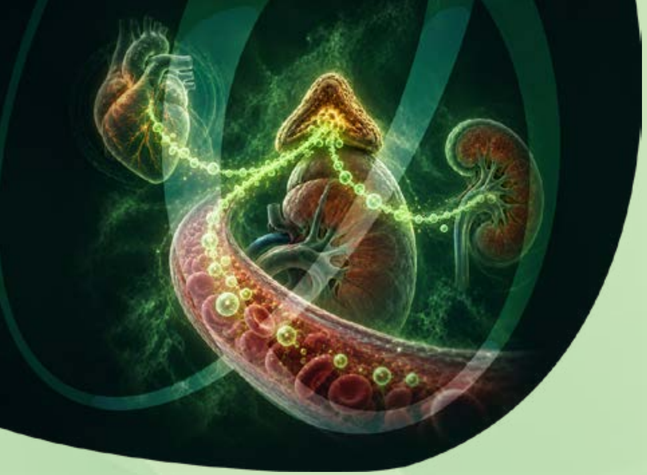


Point-of-Care Perspectives on ASI Therapy: What Clinicians Need to Know as Evidence Grows

Education provider: Nexus Healthcare Education

Diagnosis and management of uncontrolled and resistant hypertension

- Definitions
- Diagnosis of resistant hypertension
- Contributors to uncontrolled and resistant hypertension
- Clinical clues for secondary hypertension
- Referral criteria
- Core hypertension treatment
- Hypertension treatment escalation
- Other treatment options
- Rationale for new antihypertensive medications

ASI THERAPY

Practical guide to ASI therapy

- ASI monitoring requirements
- ASI eligibility and administration
- ASI clinical trials – side effects
- ASI clinical trials – comorbidities
- ASI clinical trials – patients
- ASI clinical trials – efficacy
- Rationale for ASIs

ABBREVIATIONS

REFERENCES

Disclaimer: This information is for educational purposes only and is not intended to serve as a substitute for a healthcare provider's clinical judgment. Please refer to local hypertension management guidelines and/or local regulatory authorities for up-to-date approval and prescribing information.

This activity is supported by an independent educational grant from AstraZeneca.

Definitions of uncontrolled, resistant, and refractory hypertension

	Uncontrolled hypertension[1,2] (used in some clinical trials)	Resistant hypertension[3–6]	Refractory hypertension[6,7]
Office blood pressure	Above target thresholds	Above target thresholds (vary between guidelines)	Above target thresholds (vary between guidelines)
Number of antihypertensive drug classes	≥2	≥3 (including diuretic,* RAAS inhibitor, calcium channel blocker)	≥5 (including diuretic,* MRA)
Dose of antihypertensive drug classes	Maximally tolerated doses (or lower)	Maximally tolerated doses	Maximally tolerated doses
Additional requirements	–	Various causes of pseudo-resistant and secondary hypertension must have been excluded	Various causes of pseudo-resistant and secondary hypertension must have been excluded

*Thiazide or thiazide-like diuretic.

Diagnosis of resistant hypertension

Diagnostic pathway[3–6]

BP not at target despite treatment with ≥3 antihypertensive drugs (including diuretic)

Exclude causes of pseudo-resistance:

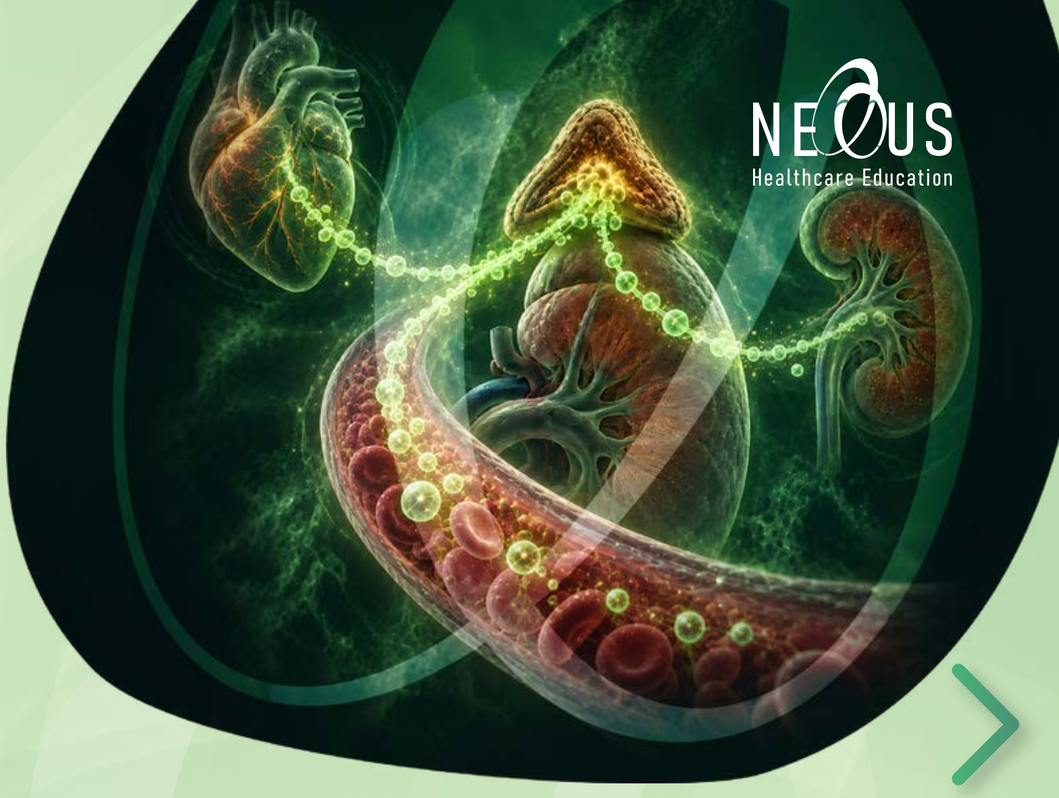
- Confirm accurate office BP measurement
- Confirm medication adherence
- Obtain HBPM or ABPM to exclude white-coat effect and masked hypertension

