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RESEARCH ARTICLE

Antihypertensive Drug Box Sales Between January 2019 - June 2024 in Turkish Drug Market: Investigating the Drug Group and Fix-Dose Combination Sales

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SUMMARY

The financial and emotional burden of chronic diseases, including hypertension, has been rising. The objective of this study was to assess the trends in box sales of antihypertensive medications in Türkiye and to compare these trends across the antihypertensive medicine subgroups. This study analyzed retail and hospital box sales of antihypertensive drug groups recommended by guidelines between January 2019 and June 2024. The data used in this study were obtained from IQVIA. While antihypertensive drugs sold a total of 176,453,254 boxes in 2019, they were sold 203,690,099 boxes in 2023, a 15.44% increase. The best-selling drug group is the Renin-Angiotensin System (RAS) antagonists. Angiotensin Receptor Blocker-Diuretic fixed-dose combination (FDC) is the best-selling subgroup in the RAS antagonists. FDCs of RAS antagonists are more often used than their mono forms, and in 2022 and 2023, FDCs of calcium channel blockers have begun to outsell their combined formulations. Triple FDCs of the RAS antagonists with calcium channel blockers and diuretics have been increasing regularly. In Türkiye, drug groups that have had the highest share in the antihypertensive drug market in recent years are the groups recommended in the guidelines. Increasing the triple FDC consumption is valuable for the rational treatment of hypertension.

Key Words: *Antihypertensive drugs; Rational drug use; box sales; Fixed-dose combination.*

Türkiye İlaç Pazarında Ocak 2019 - Haziran 2024 Arası Antihipertansif İlaç Kutusu Satışları: İlaç Grubu ve Sabit Doz Kombinasyon Satışlarının Araştırılması

ÖZ

Hipertansiyonun da içinde bulunduğu kronik hastalıkların finansal ve duygusal yükü artmaktadır. Bu çalışmanın amacı Türkiye'de antihipertansif ilaçların kutu satış eğilimlerini değerlendirmek ve bu eğilimleri antihipertansif ilaç alt grupları arasında karşılaştırmaktır. Bu çalışmada Ocak 2019 ile Haziran 2024 arasındaki kılavuzlarda önerilen antihipertansif ilaç gruplarının perakende ve hastane kutu satışları analiz edildi. Bu çalışmada kullanılan veriler IQVIA'dan elde edildi. Antihipertansif ilaçlar 2019 yılında toplam 176.453.254 kutu satarken, 2023 yılında %15,44 artarak 203.690.099 kutu satıldı. En çok satan ilaç grubu Renin-Anjiyotensin Sistem (RAS) antagonistleridir. RAS antagonistleri içinde en çok satan alt grup Anjiyotensin Reseptör Blokörü-Diüretik sabit doz kombinasyonudur (SDK). RAS antagonistlerinin SDK'ları mono formlarından daha sık kullanılmaktadır ve 2022 ve 2023'te kalsiyum kanal blokörlerinin SDK'ları da kombine formülasyonlarından daha fazla satmaya başlamıştır. RAS antagonistlerinin kalsiyum kanal blokörleri ve diüretiklerle üçlü SDK'ları düzenli olarak artmaktadır. Türkiye'de son yıllarda antihipertansif ilaç pazarında en yüksek paya sahip olan ilaç grupları kılavuzlarda önerilen gruplardır. Üçlü SDK tüketiminin artması hipertansiyonun rasyonel tedavi uygulamaları açısından değerlidir.

Anahtar Kelimeler: *Antihipertansif ilaçlar; Akılcı ilaç kullanımı; kutu satışları; Sabit doz ilaç kombinasyonu.*

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INTRODUCTION

In the last decades, the increase in the geriatric population has raised the concern of many chronic diseases in terms of the burden of disease and financial aspects. Currently, chronic diseases such as hypertension, diabetes, and coronary heart disease have been causing significant financial and emotional burdens (Sağlık Teknolojileri Değerlendirme Raporu 3). The World Health Organization (WHO) states that cardiovascular diseases cause nearly 18 million deaths worldwide each year. A significant portion of these deaths are due to heart attacks and strokes (WHO, 2021). In 2021, 28% of the total deaths in OECD countries were due to circulatory system diseases (ischemic heart disease 11%, stroke 6%), while this rate was 35% in Türkiye (ischemic heart disease 15%, stroke 7%) (Health Statistics Yearbook 2022). WHO estimates that approximately 1.28 billion adults aged 30-79 worldwide, most of whom (two-thirds) live in low- and middle-income countries, have hypertension (WHO, 2023). It is seen that the primary health problem experienced by individuals aged fifteen and over in 2022 is hypertension, with a rate of 16.1%, after waist and neck problems (Health Statistics Yearbook 2022). According to a prevalence study published in 2021, more than one-third of the adult population in Turkiye suffers from hypertension. (Bayram et al., 2021).

