone (50–100 mg/day)	$1.40–$2.79	$511–$1,022	Redbook‡
Amiloride (5–10 mg/day)	$0.56–$1.13	$206–$411	Redbook‡

*Placeholder price equal to baxdrostat WAC
†WAC ($900 per 30 tablets) used as net price; no information available to inform a discount
‡Median WAC across all generic versions
A one-time hyperkalemia monitoring cost ($11) was applied to all five treatments

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Key Model Inputs: Hypertension-Related Costs

Health State	Annual Cost*	Source
Hypertension (Annual)	$3,211	Wang et al. 2024
Stroke (Acute and Annual)	$20,442 / $20,697	Johnson et al. 2016 / Kazi et al. 2024; Kazi et al. 2019
Myocardial Infarction (Acute and Annual)	$25,832 / $17,106	Cowper et al. 2019 / Kazi et al. 2024; Kazi et al. 2016
Coronary Heart Disease (Annual)	$13,798	Kazi et al. 2024
Heart Failure (Index Hospitalization and Annual)	$16,671 / $33,890	Urbich et al. 2020
End-stage Kidney Disease (Annual)	$108,953	USRDS Annual Data Report 2025

*Adjusted to 2025 United States Dollars

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Key Model Inputs: Utilities

Health State	Value	Source
Hypertension	Age-specific	Jiang et al. 2021
Acute MI, Disutility (1 Cycle)	-0.15	Matza et al. 2015
Post-MI, Disutility	-0.041	Sullivan et al. 2006
Acute Stroke, Disutility (1 Cycle)	-0.19	Matza et al. 2015
Post-Stroke, Disutility	-0.052	Sullivan et al. 2006
CHD, Disutility	-0.034	Sullivan et al. 2006
HF, Disutility	-0.064	Sullivan et al. 2006
ESKD, Disutility	-0.170	Gorodetskaya et al. 2005

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CHD: coronary heart disease, ESKD: end stage kidney disease, HF: heart failure, MI: myocardial infarction

Results

Base-Case Results

Treatment	Intervention Acquisition Costs†	Non-Intervention Costs‡	Total Costs	Number of Strokes§	QALYs	evLYs	LYs
Baxdrostat	$27,600	$122,000	$149,600	150	9.55	9.55	11.87
Lorundrostat	$28,500*	$122,200	$150,700*	151	9.54	9.54	11.86
Spironolactone	$200	$122,600	$122,800	152	9.52	9.52	11.83
Eplerenone	$2,000	$122,200	$124,300	151	9.54	9.54	11.86
Amiloride	$830	$122,500	$123,400	152	9.52	9.52	11.84

*Based on placeholder price
†Includes one-time hyperkalemia monitoring cost ($11)
‡Health state costs, dialysis and transplant charges, unrelated medical costs, and mortality costs associated with uncontrolled hypertension
§Per 1,000 patients