Exclude other potential contributors:

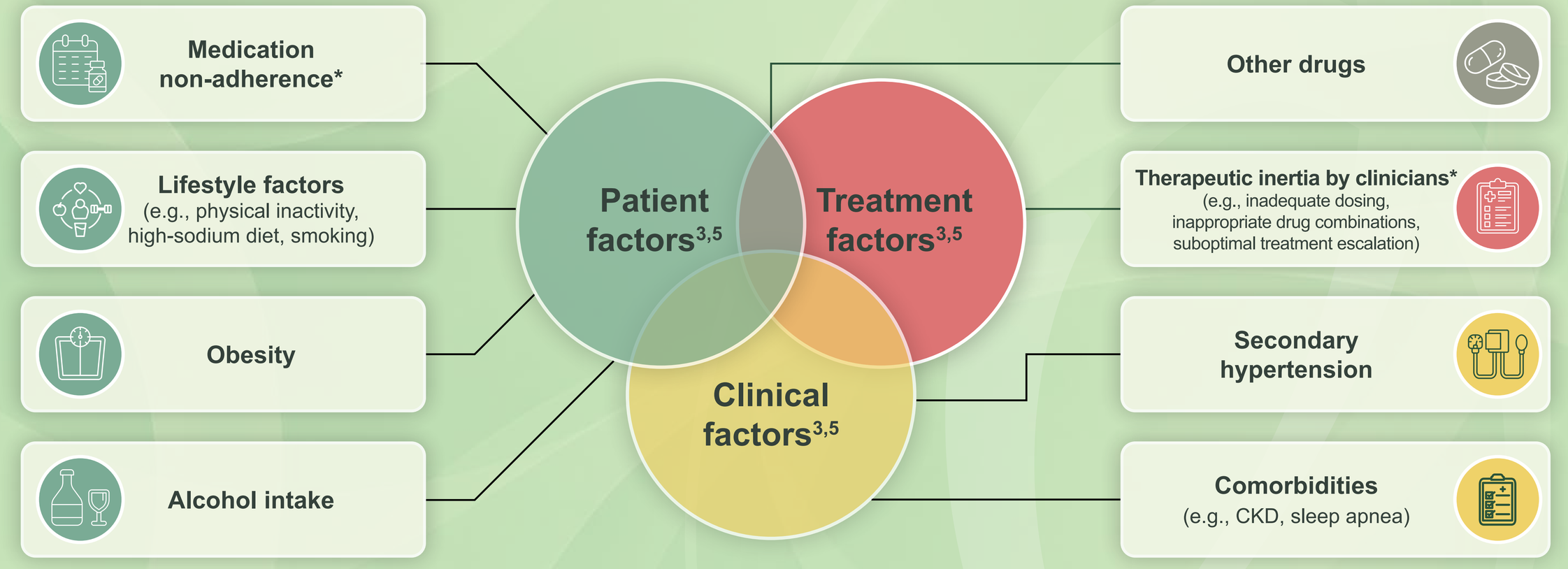
- Lifestyle factors
- Other drugs that elevate BP
- Secondary hypertension

