



Canadian Agency for
Drugs and Technologies
in Health

COMMON DRUG REVIEW

CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

ALISKIREN (Rasilez™ – Novartis Pharmaceuticals Inc.)

Description:

Aliskiren, the first marketed drug in a new class of anti-hypertensive agents called renin inhibitors, is approved for treatment of mild to moderate hypertension.

Dosage Forms:

150 and 300 mg tablets. The recommended initial dose is 150mg once daily and the maximum recommended dose is 300mg daily.

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that aliskiren not be listed.

Reasons for the Recommendation:

1. While aliskiren, alone and in combination with other antihypertensive agents, has been shown to reduce blood pressure in short-term trials, no long-term randomized trials have investigated if this translates into improvements in clinically important cardiovascular, cerebrovascular or renal outcomes.
2. There is insufficient evidence from clinical trials that aliskiren is effective and safe in patients with refractory hypertension, and there are multiple classes and types of antihypertensive agents currently funded by drug plans.
3. There are many other antihypertensive agents, lower or similar in cost compared to aliskiren, which have been demonstrated to improve clinically important cardiovascular and cerebrovascular outcomes (eg. thiazide diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers).

Summary of Committee Considerations:

The Committee considered a systematic review of double blind randomized controlled trials (RCTs) of aliskiren, alone or in combination with other antihypertensive agents, in patients with mild to moderate hypertension. Fourteen trials ranging in duration from six to 52 weeks in a total of 7,060 patients met the inclusion criteria for the systematic review. The trials compared aliskiren alone, or in combination with other agents, with placebo and a large number of other comparators. The primary outcome of all trials

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considered was blood pressure and none of these trials evaluated the effect of aliskiren on mortality and morbidity outcomes.

When used as monotherapy, aliskiren resulted in statistically significant lowering of mean sitting systolic and diastolic blood pressure compared to placebo. The additional magnitude of blood pressure lowering minus the placebo effect for aliskiren 150 mg was a mean of -5.4 mmHg for systolic and -3.0 mmHg for diastolic blood pressure and for aliskiren 300 mg it was a mean of -8.5 for systolic and -5.0 for diastolic blood pressure. In general, aliskiren monotherapy has been shown to reduce blood pressure to a similar extent as angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers and thiazide diuretics.

Compared to placebo, aliskiren caused statistically significant lowering of blood pressure when added to hydrochlorothiazide, calcium channel blockers or the combination of hydrochlorothiazide and an angiotensin receptor blocker.

There were no statistically significant differences in the incidence of serious adverse events or withdrawals due to adverse events in any of the trials. The incidence of hyperkalemia was higher in patients taking aliskiren compared to placebo. The combination of aliskiren and an angiotensin converting enzyme inhibitor is associated with a higher incidence of hyperkalemia than with aliskiren or an angiotensin converting enzyme inhibitor alone. The incidence of dry cough was approximately one-third to one-half in aliskiren treated patients compared to those treated with angiotensin converting enzyme inhibitors. Aliskiren use was associated with significantly less peripheral edema compared with calcium channel blockers.

The daily cost of aliskiren (\$1.14 for 150mg or 300mg) is higher than other antihypertensive agents such as hydrochlorothiazide, beta blockers and some angiotensin converting enzyme inhibitors and similar to angiotensin receptor blockers (\$1.02 to \$1.36). The manufacturer submitted a cost utility analyses, comparing treatment arms with aliskiren (in monotherapy or combination use) compared to other antihypertensive agents (used alone or in combination), which extrapolated short-term blood pressure lowering to a reduction in cardiovascular events (e.g., stroke, coronary heart disease) over a 40 year time horizon. As clinical trials with aliskiren are short-term and have not reported on these outcomes, the Committee felt that the true incremental cost-effectiveness of aliskiren was uncertain.

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. The listing status of aliskiren should be reviewed when the results of clinical trials evaluating the effect of aliskiren on clinically important cardiovascular and cerebrovascular outcomes are available.

Background:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.

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The CEDAC Final Recommendation and Reasons for Recommendation neither takes the place of a medical professional providing care to a particular patient nor is it intended to replace professional advice.

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