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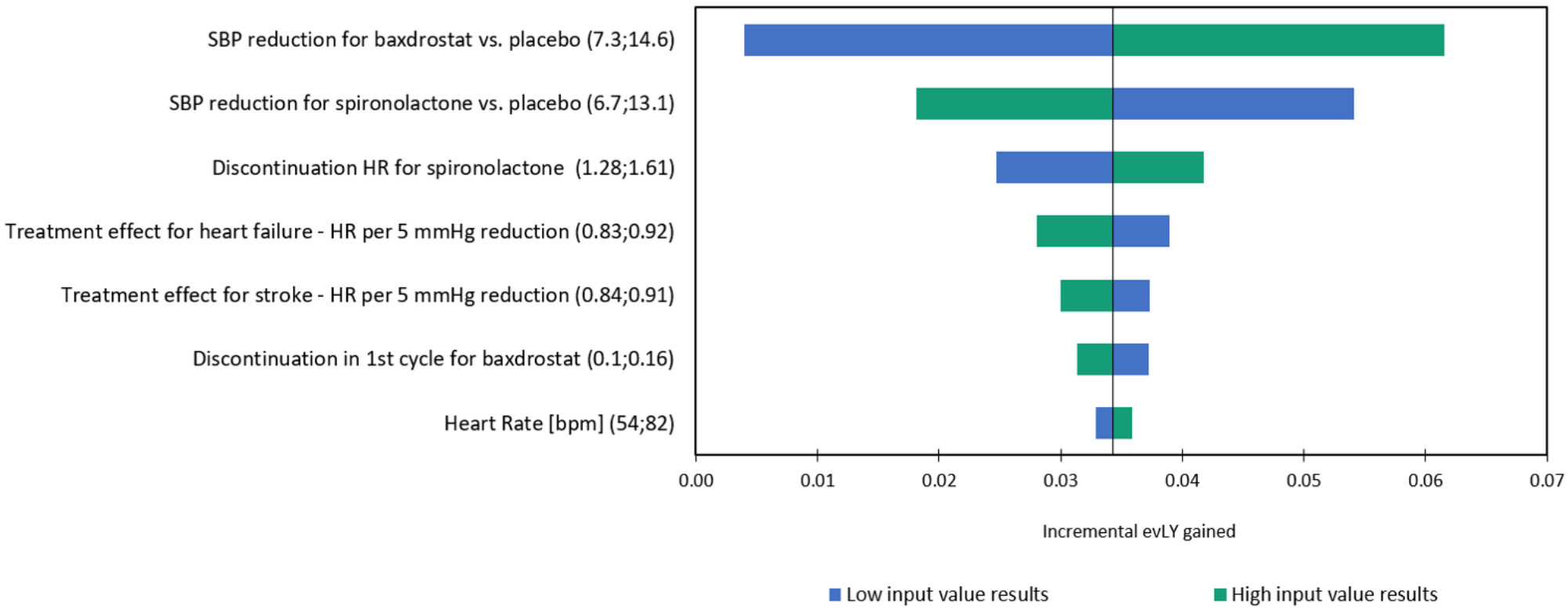
Base-Case Incremental Results

Treatment	Comparator	Cost per QALY Gained	Cost per evLY Gained
Baxdrostat	Spironolactone	$833,000	$781,000
Baxdrostat	Eplerenone	$2,077,000	$1,954,000
Baxdrostat	Amiloride	$851,000	$800,000
Lorundrostat*	Spironolactone	$1,419,000	$1,327,000
Lorundrostat*	Eplerenone	More costly, less effective	More costly, less effective
Lorundrostat*	Amiloride	$1,492,000	$1,403,000

*Based on placeholder price for lorundrostat equal to baxdrostat WAC

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evLY: equal value life year, QALY: quality-adjusted life year, WAC: wholesale acquisition cost

One-Way Sensitivity Analysis
Baxdrostat vs. Spironolactone (Incremental evLY Gained)



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bpm: beats per minute, evLY: equal value life year, HR: hazard ratio, SBP: systolic blood pressure

Probabilistic Sensitivity Analysis

Comparison	Cost-Effective at $50,000 per evLY Gained	Cost-Effective at $100,000 per evLY Gained	Cost-Effective at $150,000 per evLY Gained
Baxdrostat vs. Spironolactone	0.0%	0.0%	0.0%
Baxdrostat vs. Eplerenone	0.0%	0.0%	0.0%
Baxdrostat vs. Amiloride	0.0%	0.0%	0.0%
Lorundrostat* vs. Spironolactone	0.0%	0.0%	0.0%
Lorundrostat* vs. Eplerenone	0.0%	0.0%	0.0%
Lorundrostat* vs. Amiloride	0.0%	0.0%	0.0%

*Based on placeholder price

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Scenario Analyses

	Baxdrostat vs. Spironolactone	Lorundrostat vs. Spironolactone
	Cost per evLY Gained	
Modified Societal Perspective	$781,000	$1,313,000
Minimum Price for Spironolactone	$786,000	$1,335,000
Same Discontinuation for All Treatments	$704,000	$1,237,000

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evLY: equal value life year

Health Benefit Price Benchmark (HBPB)

