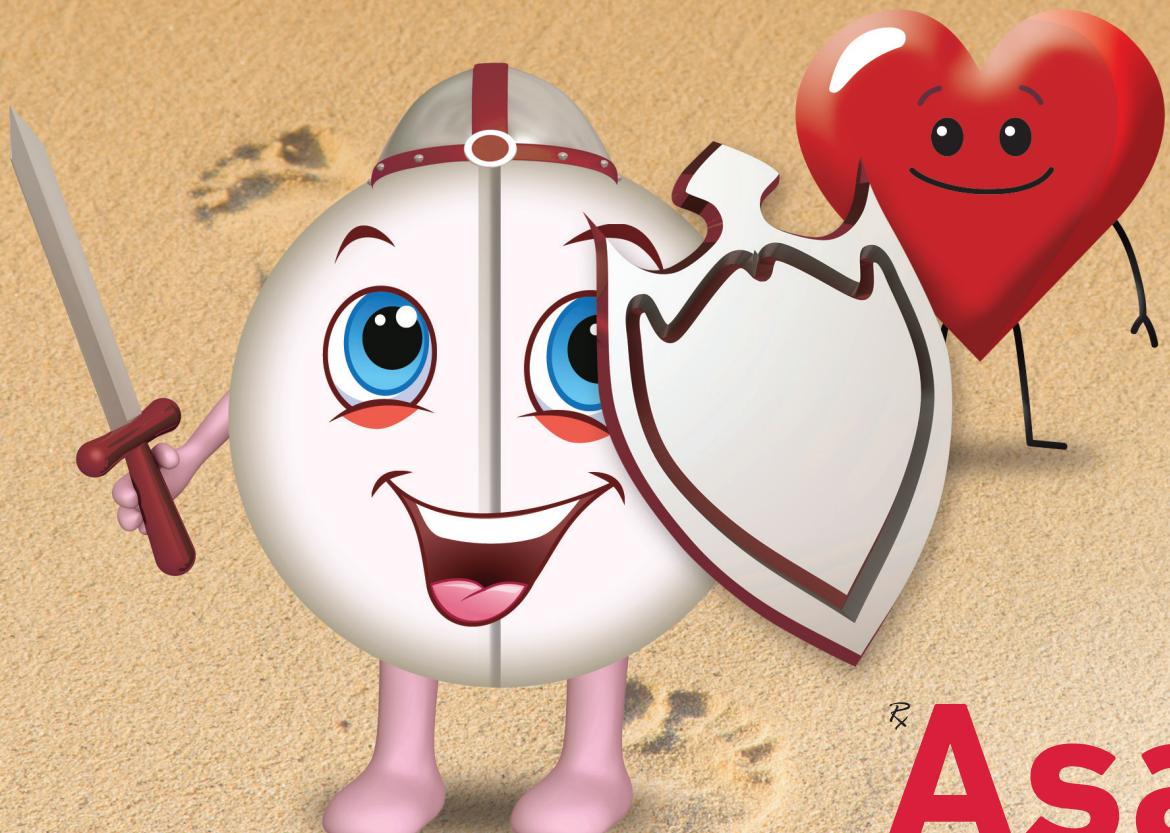


# Autobiography of Azilsartan



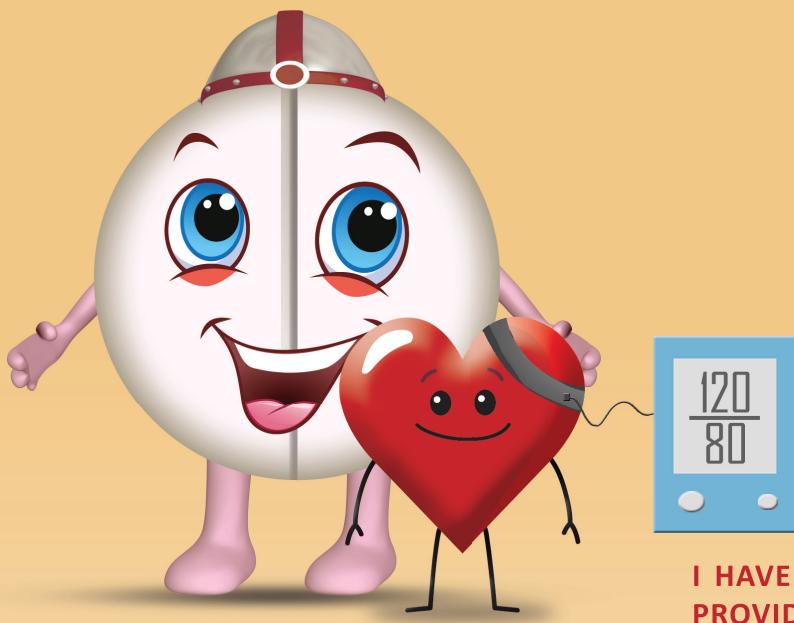
<sup>R</sup>**Asar** **40**  
**80**

Azilsartan 40/80 mg Tablets

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## I AM A RECENTLY-INTRODUCED ANGIOTENSIN II RECEPTOR BLOCKER (ARB)

Hi!

I am azilsartan, the latest inclusion to the armamentarium of ARB class for antihypertensive therapy. You may be well aware about my other colleagues, but I want you to know me better. I am the eighth member of the ARB class. I was approved by the FDA in February 2011 for the treatment of high blood pressure in adults  $\geq 18$  years of age, either as monotherapy or as combination-therapy with other antihypertensive agents.<sup>1</sup>

It is well known that hypertension is one of the main risk factors for ischemic heart disease, stroke, heart failure, and renal dysfunction.<sup>2</sup> Studies have implied that reducing mean systolic blood pressure (BP) of the order of 2 mmHg may lead to 10% decrease in the occurrence of lethal stroke and a 7% reduction in mortality due to ischemic heart disease or other vascular reasons. In contrast, target BP is attained in a meager one-fifth of the hypertensive patients.