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The Role of Azelnidipine and Telmisartan in Managing Stage-II Hypertension: A Comprehensive Review

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Abstract: Hypertension, called as high blood pres- sure, occurs when blood flows through the arteries at higher-than-normal pressures. Stage II hypertension is a more severe form of high blood pressure, where the systolic blood pressure is 140mm/Hg, or the dias- tolic blood pressure is 90mm/Hg. For improvement activity of stage II hypertension, Azelnidipine and Telmisartan are newer combination in market, which is effective in stage II Hypertension. Azelnidipine is a Calcium channel blocker, and Telmisartan is an Angi- otensin II receptor blockers. Azlenidipine offers selec- tively inhibiting calcium influx into vascular smooth muscle, leading to vasodilation with minimal reflex tachycardia, while Telmisartan works by blocking the vasoconstrictive effects of angiotensin II, providing additional protection to the cardiovascular system. This review examines the pharmacological profiles, efficacy, safety, and clinical outcomes associated with Azelnidipine and Telmisartan in the treatment of stage II Hypertension. This comprehensive review aims to provide a deeper understanding of the strate- gic use of Azelnidipine and Telmisrtan in the man- agement of stage II Hypertension.

Keywords: *Azelnidipine , Telmisartan, , Stage-II Hyperctension, Blood Pressure.*

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I. INTRODUCTION

A medical disease called hypertension, or high blood pressure, occurs when the blood pressure in the arteries remains consistently high. Blood pressure readings that are continuously high, with a systolic pressure of 140 mm/Hg or a diastolic pressure of 90 mm/Hg, are indicative of stage II hypertension. Serious health complications such as heart attacks and strokes, peripheral artery disease, kidney damage and failure, vision loss and blindness, and heart failure can result from stage II hypertension. Medication like diuretics, beta-blockers, ACE in- hibitors, calcium channel blockers, Angiotensin receptor blockers, can help lower blood pressure and reduce the risk of complication. [1]

II. INTRODUCTION OF AZELNIDIPINE

One treatment option for hypertension is azelnidipine, a lipophilic dihydropyridine calcium channel blocker that selectively targets L-type calcium channels. The use of azelnidipine is permitted in India by the Drug Controller General of India (DCGI). In 2020, it will be marketed under the Azusa brand (Ajanta Pharma Ltd.). The crystalline powder of azelnidipine ranges in color from pale yellow to yellow. 3-[1- (Benzyldrylazetidin-3-yl) is the IUPAC name. The compound 5-isopropyl-2-ami-no6methyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5dicarboxylate.
Azelnidipine's chemical formula is $C_{33}H_{34}N_4O_6$. It weighs 582.646 grams per mol. It is soluble in ethyl acetate, easily soluble in acetone, insoluble in water, and mildly soluble in methanol and acetic acid. Figure 1 depicts its chemical structure: [2,3]

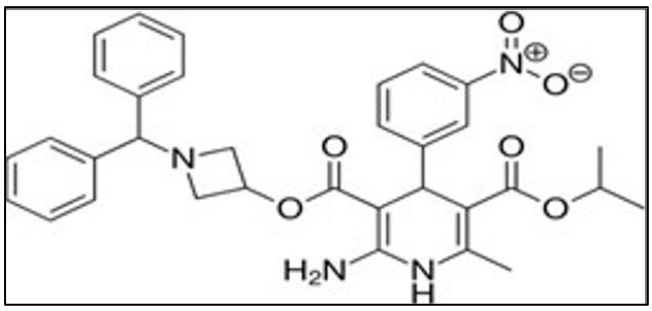

Fig 1 Chemical structure of Azelnidipine. [4]

➢ *Mechanism of Action:*

Azelnidipine inhibits trans-membrane Ca2+ influx thru the voltage-based channels of clean muscle groups in vascular partitions. Ca2+ channels are labelled into various categories, which consist of L- type, T-kind, N-type, P/Q-type, and R-type Ca2+ channels. The L-type Ca2+ channels. Normally, calcium induces muscle contraction, contributing to hypertension. When calcium channels are blocked, the vascular easy muscle does not contract, result- ing in relaxation of vascular easy muscle partitions and reduced blood strain. [5]

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➢ *Pharmacokinetics:*

Azelnidipine absorbs quickly and dose-dependently when taken orally. The liver is where azelnidipine is mostly metabolized. Hepatic cytochrome P450 (CYP) 3A4 breaks down azelnidipine; it has no active metabolite. 90% to 91% of human plasma proteins include azelnidipine. [5]

➢ *Pharmacodynamics:*

Azelnidipine works by preventing trans-membrane Ca2+ influx via voltage-dependent channels in smooth muscle cell membranes. Additionally, T-type calcium channels found in arterioles are blocked by azelnidipine. [5]

➢ *Therapeutic Uses:*

One calcium channel blocker is azelnidipine. By relaxing the blood vessels and lowering the pressure on them, it lowers blood pressure and facilitates the heart's ability to pump more blood throughout the body. In this manner, it helps patients with elevated blood pressure return to normal. [5]

➢ *Adverse Effects:*

Azelnidipine may cause common adverse effects such as headache, edema, fast heart rate, ankle swelling, sudden reddening of your face, and palpi- tations (feeling of fast or abnormal heartbeat). [5]

➢ *Contraindications:*

Azelnidipine is contraindicated in women who may be pregnant or already pregnant, as well as in com- bination with certain medications like azole anti- fungals and HIV protease inhibitors. [5]

