New Drug Overview

Baxfendy (baxdrostat)

PDL Category: Cardiovascular Agents

Introduction

Disease Background:

- Hypertension is described as a sustained increase of systemic arterial blood pressure, typically defined as a systolic blood pressure (SBP) ≥140mmHg or diastolic blood pressure (DBP) ≥90mmHg (*Bhalla et al 2026*).
  - Per the American Heart Association/American College of Cardiology, normal blood pressure is considered as SBP <120mmHg and DBP<80mmHg, while elevated blood pressure is considered as a SBP 120 to 129mmHg and DBP <80mmHg (*Basile and Bloch 2025, Bhalla et al 2026*).
    - Hypertension is classified as:
      - Stage 1- SBP 130 to 139mmHg or DBP 80 to 89mmHg.
      - Stage 2- SBP ≥140mmHg or DBP ≥90mmHg.
- Hypertension is considered a significant risk factor for heart disease and stroke and also considered the most predominant and modifiable risk factor for developing cardiovascular disease (*Basile and Bloch 2025, Jones et al 2025*).
- The prevalence of hypertension does vary based on age, sex, and race. (*Bhalla et al 2026*).
  - Obesity and weight gain, alcohol use, and high-normal blood pressure are potential risk factors for hypertension.
  - Hypertension is generally asymptomatic; it is estimated that approximately 30% of adults in the United States are not aware they have hypertension.
- Management of hypertension includes (*Bhalla et al 2026*):
  - Achieve a target blood pressure of <130/80mmHg for most adults without comorbidities.
  - Lifestyle modifications should be started and pharmacotherapy is available.
- Baxfendy was FDA approved in 2026.

Pharmacology/Usage

- Baxfendy (baxdrostat) is an inhibitor of human aldosterone synthase.
  - Aldosterone contributes to hypertension by promoting the retention of sodium and water by the kidneys, which increases blood volume, and consequently, raises blood pressure. Aldosterone can cause vascular dysfunction, inflammation, and fibrosis.
  - Inhibition of aldosterone synthase by baxdrostat decreases plasma aldosterone concentrations, thus reducing blood pressure. Baxdrostat has a higher potency and selectivity for aldosterone synthase compared to the closely related enzyme 11β-hydroxylase (final enzyme in cortisol synthesis).
  - In nonclinical and clinical studies, baxdrostat significantly lowered aldosterone concentrations without affecting cortisol responses over a wide dose range. Baxdrostat does not inhibit synthesis of sex hormones such as testosterone and estrone.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Baxfendy (baxdrostat)
• In combination with other antihypertensive drugs, for the treatment of hypertension, to lower blood pressure in adults who are not adequately controlled on other agents. [a]	√

[a] Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes. There are no controlled trials demonstrating risk reduction of these events with Baxfendy.

(Prescribing information: Baxfendy 2026)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Baxfendy (baxdrostat)	Film-Coated Tablets: 1mg and 2mg. -Swallow tablets whole; do not cut, crush, or chew tablets.	PO	Take 2mg PO QD, with or without food. -For patients at increased risk of hyperkalemia or hyponatremia, the recommended dosage is 1mg PO QD.	• Consider the patient's risk of hyperkalemia and hyponatremia before starting Baxfendy. Assess serum potassium and sodium before starting Baxfendy and periodically thereafter. Correct serum potassium and sodium abnormalities prior to initiation of Baxfendy. • If a dose is missed, take the next dose at the usual time. Do not take a double dose on the same day. • Safety and efficacy of Baxfendy initiated in patients with eGFR $<45ml/min/1.73m^2$ have not been established.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Baxfendy was assessed in a multipart, phase 3, multicenter trial that included adults with systolic blood pressure (SBP) ≥140 and <170mmHg who were prescribed at least 2 antihypertensive medications, including one diuretic and who had an eGFR≥45ml/min/1.73m^2 and a serum potassium of ≥3.5 and <5.0mEq/L.
  - Following a two-week placebo run-in period, patients (N=794) with a SBP ≥135mmHg were randomized and treated with Baxfendy 1mg, Baxfendy 2mg, or placebo QD during an initial 12-week double-blind treatment period.
    - During this period, changes to background antihypertensive medication were prohibited unless patients became hypotensive or required rescue medication.

