Rasilez® (*aliskiren)*

Pharmacology
Renin, angiotensin, and aldosterone play an important role in essential hypertension.[5] Renin is released from the kidney when there is low renal arterial pressure. Renin catalyzes the conversion of angiotensinogen to angiotensin I.[1,2,3,5] Angiotensin I is then converted to angiotensin II, an arterial vasoconstrictor, which leads to an increase in blood pressure.[1,2,5]

Current antihypertensive drugs that affect the renin-angiotensin-aldosterone system (RAAS), ACEIs and ARBs, block the conversion of angiotensinogen to angiotensin I and II. Aliskiren works by inhibiting renin activity, thus preventing the conversion of angiotensinogen and angiotensin I. All drugs that inhibit the RAAS suppress the feedback inhibition of renin secretion which leads to an increase in plasma renin concentrations. With the use of ACEIs or ARBs this results in increased plasma renin activity; aliskiren, however, suppresses the entire RAAS which results in reduced plasma renin activity as well as decreased levels of angiotensin I, angiotensin II, and aldosterone; this leads to a greater lowing of blood pressure.[1,2]

Indications
Aliskiren is a renin inhibitor indicated for the treatment of mild to moderate essential hypertension, alone or in combination with other antihypertensives.[1,2] Concomitant use of aliskiren with either hydrochlorothiazide or valsartan produces a greater drop in blood pressure than either drug alone.[1,2,4] Hypothetically, this will also occur with other classes of drugs such as ACEIs, ARBs and beta blockers.[2] This additive effect may be due to compensation by aliskiren for the increase in plasma renin activity during angiotensin receptor blockade (see pharmacology).[4]

Contraindications
None.[2]

Adverse Effects
Diarrhea occurred in 2% of patients.[4] Cough is considerably less common than with ACEI.[1,4] Other reported side effects include nasopharyngitis, peripheral edema, influenza, and constipation.[1]

Pharmacokinetics
Oral bioavailability is low (approximately 2.5%); absorption is decreased by foods high in fat. It is recommended that doses are taken consistently with respect to meals.[2] Aliskiren is metabolized by CYP3A4, but there is a low potential for drug interactions due to minimal metabolism (25% of the drug is excreted unchanged).[1,2] The drug is excreted in both feces and urine. Aliskiren is neither an inhibitor nor an inducer of CYP enzymes.[2]

Special Populations
No dosage adjustment is required in geriatric patients or patients with hepatic or moderate renal impairment.[1,2] Aliskiren should not be used during pregnancy; drugs that act directly on the RAAS can cause fetal and neonatal morbidity and mortality.[1]

Efficacy

The safety and efficacy of aliskiren for management of hypertension were established in six randomized, double-blind, placebo-controlled studies of 8 weeks duration in patients with mild to moderate hypertension.[1,2,3] Usual dosages (150 or 300 mg OD) have been shown to decrease placebo-corrected SBP by 2.1-11.2 mm Hg and DBP by 1.7-7.5 mm Hg.[2] Doses of 600 mg daily did not further decrease blood pressure.[2,4]

A response of 85-90% reduction in blood pressure can be observed within two weeks following initiation of therapy. Maximal results are seen after four weeks of therapy.[1]

Safety

Following discontinuation there is no rebound hypertension.[2,4]

Cost

$46.72 per month for both strengths (150 mg & 300 mg).[6]

Drug Status

Approved for use in Canada.[7] Currently under review by Common Drug Review (CDR).[8]

References

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