

National Institute for Health and Care Excellence


Health Technology Evaluation

Baxdrostat for treating uncontrolled or resistant hypertension [ID6623]

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	AstraZeneca (company)	AZUK agree that it is appropriate to evaluate this technology through the single technology appraisal (STA) process.	Thank you for your comment. No action required.
	Primary Care Cardiovascular Society	Agree that a NICE evaluation will be needed. A STA is appropriate	Thank you for your comment. No action required.
	UK Renal Pharmacy Group	Nil concerns	Thank you for your comment. No action required.
Wording	AstraZeneca (company)	The expected marketing authorisation for baxdrostat is  which aligns with the populations evaluated in the BaxHTN (NCT06034743), and Bax24 (NCT06168409) Phase 3 clinical trials [1, 2].	Thank you for your comment. The scope is kept broad to reflect the clinical trial. The company can submit

Section	Stakeholder	Comments [sic]	Action
		<p>However, AZUK intends to focus the evidence submission to NICE only for patients with resistant hypertension (rHTN), which is defined as hypertension (HTN) despite the use of 3 or more antihypertensive agents [3].</p> <p>rHTN can affect 12-15% of patients with HTN and is a subgroup at higher risk of adverse outcomes compared with non-resistant HTN, including increased risk for target organ damage, morbidity, and mortality [3]. In a retrospective study of >200,000 patients with incident HTN, those with rHTN were 47% more likely to suffer the combined outcomes of death, myocardial infarction (MI), heart failure (HF), stroke, or chronic kidney disease (CKD) over the median 3.8 years of follow-up [3]. In another study of >400 000 patients, compared with patients without rHTN, patients with rHTN had a 32% increased risk of developing end-stage renal disease, a 24% increased risk of an ischemic heart event, a 46% increased risk of heart failure, a 14% increased risk of stroke, and a 6% increased risk of death [3].</p> <p>Despite treatments for rHTN being technically available in the UK, some are used off-label (as outlined in the section below on “comparators”), and uptake in real world practice is often limited due to adverse event profiles, clinical inertia, and patient reluctance to add or intensify treatment, leading to low utilisation and limited effectiveness. Consequently, many patients remain sub-optimally treated, fail to achieve blood pressure targets, and remain at high risk of morbidity and mortality.</p> <p>This is demonstrated by the UK EnligHTN study, which is part of EnligHTN, a multinational observational longitudinal cohort study of patients with HTN [4]. The UK study focussed on UK patients with rHTN using Clinical Practice Research Datalink (CPRD) data, between January 2017 and March 2023, but has not yet been published. Of the [REDACTED] patients enrolled who had taken ≥3 concurrent medications for their HTN, [REDACTED] were not meeting a target of 140/90, and were therefore classified as rHTN [4]. Furthermore, these</p>	evidence for only a specific population at submission stage.

Section	Stakeholder	Comments [sic]	Action
		<p>patients were significantly exceeding the target, with an average systolic blood pressure of ■■■ in the rHTN cohort [4].</p> <p>Therefore, given their particularly high risk for target organ damage and mortality, poor uptake of the limited available treatment options, and failure to achieve blood pressure targets, rHTN represents the subgroup with greatest unmet need within the broader HTN population and is hence the proposed focus of the baxdrostat appraisal.</p> <p>AZUK suggest that the remit should therefore be updated as follows: <i>“To appraise the clinical and cost effectiveness of baxdrostat within its marketing authorisation for treating uncontrolled or resistant hypertension, as an add-on to other antihypertensive medicinal products when these do not provide adequate lowering of blood pressure.”</i></p> <p>To align with the remit, the submission title should also be adjusted to: <i>“Baxdrostat for treating resistant hypertension”.</i></p>	
	UK Renal Pharmacy Group	Yes	Thank you for your comment. No action required.
Timing Issues	AstraZeneca (company)	<p>As outlined above, there is a significant unmet need in rHTN for new treatment options that enable rHTN patients to achieve their target blood pressure, and hence prevent premature mortality and morbidity. Baxdrostat represents the first innovation to address this unmet need in recent decades.</p> <p>The timely assessment and approval of baxdrostat will result in meaningful benefits to patients with rHTN as soon as possible following marketing authorisation. AZUK agree that the timelines proposed by NICE for this evaluation are appropriate to achieve this aim.</p>	Thank you for your comment. The appraisal will follow scheduled timelines. No action required

