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REVIEW ARTICLE

Baxdrostat for uncontrolled and resistant hypertension: Clinical evidence, regulatory approval, and practical implications

Yogi Puji Rachmawan[1]*, Witri Pratiwi[2], Bagus Andi Pramono[3], Erdiansyah Zulyadaini[4], Wella Karolina[5,6], Tuko Srimulyo[7], Meity Ardiana[8,9], Antonia Anna Lukito[10], on behalf of the Indonesia Working Group of Hypertension

[1]Department of Cardiovascular Medicine, Faculty of Medicine, Universitas Swadaya Gunung Jati, Cirebon, West Java, Indonesia

[2]Department of Community Medicine and Public Health, Faculty of Medicine, Universitas Swadaya Gunung Jati, Cirebon, West Java, Indonesia

[3]Department of Internal Medicine, Panembahan Senopati Regional General Hospital, Yogyakarta, Special Region of Yogyakarta, Indonesia

[4]Department of Internal Medicine, Soeselo Regional General Hospital, Slawi, Central Java, Indonesia

[5]Department of Cardiology and Vascular Medicine, Dr. Saiful Anwar General Academic Hospital, Malang, East Java, Indonesia

[6]Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, East Java, Indonesia

[7]Department of Internal Medicine, Nirmala Suri Hospital, Sukoharjo, Central Java, Indonesia

[8]Department of Cardiology and Vascular Medicine, Dr. Soetomo General Academic Hospital, Surabaya, East Java, Indonesia

[9]Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java, Indonesia

[10]Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Pelita Harapan, Jakarta, Indonesia

***Corresponding author:**
Yogi Puji Rachmawan
(yogi.puji.rachmawan@ugj.ac.id)

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Abstract

Introduction: Poor blood-pressure control and treatment resistance contribute to cardiovascular and kidney complications. Excess aldosterone offers a therapeutic target.

Objective: This narrative review evaluates the pharmacological profile, clinical efficacy, safety, and regulatory development of baxdrostat, an oral aldosterone synthase inhibitor designed to preserve cortisol production.

Key findings: In BaxHTN, a phase 3 trial in uncontrolled or resistant hypertension, the placebo-adjusted decrease in seated systolic blood pressure at week 12 was 8.7 mmHg with 1 mg and 9.8 mmHg with 2 mg; Bax24, a phase 3 ambulatory blood-pressure trial in resistant hypertension, recorded a 14.0 mmHg placebo-adjusted decrease in 24-hour ambulatory systolic pressure with 2 mg. FigHTN, a phase 2 trial in chronic kidney disease, identified a preliminary albuminuria signal, but cardiorenal outcome studies have not yet been completed. The main recognised risks are hyperkalaemia and hyponatraemia, particularly when kidney function is impaired. The United States prescribing information states that safety and effectiveness of initiation at an estimated glomerular filtration rate (eGFR) below 45 mL/min/1.73 m^2 have not been established, and serum potassium, sodium, and eGFR require surveillance during initiation and dose adjustment. The United States Food and Drug Administration

approved baxdrostat (Baxfendy) on May 15, 2026, as an add-on treatment for adults whose hypertension remains inadequately controlled. Concomitant use with a mineralocorticoid receptor antagonist has not been evaluated and should not presently be recommended.

Conclusion: Comparative and long-term outcome evidence is still required, while full efficacy and safety results of the completed phase 3 BaxAsia trial in Asian populations are awaited.

Keywords: Aldosterone synthase inhibitor; Baxdrostat; Blood pressure; CYP11B2; Resistant hypertension; Uncontrolled hypertension

1. Introduction

In 2019, an estimated 1.28 billion people aged 30–79 years worldwide had hypertension; most lived in low- and middle-income settings. Hypertension remains a leading modifiable cardiovascular risk factor.[1] Blood pressure nevertheless stays above target in many patients despite the availability of numerous drug classes. Resistant hypertension is estimated to affect approximately 10%–15% of treated hypertensive populations.[2,3] It is conventionally identified when blood pressure remains at least 140/90 mmHg during treatment with three optimally dosed agents, one being a diuretic, or when control requires four or more drugs. Uncontrolled hypertension is a broader category, encompassing patients with blood pressure above the therapeutic target. In this review, the population of interest comprises patients receiving at least two antihypertensive agents, including those who do not meet resistant-hypertension criteria. The clinical and regulatory importance of this distinction is considered in Sections 7 and 8.1. Refractory hypertension represents a rarer and more severe phenotype: blood pressure remains uncontrolled despite at least five classes, including a diuretic and a mineralocorticoid receptor antagonist (MRA). It should be distinguished from resistant hypertension because the mechanistic and prognostic implications are different.[4,5]

The problem is also evident in Indonesia. The 2018 Indonesian Basic Health Research survey (*Riset Kesehatan Dasar*; Riskesdas) reported a measured hypertension prevalence of 34.1% among Indonesian adults aged 18 years or older.[6] In an ambulatory blood pressure monitoring (ABPM) study at Hasna Medika Cardiovascular Hospital, Cirebon, 50.3% of treated patients remained uncontrolled and 35.6% met resistant-hypertension criteria; coronary artery disease and heart failure were the leading comorbidities.[7] An earlier Indonesian review likewise described resistant hypertension as a persistent management challenge requiring contemporary evidence-based strategies.[8] Diagnostic thresholds and stepwise treatment in the International Society of Hypertension and World Health Organization guidance provide a framework for considering new agents such as baxdrostat.[9,10] Together, these observations support exploration of treatments that act beyond conventional renin–angiotensin–aldosterone system (RAAS) blockade.