According to the data of the Ministry of Health, a total of 2,268.5 million boxes of medicine were sold in Türkiye in 2017, while this number reached 2,643.2 million in 2022. The sales volume of cardiovascular system drugs was 225.9 million boxes in 2017, while it was 291 million boxes in 2022. In other words, while the total box increase was 17%, it was 29% for cardiovascular system drugs in that period. When the amount of medicine consumed per 1000 people was investigated, it was seen that the consumption of cardiovascular system drugs increased from 176.4 to 232.6 between those years (Health Statistics Yearbook 2022).

Various drug groups with different pharmacological mechanisms of action are used in the treatment of hypertension. These drug groups include diuretics (thiazide diuretics, potassium-sparing diuretics, loop diuretics), those that block angiotensin production or affect Angiotensin Receptor Blockers (ARB), Angiotensin Converting Enzyme (ACE) inhibitors, renin inhibitors, sympatholytics (alpha-blockers, beta-blockers, adrenergic neuron blockers, ganglion blockers) and vasodilators (calcium channel blockers, other direct-acting vasodilators) (Benowitz, 2018). Some of these drugs are recommended in the guidelines for the first-stage pharmacotherapy of hypertension. Although there are some differences between these guidelines, ACE inhibitors, ARBs, calcium channel blockers (some guidelines recommend dihydropyridines which are vasoselective calcium channel blockers), and diuretics (thiazide group diuretics, some guidelines also recommend potassium-sparing diuretics) are recommended as first-line hypertension pharmacotherapy. Beta-blockers are also recommended as first-line treatment in patients with ischemic heart disease or in patients who want to manage heart rate (Arıcı et al., 2015; Whelton et al., 2018; Guideline for the pharmacological treatment of hypertension in adults, 2021; Hipertansiyon Tanı Ve Tedavi Kılavuzu, 2022; McEvoy et al., 2024). In addition, the effectiveness and safety of fixed-dose combinations of these antihypertensive drugs have been demonstrated, and WHO included these drugs in the essential medicines list in 2019 (Salam et al., 2020).

In this study, we aimed to evaluate the box sales trends of essential drugs recommended in national and international guidelines for treating hypertension in Türkiye according to drug groups and subgroups and to compare these trends among themselves and with total cardiovascular system drug sales trends.

MATERIAL AND METHOD

This study analyzed retail and hospital box sales of antihypertensive drug groups recommended by national and international guidelines. The data used

in this study were obtained from IQVIA. IQVIA is a global pharmaceutical consultancy company that collects sales and price data of medicines from many different countries. The company collects data from the pharmaceutical market supply and distribution chain. The IQVIA data used herein includes the number of boxes sold from wholesalers for the selected sample of medical preparations for 66 months between January 2019 and June 2024. The data includes 3-month periods starting from the first quarter of 2019 and ending in the second quarter of 2024. Thus, 22 time points were used in the study. In addition, box sales data for 5 years between 2019 and 2023 were used as annual box sales. The data were provided by IQVIA as monthly drug box sales, indicating the active ingredients and Anatomical Therapeutic Chemical (ATC) groups. ATC is a system for the categorization of pharmaceutical active ingredients based on their effects on the organs or systems (ATC/DDD Toolkit). In the study, the pharmaceuticals were grouped according to ATC groups and active ingredients. The data does not contain any patient or personal information or prescription information.

First, cardiovascular system drugs (Class C according to ATC classification) were grouped at the ATC3 level and annual box sales volume between 2019-2023 was calculated. Data for double and triple fixed-dose combination pharmaceuticals containing active ingredients from different groups have been included only under the drug groups they are classified within the ATC system. Data for cerebral and peripheral vasotherapeutic drugs, topical antihemorrhoid drugs, and medications used in the treatment of pulmonary arterial hypertension were excluded from the study.

Then, the annual box sales data of antihypertensive drugs between 2019 and 2023 were examined. The data of drug groups included in national and international guidelines as antihypertensive drugs were examined within the framework of ATC4 level classification (Arıcı et al., 2015; Whelton et al., 2018; Guideline for the pharmacological treatment of hypertension in adults, 2021; Hipertansiyon Tani Ve Tedavi Kılavuzu, 2022; McEvoy et al., 2024). The antihypertensive drug groups whose sales data were examined were ACE inhibitors, ARBs, calcium channel blockers, beta-blockers, centrally acting sympatholytics, other peripherally acting sympatholytics, thiazide group diuretics, and potaatc4ssium-sparing diuretics. In addition to the mono forms of these drugs, their fixed-dose combination forms were also examined as separate subgroups. The fixed-dose combination subgroups are ACE inhibitors + diuretics, ACE inhibitors + calcium channel blockers, ARB + diuretics, ARB + calcium channel blockers, ARB + neprilysin inhibitors, calcium channel blockers + statins, thiazide + potassium-sparing diuretics and beta blockers + diuretics in two drug fixed-dose combinations, and ACE inhibitors + calcium channel blockers + diuretics and ARB inhibitors + calcium channel blockers + diuretics in triple-drug fixed-dose combinations.