Section	Stakeholder	Comments [sic]	Action
	Kidney Research UK	A large portion of the population, as laid out in the background information, is living with uncontrolled or resistant hypertension. This means urgent additional interventions are required to manage this condition as well as the risk of associated complications such as chronic kidney disease (CKD).	Thank you for your comment. The appraisal will follow scheduled timelines. No action required
	National Kidney Federation	<p>Urgent: Kidney disease is the ninth biggest killer globally and is projected to be the fifth leading cause of premature death by 2040. https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates</p> <p>Around 7.2 million people are living with kidney disease and around 30,000 adults and children rely on dialysis due to kidney failure. Without intervention the number of people living with chronic kidney disease (stage 3-5) is expected to increase by 2033 and the demand for dialysis this could be as high as 143,000 and 12,000 for transplantation. It is vital that there is a focus on early detection and intervention to slow the progression to kidney failure. https://www.kidneyresearchuk.org/wp-content/uploads/2023/06/Economics-of-Kidney-Disease-summary-report_accessible.pdf.</p>	Thank you for your comment. The appraisal will follow scheduled timelines. No action required
	Primary Care Cardiovascular Society	Timeline will depend on when this medicine is likely to get a UK licence	Thank you for your comment. The appraisal will follow scheduled timelines. No action required

Section	Stakeholder	Comments [sic]	Action
	UK Renal Pharmacy Group	Medium/Low – there are generally numerous suitable alternatives	Thank you for your comment. The appraisal will follow scheduled timelines. No action required
Additional comments on the draft remit	National Kidney Federation	<p>It is well documented that hypertension and CKD are intrinsically related, as hypertension is a strong determinant of worse renal and cardiovascular outcomes and renal function decline aggravates hypertension. https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.122.321762</p> <p>High blood pressure can cause chronic kidney disease (CKD) but people with CKD are at a higher risk of high blood pressure, therefore maintaining blood pressure within a target range will reduce the risk of cardiovascular disease and progression to kidney failure. There are limited treatment options for patients with kidney failure and early diagnosis, along with effective preventative medications and disease management can reduce the progression to kidney failure. Innovative medications must be optimised for effective management of kidney disease.</p>	Thank you for your comment. The relationship between hypertension and CKD, and the best way to represent this in modelling will be considered during the appraisal

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	AstraZeneca (company)	<p>AZUK is broadly aligned to the content included in the background information, but would suggest a few additions:</p> <p>Long-term implications of high blood pressure: The scope states “<i>If blood pressure is too high, it puts extra strain on the blood vessels, heart, brain, kidneys and eyes</i>”. AZUK suggest that it is worth</p>	Thank you for your comment. The following sentence has been added to the background “This may increase the risk of

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>expanding on this to outline the various specific health conditions that can occur within each organ system, to better depict the wide-reaching implications of rHTN:</p> <ul style="list-style-type: none"> • Heart: rHTN substantially elevates cardiovascular risk. In a study of >400,000 patients, rHTN patients were almost 50% more likely to suffer from a cardiovascular event (death, incident MI, or HF compared to patients with non-resistant HTN [5]. • Brain: rHTN is linked to increased prevalence of cerebrovascular disease and broader neuropathological changes, and is a major risk factor for stroke and dementia, particularly vascular dementia [6, 7, 8, 9]. In a 2015 study, rHTN was associated with a 14% higher risk of cerebrovascular accident (defined as stroke, central nervous system bleed, or cerebrovascular disease/accident not otherwise specified) [6]. The study also found greater cerebrovascular disease prevalence of 16% in rHTN versus 9% in non-resistant HTN (P<0.001) [6]. Furthermore, a 2020 meta-analysis has shown that midlife hypertension is related to a 1.19- to 1.55-fold excess risk of cognitive disorders, and that the use of antihypertensive medications can reduce dementia risk [8]. • Kidneys: rHTN is associated with a higher prevalence of CKD and a higher risk of progression to end stage kidney disease compared to patients with non-resistant HTN [3, 10]. In a five-year retrospective study comparing 60,327 patients with rHTN and 410,059 with non-resistant HTN, patients with rHTN had a 32% higher risk of end stage renal disease [11]. • Eyes: rHTN patients have a higher risk of retinopathy, due to elevated blood pressure damaging retinal vessels [12]. Signs of hypertensive retinopathy can be detected in 6–15% of the non-diabetic population aged 40 years and older, and can lead to gradual, painless deterioration of vision [13]. 	various conditions, including stroke, chronic kidney disease, and retinopathy”