Resistant hypertension

Consider additional treatment and referral



Contributors to uncontrolled and resistant hypertension



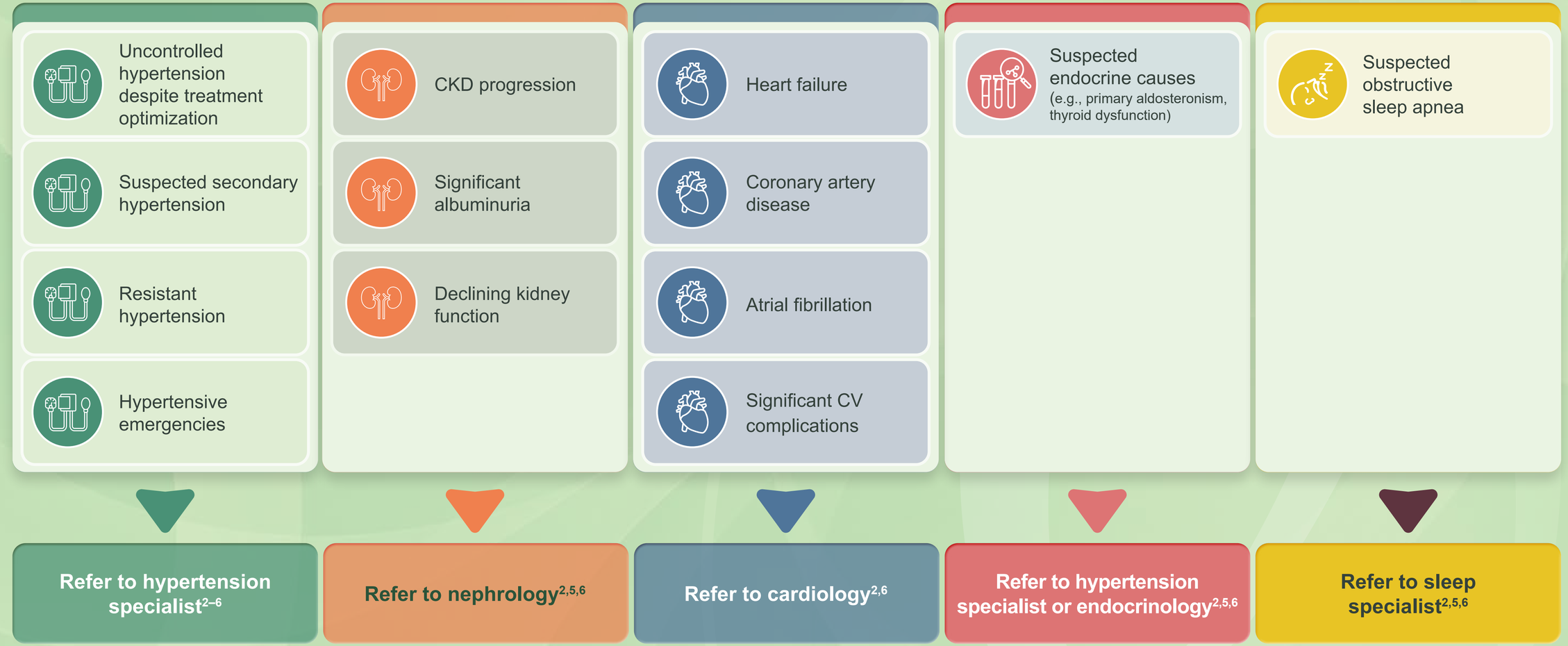
*Causes of pseudo-resistant hypertension.

Clinical clues for secondary hypertension

Clinical clues suggestive of secondary hypertension[2–5]

