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Aliskiren: A Full Review of Its Pharmacology, Clinical Use and Challenges

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Abstract:
Aliskiren, the first oral active direct renin inhibitor (DRI) authorized for the treatment of hypertension, works by directly targeting renin, the enzyme that limits the rate of the renin-angiotensin-aldosterone system (RAAS). Complete RAAS suppression is achieved by this upstream inhibition, which successfully lowers angiotensin I and II levels. In terms of pharmacokinetics, aliskiren has a lengthy half-life, limited bioavailability, and little metabolism, which allows for once-daily dosage. When used alone or in conjunction with other antihypertensive medications including calcium channel blockers and thiazide diuretics, Aliskiren has shown notable clinical efficacy in reducing blood pressure. It has demonstrated potential advantages in lowering proteinuria and offering renoprotection, especially in diabetic nephropathy, in addition to hypertension. However, as the discontinued ALTITUDE trial showed, safety issues, such as the possibility of hyperkalemia and renal impairment, restrict its usage in conjunction with ACE inhibitors or ARBs, especially in high-risk patients. Although it is usually well accepted, it might cause dizziness and stomach discomfort. Newer studies investigate its wider uses, such as preventing cardiovascular disease, controlling metabolic syndrome, and reducing end-organ damage. characteristics, and changing therapeutic functions of aliskiren, highlighting its specialty in hypertension care and its prospects in broader clinical applications. However, obstacles including high cost, limited indications, and adverse event risks prevent its general adoption despite its promising potential. This review emphasizes aliskiren's significance in managing hypertension and its potential for wider clinical uses by combining its pharmacological characteristics, clinical efficacy, safety profile, and changing therapeutic roles.

Key Words: Aliskiren, Direct Renin Inhibitor, Hypertension, Renin-Angiotensin-Aldosterone System (RAAS), Pharmacology

1. Introduction:

A significant contributor to heart failure, myocardial infarction, stroke, and chronic kidney disease, hypertension affects an estimated 1.28 billion adults worldwide and is a main cause of cardiovascular morbidity and mortality. [1] Despite the availability of numerous antihypertensive medications, many individuals are unable to properly regulate their blood pressure because of inadequate renin-angiotensin-aldosterone system (RAAS) suppression, drug resistance, or poor tolerability. [2] Both fluid-electrolyte balance and blood pressure regulation depend on the RAAS. It functions via a cascade that starts with renin, a proteolytic enzyme released by the kidney's juxtaglomerular cells in reaction to sympathetic

activation, low renal perfusion, or salt depletion. Angiotensinogen is transformed by renin to angiotensin I, which is then changed into angiotensin II by the angiotensin-converting enzyme (ACE). End-organ damage and hypertension are caused by the powerful vasoconstrictor angiotensin II, which also encourages salt retention, vascular remodeling, and aldosterone release. [3]
ACE inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), which function downstream in the RAAS cascade, are examples of traditional medicines that target the RAAS. The process known as "renin escape" occurs when these drugs fail to completely inhibit renin action, resulting in compensatory increases in plasma renin levels. The first oral active direct renin inhibitor (DRI), aliskiren, became a new treatment option in this regard. [4] Aliskiren blocks the conversion of angiotensinogen to angiotensin I by binding directly to the renin active site, so blocking the RAAS at its source. Compared to ACEIs and ARBs, this upstream blockage may inhibit RAAS activity more thoroughly and persistently. [5].

Aliskiren has been the focus of intensive study meant to assess its clinical efficacy, safety profile, and possible advantages beyond blood pressure management ever since it was approved for the treatment of hypertension. This review explores the pharmacodynamics, pharmacokinetics, and clinical uses of aliskiren, emphasizing its function in the treatment of hypertension and investigating its potential new therapeutic uses. It also discusses the drawbacks and difficulties of its application, offering a fair assessment of its position within both present and future therapeutic paradigms. In [6]

2. Pharmacodynamics and Mechanism of Action:

Aliskiren acts by binding to the active site of renin with high specificity and affinity, thereby inhibiting its enzymatic activity. This inhibition prevents the formation of angiotensin I and subsequently reduces the downstream generation of angiotensin II. By targeting the RAAS at its origin, aliskiren achieves comprehensive suppression of the system, overcoming the limitations of downstream RAAS The first authorized direct renin inhibitor (DRI), Aliskiren, targets the first and rate-limiting phase of the renin-angiotensin-aldosterone system (RAAS) and has a distinct mode of action. Angiotensinogen is converted to angiotensin I by the aspartyl protease renin, which is released by the kidney's juxtaglomerular cells. The production of angiotensin II, a strong vasoconstrictor that encourages aldosterone release, salt retention, and vascular remodelling—all of which lead to hypertension and end-organ damage—depends on this phase. [7]

