

Market Distributions and Pricing/Reimbursement Policies of Antihypertensive Drugs in Türkiye

Türkiye'de Antihipertansif İlaçların Pazar Dağılımları ve Fiyatlandırma/Geri Ödeme Politikaları

ABSTRACT

The increase in the prevalence of hypertension, the development of diagnosis and follow-up methods, the positive progress of blood pressure control rates, and the increase in access to drugs cause an increase in antihypertensive drug expenditures in Türkiye. Reducing drug spending is often not easy while ensuring equal access to drugs for the population. Countries develop appropriate policies according to their political and economic structures in drug pricing and reimbursement processes worldwide. When the pricing and reimbursement amounts of antihypertensive drugs in Türkiye are reviewed, high costs stand out especially for drugs that are not covered by the reimbursement in reference European Union countries. Although there is no evidence that molecular properties are important, there are significant differences in pricing and reimbursement of different molecules of the same class in Türkiye. National health authorities may develop a new pricing/reimbursement policies for molecules not included in the reference European Union countries. Until this happens, physicians' taking into account the prices of other molecules of the same class in their prescription preferences may benefit the country's economy in drug expenditures.

Keywords: Antihypertensive therapy, pricing, reimbursement

ÖZET

Hipertansiyon prevalansının artması, tanı ve takip yöntemlerinin gelişmesi, tansiyon kontrol oranlarındaki olumlu gelişmeler ve ilaçlara erişimin artması, Türkiye'de antihipertansif ilaç harcamalarının artmasına neden olmaktadır. Halkın ilaçlara eşit erişimini sağlarken ilaç harcamalarını azaltmak genellikle kolay değildir. İlaç fiyatlandırma ve geri ödeme süreçlerinde tüm dünyadaki ülkeler, siyasi ve ekonomik yapılarına göre uygun politikalar geliştirmektedir. Türkiye'de antihipertansif ilaçların fiyatlandırma ve geri ödeme miktarlarına bakıldığında, özellikle referans Avrupa Birliği ülkelerinde geri ödeme kapsamına girmeyen ilaçlar için yüksek maliyetler göze çarpmaktadır. Moleküler özelliklerin önemli olduğuna dair bir kanıt bulunmakla birlikte, Türkiye'de aynı sınıftaki farklı moleküllerin fiyatlandırılması ve geri ödemesi konusunda önemli farklılıklar bulunmaktadır. Ulusal sağlık otoriteleri, referans Avrupa Birliği ülkelerinde yer almayan moleküller için yeni bir fiyatlandırma/geri ödeme politikası geliştirebilir. Bu gerçekleştirene kadar, hekimlerin reçete tercihlerinde aynı sınıftaki diğer moleküllerin fiyatlarını dikkate almaları, ilaç harcamalarında ülke ekonomisine fayda sağlayabilir.

Anahtar Kelimeler: Antihipertansif tedavi, fiyatlandırma, geri ödeme

Although hypertension (HT) is a preventable and controllable disease, it is the most important reason for morbidity and mortality worldwide, and its incidence is gradually increasing. The prevalence of HT was reported between 28.9% and 31.3% in different studies conducted in Türkiye.¹

Especially drugs used in the treatment of chronic diseases have an important share in health expenditures. Increasing drug expenditures force health politicians to make continuous regulations in this area all over the world. Recently, pharmacoeconomics has gained importance due to various reasons. Health expenditures of countries are increasing faster than their gross national product worldwide. Additionally, the share allocated to drugs in health expenditures is expanding more quickly than health expenditures. Drug expenses constitute 10%-15% of the health expenditures of many countries, and it ranks second after personnel costs in total health expenditures.²

PERSPECTIVE GÖRÜŞ

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There are 2 crucial issues of drug policies: pricing and reimbursement. Countries' pricing and reimbursement policies also significantly affect individuals' access to medications. This situation is one of the most critical factors that led countries to develop strategies to ensure drug access for individuals and society. Pricing and reimbursement policies developed to control pharmaceutical expenditures include external and internal reference pricing, decision-making based on health technologies and economic evaluation, value-based pricing, and participation fee application.³ While free pricing is applied in regulating drug prices in some countries, in others, the state may intervene in price determination. As a result, countries develop appropriate policies according to their political and economic structures in drug pricing and reimbursement processes worldwide.

In this article, we aimed to provide useful information to policy-makers by examining the market distribution, pricing, and reimbursement policies of antihypertensive drugs in Türkiye.