<sup>3</sup> It therefore becomes necessary to manage hypertension with a combined approach of controlling BP as well as limiting overall cardiovascular and renal morbidity and mortality.<sup>2</sup> The advent of more effective drug for the management of hypertension seems pertinent in this scenario; thus ensues my induction into the clinical setup.<sup>3</sup>

Several studies have revealed my enhanced efficacy in reducing systolic BP compared to many other antihypertensive agents.<sup>1</sup> I, either alone or in conjunction, am regarded as one of the best available pharmacological agents for the management of hypertension.<sup>2</sup>

## I HAVE HIGH AT1 RECEPTOR SELECTIVITY; I PROVIDE VERY EFFECTIVE BLOOD PRESSURE CONTROL

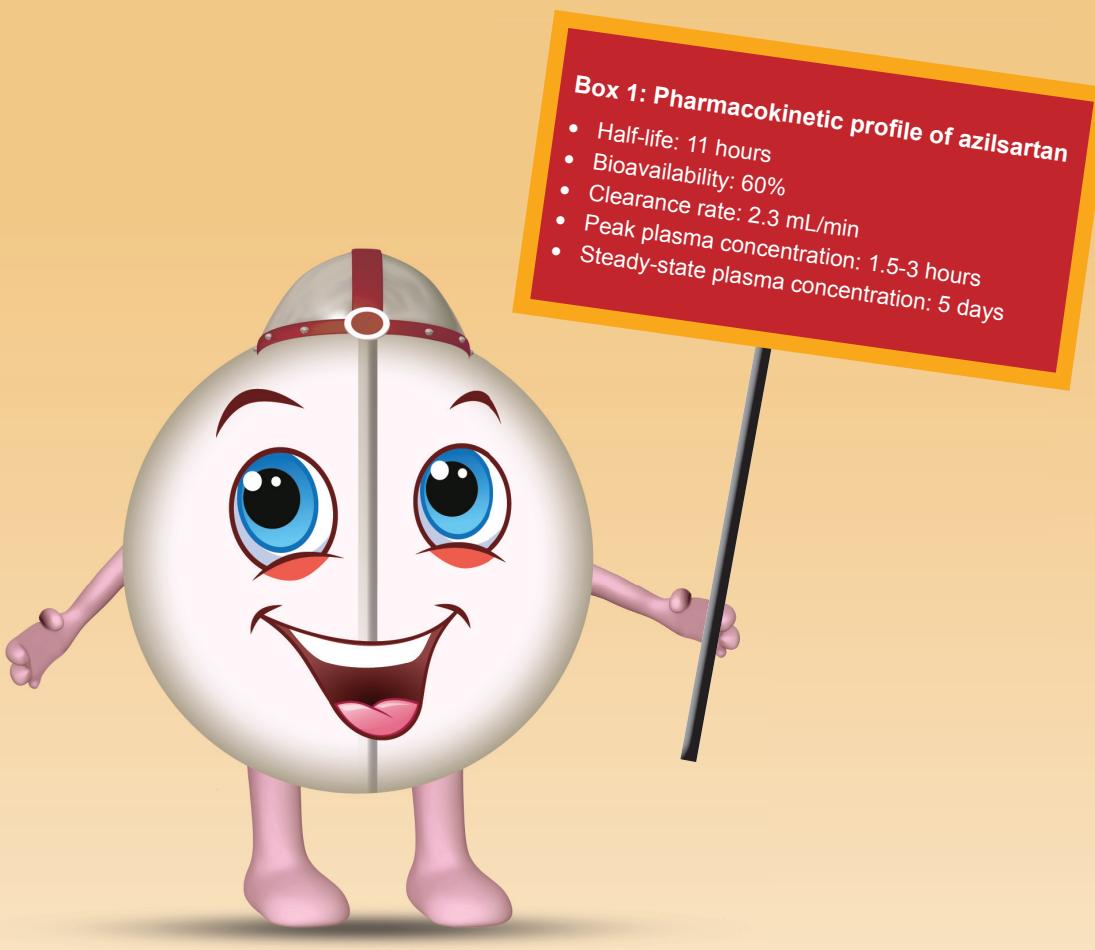
Angiotensin II, a peptide hormone, is a compelling, direct vasoconstrictor and acts as the main pressor agent in the renin-angiotensin system (RAS). It stimulates the production and secretion of aldosterone and also supports sodium reabsorption from renal tubules, leading to water retention; the final outcome being increased blood pressure.<sup>1</sup>