Annual Price Benchmarks for Baxdrostat and Lorundrostat

Intervention	Annual WAC	Annual Price at $100,000 per QALY Gained	Annual Price at $150,000 per evLY Gained	Discount from WAC to Reach Threshold Prices
Baxdrostat	$10,950	$1,400	$2,500	77.2%–87.4%
Lorundrostat	$10,950*	$760	$1,600	85.7%–93.0%

*Assumed placeholder price

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evLY: equal value life year, QALY: quality-adjusted life year, WAC: wholesale acquisition cost

Limitations

Top Limitations

- SBP effects came from indirect comparisons (NMA) with wide credible intervals, particularly for lorundrostat, eplerenone, and amiloride
- Discontinuation drawn from short-term trials and a single literature-based persistence curve, which may not reflect real-world persistence
- Not all hypertension-related complications captured (e.g. diabetes, atrial fibrillation, CKD stages, cognitive impairment)
- Placeholder price for lorundrostat

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BPLTTC: Blood Pressure Lowering Treatment Trialists' Collaboration, CKD: chronic kidney disease, NMA: network meta-analysis, SBP: systolic blood pressure

Comments Received

- Comments on the draft report included:
  - Use of dynamic pricing and future patient cohorts
  - Caregiver components such as caregiver quality of life and costs
  - Incorporating adverse events

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Conclusions

- Baxdrostat and lorundrostat generally provided small gains in QALYs, evLYs, and LYs versus spironolactone, eplerenone, and amiloride, at substantially higher total costs driven by drug costs
- At its current price, baxdrostat would not meet commonly cited cost-effectiveness thresholds versus spironolactone, eplerenone, and amiloride
- At the currently assumed placeholder price, lorundrostat would not meet commonly cited cost-effectiveness thresholds versus spironolactone, eplerenone, and amiloride

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evLYs: equal value life years, LYs: life years, QALYs: quality-adjusted life years, WAC: wholesale acquisition cost

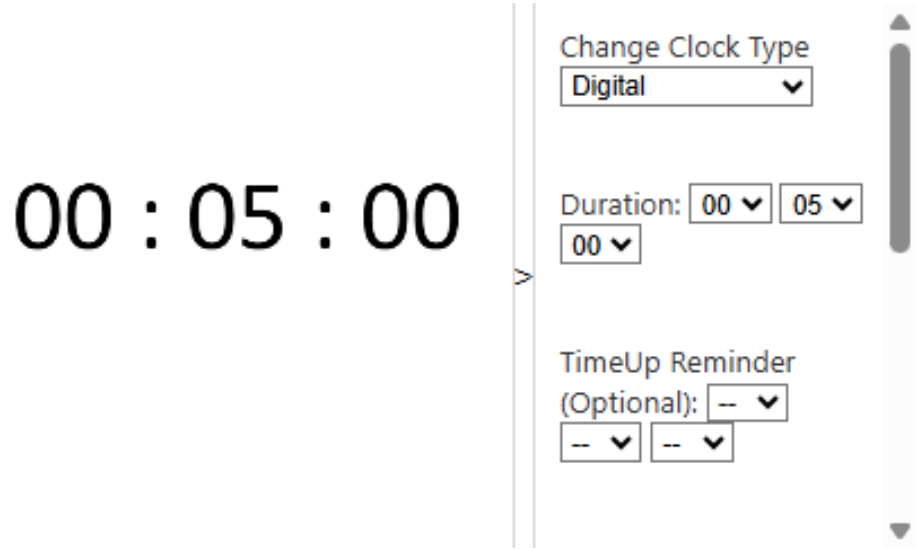
Questions?