Drug Pricing and Reimbursement Policies in Türkiye

Pharmaceutical prices in Türkiye are determined by choosing the lowest producer price as the 'reference price' among the 5 European Union (EU) countries: France, Italy, Greece, Spain, and Portugal. However, if the manufacturer's price is unavailable in the reference countries, the drug's price is calculated by deducting the profit rate and value-added tax from the pharmacy price. If a drug's manufacturing price is the lowest in the manufacturing country, the manufacturer's price in that country is taken as a reference. If the drug is not included in the reference countries, the price determined by one of the other EU countries with the lowest manufacturer price is accepted as the reference price. If the drug is unavailable in EU countries, the manufacturer's price is determined depending on that country's manufacturer price. Finally, if the drug is only available in Türkiye, the price is determined by an agreement between the manufacturer and the Ministry of Health.⁴ After the reference price is determined in Euros and converted into Turkish Liras (TL), a specific discount is applied. Additional discounts are applied to the drugs included in the reimbursement list, and the sales price is determined for the warehouse. The drugs to be included in the reimbursement list are determined by the reimbursement commission under the coordination of the Social Security Institution (SSI).

Market Distribution of Antihypertensive Drugs in Türkiye

IQVIA Holdings, Inc. sales data show an increase of 0.61% in box-based sales of antihypertensive drugs in 2021 compared to 2020 and an increase of 17.5% in the costs of antihypertensive drugs to the government (Figure 1).

According to the unit sales of antihypertensive drugs in Türkiye, beta-blockers (BBs) ranked first with 33.7%, angiotensin II receptor blockers (ARBs)+diuretic combination drugs were ranked second with 18.5%, calcium channel blockers (CCBs) were ranked third with 10.7%, and ACE inhibitors+thiazide fourth with 8.6% (Figure 2).

Considering the market shares, fixed-dose rates of renin-angiotensin-aldosterone antagonists and CCBs (7%) are pretty inadequate. It is noteworthy that ARB+diuretic fixed-dose

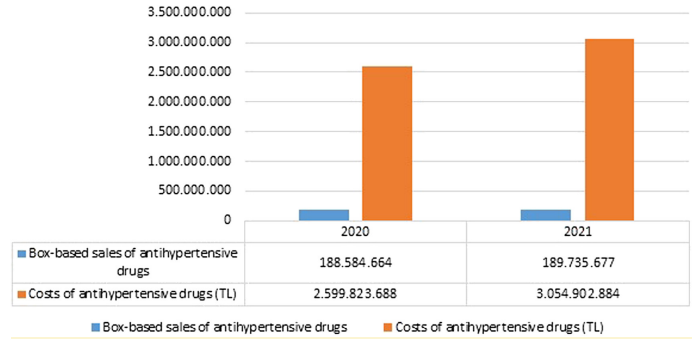


Figure 1. The unit sales and the costs of antihypertensive drugs in 2020 and 2021 of Türkiye.

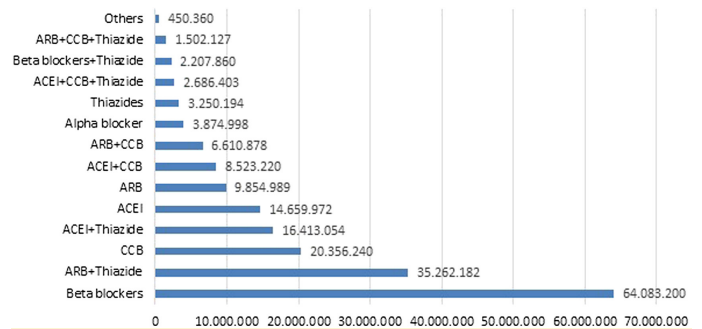


Figure 2. The unit sales of antihypertensive drugs at 2021.

combinations are highly preferred over angiotensin-converting enzyme inhibitors (ACEIs)+diuretic fixed-dose combinations. When all antihypertensive drugs were evaluated, renin-angiotensin-aldosterone system (RAAS) blockers were the most preferred antihypertensive agents. As expected, the other commonly preferred antihypertensive agents were diuretics and CCBs (Figure 3).

Evaluating the distribution of the antihypertensive market in 2021 on a budgetary basis, benidipine from the CCB group (Figure 4), eprosartan from the ARB group (Figure 5), and verapamil+trandolapril (Figure 6) from the ACEI+CCB fixed-dose drugs have higher budgetary shares compared to the other drugs in the same class, according to the box sales rates.