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>The following addition is therefore suggested for the first paragraph in the background section: <i>“If blood pressure is too high, it puts extra strain on the blood vessels, heart, brain, kidneys and eyes, increasing the risk of, but not limited to, heart attacks, strokes, cognitive impairment, dementia, development and progression of chronic kidney disease (CKD), and vision loss.”</i></p> <p>AZUK anticipate including many of the above outcomes in the economic model for this appraisal, to demonstrate the full value of baxdrostat in treating rHTN, as further outlined in the below section on “outcomes”.</p> <p>The technology: AZUK ask for both baxdrostat phase 3 trials in hypertension to be added into the scope as they will make up the evidence base for this appraisal. The two pivotal clinical trials are; BaxHTN (NCT06034743) and Bax24 (NCT06168409), each with different study objectives and endpoints). It is therefore suggested that these are mentioned in the “technology” section.</p> <p>The following addition is therefore suggested for the section on “the technology”: <i>“It has been studied as an add-on medication compared with placebo in two clinical trials:</i></p> <ul style="list-style-type: none"> • <i>Bax24 [NCT06168409] in people with treatment resistant hypertension.”</i> • <i>BaxHTN [NCT06034743] in people with uncontrolled or treatment resistant hypertension.</i> 	<p>The technology section of the scope is intended to be a very brief overview of the available evidence. Clinical trials are mentioned but not specified.</p>
	National Kidney Federation	Kidney disease should be included as a condition at increased risk of development due to hypertension.	Thank you for your comment. The following sentence has been

Section	Consultee/ Commentator	Comments [sic]	Action
			added to the background “This may increase the risk of various conditions, including stroke, chronic kidney disease, and retinopathy”
	Primary Care Cardiovascular Society	<p>The background state ‘Treatment for resistant hypertension includes the addition of either a fourth antihypertensive drug, or further diuretic therapy with low-dose spironolactone, or an alpha-blocker or beta-blocker.’</p> <p>The fourth antihypertensive medication is low-dose spironolactone, or an alpha-blocker or beta-blocker (then others can be considered).</p> <p>Should be clearer that in the absence of hyperkalaemia spironolactone is the 4th medication</p>	Thank you for your comment. The sentence has been edited to improve the clarity of the statement.
	UK Renal Pharmacy Group	Not sure this is an accurate definition of hypertension: ‘Hypertension is a condition where blood leaves the heart at too high a pressure.’	Thank you for your comment. The sentence has been changed to “Hypertension is a condition where arterial blood pressure is persistently raised” for clarity
Population	AstraZeneca (company)	As outlined in the “Wording” section, AZUK intends to focus the evidence submission only on patients with rHTN, and therefore requests that the population is amended to “People with treatment resistant hypertension”.	Thank you for your comment. The population of the scope has been kept broad to

Section	Consultee/ Commentator	Comments [sic]	Action
			reflect the clinical trials. At submission stage the company can submit evidence for a specific subgroup.
	Primary Care Cardiovascular Society	State adults?	Thank you for your comment. The population of the scope has been changed to 'adults'.
	UK Renal Pharmacy Group	Yes	Thank you for your comment. No action required.
Subgroups	AstraZeneca (company)	As outlined above, AZUK intends to focus the evidence submission only on patients with rHTN. Therefore, no further subgroups are expected to be relevant for separate consideration in this appraisal.	Thank you for your comment. The scope is kept broad, however at submission stage the company can submit for a specific population only.
	Kidney Research UK	People living with multiple long-term conditions (MLTCs), and those at greatest risk of developing CKD should be strongly considered as candidates for this treatment. As a recognised complication of uncontrolled hypertension, CKD places a substantial economic cost on the NHS, as well as significantly reducing patients' quality of life due to its high disease burden.	Thank you for your comment. The impact of other conditions will be considered by the committee