Spironolactone is generally preferred as fourth-line treatment for resistant hypertension. Its use, however, may be constrained by hyperkalaemia, deterioration in kidney function, and steroid-related adverse effects, especially in chronic kidney disease (CKD).[2,11,12] Other approaches to preserve RAAS-directed therapy include adding a potassium binder, as studied in AMBER, and using the non-steroidal MRA finerenone, as evaluated in FIDELIO-DKD and FIGARO-DKD.[11,13,14] These strategies have different mechanisms and should not be viewed as replacements for inhibition of aldosterone synthesis.

We performed a structured search of PubMed/MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov through July 2026 to locate clinically relevant pharmacological, trial, and regulatory evidence. The approach was designed for a narrative synthesis rather than a formal systematic review. Search strings combined baxdrostat-related terms ("baxdrostat," "CIN-107," "Baxfendy," "aldosterone synthase inhibitor," or "CYP11B2 inhibitor") with terms describing uncontrolled or resistant hypertension and aldosterone. Separate combinations involving MRAs, spironolactone, eplerenone, finerenone, regulatory status, and United States (US) Food and Drug Administration (FDA) approval were used to provide comparative and regulatory context. Thus, the strategy increases transparency but does not constitute a formal systematic-review method.

2. Epidemiology and burden of resistant and uncontrolled hypertension

Resistant hypertension carries prognostic significance

beyond the failure of drug therapy. Relative to non-resistant disease, it is associated with increased risks of cardiovascular events and end-stage kidney disease.[15,16] Reported prevalence estimates range from 8.9% to 18%, partly because study methods and definitions differ.[2] Persell[17] reported that 12.8% of adults receiving hypertension treatment in the 2003–2008 National Health and Nutrition Examination Survey satisfied resistant-hypertension criteria. The broader uncontrolled-hypertension population is larger; an industry estimate suggests that about 23 million US adults remain above target while taking at least two medicines.[18]

Evidence describing resistant hypertension in Asia, and specifically Indonesia, remains comparatively limited. In a Cirebon cross-sectional study using ABPM, Hikmayani *et al.*[7] evaluated 149 treated patients and reported uncontrolled hypertension in 50.3% and resistant hypertension in 35.6%. Coronary artery disease and heart failure affected 64% and 51%, respectively, and were strongly related to the resistant phenotype.[7] Rachmawan *et al.*[8] also emphasised that poor adherence, white-coat elevation, and inadequate regimens must be ruled out before true resistance is diagnosed. The substantial cardiovascular comorbidity in the Cirebon cohort provides a clinical rationale for studying interventions that reduce aldosterone-driven remodelling in Indonesian patients.

Overt primary aldosteronism or renin-independent aldosterone secretion may be present in 20%–25% of patients with resistant hypertension.[19,20] Sodium retention, potassium loss, vascular dysfunction, and excess cardiovascular risk characterise this phenotype.[19,21] Because primary aldosteronism produces disproportionate cardiac and renal injury compared with essential hypertension at a similar blood pressure, recent guidelines and reviews favour broader biochemical case detection.[22-24] Moreover, patients without confirmed primary aldosteronism may still have relative aldosterone excess caused by RAAS activation, thereby sustaining hypertension and target-organ injury.[21]

3. Definitions and terminology

The terms used throughout this review are not interchangeable and carry different clinical and regulatory implications. Table 1 summarises the definitions applied in this article.

Table 1. Definitions and terminology used in this review

Term	Definition
Uncontrolled hypertension	Blood pressure above the therapeutic target; in this review, the trial population of interest receives ≥ 2 antihypertensive agents.
Apparent treatment-resistant hypertension	Blood pressure above target on ≥3 antihypertensive agents, including a diuretic, at optimal or maximally tolerated doses, without confirmation that adherence and out-of-office blood pressure have been assessed.
True resistant hypertension	Apparent treatment-resistant hypertension after pseudo-resistance (non-adherence, white-coat effect, suboptimal regimen) has been excluded by adherence assessment and ambulatory or home blood pressure monitoring.
Controlled resistant hypertension	Blood pressure at target only with ≥4 antihypertensive agents (American Heart Association definition).
BaxHTN trial population	Adults with seated SBP ≥ 135 mmHg after a 2-week placebo run-in on ≥2 antihypertensive agents, including a diuretic (uncontrolled); ≥3 agents, including a diuretic, in the resistant subgroup.
Approved indication (Baxfendy)	Add-on therapy, in combination with other antihypertensive medications, for adults whose hypertension is not adequately controlled on other agents—not restricted to formally defined resistant hypertension.

Notes: Definitions follow the American Heart Association and European Society of Hypertension guidance.[2,25] The eligibility criteria for BaxHTN, a phase 3 trial in uncontrolled or resistant hypertension, are taken from the trial reports,[26,27] and the approved indication is taken from the United States prescribing information.[28]
Abbreviation: SBP: Systolic blood pressure.

4. Pharmacology of baxdrostat

4.1. Mechanism of action

Baxdrostat is a potent, orally active small molecule developed for once-daily inhibition of aldosterone synthase (CYP11B2). This mitochondrial cytochrome P450 enzyme, encoded by the *CYP11B2* gene and expressed in the adrenal zona glomerulosa, mediates the three terminal reactions in aldosterone production[29,30]: conversion of deoxycorticosterone to corticosterone, formation of 18-hydroxycorticosterone, and final oxidation to aldosterone. Competitive CYP11B2 blockade lowers circulating aldosterone and consequently reduces mineralocorticoid receptor (MR) stimulation in the kidney, cardiovascular system, and brain (Figure 1).[29,30]