- Treatment with potassium supplements and potassium binders was allowed during the trial, but not simultaneous use of both an angiotensin receptor blocker (ARB) and angiotensin-converting enzyme inhibitor (ACEi), or treatment with a mineralocorticoid receptor antagonist (MRA) or potassium sparing diuretic.
- At the end of the 12 weeks, patients entered a 12-week, open-label treatment period.
  - During the open-label period, patients who were on Baxfendy 2mg during the double-blind period continued the same dose of Baxfendy, patients who received Baxfendy 1mg were re-randomized to either Baxfendy 2mg or standard of care, and patients on placebo were re-randomized to either Baxfendy 2mg or standard of care.
  - At the end of the open-label period, 257 patients who were on Baxfendy 2mg in the open-label period were re-randomized to receive either Baxfendy 2mg (N=172) or placebo (N=85) QD during an 8-week double-blind, randomized withdrawal period.

- The mean age of the included population was 61 years, while 62% were male, 63% were White, and the mean body mass index (BMI) at randomization was 31kg/m^2. Patient medical history included type 2 DM (37%), heart failure (6%), myocardial infarction (5%), and stroke (4%). Mean eGFR at baseline was 85ml/min/1.73m^2.
  - Concomitant antihypertensive medications during the trial included diuretics (100% of patients), either ACEi or ARB (90%), calcium channel blockers (70%), beta-blockers (34%), and other antihypertensive medicines (17%). In addition, about 41% of patients were on 3 background antihypertensive medications.
  - At baseline, the mean SBP was 149mmHg and mean diastolic blood pressure (DBP) was 87mmHg.
- The primary endpoints were change from baseline to week 12 in seated office SBP for Baxfendy 2mg QD compared to placebo and for Baxfendy 1mg QD compared to placebo.
  - The key secondary endpoint was change in seated office SBP for Baxfendy 2mg compared with placebo from the start (week 24) to the end (week 32) of the randomized withdrawal double-blind period of the trial.
    - At week 12, both Baxfendy 1mg and 2mg were superior to placebo in reducing SBP and DBP.
    - Results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

Efficacy Parameter	Baxfendy 2mg	Baxfendy 1mg	Placebo
SBP (mmHg)	N=266	N=264	N=263
Baseline (mean)	149.1	149.7	149.0
Change from baseline (mean)	-15.7	-14.5	-5.8
Difference from placebo	-9.8	-8.7	
p-value vs placebo	<0.0001	<0.0001	
DBP (mmHg)	N=266	N=264	N=263
Baseline (mean)	85.8	88.0	85.8
Change from baseline (mean)	-6.9	-6.3	-3.0
Difference from placebo	-3.9	-3.3	
p-value vs placebo	<0.0001	0.0008	

- The treatment benefit of Baxfendy over placebo on the primary endpoints was generally consistent across pre-specified subgroups, including age, sex, BMI, renal function (eGFR), and SBP at baseline.

- Maintenance of the blood pressure lowering effect of Baxfendy was demonstrated in the double-blind randomized-withdrawal part of the trial.
  - The change in mean SBP during the 8-week randomized withdrawal period was -3.7mmHg in the Baxfendy 2mg arm and +1.4mmHg in the placebo arm, for a mean difference from placebo of -5.1mmHg (p=0.002).

Clinical guidelines

- **2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology (ACC)/American Heart Association (AHA) Joint Committee on Clinical Practice Guidelines** (*Jones et al 2025*)
  - There are recommendations for lifestyle and psychosocial approaches, including weight (reduction), diet and nutrients (DASH diet and reduce dietary sodium), alcohol (abstinence), physical activity, and stress reduction.
  - It is recommended to start medications to lower BP in adults with hypertension if average SBP is ≥140mmHg.
    - This is for reducing the risk of cardiovascular events and total mortality.
  - It is recommended to start medications to lower BP in adults with hypertension if average DBP is ≥90mmHg.
    - This is for reducing the risk of cardiovascular events and total mortality.
  - BP lowering medication is recommended in adults with hypertension and clinical cardiovascular disease (CVD) when average SBP is ≥130mmHg or when the average DBP is ≥80mmHg.
  - For adults starting antihypertensive treatment, recommended first-line treatment to prevent CVD includes thiazide-type diuretics, long-acting dihydropyridine CCB, and ACE inhibitor or ARB.
  - Starting antihypertensive therapy with 2 first-line agents of different classes, preferably in a single-pill combination (SPC) in adults with stage 2 hypertension (SBP ≥140mmHg and DBP ≥90mmHg) is recommended for BP control and adherence.
  - Starting antihypertensive therapy with a single first-line agent is reasonable in adults with stage 1 hypertension (SBP 130-139mmHg and DBP 80-89mmHg). Dosage titration and addition of other agents may be needed to obtain BP control.