Manufacturer Public Comment and Discussion

César Cerezo, MD, PhD
Vice President, US Medical, Biopharmaceuticals, AstraZeneca

Conflicts of Interest:

- *César Cerezo is a full-time employee of AstraZeneca*

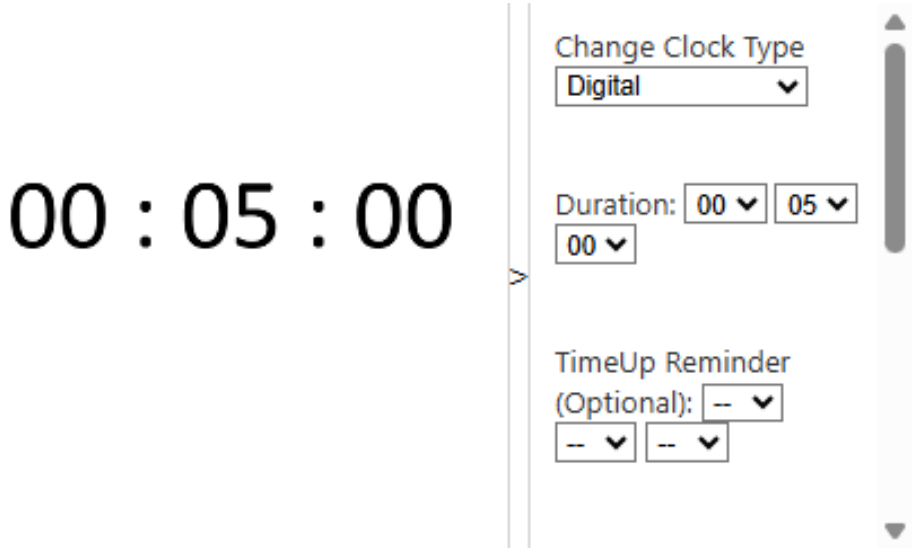


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Jon W. Mares, DO, FASN, FNKF
Executive Medical Director, Mineralys Therapeutics

Conflicts of Interest:

- *Jon W. Mares is a full-time employee of Mineralys Therapeutics*



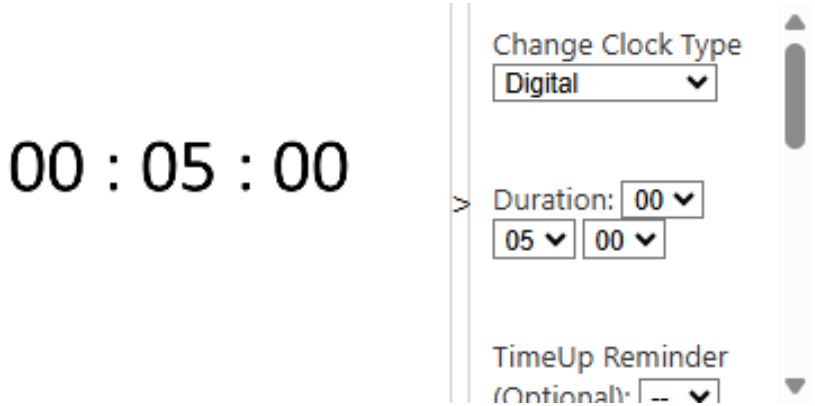
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Public Comment and Discussion

Jen Childress, MS
Director of Programs, National Forum for Heart Disease & Stroke Prevention

Conflicts of Interest:

- *Jen Childress is a full-time employee of the National Forum for Heart Disease & Stroke Prevention. The National Forum for Heart Disease & Stroke Prevention receives 72% of its annual funding from health care companies including AstraZeneca.*