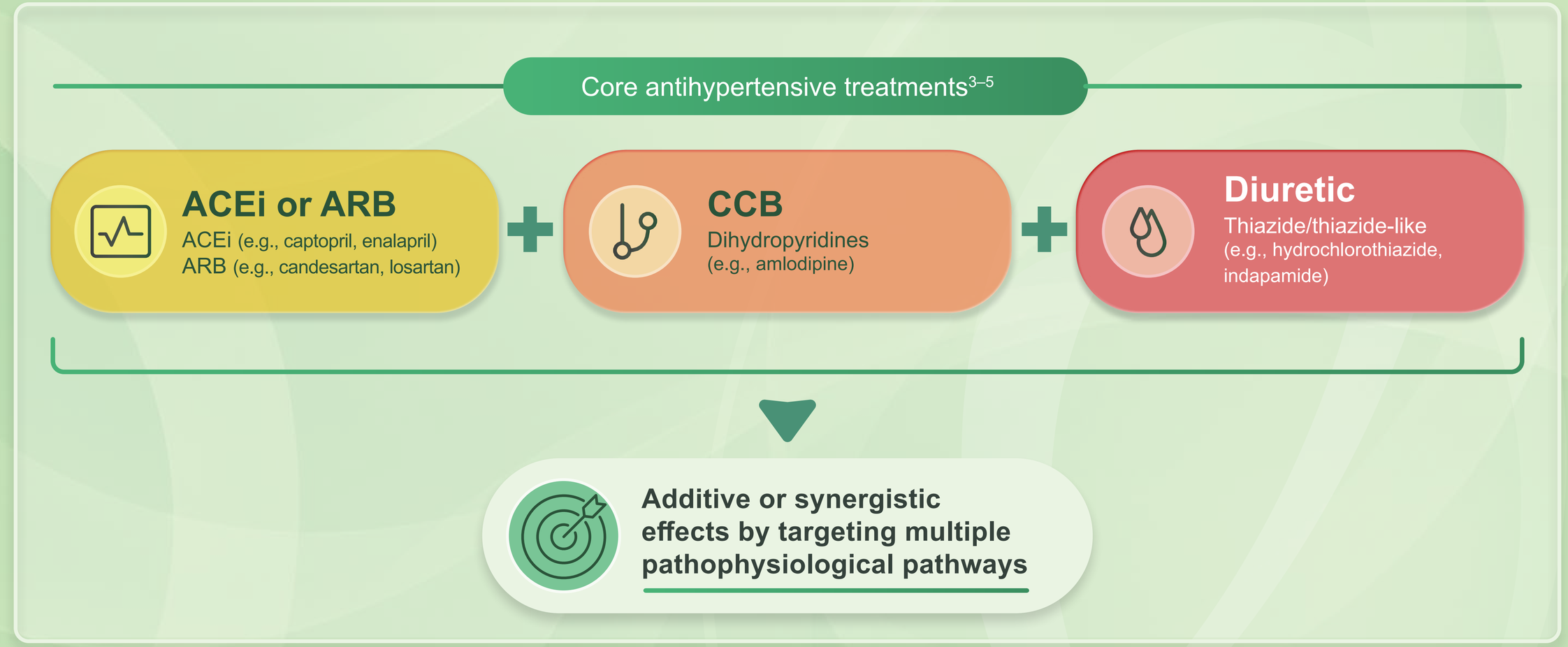
Drug-resistant/-induced hypertension	Abrupt onset of hypertension
Young age at hypertension onset (<30 years)	Worsening of previously controlled hypertension
Disproportionate target organ damage	Onset of diastolic hypertension in older adults (≥65 years)
Hypokalemia	Insomnia or daytime sleepiness
Adrenal mass	History or family history of early-onset stroke
Family history of primary aldosteronism	Accelerated/malignant hypertension
Flash pulmonary edema	Recurrent hypertensive emergencies