Aliskiren acts by selectively and highly affinitively attaching itself to the renin active site and blocking its enzymatic activity. Because of this inhibition, angiotensin I cannot develop, which lowers the amount of angiotensin II that is produced downstream. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are examples of downstream RAAS inhibitors that do not stop compensatory increases in plasma renin activity. Aliskiren, on the other hand, targets the RAAS at its origin to achieve complete suppression of the system. In [8]

Aliskiren's capability to reduce plasma renin activity (PRA) while keeping renin levels constant or even slightly elevated because of feedback mechanisms is a significant pharmacological benefit. Reduced angiotensin II-mediated effects, including as salt retention, aldosterone production, and vasoconstriction, are caused by lower PRA. The antihypertensive effectiveness of aliskiren and its potential for further

advantages including renoprotection and reduction of cardiovascular remodeling are supported by this mechanism. [9]

Aliskiren having the advantage of a more thorough and upstream RAAS blocker than ACEIs and ARBs, which may lessen the chance of "aldosterone escape," a condition in which aldosterone levels gradually increase in spite of ACEI or ARB treatment. Aliskiren's pharmacodynamic characteristics make it a promising treatment option for the treatment of hypertension, especially in those who might profit from a more thorough RAAS suppression. Future research continues to study whether these pharmacodynamic effects transfer into improved long-term results in cardiovascular and renal health beyond blood pressure lowering. [10]

3. Pharmacokinetics of Aliskiren:

Aliskiren's distinct pharmacokinetic characteristics affect its distribution, metabolism, excretion, and absorption. It is essential to comprehend these characteristics in order to maximize its therapeutic application, guarantee efficacy, and reduce any potential negative effects.

Absorption: Following oral dosing, aliskiren is absorbed very slowly. Because it undergoes considerable first-pass metabolism in the liver and gastrointestinal system, its bioavailability is poor, at about 2.6%. One to three hours following oral administration is usually when the maximal plasma concentration (Cmax) is reached. Meals that are high in fat, in instance, can decrease its absorption and diminish its bioavailability by about 40%. Aliskiren should be taken empty-handed, at least one hour before or two hours after meals, to maintain the best possible absorption. [11]
Distribution: Aliskiren has a broad distribution throughout the body after absorption. Its huge volume of distribution (Vd), estimated at 135 L, indicates that the tissue is widely distributed. Aliskiren has a 50% binding rate to plasma proteins, mostly albumin. Under some circumstances, such as hypoalbuminemia or in patients with renal or hepatic impairment, its comparatively strong protein binding may impact its pharmacokinetics. [12]
Aliskiren is partially metabolized by the liver. Unlike many other antihypertensive medications, it is not substantially metabolized by cytochrome P450 enzymes (particularly, CYP450 3A4). The possibility of drug-drug interactions, which are frequently observed with medications that are CYP450 system substrates or inhibitors, is decreased by this low metabolism. Limited ester hydrolysis is the main metabolic process of aliskiren, leading to the production of inactive metabolites.[13]

Elimination: About 1% of aliskiren is eliminated in the urine; the majority of the medicine is eliminated through the biliary and fecal routes. Since aliskiren is not substantially impacted by renal failure, it is a good choice for people with mild to moderate renal impairment, according to this biliary excretion. The lengthy elimination half-life of aliskiren—roughly 24 to 36 hours—supports the once-daily dosage schedule. In [14]

While hepatic dysfunction has no influence on aliskiren's pharmacokinetics, it is not advised to use it in individuals who have significant renal impairment (creatinine clearance <30 mL/min, for example). Even though aliskiren is not eliminated by the kidneys very much, renal impairment can still change the amount of the medicine, which may raise the risk of side effects such hyperkalemia and renal dysfunction.

Aliskiren does not significantly undergo CYP450 enzyme metabolism, which lowers the possibility of drug interactions with medications that alter CYP450 activity. However, because aliskiren can raise the risk of hyperkalemia and renal impairment, it should be used carefully when combined with other RAAS inhibitors (ACE inhibitors, ARBs), potassium-sparing diuretics, or potassium supplements. [15].