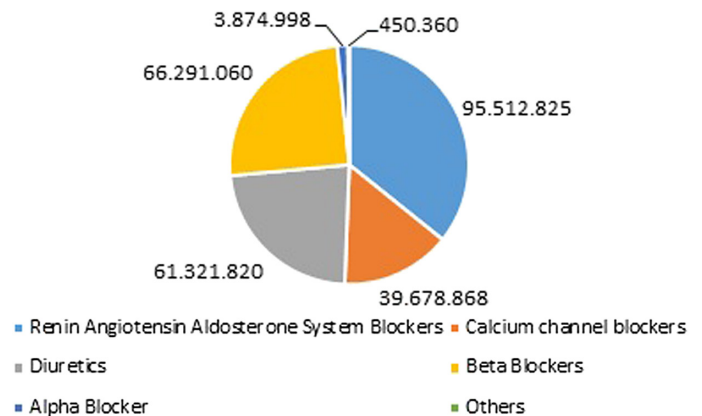


Figure 3. The distribution of the antihypertensive drugs' class.

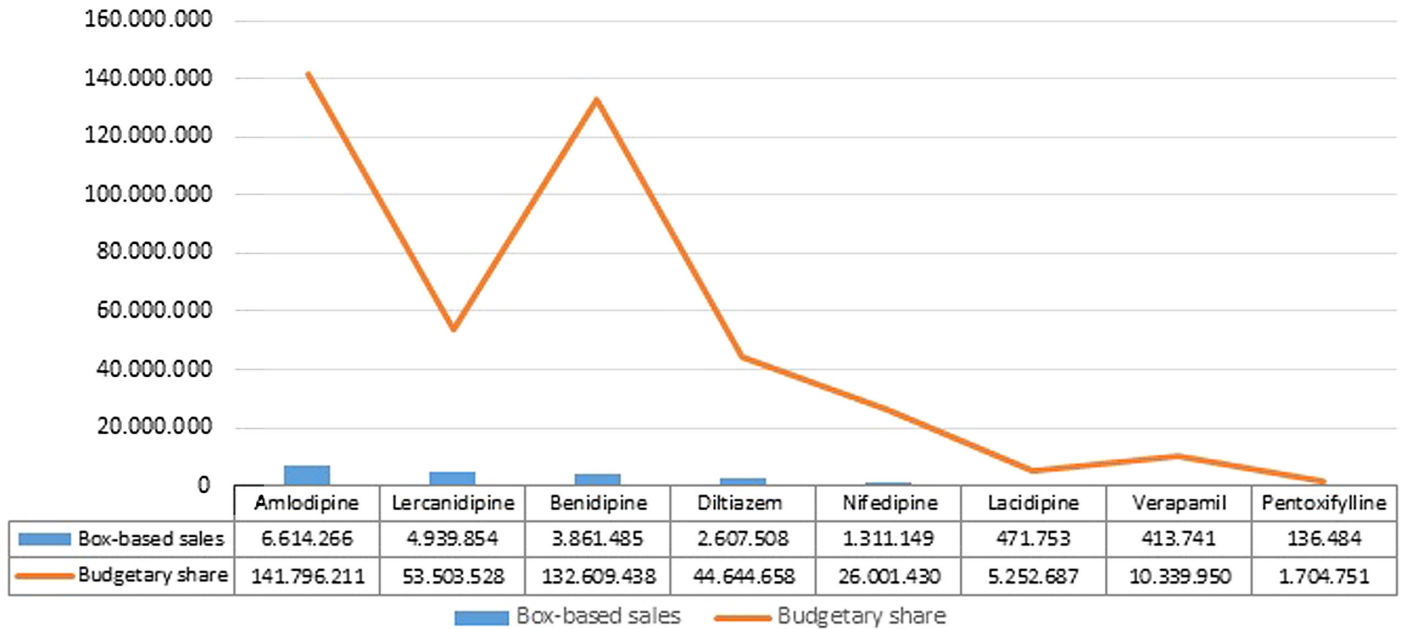


Figure 4. The unit sales and budgetary shares of calcium channel blockers (2021).