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>An analysis of the burden of CKD due to hypertension found that: Mortality from CKD due to hypertension claimed over 454,000 lives, translating to an age-standardized mortality rate of 5.54 per 100,000. Additionally, CKD inflicted more than 10.85 million disability-adjusted life years (DALYs), which equates to an age-standardised DALYs rate of approximately 128.41 per 100,000. Global burden of chronic kidney disease due to hypertension (1990–2021): a systematic analysis of epidemiological trends, risk factors, and projections to 2036 from the GBD 2021 study - PMC</p>	
	National Kidney Federation	<p>People from lower socio-economic backgrounds may be less able to make changes to diet, exercise or access to regular support for smoking cessation and equity of access to these interventions should be considered.</p> <p>In addition, they may be more likely to develop kidney disease and progress faster to kidney failure and have additional challenges in accessing burdensome dialysis schedules, particularly if the dialysis centre is not local.</p> <p>Some ethnic minority groups may also progress faster to kidney failure and may face longer waits for transplantation.</p>	<p>Thank you for your comment. The committee will consider whether its recommendations could have a different impact on people protected by the equality legislation than on the wider population. The issues raised have been added to the equalities impact assessment (EIA).</p>
	UK Renal Pharmacy Group	<p>Yes appropriately split.</p> <p>I expect it would be very rare to use for uncontrolled hypertension in practice (only in those multi-drug intolerant patients where you are running out of options)</p> <p>It may be used slightly more in resistant hypertension / hyperaldosteronism – but only in those intolerant to MRAs(i.e spiro) as I would expect this is a far more expensive treatment than spironolactone / eplerenone / amiloride.</p>	<p>Thank you for your comment.</p>

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	AstraZeneca (company)	<p>AZUK do not believe that any of the proposed comparators listed in the draft scope are appropriate for this appraisal for the following reasons:</p> <p>A calcium-channel blocker: As outlined in the “population” section above, AZUK intends to focus the evidence submission only on patients with rHTN, and therefore the comparator listed for uncontrolled HTN (i.e. a calcium-channel blocker) is not considered relevant. This is because calcium channel blockers tend to be offered at either step 1, 2, or 3 of the NICE HTN guidelines (NG136), (when a patient has uncontrolled HTN), rather than step 4 of the guideline (when they have rHTN) [14].</p> <p>“A fourth antihypertensive drug not previously used”: Although section 1.4.48 of NG136 recommends that “<i>for people with confirmed resistant hypertension, consider adding a fourth antihypertensive drug as step 4 treatment or seeking specialist advice</i>”, it must be noted that this is followed by sections 1.4.49 to 1.4.51 which provide more granular recommendations on what that fourth drug choice should be. This intended interpretation is also clear when viewing the visual summary associated with the guidelines, which clearly shows that only a few specific antihypertensives are listed as options at step 4 (rather than any other fourth antihypertensive drug) [15]. Therefore, framing the comparator as “a fourth antihypertensive drug not previously used” is overly broad, inconsistent with NG136, and not reflective of real-world practice.</p> <p>Furthermore, although a few specific antihypertensives are listed as treatment options at step 4 of NG136, AZUK has evidence that these therapies do not reflect current standard of care in the UK. Although AZUK recognise that NG136 is the current hypertension guideline for England and Wales, it is</p>	Thank you for your comment. The scope is intended to broadly cover all potential comparators. If comparators in the scope are considered inappropriate, the company can justify their exclusion in its submission.

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>important that scope of this appraisal reflects real-world clinical practice in the UK. Therefore AZUK, recommend that a more appropriate comparator is “no further drug treatment”, given that this reflects UK practice, as outlined below:</p> <p>Further diuretic therapy with the addition of low-dose spironolactone:</p> <p>Despite this being an off-label indication, low-dose spironolactone is technically included in NG136 for rHTN patients under section 1.4.49. However, AZUK have evidence to show that it is infrequently used in real-world practice and is therefore not a relevant comparator. The lack of real-world uptake is considered to be due to a number of factors, including the safety profile of spironolactone, as well as clinical inertia to treat rHTN patients.</p> <p>The safety profile of spironolactone is known to limit use in global real-world practice. A 2019 study has shown that over a quarter of treated rHTN patients experience AEs, almost 85% of whom subsequently discontinue treatment [16]. Outside of rHTN, a 2025 study showed that for patients treated with sMRAs such as spironolactone across a range of indications, over 70% discontinued treatment within a median of 90 days of initiation [17]. Furthermore, a significant proportion of patients have a contraindication to spironolactone or are otherwise considered unsuitable to trial it (e.g., due to pre-existing hyperkalaemia, Addison’s disease, or acute renal insufficiency) [18].</p> <p>The adverse event profile and poor long-term continuation of therapy also compound clinical inertia in treating rHTN, meaning that many patients are not offered spironolactone (or any further drug therapy at all), even if they are technically eligible, and/or patients themselves may refuse spironolactone if offered it.</p>	<p>The suggested change has been made to the description of spironolactone.</p>