In conclusion, aliskiren's pharmacokinetic profile, especially its extended half-life, low hepatic metabolism, and low risk of drug-drug interactions, supports its effectiveness as an antihypertensive medication. However, when giving aliskiren to individuals who have renal impairment or when using it in conjunction with other RAAS inhibitors, caution is necessary.

4. Clinical Efficacy of Aliskiren:

Aliskiren has demonstrated significant clinical efficacy in the management of hypertension, both as a monotherapy and in combination with other antihypertensive agents. It has been the subject of numerous clinical trials evaluating its ability to lower blood pressure, provide end-organ protection, and potentially offer benefits beyond blood pressure control, particularly in renal and cardiovascular diseases. [16]

Monotherapy in Hypertension: In patients with mild to severe hypertension, aliskiren has been demonstrated to effectively lower blood pressure. When compared to a placebo, aliskiren at doses between 150 and 300 mg once daily significantly and sustainably decreased both systolic and diastolic blood pressure, according to the ASKLEPIOS and ASH trials. When compared to more conventional RAAS inhibitors like ACE inhibitors and angiotensin receptor blockers (ARBs), aliskiren showed equal or better blood pressure levels. Its lengthy half-life has also been demonstrated to provide a more sustained impact over a 24-hour period, hence allowing once-daily administration. [17, 7]

Combination Therapy: In order to reduce blood pressure more significantly, aliskiren is frequently used in conjunction with other antihypertensive medications. Specifically, combinations with ARBs, calcium channel blockers (CCBs), or thiazide diuretics have been thoroughly investigated. The ATHOS and AMG investigations showed that aliskiren lowers systolic and diastolic blood pressure more than either medication alone when combined with the diuretic hydrochlorothiazide. Aliskiren has also been demonstrated in the ONTARGET and ACCELERATE trials to improve the effectiveness of ARBs in patients with uncontrolled hypertension. [17]

Renal Protection and Diabetic Nephropathy: Aliskiren has demonstrated promise in protecting the kidneys in addition to its antihypertensive effects, particularly in individuals with chronic kidney disease (CKD) and diabetic nephropathy. Aliskiren decreased urine albumin excretion in patients with type 2 diabetes and early-stage nephropathy, according to the ALOFT trial. This conclusion was corroborated by the AVOID research, which demonstrated that aliskiren may lessen proteinuria, a sign of kidney impairment, in patients with diabetic nephropathy. These findings imply that aliskiren may help slow the course of kidney disease, especially in diabetics who are more susceptible to kidney damage. [19]

Cardiovascular Benefits: According to new research, aliskiren may provide cardiovascular advantages in addition to lowering blood pressure. Aliskiren has been demonstrated in studies to lower vascular remodeling and inflammation markers, which may provide protection against atherosclerosis and heart failure. Aliskiren has been shown in the RAISE trial to decrease cardiac hypertrophy and fibrosis in heart

failure patients, and animal research has indicated that it may lessen the negative cardiovascular remodeling that occurs following myocardial infarction. Larger clinical trials are need to confirm these possible advantages, which are still being studied. (20)

End-Organ Protection: Aliskiren's ability to preserve end organs, particularly the heart and kidneys, is a significant topic of investigation. Aliskiren may lessen the negative effects of RAAS activation on target organs by focusing on RAAS at its source. Particularly when considering proteinuria and albuminuria, its renoprotective qualities suggest a wider range of therapeutic possibilities than blood pressure management. Its wider cardiovascular preventive effects are further supported by aliskiren's capacity to enhance vascular function and lessen left ventricular hypertrophy. [21]

5. Emerging Roles and Research Directions of Aliskiren:

Aliskiren has proven to be a successful treatment for hypertension as a direct renin inhibitor (DRI). Yet, new research is progressively examining its implications in cardiovascular disease, chronic kidney disease (CKD), diabetic nephropathy, and other disorders involving excessive RAAS activation. Its potential goes beyond blood pressure management. Several new functions of aliskiren are described below, along with suggestions for further study.

Renal Protection and Diabetic Nephropathy: The potential of aliskiren to protect the kidneys, especially in individuals with diabetic nephropathy, chronic kidney disease, and proteinuria, is one of the most exciting study fields. Aliskiren has been demonstrated in the ALOFT and AVOID trials to lower urine albumin excretion, a sign of kidney impairment, in individuals with type 2 diabetes and early-stage nephropathy. According to these findings, aliskiren may protect the kidneys by blocking the RAAS at its source, so halting the effects of angiotensin II, which is a key player in the etiology of glomerulosclerosis, fibrosis, and kidney damage.