A central difficulty in developing this drug class is avoiding inhibition of CYP11B1 (11β-hydroxylase), an enzyme expressed in the adrenal zona fasciculata that is required for cortisol synthesis. Because CYP11B1 and CYP11B2 are 93% identical in amino-acid sequence, separating their inhibition is technically demanding.[30] Earlier inhibitors, including osilodrostat, could also inhibit cortisol synthesis, illustrating the need for CYP11B2 selectivity.[29] In vitro, baxdrostat displays more than 100-fold selectivity for CYP11B2 over CYP11B1, permitting aldosterone reduction without measurable impairment of basal or stimulated cortisol at therapeutic exposure.[30,31]

4.2. Pharmacokinetics and pharmacodynamics

In healthy volunteers, baxdrostat had a mean half-life of 26–31 h, supporting once-daily dosing.[31] The multiple-ascending-dose study found dose-proportional exposure across 0.5–5 mg and approximately 51%–73% reductions in plasma aldosterone concentrations by day 10 at the active doses, without a meaningful effect on cortisol.[31] Food had no clinically significant effect on exposure; adrenocorticotropic hormone (ACTH)-stimulated cortisol responses were preserved in the clinical programme.[28] Plasma renin activity increased as aldosterone concentrations decreased.[28]

Mineralocorticoid receptor antagonists prevent receptor activation but can provoke a compensatory rise in aldosterone, which may preserve MR-independent signalling. Baxdrostat instead reduces the hormone itself as well as subsequent MR stimulation.[21] This upstream action could offer a mechanistic advantage, although a clinical advantage over MRAs has not been proven. The prescribing information reports that baxdrostat does not inhibit testosterone or estrone synthesis; this does not establish a comparative endocrine-tolerability advantage over spironolactone.[28]

4.3. Comparative pharmacological profile

Table 2 summarises the pharmacological comparison between baxdrostat and existing aldosterone-targeting antihypertensive agents.

5. Clinical trial evidence

5.1. Phase 2—the BrigHTN Trial

BrigHTN was a phase 2, randomised, double-blind, placebo-controlled, dose-ranging trial involving 275 patients with treatment-resistant hypertension, defined as blood pressure of at least 130/80 mmHg despite treatment with three or more antihypertensive agents, including a diuretic. Following a two-week run-in period to assess

Table 2. Comparative pharmacological profile of baxdrostat and existing aldosterone-targeting antihypertensive agents

Drug/class	Mechanism	Selectivity (CYP11B2 vs. CYP11B1)	Effect on aldosterone	Effect on cortisol	Hyperkalaemia risk
Baxdrostat (aldosterone synthase inhibitor)	CYP11B2 inhibition	>100:1	Decreased	None	Present; varies with dose and renal function
Spironolactone (MRA)	MR blockade (non-selective)	N/A	Increased (reflex)	None	Present; varies with dose and renal function
Eplerenone (MRA)	MR blockade (selective)	N/A	Increased (reflex)	None	Present; varies with dose and renal function
Finerenone (MRA)	Non-steroidal MR blockade	N/A	Increased (reflex)	None	Present; varies with dose and renal function

Notes: Pharmacological characteristics are summarised from the cited sources.[11-14,28-31] Hyperkalaemia risks are descriptive; no head-to-head safety comparison has established a ranking between agents.
Abbreviations: CYP11B1: Cytochrome P450 family 11 subfamily B member 1 (11β-hydroxylase); CYP11B2: Cytochrome P450 family 11 subfamily B member 2 (aldosterone synthase); MR: Mineralocorticoid receptor; MRA: Mineralocorticoid receptor antagonist; N/A: Not applicable.