Referral criteria

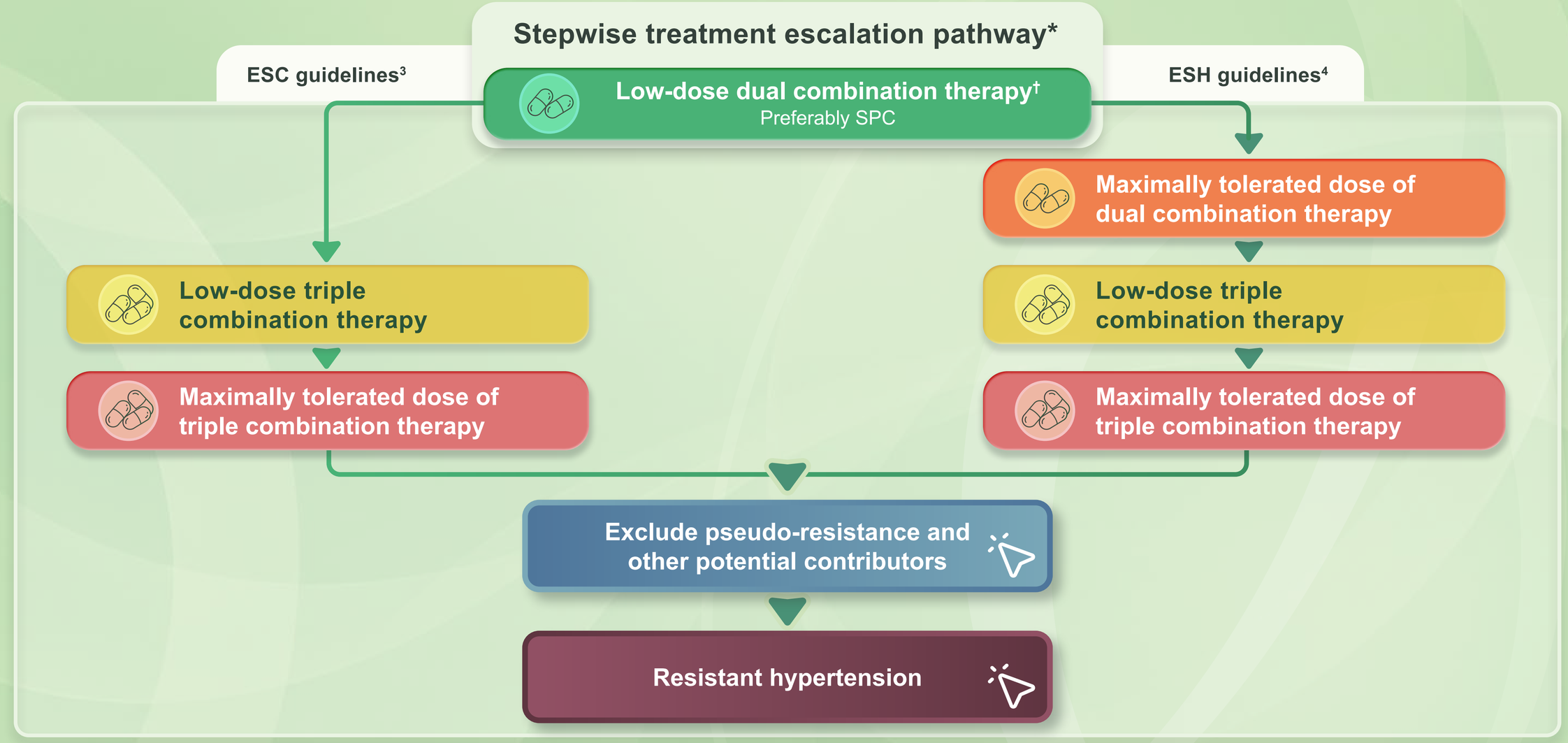


ABBREVIATIONS REFERENCES HOME

Core hypertension treatment



Hypertension treatment escalation



*US guidelines recommend starting with dual combination therapy and stepwise escalation, but do not propose a specific pathway[5]; †Start with monotherapy in selected patients (e.g., low-risk hypertension and BP <150/95 mmHg, high-normal BP and very high CV risk, frail patients and/or advanced age).

GO BACK ABBREVIATIONS REFERENCES HOME

Other treatment options

Uncontrolled hypertension[3–5,8] (± comorbidities)

- Additional core antihypertensive treatments
- ASI†

Resistant hypertension[3–6,8] (± comorbidities)

- MRA
- ASI†
- Beta blocker, alpha blocker, centrally acting agent, dual ERA
- Renal denervation‡

Additional treatment options

CKD[3,4,9,10]

- SGLT2i
- nsMRA

Heart failure[3–5,10*]

- ARNI
- SGLT2i
- Beta blocker
- MRA/nsMRA

*Treatment recommendations for heart failure vary based on LVEF. Please refer to heart failure guidelines for additional information; †Recently published expert guidance has recommended that ASIs should be considered only for patients with confirmed resistant hypertension as an adjunctive option after optimizing a standard 4-drug regimen that includes an MRA and consulting a hypertension specialist[6]; ‡Based on patient willingness[2]. Please refer to local prescribing information and guidelines for further information.

Rationale for new antihypertensive medications

Most adults living with hypertension do not have it under control despite treatment

WHO:[11]



Approximately **77%** of adults with hypertension do not have it under control

Global meta-analysis:[12]



Approximately **55%** of adults have uncontrolled hypertension*

USA:[13]

Uncontrolled hypertension†	Controlled†
77.5% (92.9 million)	22.5% (27.0 million)

Europe:[12]

Uncontrolled hypertension*	Controlled hypertension
53.7%	46.3%

China:[14]

Uncontrolled hypertension	Controlled
87.1%	12.9%

*Defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg in adults with hypertension receiving antihypertensive medications; †Includes all adults with hypertension defined as BP ≥130/80 mmHg or currently using antihypertensive medications. Uncontrolled hypertension was defined as BP ≥130/80 mmHg. All adults recommended lifestyle modifications only are considered uncontrolled as BP above threshold.