Table 1 Summary of Azelnidipine

Chemical Name	3-[(1-Diphenylmethylazetidin-3- yl)methyl] 5-isopropyl 2- amino-6-methyl-4-(3- nitrophenyl)-1,4 dihydropyridine-3,5- dicarboxylate
Category	Antihypertensive agent
Mechanism of action	L-type Calcium Channel Antagonist
Pharmacokinetic	**Steady state concentration:** 8–16 mg orally for 2–5 hours. **Excretion:** ~30% from urine and ~50% from faeces
Therapeutic Uses	Antihypertensive, Hyper-tension.
Adverse effects	**Most common:** Dizziness, Headache,Palpitations, Peripheral Edema **Rare:** Hepatotoxicity, Worsening Heart Failure

III. INTRODUCTION OF TELMISARTAN

A non-peptide angiotensin II receptor antagonist with antihypertensive properties, telmisartan is a benzimidazole derivative. Telmisartan specifically inhibits angiotensin II's binding to the vascular muscle and adrenal gland's AT1 subtype receptor. The antagonism causes vasodilation and prevents the generation of angiotensin II-mediated aldosterone, which in turn leads to a decrease in water and sodium as well as an increase in potassium excretion, both of which are necessary for a later rise in blood pressure. Telmisartan is crystal-line powder that ranges from white to off-white. 2-[4-[[4-methyl-6-(1-methylbenzimidazol-2yl)-2 –propylbenzimidazol-1yl] methyl] biphenyl)-benzoic acid is the IUPAC designation for this compound. Telmisartan's molecular formula is $C_{33}H_{30}N_4O_2$. Molecular weight is 514.6 g/mol It is insoluble in water, spar- ingly soluble in dichloromethane, strong acid, and organic solvents and soluble in strong base and methanol. Telmisartan have become patented in 1991 and got here into medical use in 1999. It is to be had as a well-known medicine. [6]

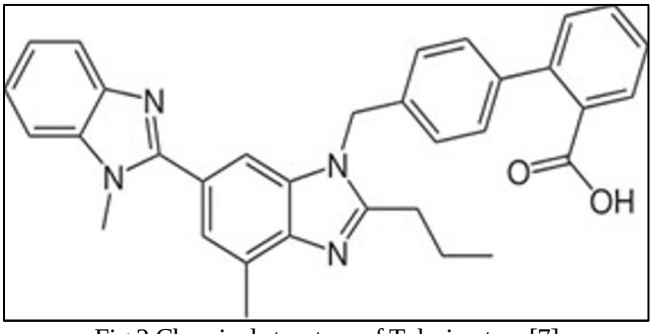

Fig 2 Chemical structure of Telmisartan. [7]

➢ *Mechanism of Action*

Telmisartan is an angiotensin II receptor blocker (ARB). It works by blocking a substance in the body that causes blood vessels to tighten. As a re- sult, telmisartan relaxes the blood vessels. This lowers blood pressure and increases the supply of blood and oxygen to the heart. [7]

➢ *Pharmacokinetics:*

Absolute bioavailability relies upon on dosage. Minimally metabolized by way of the use of conju- gation to shape pharmacologically inactive acyl- glucuronides; critical compound, glucuronide, is the metabolite identified in human plasma and urine. Cytochrome P450 isozymes do not have an effect on the metabolism of Telmisartan. [7]

➢ *Pharmacodynamics:*

Selectively blocks the AT1 receptor of angiotensin II, preventing its vasoconstrictive, aldosterone- secreting, and pro-inflammatory effects. This leads to vasodilation, reduced vascular resistance, and decreased blood pressure. High affinity and long- lasting binding to AT1 receptors, with a 24-hour duration of action, allowing once-daily dosing. No effect on AT2 receptors. [8]

➢ *Adverse Effects:*

Side results are much like specific angiotensin II receptor antagonists and embody speedy or slug- gish heartbeat, low blood strain and oedema (swell- ing of hands, legs, lips, tongue, or throat, the latter fundamental to respiratory problems). Allergic re- actions may also occur. [9]

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➢ *Contraindications:*

Telmisartan is contraindicated due to the risk of fetal toxicity, including renal dysfunction, oligohy- dramnios, and skull hypoplasia. [9]

IV. CONCLUSION

The conclusion regarding the use of azelnidipine and telmisartan in stage II hypertension can be based on their complementary pharmacological actions, Azelnidipine, with its antioxidative and vasodilatory properties, contributes to reducing arterial stiffness and improving left ventricular di- astolic function. Telmisartan's ability to inhibit the renin-angiotensin system helps to reduce the pro- gression of hypertensive organ damage, particularly in the kidneys.

Table 2 Summary of Telmiartan

Chemical Name	4'-[(1,4'-Dimethyl-2'- propyl[2,6'-bi-1H- benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]- 2-carboxylic acid.
Category	Antihypertensive agent
Mechanism of action	angiotensin II receptor blocker
Pharmacokinetic	**Steady state concentration:** 0.5 to 1 hour after oral administration **Excretion:** <1% from urine and ~97% from faeces
Therapeutic Uses	Cardiovascular Risk Reduction, Hypertension.
Adverse effects	**Most common:** Dizziness, Headache, Back Pain, Diarrhea **Rare:** Angioedema, Hepatic Dysfunction.

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