I am a selective blocker of angiotensin II type-1 (AT1) receptor. By selectively inhibiting angiotensin II from binding at AT1 receptor, I bring about a cascade of events such as vasodilation, and reduced effects of aldosterone; ultimately reducing the increased BP.<sup>1</sup>

I am more potent an antihypertensive agent than most of my other colleagues.<sup>4</sup> In a study by Ojima et al, I was found to be twice as potent as olmesartan or telmisartan- my colleagues- both of which are judged among the most potent ARBs for inhibiting angiotensin II binding to AT1 receptors. Moreover, I was found to be almost 5 to 20 times more potent than irbesartan and valsartan, respectively.<sup>5</sup> As compared to my colleagues, I am extremely selective for the AT1 receptor than the AT2 receptor.<sup>2</sup> In fact, my affinity for AT1 receptor is 10,000 times more than for the latter, which really is significant in that it results in more effective inhibition of the AT1 receptor.<sup>5,6</sup> This enables me to manage BP more effectively than maximum approved doses of my other colleagues.<sup>5</sup>

To be considered is another fact that the peak plasma concentration attained after oral administration of my maximum approved dose is 5 times higher than the peak plasma concentration attained after oral administration of olmesartan. This further explains my excellent antihypertensive action compared to my colleagues.<sup>5</sup>

  
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**Box 1: Pharmacokinetic profile of azilsartan**

- Half-life: 11 hours
- Bioavailability: 60%
- Clearance rate: 2.3 mL/min
- Peak plasma concentration: 1.5-3 hours
- Steady-state plasma concentration: 5 days

### I HAVE A FAVORABLE PHARMACOKINETIC/PHARMACODYNAMIC PROFILE

I am usually found in two forms: azilsartan- the active moiety and azilsartan medoxomil- the prodrug which hydrolyzes to the active agent in the gastrointestinal tract during absorption. My absorption remains unaffected by food. With an absolute bioavailability estimated at 60%, I attain peak plasma concentrations within 1.5 to 3 hours.<sup>1</sup>

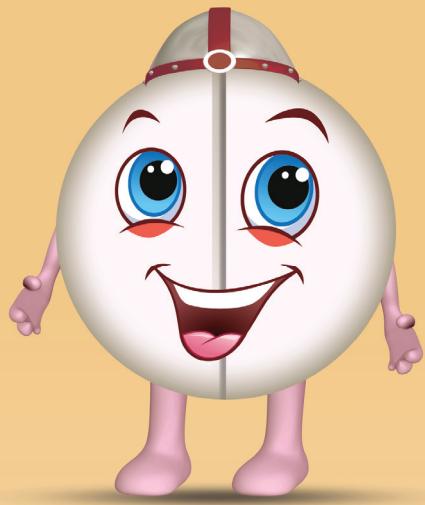
I am metabolized to an inactive metabolite M-II (formed by O-dealkylation), in the liver via cytochrome P450 (CYP) 2C9. This is followed by transformation to another inactive metabolite, M-I (formed by decarboxylation) aided by CYP2B6 and CYP2C8.