ABBREVIATIONS REFERENCES HOME

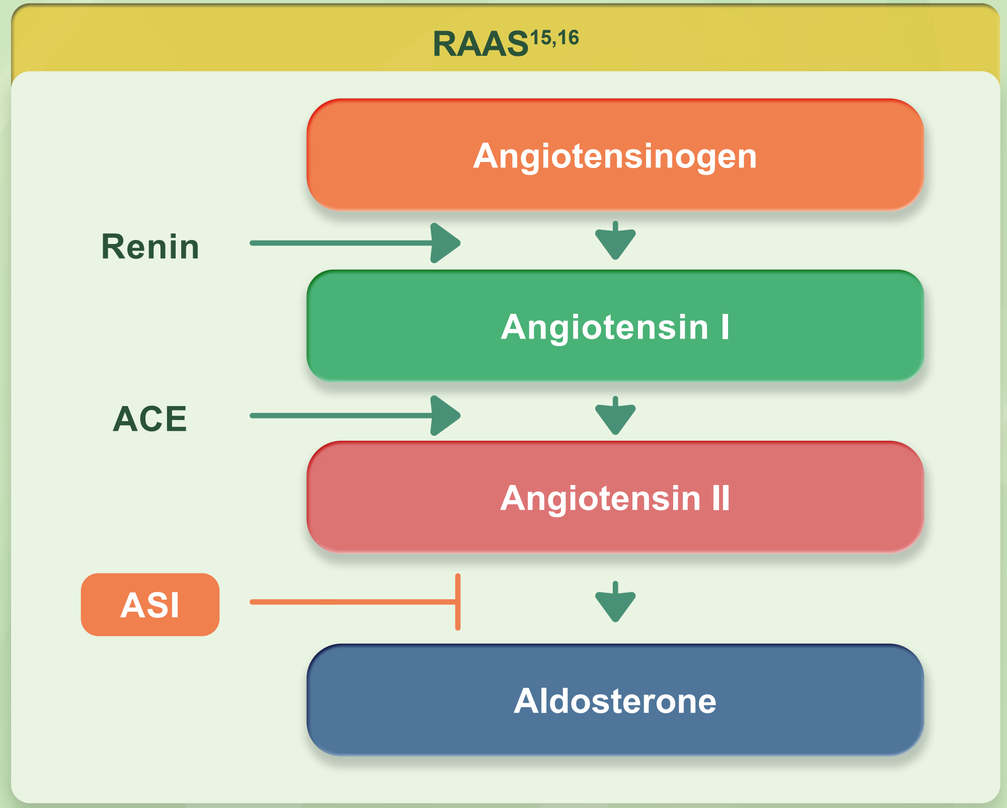
Rationale for ASIs

Aldosterone functions as part of the RAAS to regulate **sodium and water reabsorption** in the kidneys[15,16]

Aldosterone dysregulation is a major driver of **uncontrolled hypertension and cardiorenal disease**[16,17]

Aldosterone dysregulation affects many patients beyond those diagnosed with primary aldosteronism[16,18–20]

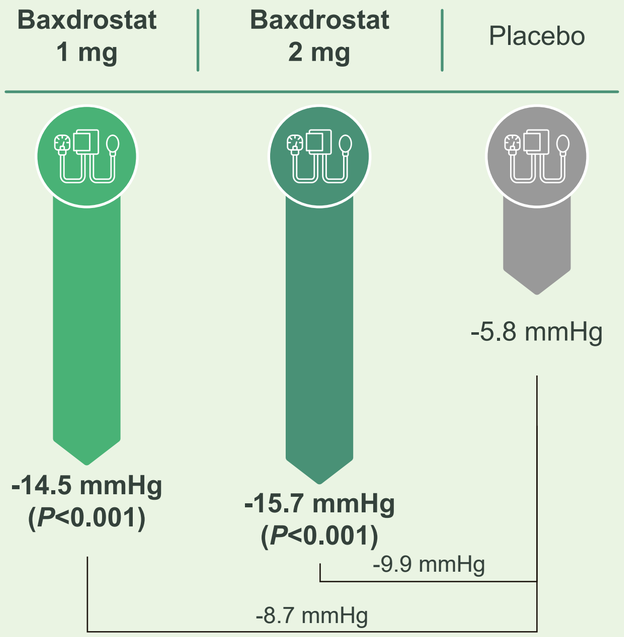
ASIs inhibit **aldosterone synthase** to reduce aldosterone production at its source[15,21]



ASI clinical trials – efficacy

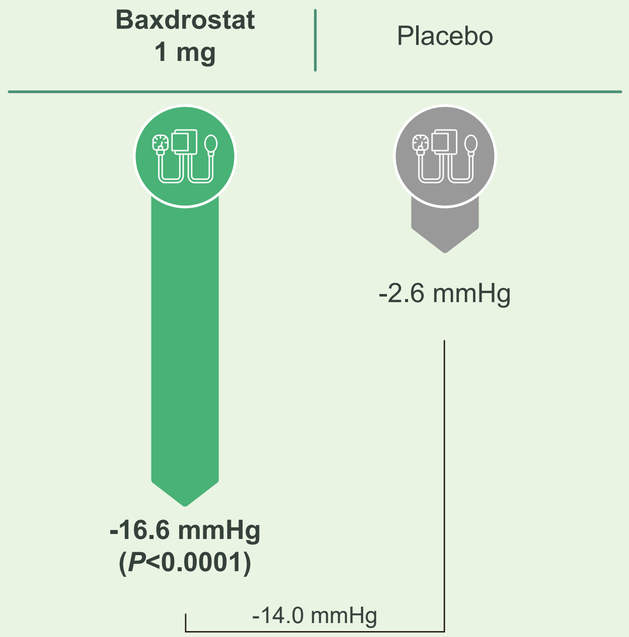
Phase 3 BaxHTN trial[1]

