Coventry & Warwickshire

Area Prescribing Committee

Drug Positioning Statement	**DPS003 (Rev)**
Aliskiren (Rasilez ®)	July 2013

VERDICT

Coventry & Warwickshire APC recommends that aliskiren has a low place in therapy because of the lack of published long term efficacy and safety data and the availability of many alternative agents. **It should be used only as a 4th or 5th line agent and prescribers should note the contraindication in combination with ACE inhibitors or ARBs in diabetic patients and the extreme caution required with other antihypertensives in general.**

Specialist Drug List status: Not listed – This drug can be initiated in primary care

Summary notes[1]

INDICATION: Aliskiren is licensed for the treatment of essential hypertension.
PHARMACOLOGICAL ACTION: Aliskiren is the first in a new class of orally active renin inhibitors, which reduces the generation of angiotensin ll rather than blocking its effects. Aliskiren may be used alone or with **extreme caution** in combination with other antihypertensive agents (**But note drug profile below and verdict above**).
DOSE: 150mg once daily, increasing to 300mg once daily in patients whose blood pressure is not adequately controlled.
COST COMPARISON: 28 days supply (Drug Tariff, eMIMs, January 2012)

Aliskiren 150mg daily	£19.80
Aliskiren 300mg daily	£23.80

Drug profile [2, 3]

In a short term (8 week), double blind RCTs, aliskiren has shown to be as effective as other anti-hypertensive agents (A2RAs, amlodipine and hydrochlorothiazide) in reducing blood pressure in patients with mild to moderate hypertension.

When added to other anti-hypertensives, (valsartan and hydrochlorothiazide), aliskiren provided additional blood pressure lowering effects. However there is no evidence that this combination is superior to other antihypertensive combinations.

There is no data on aliskiren's use in severe hypertension or in treatment resistant hypertension which could support its place in step 4 of NICE guidelines[3]. There are no long term clinical outcome data available for aliskiren and its effects on morbidity and mortality and target organ damage.

Adverse effects in the trials included hyperkalaemia (2%), when used as monotherapy, and hyperkalaemia (4%) when used in combination with valsartan. Routine monitoring of electrolytes and renal function is advisable. Diarrhoea was the only adverse effect that occurred significantly more frequently than placebo. In post-marketing experience, renal dysfunction and cases of acute renal failure have been reported in patients at risk. There have also been reports (uncommon) of peripheral oedema, increase in blood creatinine and severe cutaneous adverse reactions (SCARs) including toxic epidermal necrolysis (TEN) and oral mucosal reactions.

Interim results from the Aliskiren Trial in Type 2 Diabetes Using Cardio-Renal Endpoints, 'ALTITUDE', (where Aliskiren 300mg, was given in addition to standard care, including an ACE inhibitor or ARB to type 2 diabetic patients at high risk of fatal or non fatal cardiovascular and renal events) suggest a higher incidence of adverse events related to non-fatal stroke, renal complications, hyperkalaemia and hypotension in this high-risk population. **Analysis of these data are ongoing by the European Medicines Agency (EMA), however as a precautionary measure, recommendations are that Aliskiren or aliskiren-containing fixed combination products should not be used in combination with angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) in patients with diabetes[6].**

Current place in therapy

NICE[4]

Although newer therapies such as the direct renin inhibitor aliskiren were discussed by the guideline development group, it concluded that there was **insufficient evidence of its effectiveness to determine its suitability for use in resistant hypertension**. For resistant hypertension NICE recommends considering further diuretic therapy with low-dose (25mg daily) spironolactone if the blood potassium level is 4.5 mmol/l or lower and to consider higher-dose thiazide-like diuretic treatment if the blood potassium level is higher than 4.5 mmol/l. If further diuretic therapy is not tolerated or is contra-indicated or ineffective consider an alpha-blocker or a beta-blocker.

SMC[5]

Aliskiren (Rasilez) is not recommended for use within NHS Scotland for the treatment of essential hypertension. Aliskiren has shown comparable efficacy to other antihypertensive agents in terms of blood pressure reduction, though its effects on mortality and long-term morbidity are currently unknown.

MTRAC[3]

Considered suitable for prescribing in primary care, however it has a lower place in therapy because of the lack of published long term efficacy and safety data and the availability of many alternative agents.

Summary

At present there is no convincing evidence to support the choice of aliskiren above other established antihypertensive agents. Its role in combination therapy has not been fully explored and its efficacy in severe hypertension is unknown.

In contrast to other antihypertensive agents, there are no long term clinical outcome data. Recent NICE guidance on hypertension does not support its role for resistant hypertension (at step 4).

References

1. SPC (Aliskiren). Novartis 14/12/2011. Available from www.medicines.org.uk
2. UKMI New Medicines Profile March 2008. No 08/04
3. MTRAC. Aliskiren. Verdict and Summary. November 2007
4. NICE CG 127. Hypertension. August 2011
5. Scottish Medicines Consortium (SMC). No 462/08: Aliskiren (Rasilez ®). 8/2/2010
6. Communication from Novartis. Direct Healthcare Professional Communication on potential risks of cardiovascular and renal adverse events with aliskiren (Rasilez™) 30/12/11