PrescQIPP Community Interest Company

# Aliskiren

In England, Scotland and Wales, over £586k is spent aliskiren (NHSBSA prescribing data Feb-April 2021 and Public Health Scotland January to March 2021).

QIPP projects in this area are aimed at reviewing the continued need for aliskiren and switching to an alternative antihypertensive with better safety and efficacy and a lower acquisition cost. This bulletin reviews the place in therapy of aliskiren and offers guidance and support material for organisations considering reviewing the prescribing of aliskiren as a QIPP project.

## Recommendations

- Ensure that prescribing of antihypertensives is in line with national guidance for hypertension in adults.[1]
- Commence new patients requiring an antihypertensive on a treatment recommended by NICE or other national guidance.
- Review all patients taking aliskiren and discontinue treatment, switching to an appropriate alternative antihypertensive.
- As with all switches, these should be tailored to the individual patient.

## National guidance

The current NICE Guideline for diagnosis and management of hypertension in adults [NG136] does not recommend aliskiren, a direct renin inhibitor, as a treatment option for resistant hypertension.[1]

A joint clinical working group of NHS England and NHS Clinical Commissioners representatives determined that aliskiren is an item that should not be routinely prescribed in primary care in England, based on the insufficient evidence of its effectiveness to determine its suitability for use in the treatment of resistant hypertension.[2] The All Wales Medicines Strategy Group have also identified aliskiren as an item of low value for prescribing in NHS Wales as there are more cost-effective alternatives available.[3]

Aliskiren is not recommended for use in NHS Scotland for the treatment of essential hypertension.[4]

## Clinical effectiveness

The previous NICE clinical guideline for management of primary hypertension in adults [CG127] stated that there was insufficient evidence of effectiveness for aliskiren to determine its suitability for use in the treatment of resistant hypertension.[5] Aliskiren is licensed for treatment of essential hypertension in adults.[6] A Cochrane Clinical Answer prepared in December 2020 stated that very low- to low-certainty evidence suggests little to no difference between renin inhibitors and ACE inhibitors for control of mild to moderate primary hypertension in adults. Of the 11 randomised controlled trials (RCTs) identified, one included only people with chronic heart failure (7064 participants) and one included only people with type 1 or 2 diabetes (837 participants). In the other nine RCTs (5696 participants), when reported, 7% to 58.6% of participants had diabetes or metabolic syndrome.[7] Whilst aliskiren has shown comparable efficacy to angiotensin converting enzyme inhibitors (ACE inhibitors) and Angiotensin II receptor antagonist in terms of blood pressure reduction, its effects on mortality and long-term morbidity are

currently unknown.[2,8] A systematic review and meta-analysis of the role of aliskiren in the management of hypertension and major cardiovascular outcomes concluded that data from 37 RCTs (35,916 patients) showed aliskiren did not reduce mortality or cardiovascular death. In patients with diabetes, aliskiren add-on therapy may have the potential to increase total mortality and cardiovascular death (weighted relative risk (WRR) 1.06, 95% confidence interval (CI) [0.88;1.28] and WRR 1.09, 95% CI [0.94;1.24], respectively).[9]

## Safety

A Drug Safety Update in 2009 highlighted that aliskiren may rarely cause angioedema and patients should be advised that they should stop aliskiren and seek medical advice straight away if they develop symptoms of angioedema, such as swelling of the face, eyes, lips or tongue (or both), hands and feet, or difficulty breathing or swallowing. Extreme caution is required if aliskiren is used in patients with renal artery stenosis or conditions predisposing to kidney dysfunction (such as hypovolaemia, heart disease, liver disease, or kidney disease) because of a risk of acute renal failure. If any signs of renal failure occur, aliskiren should be promptly discontinued. NSAIDs may reduce the antihypertensive effect of aliskiren. Elderly patients or patients with compromised renal function may be at risk of further deterioration of renal function if NSAIDs and aliskiren are used together.[10]

In 2012 the Medicines and Healthcare products Regulatory Agency (MHRA) reviewed the combination use of medicines from different classes of renin-angiotensin system blocking agents. They concluded that the combination use of medicines from two classes of renin-angiotensin system blocking agents (ACE-inhibitors, Angiotensin II receptor antagonist, or aliskiren) is not recommended due to the risk of hypotension, syncope, stroke, hyperkalaemia and change in renal function including acute renal failure. They also summarised that combining the direct renin inhibitor, aliskiren, with an ACE inhibitor or an Angiotensin II receptor antagonist is strictly contraindicated in people with kidney impairment (estimated glomerular filtration rate <60 ml/minute/1.73 $m^2$) or diabetes, due to similar safety concerns.[11]

## Patient factors

There are alternative oral daily preparations available for the treatment of hypertension, so no significant patient factors are foreseen.