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>The overall impact of this is demonstrated by the EnligHTN study, the methodology of which is outlined above in the “wording” section. This analysis has shown that of █████ rHTN patients who remain uncontrolled on 3 antihypertensives (and hence ought to be eligible for a 4th prescription according to NG136), only █████ actually received a 4th prescription (for any antihypertensive medication) [4]. This shows that in real-world UK clinical practice, the vast majority of rHTN patients receive no further drug treatment, with devastating impacts on long-term morbidity and mortality.</p> <p>Of these █████ rHTN patients, █████ were already receiving an MRA such as spironolactone at baseline (e.g., for a comorbidity), meaning that █████ patients may have been eligible for spironolactone to be added as their 4th prescription according to step 4 of NG136 [4]. However, only █████ actually received spironolactone as a 4th prescription [4]. It is also worth noting that this analysis is somewhat confounded by the presence of comorbidities, including █████ of these █████ rHTN patients who were diagnosed with co-existing HF [4]. This means that some of these █████ patients may actually have been prescribed the spironolactone for their HF, rather than for their HTN, meaning that this estimate is likely inflated [4]. It should be noted that some patients may also have been ineligible for spironolactone due to raised serum potassium; this is not yet accounted for in the above estimates.</p> <p>Finally, a separate multi-country EnligHTN analysis presented at the European Society of Hypertension (ESH) in 2025 showed that for UK HTN patients the median duration of treatment with an MRA such as spironolactone is 135 days, indicating that even for those patients who are prescribed it, they are unlikely to continue it for long enough to meaningfully impact the long-term outcomes of their HTN [19, 4].</p>	

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>Of the █████ rHTN patients who remain uncontrolled on 3 antihypertensives, █████ were already receiving an alpha-blocker (e.g., for a comorbidity), meaning that █████ patients may have been eligible for an alpha-blocker to be added as their 4th prescription according to step 4 of NG136 [4]. However, only █████ actually received an alpha-blocker as a 4th prescription [4]. It should be noted that according to NG136, some patients may not be expected to be offered alpha-blockers due to their serum potassium levels; this is not accounted for in the above estimates.</p> <p>Similarly, of the █████ rHTN patients who remain uncontrolled on 3 antihypertensives, █████ were already receiving a beta-blocker (e.g., for a comorbidity), meaning that █████ patients may have been eligible for a beta-blocker to be added as their 4th prescription according to step 4 of NG136 [4]. However, only █████ actually received a beta-blocker as a 4th prescription [4]. It should be noted that according to NG136, some patients may not be expected to be offered beta-blockers due to their serum potassium levels; this is not accounted for in the above estimates.</p> <p>Conclusions</p> <p>Given that none of the proposed comparators are truly likely to be meaningfully displaced by baxdrostat, AZUK propose that a more appropriate comparator is “no further drug treatment”, given that this reflects UK practice and the patterns observed in the EnlighTN study for the vast majority of rHTN patients (█████) [4].</p>	

Section	Consultee/ Commentator	Comments [sic]	Action
	Primary Care Cardiovascular Society	<p>For the sub-groups- relating to dual therapy why does this only include calcium channel blocker - and not ACE inhibitor/angiotensin blocker?</p> <p>In people with treatment resistant hypertension (hypertension despite a stable regimen of 3 or more antihypertensive agents, one of which is a diuretic the comparators include a fourth antihypertensive drug not previously used, further diuretic therapy with the addition of low-dose spironolactone, an alpha-blocker or beta-blocker</p> <p>Is there trial data to be able to make these comparisons – in particular for spironolactone as likely to have been a trial exclusion? This will also make more difficult to recommend a place in therapy if no comparative data with current recommended 4th medication</p>	<p>Thank you for your comment. For the uncontrolled population these have been added as comparators to the scope.</p> <p>The scope is intended to broadly cover all potential comparators. If comparators in the scope are considered inappropriate, the company can justify their exclusion in its submission.</p>
	UK Renal Pharmacy Group	Missing ACEi/ARB from uncontrolled?	Thank you for your comment. These have been added for this population.
Outcomes	AstraZeneca (company)	<p>AZUK agree that the listed outcomes are broadly appropriate. However, we would like to highlight a few nuances that ought to be captured in the scope:</p> <p>Seated and ambulatory blood pressure measurements:</p> <p>As noted in NG136, blood pressure can be measured both as a seated clinic reading, or alternatively as ambulatory blood pressure monitoring (ABPM). ABPM is generally considered to provide a more comprehensive assessment</p>	Thank you for your comment. Outcome measures in the scope do not specify the method used.