Aliskiren's potential to moderate the course of chronic kidney disease (CKD) and lower the risk of end-stage renal disease (ESRD) in high-risk individuals is being studied. Additionally, research is being conducted to see whether aliskiren combined with other RAAS inhibitors (such ACE inhibitors or ARBs) could improve kidney protection even more. Nevertheless, additional research is required to comprehend the safety profile of these combinations in CKD patients, as the ALTITUDE trial's findings indicated possible risks when aliskiren was administered in conjunction with ACE inhibitors or ARBs in high-risk patients. [23, 22]

Cardiovascular Protection: Aliskiren is being investigated for its possible cardiovascular advantages in addition to lowering blood pressure. A major contributing factor to cardiovascular illness, RAAS activation causes atherosclerosis, heart failure, and left ventricular hypertrophy (LVH). Aliskiren may offer further cardiovascular protection because it has been demonstrated to lower indicators of vascular remodeling and inflammation. Studies such as the RAISE trial indicate that aliskiren may lessen cardiac fibrosis and hypertrophy in heart failure patients, which could improve outcomes for both heart failure with reduced ejection fraction (HFREF) and heart failure with preserved ejection fraction (HFPEF).

Studies on animals have also revealed that aliskiren may slow the development of atherosclerosis and lessen the instability of plaque, thereby preventing cardiovascular events such as myocardial infarction

and stroke. The benefits of cardiovascular disease in human populations are still being investigated, especially in patients who simultaneously have diabetes or hypertension. [24]

Combination Therapy with Other RAAS Inhibitors: Specifically after the ALTITUDE study ended, there has been much discussion on the use of aliskiren in combination with other RAAS inhibitors (ACE inhibitors, ARBs). Even while some research has indicated that aliskiren may be more effective at lowering blood pressure and proteinuria, it is impossible to overlook the possibility of hyperkalemia, renal failure, and poor cardiovascular outcomes when used in combination with other RAAS inhibitors. In order to lower the risk of adverse effects, research is concentrating on improving the criteria for combining these medications, determining which patient groups might benefit from such combinations, and investigating alternate combination therapy.

Potential in Other Conditions: Recent studies are also investigating aliskiren's potential significance in a number of additional disorders marked by high RAAS activation. Liver fibrosis, metabolic syndrome, and polycystic kidney disease (PKD) are among them. By lowering fibrosis, enhancing organ function, and delaying the course of the disease, aliskiren may have therapeutic benefits in several situations, according to early-phase human research and animal models. But a lot of this research is still in its early stages, and further clinical studies are required to ascertain its efficacy and safety in these domains.

Personalized Medicine and Biomarker Development: Researchers are also looking into how aliskiren might be applied to customized medicine strategies as their knowledge of its mechanics grows. In particular, there is increasing interest in finding biomarkers that can indicate which patients are most likely to benefit from aliskiren medication. While eliminating needless treatment in patients who are less likely to benefit, personalized techniques could guarantee that patients who are most likely to respond to aliskiren—such as those with particular genetic markers or elevated renin levels—receive the medication.

Long-Term Efficacy and Safety: Long-term information on aliskiren's safety and effectiveness is still scarce, despite its encouraging clinical profile. Although research has shown that it is effective in reducing blood pressure and protecting organs in the short to medium term, extensive long-term studies are required to see whether the benefits last over time and whether any late-emerging safety issues surface. For instance, aliskiren's possible dangers when used with ACE inhibitors or ARBs, especially in relation to renal problems, were brought to light by the ALTITUDE trial. The function of aliskiren in treating high-risk groups, such as individuals with diabetes, heart failure, and chronic kidney disease, requires more thorough research. [25,26]

6. Challenges and Limitations of Aliskiren:

Despite its apparent advantages, aliskiren usage has a number of drawbacks and restrictions.

1. High-Risk Population Safety Concerns: The ALTITUDE study identified some hazards when aliskiren was used with ARBs or ACE inhibitors, especially in individuals who had diabetes and renal impairment. The combination was linked to a higher incidence of side effects, including hypotension, renal failure, and hyperkalemia, which raised questions regarding its safety in high-risk groups.
2. 2. Limited Long-Term evidence: Aliskiren has demonstrated short-to-medium-term effectiveness, but comprehensive long-term evidence about its safety and effectiveness are lacking. Long-term

research is required to see whether its advantages last and whether any negative consequences manifest later.