## Costs

There is a significant difference in cost between antihypertensives. Table 1 below illustrates the cost differences.

**Table 1: Antihypertensive product and price comparison – Drug Tariff May 2021[12]**

| Product* | Cost per 28 days |
|---|---|
| ACE inhibitor – lisinopril 10mg tablets | £1.08 |
| ACE inhibitor – ramipril 2.5mg capsules | £1.12 |
| Angiotensin II receptor antagonist – losartan 50mg tablets | £1.45 |
| Calcium channel blocker – amlodipine 5mg tablets | £1.05 |
| Thiazide diuretic – indapamide 2.5mg tablets | £3.04 |
| Potassium sparing diuretic – spironolactone 25mg tablets (unlicensed) | £1.70 |
| Alpha blocker – doxazosin 2mg tablets | £1.17 |
| Beta blocker – bisoprolol 2.5mg tablets | £1.00 |
| Renin inhibitor - aliskiren 150mg tablets | £28.51 |
| Renin inhibitor – aliskiren 300mg tablets | £34.27 |

*Preparations included in this table provide an example of commonly prescribed strengths only and should not be taken to imply equivalence.

## Switching options

There are several potential switch options from aliskiren to alternative products depending on other antihypertensive treatments already prescribed or considered (although clinicians may choose other options according to the clinical need of the patient).

These include:

If a renin-angiotensin system drug is indicated, a low-cost ACE inhibitor or angiotensin II receptor blocker (ARB) is preferred. Generic lisinopril tablets and ramipril capsules are cost-effective choices for an ACE inhibitor and generic losartan is a low-cost Angiotensin II receptor antagonist.[12]

For resistant hypertension, clinicians should follow NICE guidance. Initially steps 1-3 include optimising therapy with an ACE inhibitor or Angiotensin II receptor antagonist plus a calcium channel blocker plus a thiazide-like diuretic. At step 4, consider further diuretic therapy with low-dose spironolactone (25 mg once daily) if the blood potassium level is 4.5mmol/l or lower, or higher dose thiazide-like diuretic treatment if blood potassium is higher than 4.5mmol/l. If further diuretic therapy for resistant hypertension at step 4 is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker. If blood pressure remains uncontrolled with the optimal or maximum tolerated doses of four drugs, seek specialist advice.[1]

## Switch savings

There is a significant difference in cost between aliskiren and alternative antihypertensives including renin-angiotensin system drugs. In England, Scotland and Wales, over £586k (£554k England, £17k Scotland, 15k Wales) is spent on aliskiren per year.

**Switching from aliskiren to an alternative antihypertensive could release savings of up to £513k nationally. This equates to savings of £801 per 100,000 patients nationally.**

## Summary

There is no data to suggest that aliskiren is more effective than other renin-angiotensin system drugs at controlling hypertension and there is no long-term safety data to warrant its use ahead of other established treatment options. Furthermore, there are significant safety concerns around adding aliskiren to other renin-angiotensin drug therapy.[1-11] In addition, aliskiren is significantly more costly than alternative antihypertensives.[12] Consequently, aliskiren is not recommended for prescribing.

## References

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12. NHS Business Services Authority. Drug Tariff May 2021. https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariff


## Additional PrescQIPP resources

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| Briefing | https://www.prescqipp.info/our-resources/bulletins/bulletin-247-aliskiren/ |
| Implementation tools | |
| Data pack | https://data.prescqipp.info/views/B247_NHSELPPAliskiren/FrontPage?:iid=1&:isGuestRedirectFromVizportal=y&:embed=y |

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