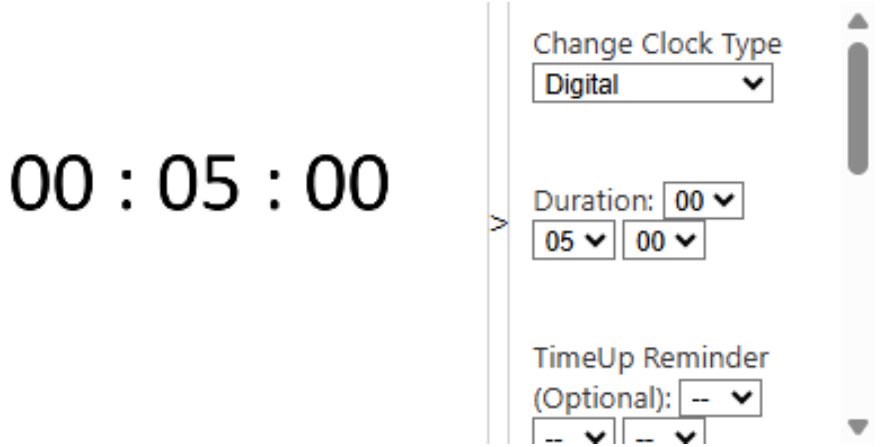


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Michael J. McGowan
Board Member, Primary Aldosteronism Foundation

Conflicts of Interest:

- *The Primary Aldosteronism Foundation receives about one-third of its annual funding from healthcare companies, including AstraZeneca and Mineralys.*

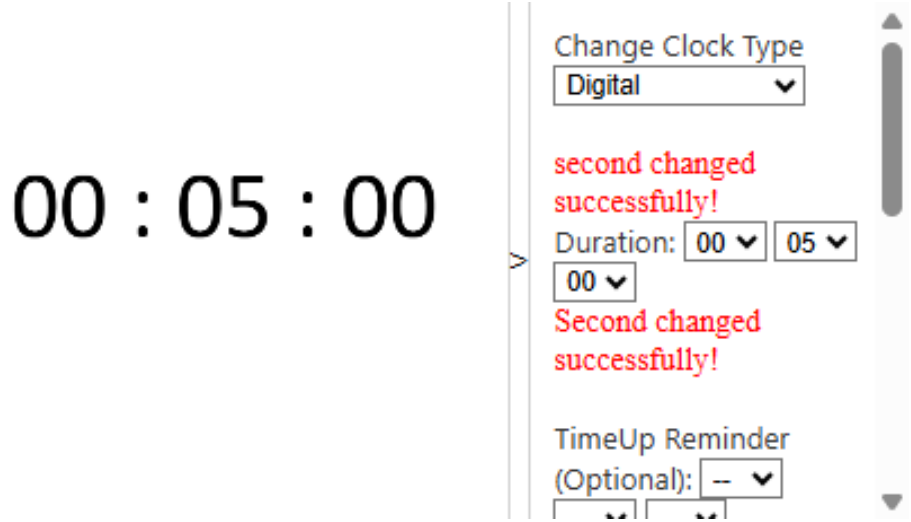


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Mandy Sandkuhler
Director, Partnerships and Communications, The Mended Hearts Inc.

Conflicts of Interest:

- *Mandy Sandkuhler is a full-time employee of The Mended Hearts Inc. The Mended Hearts Inc. receives 89% of its annual funding from healthcare companies including AstraZeneca.*



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Lunch

Meeting will resume at 12:50 PM CT

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Voting Questions

Special Ethical Priorities

To help inform judgments of overall long-term value for money, please answer the following questions:



1. Are there particular obligations to people with hypertension that are not adequately controlled with available first-line agents because of disease severity and/or unmet need with currently available therapies?



2. Are there particular obligations to people with hypertension not adequately controlled with available first-line agents because it disproportionately affects those from a racial/ethnic group that have not been equitably served by the health care system?



3. Apart from issues around disease severity/unmet need and race/ethnicity, are there other particular obligations to people with hypertension that are not adequately controlled with available first-line agents?

Clinical Evidence

4. For patients with resistant hypertension not at goal despite use of three or more antihypertensive medications (Population 1)…



4. Is the current evidence adequate to demonstrate that the net health benefit of baxdrostat is greater than that of spironolactone, eplerenone, or amiloride?

5. For patients with resistant hypertension not at goal despite use of three or more antihypertensive medications (Population 1)…



5. Is the current evidence adequate to demonstrate that the net health benefit of lorundrostat is greater than that of spironolactone, eplerenone, or amiloride?

6. For patients on two antihypertensive medications not at goal who cannot tolerate a third first-line medication (Population 2)…



6. Is the current evidence adequate to demonstrate that the net health benefit of baxdrostat is greater than that of spironolactone, eplerenone, or amiloride?