I am mostly excreted as inactive metabolites by the kidney, with a clearance of 2.3 mL/min. Subsequent to oral administration, I attain steady-state plasma concentration in five days; my elimination half-life being around 11 hours (Box 1).<sup>2</sup>

I induce a dose-dependent antihypertensive effect. This feature was studied after an infusion of angiotensin II in healthy individuals. I, in a dose of 32 mg reduced the maximal pressor effect of angiotensin II by about 90% at my peak plasma concentration. 24 hours post-administration, I decreased the pressor effect by about 60%.<sup>1</sup>

My favorable pharmacokinetic/pharmacodynamic profile implies that I should be preferred for mild-to-moderate hypertension.<sup>7</sup>

  
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## I HAVE GOOD TOLERABILITY AT ALL DOSES

I am used in dosages of 20, 40 and 80 mg daily without the need of any dose adjustment based on patient's age, sex, race, or extent of renal/hepatic injury.<sup>2</sup> A study by White et al. comparing my two dose ranges (40 and 80 mg) with that of valsartan (320 mg) and olmesartan (40 mg) revealed that I, at my maximum dose had enhanced efficacy than both colleagues in lowering systolic BP without increasing untoward events.<sup>8</sup> In another study, Bönnér et al revealed that my dose of 40 and 80 mg resulted

in significant decrease in systolic BP compared to ramipril, with remarkably increased response rates. Additionally, I was associated with less frequent adverse events.<sup>1</sup> Of special consideration is the fact that using me in 40 mg requires no dose adjustment for patients with mild, moderate, or severe chronic kidney disease, or those with end-stage renal disease in need of hemodialysis.<sup>2</sup>

The above studies and findings insinuate that coupled with good tolerability, I provide an effective treatment choice for hypertension.

**Sources:** 1. Jones JD, Jackson SH, Agboto C, Martin TS. Azilsartan Medoxomil (Edarbi): The Eighth Angiotensin II Receptor Blocker. *Pharmacy and Therapeutics*. 2011;36(10):634-640. 2. Angeloni E. Azilsartan medoxomil in the management of hypertension: an evidence-based review of its place in therapy. *Core Evidence*. 2016;11:1-10. doi:10.2147/CE.S81776. 3. Gitt AK, Bramlage P, Potthoff SA, et al. Azilsartan compared to ACE inhibitors in anti-hypertensive therapy: one-year outcomes of the observational EARLY registry. *BMC Cardiovascular Disorders*. 2016;16:56. 4. Miura S, Okabe A, Matsuo Y, Karnik SS, Saku K. Unique binding behavior of the recently approved angiotensin II receptor blocker azilsartan compared with that of candesartan. *Hypertension research: official journal of the Japanese Society of Hypertension*. 2013;36(2):134-139. 5. Kurtz TW, Kajiyama T. Differential pharmacology and benefit/risk of azilsartan compared to other sartans. *Vascular Health and Risk Management*. 2012;8:133-143. 6. De Caterina AR, Harper AR, Cuculi F. Critical evaluation of the efficacy and tolerability of azilsartan. *Vascular Health and Risk Management*. 2012;8:299-305. 7. Volpe M, Savoia C. New treatment options in the management of hypertension: appraising the potential role of azilsartan medoxomil. *Integrated Blood Pressure Control*. 2012;5:19-25. 8. White WB, Weber MA, Sica D, Bakris GL, Perez A, Cao C, Kupfer S. Effects of the Angiotensin Receptor Blocker Azilsartan Medoxomil Versus Olmesartan and Valsartan on Ambulatory and Clinic Blood Pressure in Patients With Stages 1 and 2 Hypertension. *Hypertension*. 2011; 57: 413-420.

In hypertension, 

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