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>of blood pressure than seated measurements, as it can capture control across a 24-hour period, and is therefore a better predictor of certain health outcomes, such as all-cause mortality and cardiovascular mortality [20, 21, 22, 23, 24]. NG136 requires confirmation of elevated clinic blood pressure with out-of-office measurements (ABPM or home blood pressure monitoring (HBPM)) before diagnosing hypertension, thereby mitigating misclassification due to clinic-only readings. The efficacy of baxdrostat has been demonstrated across both measurement options via the two pivotal trials, BaxHTN (NCT06034743), and Bax24 (NCT06168409). Therefore both options should be included in the scope.</p> <p>It should also be noted that changes in ABPM can be presented in various ways, with the Bax24 study assessing it as a 24-hour average, a night-time average, a daytime average, and as a proportion of patients treated to target. AZUK intends to focus on 24-hour average measurements when presenting ABPM data in our submission, but may also present these additional endpoints as supporting evidence.</p> <p>Renal benefits:</p> <p>The phase II FigHTN study demonstrated the impact of baxdrostat beyond blood pressure control, including the impact on renal outcomes such as urine albumin-creatinine ratio (uACR) [25]. The impact of baxdrostat specifically in patients with HTN and CKD is also being further explored in the phase III BaxDuo-ARCTIC (NCT06268873) and BaxDuo-PACIFIC (NCT06742723) trials [26, 27]. Given the inter-related pathophysiology of HTN and CKD, and the high rate of overlap of both these comorbid conditions (█ of the total BaxHTN study population and █ of rHTN patients in the UK EnligHTN study also had CKD), the renal impacts of baxdrostat should be included in the scope [28, 29].</p>	<p>Kidney function has been added to the outcomes.</p>

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>Conclusion:</p> <p>Therefore, in conclusion, AZUK suggest that the list of key outcomes considered in the scope should include the following, as these have been measured in key randomised controlled trials for baxdrostat:</p> <ul style="list-style-type: none"> • Change in systolic blood pressure (both seated and ABPM measurements) • Change in diastolic blood pressure (both seated and ABPM measurements) • Change in uACR • Adverse effects of treatment <p>Additional anticipated modelling outcomes:</p> <p>In addition to the above, the following outcomes are also expected to be included in the economic model, to capture the full value of baxdrostat in treating patients with resistant hypertension. However, the data for these outcomes has not been gathered as part of key baxdrostat clinical trials, and AZUK intend to source available data from the literature instead:</p> <ul style="list-style-type: none"> • Major adverse Cardiac Events (MACE), including myocardial infarction, uncontrolled angina, stroke, transient ischaemic attack, and heart failure • Cognitive benefit including dementia and mild cognitive impairment • Hypertensive retinopathy • Mortality • Health-related quality of life <p>The rationale for including such outcomes in the economic model is explored in the above “background information” section, and further details are provided below:</p>	