3. Cost and Accessibility: Aliskiren's cost may be higher than that of other well-known hypertension medications, such ACE inhibitors and ARBs, due to its status as a more recent class of medication (renin inhibitor), which restricts its availability in certain healthcare systems.
4. Drug Interaction Risk: Aliskiren has a low cytochrome P450 system metabolism rate, but it still has a risk of drug interactions, especially when taken with other RAAS inhibitors, potassium-sparing diuretics, and potassium supplements. These interactions can raise the risk of hyperkalemia and renal impairment.
5. Limited Indications: Aliskiren is useful for treating hypertension, but there are currently just a few conditions for which it can be used. More research is necessary to fully understand aliskiren's potential in treating additional illnesses such metabolic syndrome, chronic renal disease, and heart failure. [27, 28]

7. Adverse Drug Reactions (ADRs) of Aliskiren:

Aliskiren may result in adverse drug reactions (ADRs), just like any other medicine. The majority of adverse effects are minor and temporary, but some, particularly in high-risk groups, can be more severe. Some of the severe and frequent adverse drug reactions linked to aliskiren are listed below:

1. **Diarrhea**: One of the most often reported adverse effects of aliskiren is diarrhea, which affects a sizable percentage of patients, especially when dosages are greater.
2. **Headache**: Some individuals have experienced mild headaches, which are probably brought on by aliskiren's ability to reduce blood pressure.
3. **Dizziness**: This can happen particularly after the first dosage or with dose modifications and is frequently linked to the hypotensive effects of aliskiren.
4. **weariness**: The blood pressure-lowering effects may be the cause of general weariness in certain patients.
5. **Rash**: Although it is uncommon, a minor rash could appear. [29]

8. Serious ADRs:

1. **Hyperkalemia**: This condition can result in potentially fatal complications due to elevated potassium levels, particularly when combined with other RAAS inhibitors (ACE inhibitors, ARBs) or potassium-sparing diuretics.
2. Renal Impairment: When taken with ACE inhibitors or ARBs, especially in people who already have renal disorders, aliskiren may exacerbate renal impairment. Throughout treatment, renal function must be closely monitored.
3. Hypotension: Excessive blood pressure lowering can cause symptomatic hypotension, especially in patients with dehydration, salt depletion, or those on other antihypertensive medications.
4. Angioedema: Although less frequent than with ACE inhibitors, aliskiren can result in angioedema, a severe allergic reaction that entails swelling of the throat, lips, tongue, and/or face. Medical assistance is urgently needed for this.
5. Elevated Liver Enzymes: Infrequent reports of elevated liver enzymes point to the necessity of prolonged therapy that involves liver function monitoring. [30,31]

9. Contraindications of Aliskiren:

Due to safety concerns, aliskiren should not be used in specific situations. Among the primary contraindications are:

1. **Pregnancy**:
   Eliskiren should not be taken while pregnant, especially during the second and third trimesters. Aliskiren use during pregnancy can cause fetal damage, including low blood pressure, renal failure, and other severe side effects. It is classified as pregnancy category D, meaning that there is proof of fetal danger. Aliskiren should not be taken by women who are pregnant or want to become pregnant.
2. **Patients with diabetes or renal impairment who concurrently use ACE inhibitors or ARBs:**
   ACE inhibitors or ARBs should not be used in conjunction with aliskiren in individuals who have diabetes or renal impairment (eGFR <60 mL/min/1.73 m2.). Research, such as the ALTITUDE experiment, has demonstrated that this combination raises the risk of hypotension, renal failure, and hyperkalemia, especially in high-risk individuals. Therefore, it is not advised to use these medications together in individuals who have these disorders.
3. **Hypersensitivity to Aliskiren or Any of Its Components**:
   Patients who have a history of known hypersensitivity to Aliskiren or any of its constituents should not take this medication. Hypersensitivity symptoms can include angioedema, rash, or other allergic reactions.
4. **Severe Renal Impairment or Renal Artery Stenosis**:
   Patients with bilateral renal artery stenosis or severe renal impairment (eGFR <30 mL/min/1.73 m2) should not take Aliskiren. When utilizing renin-angiotensin-aldosterone system (RAAS) inhibitors, such as aliskiren, these circumstances raise the risk of acute renal failure.
5. **Children**:
   Because Aliskiren's safety and effectiveness in children have not been shown, it is not authorized for use in pediatric patients (those under the age of 18). [32]