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Baxfendy can cause hyperkalemia.
    - Assess serum potassium prior to starting Baxfendy and monitor periodically during treatment.
    - Correct serum potassium abnormalities prior to starting Baxfendy.
    - More frequent monitoring is recommended for patients at increased risk of hyperkalemia. If hyperkalemia occurs, treat hyperkalemia and consider interrupting or discontinuing Baxfendy. Consider more frequent monitoring of serum potassium in patients who restart Baxfendy after experiencing hyperkalemia. Permanently discontinue Baxfendy if clinically significant hyperkalemia recurs.
  - Baxfendy can cause hyponatremia.
    - Assess serum sodium prior to starting Baxfendy and monitor periodically during treatment.
    - Correct serum sodium abnormalities prior to starting Baxfendy.
    - More frequent monitoring is recommended for patients with low baseline serum sodium concentrations and those at risk of hyponatremia, such as those receiving concomitant medications that may cause hyponatremia.

- If clinically significant hyponatremia occurs, treat the hyponatremia and consider interrupting or discontinuing Baxfendy. Consider more frequent monitoring of serum sodium in patients who restart Baxfendy after experiencing hyponatremia. Permanently discontinue Baxfendy if clinically significant hyponatremia recurs.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Baxfendy 2mg) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo
    - The most frequently reported adverse events included hyperkalemia (7.7%), hypotension (3.1%), hyponatremia (2.3%), dizziness (2%), and muscle spasms (2.2%).
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Baxfendy 1mg) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo
    - The most frequently reported adverse events included hyperkalemia (4.1%), hypotension (1.6%), hyponatremia (1.2%), dizziness (2.1%), and muscle spasms (1.1%).

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

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use of Baxfendy during pregnancy to assess for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
    - Hypertension during pregnancy poses a risk to the mother and fetus.
    - Report any pregnancies while treated with Baxfendy to AstraZeneca at 1-800-236-9933.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- Hypertension is described as a sustained increase of systemic arterial blood pressure, typically defined as a systolic blood pressure (SBP) ≥140mmHg or diastolic blood pressure (DBP) ≥90mmHg (*Bhalla et al 2026*).
- Baxfendy is an aldosterone synthase inhibitor indicated for the treatment of hypertension in combination with other antihypertensive drugs, to lower blood pressure in adults who are not adequately controlled on other agents.
  - Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes. There are no controlled trials demonstrating risk reduction of these events with Baxfendy.
- Baxfendy can cause hyperkalemia and can cause hyponatremia.
  - Assess serum potassium and serum sodium prior to initiation of Baxfendy and monitor periodically during treatment.
- The efficacy of Baxfendy was assessed in a multipart, phase 3 multicenter trial that included adults with SBP ≥140mmHg and <170mmHg who were prescribed at least 2 antihypertensive medications, including one diuretic, and who had an eGFR ≥45ml/min/1.73m^2 and a serum potassium of ≥3.5 and <5mEq/L.

    - The primary endpoints were change from baseline to week 12 in seated office SBP for Baxfendy 2mg compared to placebo and for Baxfendy 1mg compared to placebo.
        - At week 12, both Baxfendy 1mg and 2mg were superior to placebo in reducing SBP and DBP.
- Guidelines do not currently include Baxfendy as it was most recently FDA approved, but guidelines do recommend starting most patients with antihypertensive therapy that includes either a thiazide-type diuretic, long-acting dihydropyridine CCB, and ACE inhibitor or ARB.
- Baxfendy is indicated for use in combination with other antihypertensive agents for hypertension treatment in adults not adequately controlled on other agents. A comparator with Baxfendy may include Tryvio (aprocitentan), which has the same indication as Baxfendy.

- There is no evidence to suggest that Baxfendy is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Baxfendy remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

- **PDL Placement:**
    - ☐ Preferred
    - ☒ Non-Preferred

References

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