PRIMARY ENDPOINT: Mean change in **seated SBP** from baseline to Week 12



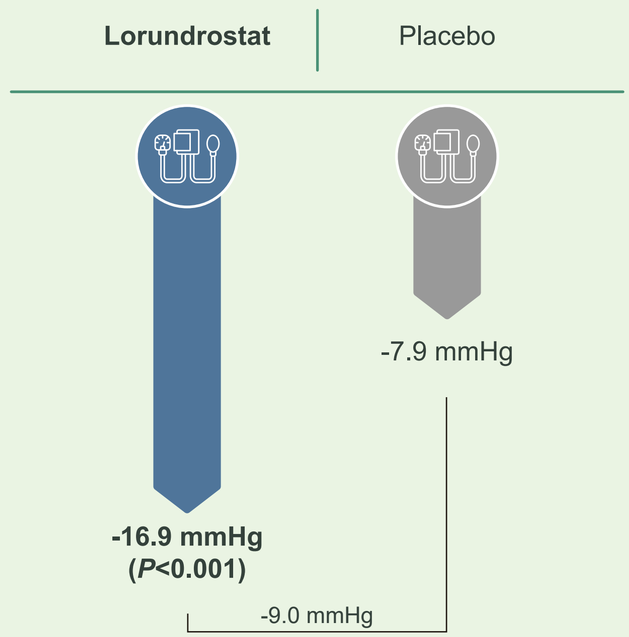
Phase 3 Bax24 trial[22]

PRIMARY ENDPOINT: Mean change in **ambulatory SBP** from baseline to Week 12



Phase 3 Launch-HTN trial[23]

PRIMARY ENDPOINT: Mean change in **office SBP** from baseline to Week 6



ASI clinical trials – patient eligibility criteria

Phase 3 BaxHTN trial[1]

RESISTANT HYPERTENSION

- Office seated SBP 140–<170 mmHg
- ≥3 antihypertensive medications (including a diuretic)

UNCONTROLLED HYPERTENSION

- Office seated SBP 140–<170 mmHg
- 2 antihypertensive medications (including a diuretic)

Phase 3 Bax24 trial[22]

RESISTANT HYPERTENSION

- Office seated SBP 140–<170 mmHg
- ≥3 antihypertensive medications (including a diuretic)

Phase 3 Launch-HTN trial[23]

UNCONTROLLED OR RESISTANT HYPERTENSION

- Unattended automated office BP 135–180/65–110 mmHg or isolated automated office DBP 90–110 mmHg
- 2–5 antihypertensive medications (including a thiazide or thiazide-like diuretic)

ASI clinical trials – comorbidities

	BaxHTN[1]	Bax24[22]	Launch-HTN[23]
Mean age	~60 years	~60 years	~61 years
Obesity (BMI ≥30 kg/m²)	52%	63%	63%
Diabetes	38%	34%*	31%
CKD (<60 mL/min/1.73 m²)	11%	12%	6%
Dyslipidemia	NR	30%	NR
Sleep apnea	NR	10%	NR
Heart failure	NR	6%	NR

*Type 2 diabetes only.

ASI clinical trials – side effects

Hyperkalemia



- Baxdrostat: 3% (placebo) vs **7%** (1 mg) and **10%** (2 mg)[8]
- Lorundrostat: <1% (placebo) vs **2%** (50 mg)[23]

Hyponatremia



- Baxdrostat: 1% (placebo) vs **2%** (1 mg) and **3%** (2 mg)[8]
- Lorundrostat: 3% (placebo) vs **7%** (50 mg)[23]

Hypotension



- Baxdrostat: 1% (placebo) vs **2%** (1 mg) and **4%** (2 mg)[8]
- Lorundrostat: <1% (placebo) vs **2%** (50 mg)[23]

Dizziness



- Baxdrostat: 1% (placebo) vs **3%** (1 mg) and **3%** (2 mg)[8]
- Lorundrostat: NR[23]

Muscle spasms



- Baxdrostat: 1% (placebo) vs **2%** (1 mg) and **3%** (2 mg)[8]
- Lorundrostat: NR[23]

eGFR reduction



- Baxdrostat:* **7.1** and **8.0** mL/min/1.73 m^2 (1 mg and 2 mg)[8]
- Lorundrostat: 1% (placebo) vs **3%** (50 mg)[23]

*Mean placebo-corrected eGFR reduction.

ABBREVIATIONS REFERENCES HOME

ASI eligibility and administration



Hypertension[8]*



In combination with other antihypertensive medications[8]*



BP not adequately controlled on other agents[8]*

Dosage and administration[8]

- Recommended baxdrostat dosage: **2 mg** orally OD
- For patients at increased risk of hyperkalemia or hyponatremia, recommended baxdrostat dosage: **1 mg** orally OD
- Baxdrostat can be taken with or without food
- Consider the patient's risk of hyperkalemia and hyponatremia before initiating baxdrostat

Drug interactions[8]

- Monitor the therapeutic effect of baxdrostat more frequently when concomitantly used with **strong or moderate CYP3A inducers**
  - Strong or moderate CYP3A inducers may decrease baxdrostat plasma concentration, which may reduce efficacy
- Monitor serum potassium more frequently when baxdrostat is used concomitantly with **drugs that impair potassium excretion or increase serum potassium**. Concomitant use may increase hyperkalemia risk

*Recently published expert guidance has recommended that ASIs should be considered only for patients with confirmed resistant hypertension as an adjunctive option after optimizing a standard 4-drug regimen that includes an MRA and consulting a hypertension specialist.[6]
Please refer to local prescribing information and guidelines for further information.

