

Aliskiren

Product:

ALISKIREN (Rasilez®) 150mg, 300mg tablets

Class of drugs:

Renin inhibitor

Indication:

Treatment of high blood pressure

Manufacturer:

Novartis Pharmaceuticals Canada Inc.

CED Recommendation

The CED recommended that aliskiren (Rasilez) not be funded. The CED noted that aliskiren (Rasilez) has not been shown to provide improvements in long-term health outcomes or to be effective in patients whose blood pressure is difficult to control with existing treatments. Given that there are many alternatives with proven morbidity and mortality benefits, the CED recommended that aliskiren (Rasilez) not be funded until more clinical evidence is available to address concerns around effectiveness and safety.

Executive Officer Decision

Taking into consideration the CED's recommendation, the Executive Officer decided to list aliskiren (Rasilez) on the Ontario Drug Benefit Formulary based on a listing agreement with the manufacturer that addresses price, appropriate utilization, and evidence development.

Status

Listed on the Ontario Drug Benefit Formulary.

Highlights of Recommendation:

- ◆ Aliskiren (Rasilez) is used for the treatment of high blood pressure (hypertension).
- ◆ Evidence from short-term studies (ranging in duration from six to 52 weeks) has shown that aliskiren (Rasilez) is effective for lowering blood pressure when compared with placebo or other first-line blood pressure treatments, or when added to first-line therapies.
- ◆ There are no long-term studies to demonstrate that aliskiren (Rasilez) provides improvements in important clinical outcomes, such as reductions in the risk of stroke, heart attack, kidney disease and death.
- ◆ The Committee noted that more than 45 medications for high blood pressure are already funded on the Formulary. Many of these treatments have been proven to provide important long-term health benefits, including reductions in the risk of heart attack, stroke, and kidney disease, in addition to blood pressure lowering. Agents with proven benefits on these important outcomes should be used preferentially.
- ◆ The Committee considered whether aliskiren (Rasilez) should be funded for patients who do not achieve adequate blood pressure control from current therapies (i.e. as third- or fourth-line therapy), but concluded there is limited evidence that aliskiren (Rasilez) is effective in these patients.
- ◆ Because only short-term studies are available, long-term safety data on aliskiren (Rasilez) are lacking.
- ◆ Aliskiren (Rasilez) costs \$1.14 per day. Most other treatments on the Formulary, including diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, are either lower or similar in cost. Aliskiren (Rasilez) costs less than some calcium channel blockers.

◆ Overall, the Committee noted that aliskiren (Rasilez) has not proven to improve long-term health outcomes, while the Formulary currently lists many blood pressure therapies with proven morbidity and mortality benefits. Furthermore, there is currently limited clinical trial data on the proposed use of aliskiren (Rasilez) as a third- or fourth-line treatment after failure to other blood pressure drugs. The CED concluded that aliskiren (Rasilez) should not be funded until more clinical evidence is available to address concerns around effectiveness and safety.

Background:

High blood pressure (hypertension) affects one in five Canadians. Untreated, high blood pressure can lead to heart attack, stroke and kidney failure. Risk factors for hypertension include excess weight, lack of exercise, unhealthy diet, stress, and excessive alcohol consumption. Modifying these risk factors is the first approach in managing high blood pressure. Medications are required to manage patients who have high blood pressure despite lifestyle changes.

There are many types of medication used to treat high blood pressure. These include diuretics, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, calcium channel blockers, alpha-blockers, vasodilators, and central-acting agents. Some patients require multiple drugs to reduce blood pressure to acceptable levels.

Aliskiren (Rasilez) belongs to a new class of drugs, called renin inhibitors.

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Detailed Discussion:

- ◆ The Committee considered evidence from 14 randomized controlled trials. The studies were conducted in patients with mild to moderate hypertension and evaluated aliskiren (Rasilez) as a single-agent treatment or as an add-on to other antihypertensive agents.
- ◆ The majority of the studies were less than six months in duration. The primary efficacy measure used in all the trials was blood pressure lowering. None of the studies assessed the effect of aliskiren (Rasilez) on mortality, stroke, heart attack, or kidney failure.
- ◆ When used as a single-agent treatment, aliskiren (Rasilez) was shown to provide similar efficacy in blood pressure reduction as ACE inhibitors, angiotensin II receptor blockers, beta-blockers and thiazide diuretics.
- ◆ The use of aliskiren (Rasilez) as add-on treatment was evaluated in several studies. In one study, combination regimens using aliskiren (Rasilez) was assessed in patients who were unable to achieve adequate blood pressure reduction with hydrochlorothiazide alone. The study reported that the addition of aliskiren (Rasilez) to hydrochlorothiazide or to hydrochlorothiazide plus an angiotensin receptor blocker provided greater blood pressure reduction than each of the respective regimens without aliskiren (Rasilez).
- ◆ The Committee noted that more than 45 antihypertensive medications from multiple drug classes are currently available on the Formulary. Data on long-term mortality and morbidity benefits are available for drugs such as ACE inhibitors, beta-blockers, and angiotensin receptor blockers, particularly in high-risk patient subgroups, such as those with diabetes, previous heart attacks, and congestive heart failure. In comparison, aliskiren (Rasilez) has not been shown to improve long-term outcomes.
- ◆ The Committee considered whether there is a therapeutic role for aliskiren (Rasilez) in patients who are unable to achieve adequate blood pressure reduction with current therapies. It was noted that there are insufficient data on the efficacy of aliskiren (Rasilez) in these patients, and there is no evidence that aliskiren (Rasilez) is more effective in this setting than existing antihypertensive agents.
- ◆ Although aliskiren (Rasilez) was generally well-tolerated in short-term clinical studies, long-term safety data are lacking. The Committee expressed concern regarding the understudied potential for adverse effects when combined with other agents that inhibit the renin-angiotensin-aldosterone system (such as ACE inhibitors and angiotensin receptor blockers).
- ◆ Aliskiren (Rasilez) costs \$1.14 per day (for both the 150mg and 300mg tablets). It is significantly more expensive than diuretics and beta blockers, and more expensive than some ACE inhibitors. The cost of aliskiren (Rasilez) is similar to angiotensin receptor blockers. Aliskiren (Rasilez) costs less than some calcium channel blockers (e.g. amlodipine).
- ◆ Overall, the Committee noted that aliskiren (Rasilez) has not been shown to provide improvements in long-term health outcomes or to be effective in patients who are refractory to existing treatments. Given that there are many alternatives with better evidence of benefit, the Committee recommended that aliskiren (Rasilez) not be funded until more clinical evidence is available to address concerns around effectiveness and safety.

Funding Status:

Aliskiren (Rasilez) is listed on the Ontario Drug Benefit Formulary with the following therapeutic note:

For patients with moderate hypertension who have not achieved blood pressure targets while on maximally optimized therapy with a thiazide-diuretic and an angiotensin converting enzyme inhibitor (ACE-I) OR a thiazide-diuretic and an angiotensin II receptor blocker (ARB).

CEDAC Recommendation:

<http://www.cadth.ca/index.php/en/cdr/recommendations>

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



Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

For more information, please contact:

Ministry of Health and Long-Term Care

Ontario Public Drug Programs
Hepburn Block, 9th Floor
80 Grosvenor Street, Queen's Park
Toronto, Ontario M7A 1R3

or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html