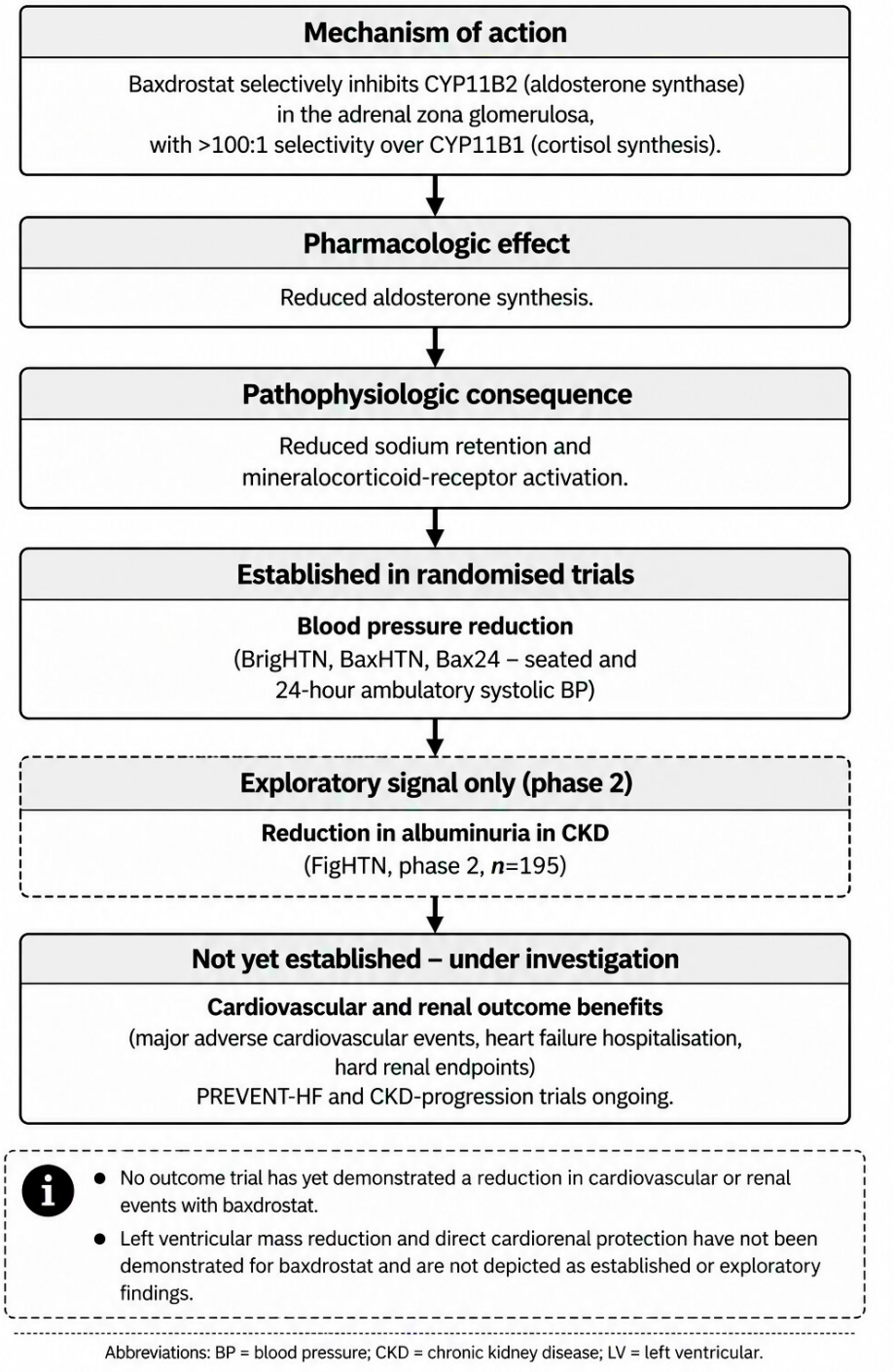


Figure 1. Mechanism of action of baxdrostat and the current level of evidence for its downstream effects. By selectively blocking CYP11B2, baxdrostat decreases aldosterone production and consequently limits sodium retention and MR stimulation. BrigHTN (phase 2 resistant-hypertension trial), BaxHTN (phase 3 uncontrolled- or resistant-hypertension trial), and Bax24 (phase 3 ambulatory blood-pressure trial in resistant hypertension) have established the blood-pressure effect. FigHTN, a phase 2 trial in CKD, provides only preliminary, hypothesis-generating evidence for reduced albuminuria. Completed trials have not demonstrated regression of left-ventricular mass, direct cardiorenal protection, or improved cardiovascular and renal outcomes; cardiorenal outcomes are being investigated in PREVENT-HF and CKD-progression studies. The figure was developed by the authors from the cited sources.[26,27,29-36]
Abbreviations: BP: Blood pressure; CKD: Chronic kidney disease; CYP11B1: Cytochrome P450 family 11 subfamily B member 1 (11β-hydroxylase); CYP11B2: Cytochrome P450 family 11 subfamily B member 2 (aldosterone synthase); LV: Left ventricular; MR: Mineralocorticoid receptor.

treatment adherence, participants were randomised to receive baxdrostat 0.5, 1, or 2 mg or placebo once daily for 12 weeks. The primary endpoint was the change in seated systolic blood pressure (SBP) from baseline to week 12. Of the 275 randomised participants, 248 completed the trial. The findings were published online in November 2022 and subsequently appeared in the February 2023 print issue.[32]

Mean reductions were 9.4 mmHg with placebo and 12.1, 17.5, and 20.3 mmHg with baxdrostat 0.5, 1, and 2 mg, respectively. For 2 mg, the adjusted difference from placebo was approximately 11.0 mmHg ($p < 0.001$). Serum aldosterone decreased without evidence of cortisol suppression, consistent with the endocrine selectivity demonstrated in phase 1.[32]

Baxdrostat was generally tolerated in BrigHTN. Two patients had baxdrostat-related potassium elevations to at least 6.0 mmol/L; these did not recur after temporary withdrawal and reinitiation. No cases of adrenocortical insufficiency were reported.[32] Patients with an estimated glomerular filtration rate (eGFR) below 45 mL/min/1.73 m^2 were excluded, limiting generalisability to more advanced CKD.[32]

5.2. The HALO Trial—a cautionary observation

HALO was a phase 2, randomised, double-blind, placebo-controlled trial involving 249 patients with hypertension that remained uncontrolled despite treatment with one or two background antihypertensive agents. Participants were randomised to receive baxdrostat 0.5, 1, or 2 mg, or placebo, once daily for eight weeks. The primary endpoint was the change in mean seated SBP from baseline to week 8 compared with placebo. Unlike BrigHTN, HALO did not demonstrate a statistically significant reduction in seated SBP with baxdrostat relative to placebo.[37]

Subsequent testing of plasma baxdrostat concentrations identified substantial non-adherence in the active-treatment groups that had not been detected through pill counts. A subsequent development-programme report described a post hoc analysis of participants assigned to the 2-mg dose who had plasma drug concentrations consistent with adherence, suggesting a placebo-adjusted SBP reduction of approximately 7.9 mmHg.[27] The discrepancy between pill-count and drug-concentration findings highlights the challenges of assessing treatment adherence, which have also been documented in studies such as SYMPATHY.[38] These observations informed the implementation of more stringent run-in and adherence-assessment procedures in the phase 3 development programme.

