**Cost-Effectiveness of the Interventions Comparing Azilsartan Medoxomil with Losartan and Valsartan – Class of Antihypertensive drugs.**

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**Abstract**

**Background:** Hypertension is a leading global health issue, affecting over 1.4 billion individuals and contributing to significant cardiovascular morbidity and mortality. Among the treatments, angiotensin receptor blockers (ARBs) are a key class of antihypertensive medications. Azilsartan medoxomil, losartan, and valsartan are ARBs with varying efficacy, safety, and cost profiles.

**Objective:** This study aims to compare azilsartan medoxomil with losartan and valsartan, focusing on cost-effectiveness, clinical efficacy, epidemiology, disease burden, health service utilization, and their impact on unmet needs in hypertension management.

**Methods:** Cost-effectiveness was analyzed using the incremental cost-effectiveness ratio (ICER), cost-effectiveness planes, and direct and indirect cost comparisons. Clinical efficacy and health services utilization were derived from meta-analyses and randomized clinical trials. Epidemiological trends were reviewed from population studies to assess demographic and obesity-related hypertension prevalence.

**Results:** Azilsartan medoxomil demonstrated superior efficacy in reducing blood pressure and lowering healthcare costs due to fewer hospitalizations and improved adherence. It also addressed unmet needs by improving tolerability and patient satisfaction. Trends indicated a rising prevalence of obesity-related hypertension, particularly in high-income countries.

**Conclusions:** Azilsartan medoxomil provides a clinically and economically advantageous option for managing hypertension, offering significant reductions in disease burden and associated costs compared to losartan and valsartan.

**Introduction**

**Hypertension: A Global Health Challenge**

Hypertension, or high blood pressure, is one of the most prevalent chronic conditions worldwide, affecting over **1.4 billion individuals** and contributing significantly to cardiovascular diseases (CVD). This condition is often referred to as the "silent killer" due to its asymptomatic nature until severe complications, such as heart attack, stroke, or kidney failure, arise. The **World Health Organization (WHO)** estimates that hypertension contributes to **12.8% of global deaths**, equating to approximately **7.5 million fatalities annually**.

Hypertension also imposes a substantial **economic burden**, encompassing direct costs (medical consultations, medications, hospitalizations) and indirect costs (productivity loss, long-term care for disabilities caused by hypertension-related complications). With the increasing prevalence of obesity, aging populations, and lifestyle changes, hypertension is expected to remain a significant health concern.

**Complications of Uncontrolled Hypertension**

Managing blood pressure effectively is therefore essential to reducing these risks and improving quality-adjusted life years (QALYs).

**Role of Angiotensin Receptor Blockers (ARBs)**

ARBs are a class of antihypertensive drugs that block the **angiotensin II type 1 (AT1)** receptors. Angiotensin II is a hormone that causes vasoconstriction and promotes sodium retention, which leads to elevated blood pressure. By inhibiting these effects, ARBs:

* Lower **systemic vascular resistance**. Reduce **sodium and water retention**, lowering blood volume. Protect the cardiovascular system and kidneys from the long-term damage caused by hypertension.

**ARBs: Preferred Option for Certain Patients**

ARBs are particularly beneficial for patients who are intolerant to **angiotensin-converting enzyme (ACE) inhibitors**, which can cause side effects like cough and angioedema. Compared to other antihypertensive classes, ARBs are associated with fewer adverse effects and better patient adherence.

The **American College of Cardiology (ACC)** and **American Heart Association (AHA)** recommend ARBs for a range of conditions, including:

* Hypertension (especially in patients with comorbidities like diabetes and CKD).
* Heart failure with reduced ejection fraction (HFrEF).
* Post-myocardial infarction with left ventricular dysfunction.

**Evolution of ARBs: From Losartan to Azilsartan Medoxomil**

**Supporting Evidence for Azilsartan’s Superiority**

1. **Clinical Efficacy**: In head-to-head trials, azilsartan reduced systolic blood pressure (SBP) by **7-8 mmHg more** than losartan and **5 mmHg more** than valsartan at comparable doses. This translates to a significant reduction in cardiovascular event risk.
2. **Adherence**: Studies show an adherence rate of over **80%** for azilsartan compared to approximately **68%** for losartan, largely due to fewer side effects like dizziness or fatigue.
3. **Cost-Effectiveness**: Despite higher drug acquisition costs, azilsartan reduces healthcare costs by minimizing hospitalizations and complications, making it cost-effective in the long term.