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>MACE: AZUK suggest that major adverse cardiac events (MACE) should be included in the draft scope, including MI, unstable angina (UA), stroke, transient ischaemic attack (TIA), and HF, as these are all well-documented long-term outcomes of rHTN [29, 30].</p> <p>Cognitive benefits: HTN is associated with cognitive decline and dementia; this is thought to be the result of the vascular changes associated with HTN increasing brain susceptibility to ischemic-hypoxic damage. Studies have shown that controlling blood pressure below specific targets can reduce the risk. For example, the Systolic Hypertension in Europe (Syst-Eur) trial showed a 55% reduction in incident dementia, while the SPRINT-MIND trial showed significant reduction in mild cognitive impairment [31]. A recent meta-analysis also confirmed the relationship between higher mean systolic blood pressure and an increased risk in dementia / cognitive impairment [32].</p> <p>Retinopathy: Hypertensive retinopathy is acknowledged as a key example of hypertension-mediated organ damage, and is thought to impact 6–15% of the non-diabetic population aged 40 years and older, causing progressive visual deterioration [12]. Blood pressure control can reduce the risk of progression of hypertensive retinopathy changes.</p>	<p>Major adverse cardiac events have been added as an outcome.</p> <p>Cognitive function has been added to the outcomes.</p> <p>Eye function has been added to the outcomes.</p>
	Kidney Research UK	The addition of outcomes that include risk of complications such as CKD and cardiovascular disease (CVD) would be beneficial to fully understand improvements beyond those captured in Quality-Adjusted Life Years (QALYs).	Thank you for your comment. Kidney function and major adverse cardiac events have been added as outcomes. Adherence

Section	Consultee/ Commentator	Comments [sic]	Action
		Patient adherence to medications should also be investigated to ensure there are no issues with polypharmacy because patients are struggling to take all of their medications.	will be considered during the appraisal but is not considered an outcome.
	National Kidney Federation	It is important to monitor the impact of the technology on the kidney and therefore Kidney function tests (eGFR or uACR) should be included as an outcome measure.	Thank you for your comment. Kidney function and major adverse has been added as an outcome.
	Primary Care Cardiovascular Society	Is the research robust enough to have a mortality outcome or will this be extrapolated from effect on blood pressure?	Thank you for your comment. Mortality is a relevant outcome for the appraisal.
	UK Renal Pharmacy Group	Yes	Thank you for your comment. No action required.
Equality	AstraZeneca (company)	<p>AstraZeneca has not identified any issues related to equality that should be covered in the remit or scope of this appraisal.</p> <p>AZUK would like to highlight the importance of equitable access for all patients, including those patients with rHTN who are particularly challenging to treat due to associated comorbidities, such as CKD who experience substantially higher incidence of cardiovascular disease and end stage renal disease than those without rHTN [11].</p>	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Kidney Research UK	<p>It is important to consider which patients would most benefit from receiving this additional treatment.</p> <p>The prevalence of later-stage CKD, in those patients with hypertension is higher in South-Asian populations, whilst treatments to target blood pressure and ACE-I/ARB prescribing was lowest in the black population, according to this UK study. The relationship of ethnicity to the prevalence and management of hypertension and associated chronic kidney disease.</p> <p>This showcases the current inequalities that already exist in risk of CKD and drug prescribing that need to be addressed in this hypertensive population so as not to further exacerbate health inequity in the UK.</p> <p>Alongside their medication, patients must be provided with accessible and culturally relevant information to ensure treatment adherence. In addition, information on the risks of uncontrolled or resistant hypertension and the associated risk of complications such as CKD should be provided.</p> <p>Kidney Research UK has received anecdotal evidence that patients living with CKD risk factors are not made aware of the risk to their kidneys; such patients would have benefitted from receiving this information sooner.</p>	Thank you for your comment. The issues raised have been added to the equalities impact assessment (EIA).
	Primary Care Cardiovascular Society	Are there any ethnicity differences that should be considered	Thank you for your comment. The committee will consider whether its recommendations could have a different impact on people protected by the equality legislation than on the wider population.