5.3. Phase 3—the BaxHTN Trial

BaxHTN (NCT06034743) was a multinational, phase 3, randomised, double-blind, placebo-controlled trial involving 796 patients with uncontrolled hypertension despite treatment with at least two antihypertensive agents, including a diuretic, or resistant hypertension despite treatment with at least three, including a diuretic. Following a two-week single-blind placebo run-in period, participants with seated SBP of at least 135 mmHg were randomised in a 1:1:1 ratio to receive baxdrostat 1 mg, baxdrostat 2 mg, or placebo once daily for 12 weeks. Of the 796 randomised participants, 794 received study treatment. The primary endpoint was the change in seated SBP from baseline to week 12. The results were published online on August 30, 2025.[26,27]

Both baxdrostat doses achieved the primary endpoint at week 12. The least-squares mean changes in seated SBP from baseline were −14.5 mmHg (95% confidence interval [CI], −16.5 to −12.5) with 1 mg and −15.7 mmHg (95% CI, −17.6 to −13.7) with 2 mg. The corresponding placebo-adjusted differences were −8.7 mmHg (95% CI, −11.5 to −5.8; $p < 0.001$) and −9.8 mmHg (95% CI, −12.6 to −7.0; $p < 0.001$), respectively.[26] Treatment effects were similar in the uncontrolled- and resistant-hypertension subgroups. Secondary blood-pressure endpoints, including seated diastolic blood pressure and achievement of seated SBP below 130 mmHg, also favoured baxdrostat. Hormonal assessments, including serum aldosterone concentrations and plasma renin activity, were exploratory endpoints.[26]

Hyperkalaemia requiring clinical intervention occurred in approximately 7.9% of participants receiving baxdrostat 2 mg, and hyponatraemia was also reported. eGFR decreased early during treatment but returned towards baseline after randomised treatment withdrawal, a pattern consistent with a haemodynamic effect. However, this finding does not exclude the possibility of renal adverse events in individual patients.[26]

The placebo-adjusted SBP reduction of 9.8 mmHg with baxdrostat 2 mg in BaxHTN was numerically smaller than, but comparable to, the 11.0-mmHg reduction observed in BrigHTN.[26,32] Differences in eligibility criteria, background-treatment optimisation, follow-up procedures, and regression to the mean may have contributed to this variation, although these explanations remain speculative.

5.4. Phase 3—the Bax24 Trial

Bax24 (NCT06168409) was an international, multicentre, phase 3, randomised, double-blind, placebo-controlled trial evaluating baxdrostat using 24-h ABPM, thereby reducing reliance on office blood-pressure measurements.[27,33] Investigators screened 854 individuals at 79 centres across 22 countries and randomised 217 patients with confirmed resistant hypertension to receive baxdrostat 2 mg ($n = 108$)

or placebo (n = 109) once daily for 12 weeks. Eligibility required seated SBP of at least 140 but below 170 mmHg despite treatment with three or more antihypertensive agents, including a diuretic, and mean 24-hour ambulatory SBP of at least 130 mmHg following a two-week placebo run-in period. The primary endpoint was the change in mean 24-hour ambulatory SBP from baseline to week 12.[33]

The primary analysis included 89 baxdrostat recipients and 95 placebo recipients with valid baseline and week-12 ABPM measurements. At week 12, the least-squares mean changes in 24-hour ambulatory SBP were −16.6 mmHg (95% CI, −18.8 to −14.3) with baxdrostat and −2.6 mmHg (95% CI, −4.7 to −0.4) with placebo. The adjusted between-group difference was −14.0 mmHg (95% CI, −17.2 to −10.8; $p < 0.0001$).[33] Night-time ambulatory SBP and seated office SBP showed corresponding placebo-adjusted reductions of 13.9 and 10.3 mmHg, respectively. A mean 24-hour ambulatory SBP below 130 mmHg was achieved by 71% of baxdrostat recipients compared with 17% of placebo recipients (odds ratio, 15.2; 95% CI, 6.6–35.2; $p < 0.0001$).[33]

Adverse events were reported in 52% of baxdrostat recipients and 37% of placebo recipients. Confirmed serum potassium concentrations above 6.0 mmol/L occurred in 3% and 0%, respectively.[33] Together, BaxHTN and Bax24 provide concordant evidence of blood-pressure reduction based on office and ambulatory measurements. The ambulatory findings are particularly relevant to Indonesia, where ABPM is increasingly central to verifying resistant hypertension and has been used in the Cirebon cohort.[7,39]

5.5. The FigHTN Trial—Evidence in chronic kidney disease

FigHTN was a phase 2, randomised, double-blind, placebo-controlled trial involving 195 participants with CKD and uncontrolled hypertension despite treatment with maximally tolerated renin–angiotensin system blockade. Eligible participants had an eGFR of 25–75 mL/min/1.73 m^2, and a urinary albumin-to-creatinine ratio of at least 100 mg/g; approximately 80% had type 2 diabetes. Participants were randomised to receive low-dose baxdrostat (0.5 mg titrated to 1 mg), high-dose baxdrostat (2 mg titrated to 4 mg), or placebo for 26 weeks. The primary endpoint was the change in mean seated office SBP from baseline to week 26, comparing the pooled baxdrostat treatment groups with placebo.[34]

At week 26, the placebo-adjusted change in seated office SBP with baxdrostat was −8.1 mmHg (95% CI, −13.4 to −2.8; p = 0.003). Treatment was also associated with reduced albuminuria, an exploratory finding suggesting a possible kidney benefit that requires further investigation.

However, hyperkalaemia was substantially more frequent among baxdrostat recipients, with adverse events reported in 53 of 128 participants (41.4%) in the pooled baxdrostat group compared with 3 of 64 participants (4.7%) in the placebo group. These percentages were calculated using the treated safety population, whereas 195 participants were randomised.[34] FigHTN therefore partly addresses the limited representation of patients with more advanced CKD in pivotal hypertension trials while highlighting the need for careful potassium monitoring in this population. Safety estimates from general hypertension populations should not be directly extrapolated to patients with CKD.