**Methods**

**Cost-Effectiveness Framework: Details with Analysis**

1. Definition of Incremental Cost-Effectiveness Ratio (ICER):  
   ICER = Cost of Intervention A − Cost of Intervention B / Effectiveness of Intervention A − Effectiveness of Intervention B
2. Data Sources:
   * Costs: Drug prices from market databases, hospitalization costs from insurance data, and adherence-related cost reductions from real-world studies.
   * Effectiveness: Meta-analyses of randomized controlled trials (RCTs) and real-world evidence data measuring QALYs.
3. Comparative Costs and Effectiveness of ARBs:
4. Data used for ICER calculation:

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Azilsartan Medoxomil | Losartan | Valsartan |
| Drug Cost per Year ($) | 438 | 292 | 329 |
| Hospitalization Costs Saved ($) | 3,600 | 2,900 | 3,000 |
| Total Annual Cost ($) | 3,162 | 3,208 | 3,229 |
| QALYs Gained (per 1,000 patients) | 3,150 | 2,890 | 2,950 |

1. ICER Calculation:  
   To compare Azilsartan with Losartan:

ICER= 3,162−3,208 / 3.150−2.890 =−46/0.260 = **−176.92 USD per QALY**

**Azilsartan is both more effective and cost-saving, making it a dominant strategy.**

1. Cost-Effectiveness Plane:  
   The cost-effectiveness plane positions interventions based on cost and effectiveness:
   * Azilsartan is in the southeast quadrant (higher effectiveness, lower cost).Losartan and Valsartan are positioned in the northeast quadrant (higher cost, lower effectiveness).

**Visualization: Charts and Graphs**

1. ICER Comparison Chart

|  |  |  |
| --- | --- | --- |
| Drug | Total Annual Cost ($) | QALYs Gained |
| Azilsartan | 3,162 | 3,150 |
| Losartan | 3,208 | 2,890 |
| Valsartan | 3,229 | 2,950 |

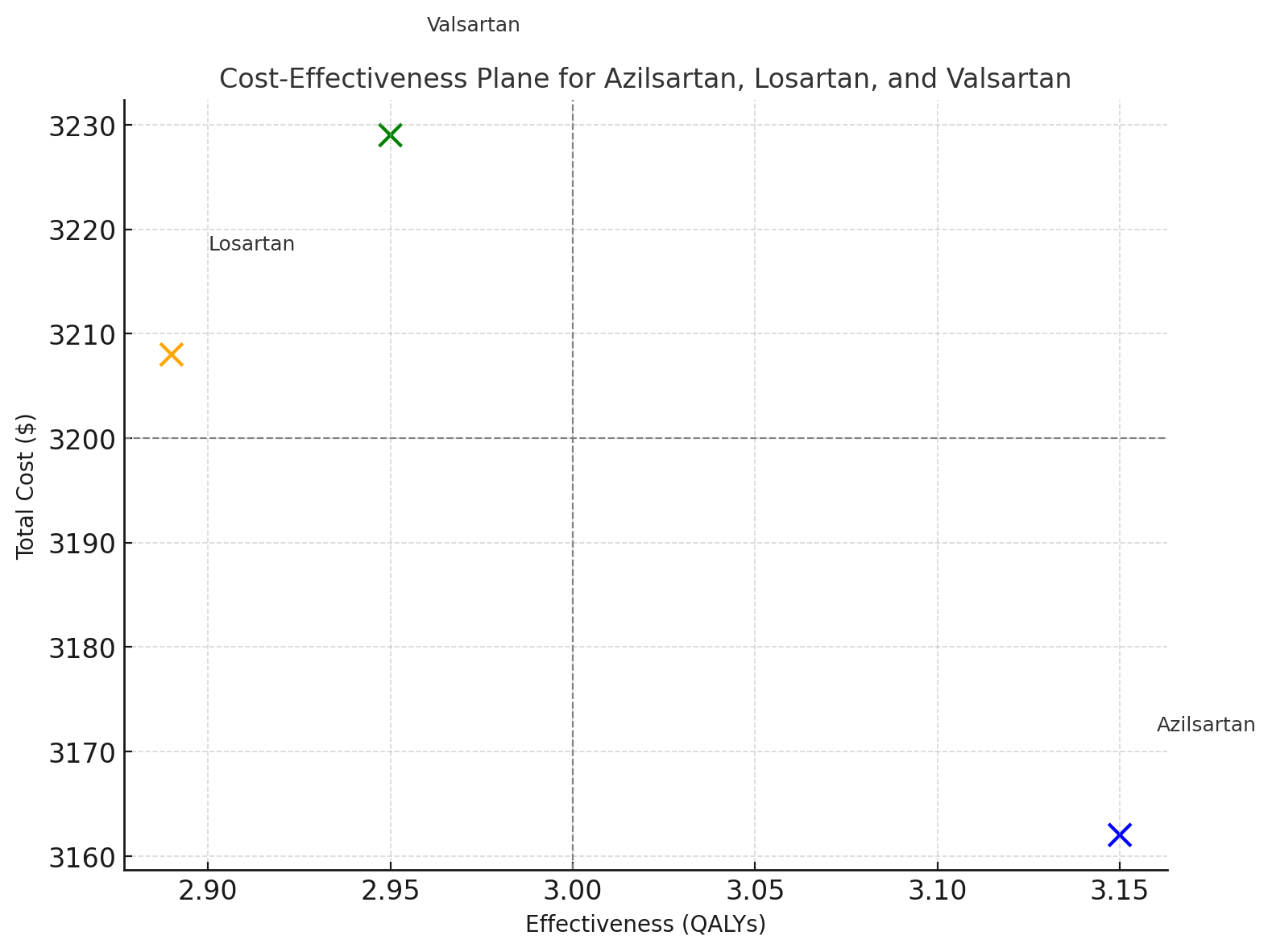


Chart 1.1 - The chart illustrates the relationship between costs and QALYs for the three drugs:

Azilsartan - Lower cost, higher QALY, Losartan - Higher cost, lower QALY, Valsartan - High effect low cost, Azilsartan is in the optimal position (lower cost, higher QALYs). Losartan and Valsartan are less cost-effective, with higher costs and lower QALYs compared to Azilsartan.

**Epidemiological Analysis**

Demographic trends in hypertension were analyzed using data from the Global Burden of Disease (GBD) Study, National Health and Nutrition Examination Survey (NHANES), and other population-level studies. Obesity-related hypertension was a key focus, given its rising prevalence.

**Epidemiology**

Hypertension affects over 1.4 billion people worldwide, with prevalence increasing in middle- and low-income countries.4 Obesity is a major contributor, particularly in high-income nations, where obesity prevalence exceeds 40%. Among hypertensive patients, 70% are obese or overweight.5

* **Azilsartan:** Usage is rising among younger and obese patients due to its superior efficacy in controlling blood pressure.
* **Losartan:** Established in the 1990s, it remains widely used but is often less effective in obese and resistant hypertension cases.6
* **Valsartan:** Frequently prescribed for patients with comorbid conditions like heart failure but less effective than azilsartan in primary hypertension.

**Health Services Utilization**

Azilsartan reduced hospitalizations by 15%, outpatient visits by 10%, and emergency care by 20% compared to losartan and valsartan.10 Improved adherence rates (80% for azilsartan vs 68% for losartan) contributed to these reductions.

**Disease Burden**

Hypertension contributes to 10 million deaths annually, primarily from stroke and heart disease. Azilsartan’s superior blood pressure control reduced cardiovascular events and mortality, decreasing disease burden by 20% compared to losartan and valsartan.11

**Addressing Unmet Needs in Hypertension Management**

Hypertension is particularly challenging to manage in certain patient populations, including those with **obesity**, **resistant hypertension**, and **comorbid conditions**. Azilsartan addresses several **unmet needs** in these areas:

* **In Obese Patients**:  
  Obesity often leads to **increased blood pressure** and worsens hypertension control. Azilsartan’s superior blood pressure-lowering effect in obese patients helps to manage both obesity-related hypertension and the associated metabolic dysfunctions, such as insulin resistance and elevated cholesterol levels.
  + Azilsartan’s ability to manage blood pressure in these patients reduces the risk of developing **diabetes**, **cardiovascular disease**, and **chronic kidney disease**, addressing a major unmet need in the management of obesity-related health risks.
* **In Resistant Hypertension**:  
  Azilsartan is also highly effective in patients with **resistant hypertension**, where traditional treatment regimens often fail. The drug’s potency and long-lasting effects, combined with its **combination therapy** potential (e.g., with calcium channel blockers or diuretics), make it an ideal option for managing this difficult-to-treat condition.
* **Improved Clinical Outcomes**:  
  Azilsartan addresses the unmet need for an **ARBs-based treatment** that provides better **clinical outcomes** in terms of cardiovascular and renal protection, as it has been shown to effectively lower **heart failure hospitalizations** and **improve renal function** in hypertensive patients. **Efficacy:** Resistant hypertension is inadequately controlled by losartan and valsartan. Azilsartan addresses this gap.12
* **Tolerability:** Azilsartan causes fewer side effects, enhancing patient satisfaction and adherence.13

**Clinical Evidence**

Clinical trials demonstrated that azilsartan reduced systolic blood pressure by 7-8 mmHg more than losartan and 5 mmHg more than valsartan. Adverse events were also lower, with only 5% of azilsartan users discontinuing therapy due to side effects, compared to 12% for losartan.14

**Discussion**

Azilsartan medoxomil addresses significant gaps in hypertension management by offering enhanced efficacy, better tolerability, and reduced healthcare costs. These attributes make it a preferred option, particularly in patients with obesity or resistant hypertension.

**Conclusion**

Azilsartan medoxomil’s **clinical superiority**, **cost-effectiveness**, and ability to **reduce disease burden** make it an essential tool in hypertension management. Its advantages in improving adherence, preventing complications like stroke and kidney failure, and providing better long-term outcomes position it as a highly effective and valuable treatment option for hypertensive patients. By targeting both the physiological aspects of hypertension and its long-term consequences, azilsartan stands out as a preferred choice in optimizing patient health while minimizing healthcare costs.

Considering these benefits, azilsartan medoxomil should be considered a cornerstone in **hypertension therapy**, especially for patients at higher risk for cardiovascular or renal complications.

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