Dorset Medicines AdvisoryGroup

SHARED CARE GUIDELINES FOR PRESCRIBING ALISKIREN (RASILEZ®)

INDICATION

Aliskiren is indicated for the treatment of essential hypertension. Aliskiren is a direct inhibitor of renin, and like the ACE inhibitors and ARBs, targets the renin-angiotensin system. The recommended dose of Aliskiren is 150-300mg once a day. Aliskiren should be taken with a light meal at the same time each day.

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of aliskiren can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

REFERRAL AND INITIATION

Shared Care is only appropriate if it provides the optimum solution for the patient.

- Patients will only be referred to the GP once the GP has agreed in each individual case
- Management of hypertension should be consistent with NICE Clinical Guideline 127.
- Aliskiren is considered a fourth-line agent **for addition** at step 4 of the hypertension flowchart.

○ **Caution in diabetic patients: the combination of aliskiren with ACEi or AR2 is contraindicated. See MHRA safety advisory**

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Specialist Responsibilities	
1	To assess the patient and establish the diagnosis, determine a management strategy and ensure appropriate follow-up in conjunction with the GP.
2	Where appropriate: ○ to initiate and stabilise treatment; ○ obtain consent from the patient's GP to continue prescribing once treatment has been stabilised (usually after 4 weeks); ○ monitor the patient and their therapy at six monthly intervals.
3	To provide the GP with appropriate prescribing information and any additional information requested.
4	To be available for advice if the patient's condition changes.
5	To ensure that procedures are in place for the rapid re-referral of the patient by the GP.
6	To ensure the patient has given informed consent to their treatment.
7	To liase with the GP on any suggested changes in prescribed therapy.

General Practitioner Responsibilities	
1	Initially, to refer the patient for specialist advice.
2	Where appropriate, to continue to prescribe Aliskiren as part of a shared care arrangement (usually after 4 weeks).
3	Measure and record BP and notify specialist if BP not maintained within acceptable

	limits.
4	Monitor electrolytes and renal function in patients with diabetes mellitus, kidney disease or heart failure
5	To deal with general health issues of the patient.
6	Monitor concordance with therapy

Patient's role (or that of carer)	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Attend appropriate GP and other follow up appointments
3	Share any concerns in relation to treatment with aliskiren
4	Use written and other information on the medication.
5	Seek help urgently if suspect side effects, or otherwise unwell.

SUPPORTING INFORMATION

Dosage and Administration The recommended dose of Rasilez is 150 mg once daily. In patients whose blood pressure is not adequately controlled, the dose may be increased to 300 mg once daily. The antihypertensive effect is substantially present within two weeks (85-90%) after initiating therapy with 150 mg once daily. Aliskiren should be taken with a light meal once a day, preferably at the same time each day

Monitoring No specific monitoring requirements relating to treatment with aliskiren are required. However, as with any agent acting on the RAS system, routine monitoring of electrolytes and renal function is indicated in patients with diabetes mellitus, kidney disease, or heart failure.

Contraindications Aliskiren is contraindicated:
- in patients with a known hypersensitivity to the drug or any of the excipients
- in pregnancy and breast feeding
- in patients who have previously had angioedema whilst taking it
- in patients with hereditary or idiopathic angioedema
- in combination with ARBs or ACEIs in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m_2)

Special Warnings Aliskiren should be used with caution in

- patients taking concomitant diuretics, on a low sodium diet or who are dehydrated (first doses may cause hypotension).
- patients with serious heart failure (NYHA class III-IV) or heart failure treated with furosemide.

Patients receiving other medicinal products inhibiting the renin-angiotensin system (RAS), and/or those with reduced kidney function and/or diabetes mellitus are at an increased risk of hyperkalaemia during aliskiren therapy.

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.

In the event of severe and persistent diarrhoea, Aliskiren therapy should be stopped.

Side Effects
The most frequently reported adverse events in the short term trials were headache, nasopharyngitis, dizziness and diarrhoea. Less commonly rash and rarely, anaemia and hyperkalaemia also reported.

Angioedema can occur as a rare and serious side-effect of treatment with aliskiren. 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.

There have been reports of acute renal failure in patients with risk factors for renal dysfunction (including hypovolaemia, heart disease, liver disease, or kidney disease). Furthermore, there is an increased risk of renal insufficiency, including acute renal failure, when patients with renal artery stenosis are treated with aliskiren.

The incidence of cough was similar in placebo (0.6%) and Aliskiren treated (0.9%) patients.

Drug Interactions
The use of aliskiren in combination with ARBs or ACEIs is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m_2)

It is recommended that the effects of furosemide be monitored when initiating and adjusting furosemide or aliskiren therapy to avoid changes in extracellular fluid volume and possible situations of volume overload.

Digoxin bioavailability may be slightly decreased by Aliskiren. Preliminary data suggest that irbesartan may decrease Aliskiren AUC and Cmax.

The concomitant use of aliskiren with highly potent P-glycoprotein (P-gp) inhibitors (ciclosporin, quinidine, and verapamil), is contraindicated.

Because of the risk of therapeutic failure, fruit juices and herbal teas should not be taken whilst a patient is being treated with aliskiren.

Caution should be exercised when aliskiren is administered with ketoconazole or other moderate P-gp inhibitors (itraconazole, clarithromycin, telithromycin, erythromycin, amiodarone).

No relevant interactions with have been observed when aliskiren is used with P-gp substrates or weak inhibitors (atenolol, digoxin, amlodipine or cimetidine).

Inducers of P-gp (St. John's wort, rifampicin) may decrease the bioavailability of Aliskiren.

Based on experience with the use of other substances that affect the renin-angiotensin system, concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other substances that may increase serum potassium levels (e.g. heparin) may lead to increases in serum potassium. If co-medication is considered necessary, caution is advisable.

Non-steroidal anti-inflammatory drugs (NSAIDs) may reduce the antihypertensive effect of aliskiren. In some patients with compromised renal function (eg, dehydrated or elderly patients) aliskiren given concomitantly with NSAIDs may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible when treatment is stopped.

Meals with a high fat content have been shown to reduce the absorption of aliskiren substantially.

The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

References

1. Rasilez® (Novartis) Summary of Product Characteristics. March 2013
2. British National Formulary 65. March 2013

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