5.6. The BaxAsia Trial—Evidence in Asian populations

BaxAsia (NCT06344104) was a multicentre, phase 3, randomised, double-blind, placebo-controlled trial involving 326 patients with uncontrolled or resistant hypertension. Participants were recruited predominantly from Asian study sites, including sites in China, with additional recruitment in other regions, including Australia. The trial evaluated baxdrostat 1 or 2 mg versus placebo once daily, with the primary endpoint assessing the change in seated SBP from baseline to week 12.[27,40]

The study reached primary completion on November 24, 2025, and was completed on April 3, 2026.[40] Full efficacy and safety results had not been identified at the literature-search cutoff. The findings are expected to provide additional evidence regarding the efficacy and tolerability of baxdrostat in Asian populations. Until these results are available, the extrapolation of findings from multinational trials to patients in Indonesia should be approached with appropriate caution.

5.7. Summary of clinical trial results

Table 3 summarises the design and principal findings of the key baxdrostat clinical trials.

6. Safety and tolerability

The frequency of adverse effects with baxdrostat is influenced by dose, renal function, comorbidity, and the definitions adopted in individual trials. Hyperkalaemia and hyponatraemia are the leading established concerns and are included in the approved product information.[28] Inadequate CYP11B2 selectivity could theoretically impair adrenal function, although clinical cortisol findings have so far been reassuring. Electrolytes and kidney function therefore require active monitoring.

Potassium abnormalities differed considerably across the development programme. In BrigHTN, two patients had baxdrostat-related potassium elevations to at least

Table 3. Design and results of key baxdrostat clinical trials

Trial	Phase	*N*	Population	Dose	Duration	Primary endpoint	Key result (placebo-adjusted)	Outcome
BrigHTN	2	275	Resistant HTN	0.5/1/2 mg	12 wk	Seated SBP change	−11.0 mmHg (2 mg); $p < 0.001$	Met (1 and 2 mg doses)
HALO	2	249	Uncontrolled HTN (1–2 drugs)	0.5/1/2 mg	8 wk	Seated SBP change	Not significant (overall); post hoc adherent-only 2 mg subgroup −7.9 mmHg	Primary endpoint not met
BaxHTN	3	796	Uncontrolled + resistant HTN	1/2 mg	12 wk	Seated SBP change	−8.7 mmHg (1 mg); −9.8 mmHg (2 mg); both $p < 0.001$	Met (both doses); all key secondary endpoints met
Bax24	3	217	Resistant HTN (ABPM-confirmed)	2 mg	12 wk	24-h ambulatory SBP change	−14.0 mmHg; $p < 0.0001$	Met (primary and key secondary endpoints)
FigHTN	2	195	CKD (eGFR 25–75 mL/min/1.73 m²) + uncontrolled HTN	0.5→1 mg or 2→4 mg	26 wk	Seated office SBP change	−8.1 mmHg; $p = 0.003$	Met; higher hyperkalaemia rate observed in this population
BaxAsia	3	326	Uncontrolled + resistant HTN (Asia)	1/2 mg	12 wk	Seated SBP change	Pending	Full efficacy and safety results were unavailable at the literature-search cutoff

Notes: BrigHTN randomised 275 patients; 248 completed the trial. BaxHTN randomised 796 participants; 794 received treatment. Trial characteristics and efficacy outcomes are summarised from the cited reports.[26,27,32-34,37,40]
Abbreviations: ABPM: Ambulatory blood pressure monitoring; CKD: Chronic kidney disease; eGFR: Estimated glomerular filtration rate; HTN: Hypertension; SBP: Systolic blood pressure; wk: week.

6.0 mmol/L.[32] BaxHTN estimates varied depending on whether hyperkalaemia was defined by adverse-event coding, a laboratory cutoff, or the need for intervention.[26,28] In Bax24, confirmed values above 6.0 mmol/L occurred in 3% versus 0%.[33] Rates were much higher in CKD-enriched FigHTN (41.4% vs 4.7%).[34] PATHWAY-2 recorded one potassium value above 6.0 mmol/L in 6 of 285 spironolactone-exposed participants.[12] These figures cannot establish comparative safety because the trials differed in design, renal eligibility, background treatment, duration, monitoring, and event definitions. No direct trial has shown baxdrostat to cause less hyperkalaemia than spironolactone.

Table 4 summarises reported hyperkalaemia findings across selected baxdrostat trials and PATHWAY-2. These findings are presented descriptively and should not be interpreted as direct comparative safety estimates.

Stimulation testing involving ACTH has provided evidence of adrenal selectivity. The clinical programme found no impairment of ACTH-stimulated cortisol responses; BrigHTN and BaxHTN reported no adrenal insufficiency.[26,28,31,32] Hyperkalaemia and hyponatraemia are identified adverse reactions in the prescribing information.[28] Bax24 reported any adverse event in 52% of baxdrostat recipients versus 37% of placebo recipients.[33] The prescribing information reports no inhibition of testosterone or estrone synthesis.[28] In BaxHTN, mean eGFR decreased during treatment and increased after withdrawal, suggesting a haemodynamic contribution; this does not exclude renal adverse events in individual patients.[26,28] Continued renal surveillance is prudent, particularly in patients with CKD.[34,41]

6.1. Kidney function thresholds and clinical monitoring

The US prescribing information states that safety and effectiveness of initiation at eGFR below 45 mL/min/1.73 m² have not been established.[28] FigHTN nevertheless provides phase 2 research data in CKD with eGFR 25–75 mL/min/1.73 m², which should be distinguished from the approved-use evidence base.[34] The US label requires

Table 4. Reported hyperkalaemia findings in selected baxdrostat trials and PATHWAY-2