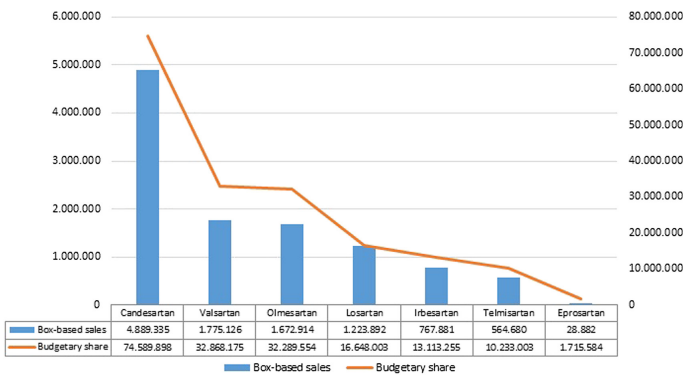


Figure 5. The unit sales and budgetary shares of angiotensin II receptor blockers (2021).

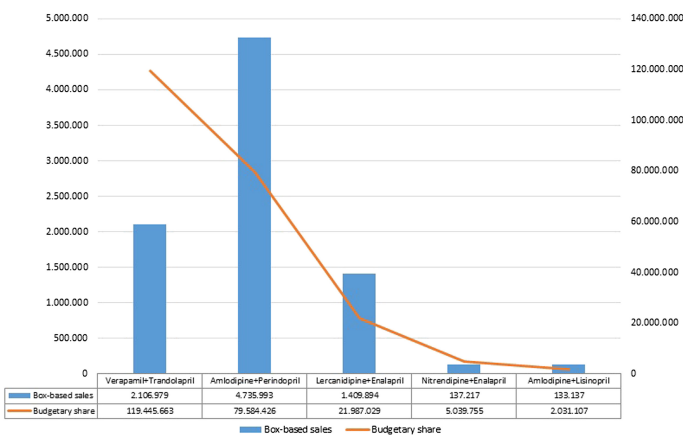


Figure 6. The unit sales and budgetary shares of combination angiotensin II receptor blockers (2021).

Table 1 shows the drug classes within the scope of reimbursement in Türkiye and the lowest and highest reimbursement amounts for 2022.

Table 2 compares the reimbursement amounts for eprosartan, benidipine, and verapamil+trandolapril with the best-selling molecules in their class.

Discussion

The growth rate of the anti-hypertensive market in 2020 (0.61%) was slower than expected, probably due to the coronavirus disease 2019 pandemic. However, contrary to expectations, antihypertensive drug expenditures increased (17.5%) during the pandemic. The impact of the ongoing economic crisis

Table 1. Drug Classes Within the Scope of Reimbursement in Türkiye and the Lowest and Highest Reimbursement Amounts for 2022

Drug Class	The Lowest Reimbursement Amounts (TL)	The Highest Reimbursement Amounts (TL)
Beta-blockers	21.48	40.64
ACEIs	22.25	41.32
ARB	29.44	149.57
CCBs	14.15	117.53
ACEI + CCB	34.49	185.07
ARB + CCB	34.37	56.82
ACEI + CCB + diuretic	36.58	50.14
ARB + CCB + diuretic	33.86	48.90

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; TL, Turkish Liras.

Table 2. Reimbursement Amounts of Eprosartan, Benidipine, and Verapamil+Trandolapril Compared to the Best-Selling Molecules in Their Class

Drug Class	Best-Selling Molecule	2022 Reimbursement Price (TL)	Molecule	2022 Reimbursement Price (TL)
ARBs	Candesartan		Eprosartan	
	8 mg	32.63	600 mg	149.57
	16 mg	39.63		
	32 mg	79.82		
CCBs	Amlodipine		Benidipine	
	5 mg	14.15	4 mg	68.20
	10 mg	28.21	8 mg	117.53
ACEI+CCB	Amlodipine + perindopril		Verapamil + trandolapril	
	5 mg/5 mm	38.41	180 mg/2 mg	185.07
	10 mg/10 mm	50.42	240 mg/4 mg	91.04

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; TL, Turkish Liras.

due to the worldwide pandemic on this increase is undeniable. In addition, finding raw materials due to the pandemic, a severe problem, has also affected the pharmaceutical industry, thus increasing costs.

Considering the unit sales of antihypertensive agents, doctors' preferences in Türkiye are in accord with the recommendations in national and international HT treatment guidelines. This situation is also the result of the Rational Drug Use Incentive Program carried out by the Ministry of Health of the Republic of Türkiye for a long time. The fact that BBs are the best sellers in terms of unit sales in Türkiye may be due to their widespread use in cardiovascular and neuropsychiatric fields such as heart failure, coronary artery disease, tachycardia, anxiety, and tremor. However, since diagnostic information is not available from IQVIA sales data, it is not possible to infer the rate of use of these drugs in the diagnosis of HT.