ASI monitoring requirements



Prior to initiation:[8]

- Assess serum potassium and sodium
- Correct serum potassium and sodium abnormalities prior to initiation

After initiation:[8]

- Monitor serum potassium and sodium periodically during treatment
- More frequent monitoring is recommended for patients with low baseline serum sodium or at increased risk of:
  - Hyperkalemia (e.g., age ≥65 years, diabetes, CKD, concomitant medications that increase serum potassium)
  - Hyponatremia (e.g., receiving concomitant medications that may cause hyponatremia)

Hyperkalemia management[8]

- Treat hyperkalemia and consider interruption or discontinuation of ASI
- Consider more frequent monitoring of serum potassium in those restarting after interruption due to hyperkalemia
- Permanently discontinue if clinically significant hyperkalemia occurs

Hyponatremia management[8]

- Treat clinically significant hyponatremia and consider interruption or discontinuation of ASI
- Consider more frequent monitoring of serum sodium in those restarting after interruption due to hyponatremia
- Permanently discontinue if clinically significant hyponatremia recurs

Abbreviations

ABPM, ambulatory blood pressure monitoring.

ACE, angiotensin-converting enzyme.

ACEi, angiotensin-converting enzyme inhibitor.

ARB, angiotensin receptor blocker.

ARNI, angiotensin receptor-neprilysin inhibitor.

ASI, aldosterone synthase inhibitor.

BMI, body mass index.

BP, blood pressure.

CCB, calcium channel blocker.

CKD, chronic kidney disease.

CV, cardiovascular.

DBP, diastolic blood pressure.

eGFR, estimated glomerular filtration rate.

ERA, endothelin receptor antagonist.

ESC, European Society of Cardiology.

ESH, European Society of Hypertension.

HBPM, home blood pressure monitoring.

LVEF, left ventricular ejection fraction.

MRA, mineralocorticoid receptor antagonist.

NR, not reported.

nsMRA, nonsteroidal mineralocorticoid receptor antagonist.

OD, once daily.

RAAS, renin–angiotensin–aldosterone system.

SBP, systolic blood pressure.

SGLT2i, sodium–glucose cotransporter-2 inhibitor.

SPC, single-pill combination.

WHO, World Health Organization.

References

1. Flack JM, et al. *N Engl J Med*. 2025;393:1363–74.
2. Faculty opinion.
3. McEvoy JW, et al. *Eur Heart J*. 2024;45:3912–4018.
4. Kreutz R, et al. *Eur J Int Med*. 2024;126:1–15.
5. Jones DW, et al. *Circulation*. 2025;152:e114–218.
6. Davis LL, et al. *J Am Coll Cardiol*. 2026; doi:10.1016/j.jacc.2026.08.028.
7. Matanes F, et al. *Curr Hypertens Rep*. 2022;24:225–34.
8. BAXFENDY (baxdrostat) US Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/219878Orig1s000lbl.pdf. Accessed November 2026.
9. KDIGO CKD Work Group. *Kidney Int.* 2024;105(Suppl 4S):S117–314.
10. KERENDIA (finerenone) US Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/215341Orig1s009lbl.pdf. Accessed November 2026.
11. WHO Hypertension Factsheet. Available at: https://www.who.int/news-room/fact-sheets/detail/hypertension. Accessed November 2026.
12. Cheraghi Z, et al. *BMC Public Health*. 2025;25:4259.
13. Million Hearts. Estimated Hypertension Prevalence, Treatment, and Control Among US Adults. Available at: https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html. Accessed November 2026.
14. Liu M, et al. *Chin Med J (Engl)*. 2025;138:3037–49.
15. Młynarska E, et al. *Biomolecules*. 2025;15:1439.
16. Ananda RA, et al. *Metabolites*. 2025;15:553.
17. Brown JM. *J Am Heart Assoc*. 2024;13:e030142.
18. Brown JM, et al. *Ann Intern Med*. 2017;167:630–41.
19. Hundemer GL, et al. *Circulation*. 2024;149:124–34.
20. Parksook WW, et al. *J Clin Endocrinol Metab*. 2024;109:2220–32.
21. Mazzieri A, et al. *Curr Opin Nephrol Hypertens*. 2026;35:337–46.
22. Azizi M, et al. *Lancet*. 2026;407:988–99.
23. Saxena M, et al. *JAMA*. 2025;334:409–18.