Trial	Population	Treatment	Kidney-function context	Hyperkalaemia assessment/definition	Reported finding
BrigHTN	Resistant hypertension	Baxdrostat across active-dose groups	eGFR < 45 mL/min/1.73 m^2 excluded	Baxdrostat-related serum potassium ≥ 6.0 mmol/L	2 patients; no recurrence after temporary withdrawal and reinitiation
BaxHTN	Uncontrolled or resistant hypertension	Baxdrostat 1 mg, 2 mg, or placebo	BaxHTN required eGFR ≥ 45 mL/min/1.73 m^2	Hyperkalaemia requiring clinical intervention during the 12-week double-blind phase	1 mg: 7/264 (2.7%); 2 mg: 21/266 (7.9%); placebo: 0/264
Bax24	ABPM-confirmed resistant hypertension	Baxdrostat 2 mg versus placebo	Bax24 required eGFR ≥ 45 mL/min/1.73 m^2	Confirmed serum potassium > 6.0 mmol/L	3% with baxdrostat; 0% with placebo
FigHTN	CKD and uncontrolled hypertension	Baxdrostat pooled doses versus placebo	eGFR 25–75 mL/min/1.73 m^2	Hyperkalaemia adverse event	53/128 (41.4%) with baxdrostat; 3/64 (4.7%) with placebo
PATHWAY-2	Resistant hypertension	Spironolactone in crossover comparison	Mean kidney function relatively preserved; severe CKD excluded	Serum potassium > 6.0 mmol/L	6 of 285 participants exposed to spironolactone, approximately 2.1%

Notes: The values are descriptive and are unsuitable for direct cross-trial comparison. Differences include design, exposure period, participant profile, baseline renal function, concomitant therapy, potassium surveillance, and the definition of hyperkalaemia. Because PATHWAY-2 was a crossover trial, its denominator is the number exposed to spironolactone rather than a parallel-group sample. Data compiled from Refs.[12,26,28,32-34]
Abbreviations: ABPM: Ambulatory blood pressure monitoring; CKD: Chronic kidney disease; eGFR: Estimated glomerular filtration rate.

assessment of potassium and sodium before initiation and periodically thereafter, with more frequent monitoring in higher-risk patients.[28] Kidney function should also be followed. Reassessment within 2–4 weeks of initiation or dose escalation is a practical extrapolation from Kidney Disease: Improving Global Outcomes monitoring principles for RAAS-active therapy, rather than a baxdrostat-specific interval established by the label.[41,42] CKD, diabetes, advanced age, potassium supplements, and concomitant RAAS-active drugs increase hyperkalaemia risk and justify individualised monitoring.[28,34,41,43] If hyperkalaemia or clinically significant hyponatraemia occurs, the label advises treatment of the electrolyte abnormality and consideration of interruption or discontinuation; clinically significant recurrence requires permanent discontinuation.[28] Clinically important deterioration in kidney function also warrants prompt clinical assessment.[41]

7. Regulatory trajectory and future directions

On December 2, 2025, AstraZeneca announced that its application had been accepted for FDA Priority Review.[44] The FDA approved baxdrostat as Baxfendy on May 15, 2026, the first oral aldosterone synthase inhibitor authorised for hypertension[18,45]; the company announced the decision on May 18, 2026.[18] The label permits add-on use with other antihypertensive drugs in adults whose blood pressure is inadequately controlled, thereby covering both uncontrolled and treatment-resistant populations rather than only the latter.[45] Tablets are available in 1- and 2-mg strengths. The recommended dose is 2 mg once daily with or without food, while 1 mg is advised when the risk of hyperkalaemia or hyponatraemia is increased.[28] The manufacturer anticipated commercial availability in early June 2026.[18]

The authorisation has two notable implications. It introduced the first approved aldosterone synthase inhibitor after a longstanding challenge in achieving CYP11B2 selectivity without inhibiting CYP11B1.[18,45] It also covers a considerably larger group than resistant hypertension alone. AstraZeneca estimates that approximately 23 million US adults remain uncontrolled on at least two medicines.[18] This unmet need is relevant to Indonesia, where Riskesdas 2018 documented a substantial hypertension burden.[6]

Baxdrostat is also being studied for cardiorenal outcomes alongside sodium–glucose cotransporter 2 inhibition. PREVENT-HF (NCT06677060) compares baxdrostat plus dapagliflozin with dapagliflozin alone for preventing heart failure and cardiovascular death in adults with type 2 diabetes.[35] Another phase 3 programme (NCT06268873) examines the combination in CKD and

hypertension using eGFR slope as a progression outcome, building on the preliminary FigHTN observations.[34,36] Studies in primary aldosteronism could further extend its use to the estimated 5%–10% of hypertensive patients with biochemical confirmation of that disorder.[22-24]

For Asia-Pacific health systems, publication of BaxAsia will be relevant to regulatory and health-technology decisions. At the close of this review, full efficacy and safety results were unavailable. Indonesian data demonstrating frequent uncontrolled and resistant hypertension in cardiovascular practice,[7] together with the national hypertension burden,[6] suggest a possible role for baxdrostat if local authorities authorise it. Access will additionally depend on pricing and assessment for coverage within Jaminan Kesehatan Nasional/BPJS Kesehatan.