Considering the distribution of all antihypertensive agents, the fact that RAAS blockers are the most preferred shows that RAAS blockade-based combination therapies are accepted in Türkiye.⁴ The second most frequently preferred drug class is diuretics, which comes from the fact that salt consumption is significantly higher in Türkiye than in other societies.¹ RAAS blocker+ diuretic combination constitutes 30% of all antihypertensive agents. The class of antihypertensive drugs most commonly combined with diuretics are ARBs.

The ACEI+CCB fixed-dose combination accounts for 4% of the antihypertensive market; ARB+CCB fixed-dose combination constitutes 3%. The usage rates of fixed-dose drugs are lower than expected. In the HT treatment guideline published recently, the European Society of Cardiology emphasizes that the use of fixed-dose single-tablet combination drugs will increase patient compliance and provide economic benefits in drug costs.⁵ If the prescription rates of these fixed-dose drugs are increased, it is clear that it will contribute to the country's economy when the reimbursement amounts are taken into account. Especially, a significant advantage is seen in the prices of fixed-dose single-tablet triple combination drugs with diuretics. For this reason,

the preference of these drugs in appropriate patient groups will be beneficial in reducing drug expenditures.

The prices of different molecules in different groups and even in the same class vary. The price of the molecule alone is not the determining factor when deciding which molecules to include in reimbursement. Many countries use pharmacoeconomic assessments to make reimbursement decisions and develop guidelines. This indicates that health authorities may exclude drugs that do not offer advantages in cost-effectiveness analyses from the scope of reimbursement. The prices of eprosartan, benidipine, and verapamil+trandolapril in Türkiye are significantly higher than that of similar molecules in their groups because these drugs are not covered for reimbursement in reference European countries. The prices of these drugs in Türkiye are determined according to their costs in the countries where they are produced.

Numerous randomized studies on antihypertensive therapy have been reviewed in many international HT treatment guidelines published to date. It has been concluded that the main benefits of antihypertensive therapy are primarily due to blood pressure reduction and are largely independent of the drugs used. However, there is uncertainty and even controversy over treatment thresholds, first-choice drugs, and add-on drugs. The controversy is partly related to the price of different drugs and partly to disagreements about how to interpret the available evidence about the efficacy and side effects of different drugs. Although meta-analyses sometimes seem to claim the superiority of one drug class over others, this conclusion is primarily based on the selection of studies. Current large-scale meta-analyses have not shown clinically significant differences between drug classes. Therefore, current guidelines emphasize that diuretics, BBs, CCBs, ACE inhibitors, and ARBs are all appropriate for initiating or maintaining antihypertensive therapy, either as monotherapy or in combination. Specific drug groups with evidence-based data may be preferred only in some patient groups. There is no evidence to suggest that molecular properties are important among the drug classes preferred for mandatory indications. It cannot be said that one molecule is superior to another within the same drug class. Molecular features can change tolerance

rates by making a difference in terms of side effects such as cough and ankle edema. For example, in a study investigating the long-term tolerability of lercanidipine, amlodipine, and lacidipine in elderly hypertensives, it was found that lercanidipine is more easily tolerated in the elderly. However, all 3 molecules reduce blood pressure equally.⁶ Therefore, cost-effectiveness should also be considered, since clinical benefit will not differ in pricing and reimbursement of different molecules from the same drug class.

Conclusion

The increase in the prevalence of HT, the development of diagnosis and follow-up methods, the positive progress of blood pressure control rates, and the increase in access to drugs cause an increase in antihypertensive drug expenditures in Türkiye. Reducing drug spending is often not easy while ensuring equal access to drugs for the population. Regulations made for this purpose are mainly related to pricing and reimbursement of drugs.

Since SSI is the primary source of financing the ever-increasing pharmaceutical expenditures in Türkiye, we believe that policymakers should make arrangements for the pricing and reimbursement policies to be sustainable in the long term. Preferring fixed-dose combination regimens and generic drugs in antihypertensive treatment is very likely to reduce drug expenditures.

When the pricing and reimbursement amounts of antihypertensive drugs in Türkiye are reviewed, high costs stand out especially for drugs that are not covered by the reimbursement in reference EU countries. Although there is no evidence that molecular properties are important and that the class effect of drugs is accepted, there are significant differences in pricing and reimbursement of different molecules of the same class in Türkiye. National health authorities may develop a new pricing/reimbursement policies for molecules not included in the reference EU countries. Until this happens, physicians' taking into

account the prices of other molecules of the same class in their prescription preferences may benefit the country's economy in drug expenditures.

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