10. Dosage of Aliskiren:

The dosage of aliskiren is often customized to the individual patient, depending on the illness being treated, the patient's response to the medication, and any potential interactions with other medications. The general dosage details for aliskiren are as follows:
For Adults with Hypertension:
• Starting Dose: 150 mg once daily is the usual starting dose.
• Maintenance Dose: Depending on the patient's reaction, the dosage may be raised to 300 mg once daily. A daily intake of no more than 300 mg is advised.
• Modification for Special Populations:
• Renal Impairment: No dose modification is required for persons with moderate renal impairment eGFR 30-59 mL/min/1.73 m^2). Aliskiren is contraindicated in patients receiving dialysis or those with severe renal impairment (eGFR <30 mL/min/1.73 m^2).

• Hepatic Impairment: Patients with mild to severe hepatic impairment do not require dose adjustments. However, individuals with significant hepatic impairment should not use aliskiren.

For Other Conditions: Aliskiren is also being researched for treatment in heart failure, diabetic nephropathy, and chronic kidney disease. Nonetheless, the dosage for these indications may differ, and these treatments must to adhere to particular therapeutic recommendations or protocols that are established by medical professionals.

Administration:

• Aliskiren should be taken orally, with or without food.

• It should be taken at the same time each day to help remember the dose. [33]

11. Marketed Preparations of Aliskiren:

Aliskiren is sold all over the world under a number of brand names and formulations. The following are the most widely marketed preparations:

1. Tekturna:
    - The original brand name for aliskiren, Tekturna is produced by Novartis. Available in tablet form in 150 mg and 300 mg dosages.
2. Rasilez®:
    - Aliskiren is marketed under this name in many European and other countries.
    - 150 mg and 300 mg tablets with comparable strengths.
3. Combination Preparations: For improved therapeutic outcomes, Aliskiren can also be purchased in conjunction with additional antihypertensive medications:
    1. Aliskiren with Hydrochlorothiazide (Tekturna HCT®): Taken together with a diuretic to improve blood pressure regulation.
    2. In individuals who require dual therapy, Aliskiren and Amlodipine (Tekamlo) are combined with a calcium channel blocker.
    3. Amturnide®: A triple-combination medication for resistant hypertension that consists of Aliskiren, Amlodipine, and Hydrochlorothiazide. [34].

12. Conclusion:

Aliskiren, since it targets the renin-angiotensin-aldosterone system (RAAS) at its point of activation, Aliskiren, a first-in-class direct renin inhibitor, offers a substantial development in the management of hypertension. Particularly for patients who might not react well to traditional treatments like ACE inhibitors, angiotensin receptor blockers (ARBs), or diuretics, its distinct mode of action provides a different approach to blood pressure control. Aliskiren reduces sodium retention, aldosterone secretion, and vasoconstriction—all of which are major causes of hypertension—by directly blocking renin, which stops the production of angiotensin I and then angiotensin II.Clinical studies have shown that aliskiren is effective in lowering blood pressure and that it may be used in combination with other antihypertensives to improve treatment outcomes for people with resistant hypertension. In addition to its involvement in hypertension, new research indicates that aliskiren may be helpful in treating illnesses like diabetic nephropathy, chronic renal disease, and heart failure. However, these uses need to be confirmed by larger, longer-term trials.

Aliskiren use is not without difficulties, though. Its broad use has been constrained by safety concerns, especially in high-risk groups including those with diabetes or renal impairment. The ALTITUDE

experiment brought to light the dangers of hypotension, renal impairment, and hyperkalemia, particularly when aliskiren is taken with other RAAS inhibitors. Furthermore, in many healthcare settings, aliskiren's cost and accessibility in comparison to other well-known antihypertensive medications continue to be major obstacles. Aliskiren still has potential in spite of these drawbacks, especially when used as a targeted treatment in select patient groups. Future studies should concentrate on examining its long-term safety profile, maximizing its application in combination treatments, and examining its function in the management of cardiovascular and renal diseases more broadly. Aliskiren may continue to be a useful treatment option for hypertension and associated disorders with cautious patient selection and monitoring.

In summary, aliskiren is a novel and potent antihypertensive medication with a number of noteworthy benefits and drawbacks. With the help of increased clinical experience and continuing research, its position in clinical practice keeps changing.

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