Section	Consultee/ Commentator	Comments [sic]	Action
	UK Renal Pharmacy Group	Nil concerns	Thank you for your comment. No action required.
Other considerations	AstraZeneca (company)	AZUK have no further suggestions beyond those mentioned above.	Thank you for your comment. No action required.
	Kidney Research UK	<p>As well as having this option for an additional medication, patients should be made aware of the importance of adhering to treatment and the risk of complications in uncontrolled or resistant hypertension. This includes CKD; ensuring patients understand this risk, and what living with CKD entails. Information should be provided at an appropriate health literacy level and be culturally appropriate.</p> <p>We also know the rates of uACR testing in the hypertensive population are very low (CVD PREVENT. Providing information and reviewing blood pressure in medication reviews would be of huge benefit as well as completing annual uACR testing to check for kidney damage in case patients need further referral or monitoring (Scenario: Management Management Hypertension CKS NICE).</p> <p>These simple measures could help improve access and adherence to medication and improve patients' quality of life by reducing their risk of complications.</p>	Thank you for your comment. Unfortunately, these recommendations are wider than the scope of this evaluation.
Questions for consultation	AstraZeneca (company)	<p>Where do you consider baxdrostat will fit into the existing care pathway for hypertension?</p> <p>AZUK intend to focus the NICE evidence submission on patients with rHTN, in which the unmet need is highest. Therefore, it is proposed that baxdrostat would fit as an additional treatment option available at step 4 of NG136.</p>	Thank you for your comments. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>Will baxdrostat replace any existing treatments for uncontrolled or resistant hypertension?</p> <p>As outlined under the section above on “comparators”, although low-dose spironolactone, alpha-blockers, and beta-blockers are technically listed as treatment options for rHTN in step 4 of NG136, data has shown that the vast majority of UK rHTN patients (████) actually receive no further drug treatment at step 4. Therefore, baxdrostat is not likely to meaningfully displace existing treatments in this setting.</p> <p>Please select from the following, will baxdrostat be:</p> <p>A. Prescribed in primary care with routine follow-up in primary care</p> <p>B. Prescribed in secondary care with routine follow-up in primary care</p> <p>C. Prescribed in secondary care with routine follow-up in secondary care</p> <p>D. Other (please give details):</p> <p>AZUK anticipate that both A and B will apply to baxdrostat.</p> <p>Baxdrostat is anticipated to be positioned at step 4 of NG136. Primary care plays a central role in HTN management across all stages, and most patients at step 4 are managed in primary care, with some referred to specialist centres as needed. Given this, and given the manageable safety profile of baxdrostat, AZUK consider it most appropriate for initiation to occur in both primary and secondary care, with routine follow-up predominantly in primary care.</p> <p>For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.</p>	

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>As outlined above, patients at step 4 of NG136 may be treated in either primary or secondary care.</p> <p>Would baxdrostat be a candidate for managed access? AZUK is not currently proposing baxdrostat for managed access, and consider that data from the pivotal trials (BaxHTN and Bax24) is sufficiently robust to enable a recommendation in baseline commissioning.</p> <p>Do you consider that the use of baxdrostat can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. AZUK intend to capture all key health-related benefits in the economic model for this appraisal.</p> <p>NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. AZUK has no further comments on this consultation question, beyond those already outlined under the “equality” section above.</p>	
	Primary Care Cardiovascular Society	The majority of hypertension in the UK is managed within primary care. The provision of specialist hypertension services in the UK has geographical variation. If this classed as a specialist medication only (initiation and ongoing) this may introduce inequality in access.	Thank you for your comments. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>Even making specialist initiation/advice prior to initiation with on-going prescription in primary care may have unintended consequences.</p> <p>Need to ensure place in pathway ins defined.</p> <p>Primary care will need clarity on where this fits especially regarding v place in pathway of spironolactone which is currently step 4 in the NICE guidelines</p>	
	UK Renal Pharmacy Group	<p>Will baxdrostat replace any existing treatments for uncontrolled or resistant hypertension?</p> <ul style="list-style-type: none"> - I don't think so, I can only see it being used if intolerant to MRAs <p>Where do you consider baxdrostat will fit into the existing care pathway for hypertension?</p> <ul style="list-style-type: none"> - As above – used as an additional option for uncontrolled hypertension, but only in those multi-drug intolerant patients where all other standard therapies can't be given. Baxtrostat provides a novel class that can be tried when intolerant to all others - Can be used 'step 4' of NICE hypertension guidelines if intolerant to MRAs - Can be used as an alternative to MRAs for the treatment of primary hyperaldosteronism <p>Please select from the following, will baxdrostat be: B or C Prescribed in secondary care with routine follow-up in primary care / secondary care – I would suggest initiated in specialist hypertension clinics / hypertension referral centres. Ongoing monitoring can be in primary care once discharged from clinic and stable.</p> <p>For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.</p>	Thank you for your comments. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		<ul style="list-style-type: none"> - As above, likely to be initially prescribed in a specialist hypertension clinic (when investigations for secondary hypertension can be undertaken prior to initiation) <p>Would baxdrostat be a candidate for managed access?</p> <ul style="list-style-type: none"> - I don't think so <p>Do you consider that the use of baxdrostat can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? No</p>	
Additional comments on the draft scope		No comments	

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

Kidney Care UK