7. For patients on two antihypertensive medications not at goal who cannot tolerate a third first-line medication (Population 2)…



7. Is the current evidence adequate to demonstrate that the net health benefit of lorundrostat is greater than that of spironolactone, eplerenone, or amiloride?

8. For patients with hypertension not at goal on two antihypertensive medications who have not yet tried a third first-line agent (Population 3)…



8. Is the current evidence adequate to demonstrate that the net health benefit of baxdrostat is greater than that of amlodipine?

9. For patients with hypertension not at goal on two antihypertensive medications who have not yet tried a third first-line agent (Population 3)…



9. Is the current evidence adequate to demonstrate that the net health benefit of lorundrostat is greater than that of amlodipine?

10. For patients with resistant hypertension not at goal, patients on two antihypertensive medications not at goal who cannot tolerate a third first-line medication, and patients with hypertension not at goal on two antihypertensive medications who have not yet tried a third first-line agent (All Populations)…



10. Is the currently available evidence adequate to distinguish the net health benefit between baxdrostat and lorundrostat?

Benefits Beyond Health

To help inform judgments of overall long-term value for money, please answer the following questions about the aldosterone synthase inhibitors (ASIs), baxdrostat and lorundrostat, when used for patients with resistant hypertension that is not at goal.



11. Are the aldosterone synthase inhibitors likely to improve caregivers' quality of life and/or ability to pursue their own education, work, and family life?



12. If payment/cost were not an issue, would the aldosterone synthase inhibitors be likely to improve access to treatment because of its method of delivery and/or treatment setting?

Long-Term Value for Money

Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering benefits beyond health and special ethical priorities…



13. What is the long-term value for money of baxdrostat at current pricing for patients with resistant hypertension not at goal despite use of three or more antihypertensive medications?

Break

Meeting will resume at 2:00 PM CT

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Policy Roundtable

Policy Roundtable

Participant	Conflict of Interest
Victoria (Vicky) Brown, PharmD, BCOP Associate Vice President, Clinical Drug Strategy, Humana Pharmacy Solutions	Vicky Brown is a full-time employee at Humana Pharmacy Solutions.
Andrew Bzowyckyj, PharmD, BCPS, CDCES Senior Scientific Director, Learning Consultant; National Kidney Foundation	Andrew Bzowyckyj is a full-time employee of the National Kidney Foundation (NKF). NKF receives 64% of its annual funding from health care companies including AstraZeneca.
Jordana (Jordy) Cohen, MD, MSCE Associate Professor of Medicine and Epidemiology, University of Pennsylvania	Jordana Cohen has no conflicts to disclose.
Brittany Dickerson Kidney Health Advocate	Brittany Dickerson serves as an ambassador and committee member on multiple initiatives for the National Kidney Foundation. She also volunteers with American Kidney Fund, Chronic Disease Coalition, IPRO End Stage Renal Disease Network Program, NephCure, Sharing Hope SC. She receives compensation from Ardelyx as their Kidney Patient Advisory Committee member.
Benjamin (Ben) A. Kruskal, MD, PhD Medical Director for Clinical Integration, Blue Cross Blue Shield of Massachusetts	Benjamin Kruskal is a full-time employee of Blue Cross Blue Shield of Massachusetts.
Kay Sadik, PharmD, PhD Director, Health Economics and Outcomes Research, Mineralys Therapeutics	Kay Sadik is a full-time employee of Mineralys Therapeutics.
Karol Watson, MD, PhD Professor of Medicine/Cardiology and John Mazziotta Endowed Chair in Medicine, David Geffen School of Medicine at UCLA; Co-director, UCLA Program in Preventive Cardiology; Director, UCLA Barbra Streisand Women's Heart Health Program	Karol Watson has served as consultant for Boehringer Ingelheim, Eli Lilly, Merck, Novartis, Novo Nordisk, and Regeneron.

Midwest CEPAC Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around November 30, 2026
    - Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/hypertension-2026/

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Adjourn

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