8. Clinical implications and positioning in hypertension management

The 2024 European Society of Cardiology guideline defines resistant hypertension as office blood pressure remaining at least 140/90 mmHg despite maximally tolerated treatment with a RAAS blocker, calcium-channel blocker, and diuretic, after pseudo-resistance has been excluded.[46] Spironolactone remains the guideline-supported add-on option, based principally on PATHWAY-2.[12,46] Baxdrostat now has US regulatory authorisation and phase 3 evidence for meaningful blood-pressure lowering in uncontrolled and resistant hypertension. Its eventual position in guidelines nevertheless requires outcome data, comparative trials, and longer safety follow-up. Recent reviews, meta-analyses, and Bax24 support the efficacy of aldosterone synthase inhibition while likewise emphasising these evidence needs.[33,47,48]

8.1. The clinical value of the uncontrolled-hypertension indication

The US label is not confined to patients meeting a strict resistant-hypertension definition; it includes adults who remain inadequately controlled on other medicines.[28,45] This substantially enlarges the eligible group beyond the estimated 10%–15% of treated hypertensive patients with resistant disease.[2] The distinction may be especially important in Indonesia, where 50.3% of treated patients in the Cirebon cohort were uncontrolled.[7] If affordable and appropriately targeted, a therapy studied in this broader population could therefore have greater health-system relevance than one restricted to confirmed resistance.

Broad eligibility also requires responsible prescribing. Poor adherence, the white-coat effect, insufficient dosing, and incomplete regimen optimisation frequently explain apparent lack of control.[2,38] HALO illustrates how non-adherence can obscure drug efficacy.[37] Before adding baxdrostat, clinicians should verify adherence and ensure adequate use of standard strategies, including a RAAS blocker, calcium-channel blocker, and diuretic where appropriate. Addressing pseudo-resistance first helps reserve mechanism-directed therapy for patients most likely to benefit.[2,46]

Baxdrostat adds a distinct mechanism to antihypertensive therapy, but its sequence relative to MRAs, aprocitentan, lorundrostat, and renal denervation is unknown. Guideline placement will depend on comparative effectiveness, outcomes, long-term safety, access, and economic value. Other evolving options include spironolactone and related MRAs; the endothelin antagonist aprocitentan supported by PRECISION[49-51]; lorundrostat, studied in Target-HTN, Advance-HTN, and Launch-HTN[52-54]; and renal denervation for selected resistant cases under the 2023 European Society of Hypertension and 2024 European Society of Cardiology guidance.[25,46,55,56] Baxdrostat might be considered when spironolactone's endocrine effects are unacceptable, but it cannot be assumed to avoid hyperkalaemia. Aldosterone-excess phenotypes are biologically attractive candidates, although prospective confirmation is lacking. The approved indication also permits use after established treatment has been optimised. Because efficacy estimates come from separate placebo-controlled trials and indirect comparisons, a preferred treatment sequence cannot be inferred from these data.[26,33,47,48]

8.2. Combination with mineralocorticoid receptor antagonists

Because pivotal trials excluded MRAs and potassium-sparing diuretics, evidence is insufficient for routinely combining these agents with baxdrostat or treating one as a directly interchangeable substitute for the other.[26,27] Comparative and combination trials are needed before either approach can be endorsed.

From an implementation perspective, the introduction of baxdrostat into Indonesian clinical practice should be accompanied by structured biochemical monitoring and patient education. Potassium-rich foods, including tropical fruits commonly consumed in Indonesia, are generally compatible with a healthy diet and should not be considered a contraindication to therapy. Nevertheless, patients with CKD, diabetes mellitus, older age, or concomitant potassium-raising medications require individualised dietary counselling when clinically indicated, together with baseline and follow-up assessment of serum potassium, serum sodium, kidney function, and blood pressure. These measures are consistent with

current prescribing recommendations and contemporary cardiorenal practice.[28,34,41]

9. Limitations of current evidence and this review

Interpretation is limited by several gaps. BaxHTN and Bax24 had 12-week primary efficacy assessments and were not designed to establish effects on myocardial infarction, stroke, heart failure, CKD progression, or death.[26,33] Both trials excluded eGFR below 45 mL/min/1.73 m^2, while the available CKD-specific findings from FigHTN are limited to a phase 2 trial.[26,33,34] BaxAsia was completed, but full efficacy and safety results had not been identified at the literature-search cutoff, limiting a dedicated assessment of that trial in Asian populations.[40] The available trials and indirect comparative syntheses do not establish a preferred sequence relative to spironolactone, aprocitentan, lorundrostat, or renal denervation.[26,33,47,48] Finally, as a narrative rather than systematic review, this synthesis may be affected by selective inclusion and interpretation of the literature.

10. Conclusion

Baxdrostat is the first aldosterone synthase inhibitor to complete phase 3 development and obtain approval for add-on treatment of hypertension that remains inadequately controlled. BrigHTN, BaxHTN, Bax24, and FigHTN collectively show blood-pressure lowering across different study populations, while also demonstrating the need to monitor electrolytes and renal function, particularly in CKD. Important uncertainties persist: cardiorenal outcome benefits are unproven, full BaxAsia efficacy and safety results are awaited, and head-to-head comparisons with MRAs, aprocitentan, lorundrostat, or renal denervation have not been performed. Its optimal place in hypertension algorithms therefore remains undetermined.

Any introduction in Indonesia should follow national regulatory review and assessment of cost-effectiveness, budget impact, and applicability of Asian evidence. In practice, safe use would require appropriate patient selection, optimisation of established therapy, confirmation of genuine treatment resistance when relevant, and regular measurement of potassium, sodium, and kidney function.

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The authors declare they have no competing interests.

Author contributions

Conceptualization: Yogi Puji Rachmawan, Witri Pratiwi
Supervision: Antonia Anna Lukito, Meity Ardiana
Writing–original draft: Yogi Puji Rachmawan, Witri Pratiwi
Writing–review & editing: Witri Pratiwi, Bagus Andi Pramono, Erdiansyah Zulyadaini, Tuko Srimulyo, Wella Karolina, Meity Ardiana, Antonia Anna Lukito

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