The box sales data of diuretics, drugs that block angiotensin production or effect (ARB and ACE inhibitors), beta-blockers, and calcium channel blockers were examined independently. These four groups were classified separately according to their mono and fixed-dose combination, and the 3-month box sales data between the first quarter of 2019 and the second quarter of 2024, change rates, and the amounts of medical preparations in these groups were shared separately.

The changes in the total sales volume data of the drugs examined in the study were compared with the sales volume changes of cardiovascular system drugs in the same period. In this study, grouping, addition, and percentage calculations were performed using Microsoft Excel. Additionally, graphs and tables were created with Microsoft Excel.

RESULTS AND DISCUSSION

While cardiovascular system drugs sold a total of 225,038,590 boxes in 2019, it increased by 18.10% and sold 265,766,918 boxes in 2023. Below are box sales for cardiovascular system medication classes at the ATC3 level from 2019 to 2023 (Table 1).

Table 1. Box sales for cardiovascular system medication classes at the ATC 3 level between 2019-2023.

Drug Groups (ATC3 Level)	2019	2020	2021	2022	2023
Cardiac Glycosides	685,330	694,589	709,389	658,176	576,250
Antiarithymics	2,478.259	2,387,156	2,602,548	3,036,789	2,949,973
Other Vasodilators Used in Cardiac Diseases (excluding nitrates, calcium canal blockers, renin-angiotensin system inhibitors)	8,401,191	9,383,448	9,630,685	9,110,695	8,893,443
Nitrites and Nitrates	4,330,763	4,498,612	4,166,555	4,053,054	3,786,499
Cardiac Stimulants (excluding cardiac glycosides)	84,090	80,810	110,709	94,500	99,471
Other Antihypertensives (Central and Peripheral Effects)	4,154,420	4,415,927	4,354,237	5,002,136	5,290,594
Diuretics (mono and fixed-dose combination)*	15,229,910	16,001,615	16,286,815	15,311,724	15,949,625
Beta Blockers (mono and fixed-dose combination)*	60,543,231	65,598,097	67,151,393	67,979,337	70,110,291
Calcium Canal Blockers (mono and fixed-dose combination)*	19,525,661	21,304,975	21,148,323	20,891,310	21,146,152
Angiotensin Converting Enzyme Inhibitors (mono and fixed-dose combination)*	37,194,441	40,861,750	42,420,237	43,293,906	43,764,708
Angiotensin Receptor Blockers (mono and fixed-dose combination)*	49,635,836	55,163,416	53,396,957	57,628,803	58,367,238
Cholesterol and Triglyceride Regulators (mono)	22,710,158	28,143,144	30,264,136	34,448,434	34,603,590
Cholesterol and Triglyceride Regulators (fixed-dose combination)	0	0	4,268	88,761	173,076
Cholesterol and Triglyceride Regulators (fixed-dose combinations with other groups)*	65,300	69,567	71,711	65,579	56,008
TOTAL	**225,038,590**	**248,603,106**	**252,317,963**	**261,663,204**	**265,766,918**

* Data for double and triple fixed-dose combination pharmaceuticals containing active ingredients from different groups have been included only in the drug groups they are included in the ATC classification

Among the antihypertensive drug groups whose sales data were investigated, box sales of ACE inhibitors increased by 17.67% in 2023 compared to 2019, while ARBs increased by 17.59%. The increase rate for this period was 8.30% for calcium channel blockers, 15.80% for beta blockers, and 4.73% for diuretics. The following table presents the sales of antihypertensive medications from 2019 to 2023, which were examined by categorizing them at the ATC4 level by national and international norms (Table 2).

Table 2. Box sales for antihypertensive medications at the ATC4 level between 2019 – 2023.

Drug Groups (ATC4 Level)	2019	2020	2021	2022	2023
Potassium-Sparing Diuretics (mono)	458,448	513,015	516,805	567,169	619,750
Thiazide Group Diuretics (mono)	3,129,853	3,302,538	3,251,199	2,957,196	2,834,971
Potassium-Sparing Diuretics+Thiazide Group Diuretics (Fixed-Dose Combination)	1,713,848	1,550,639	1,527,162	1,499,500	1,473,525
Vasopressin Antagonist Diuretics (mono)	32,216	72,456	99,237	8,791	26,862
Centrally Acting Sympatholytics (mono)	521,857	524,883	458,251	482,232	479,470
Peripherally Acting Sympatholytics (excluding beta blockers) (mono)	3,632,563	3,891,044	3,895,986	4,519,904	4,811,124
Beta Blockers (mono)	58,826,819	63,632,381	64,943,282	65,614,292	67,418,808
Beta Blockers+Diuretics (Fixed-Dose Combination)	1,716,412	1,965,716	2,208,111	2,365,045	2,691,483
Calcium Channel Blockers (mono)	19,525,661	21,304,975	21,148,323	20,891,310	21,146,152
Calcium Channel Blockers+Statines (Fixed-Dose Combination)	65,300	69,567	71,711	65,579	56,008
Angiotensin Converting Enzyme Inhibitors (mono)	13,335,618	14,412,486	14,782,213	15,134,327	15,163,892
Angiotensin Converting Enzyme Inhibitors+ Diuretics (Fixed-Dose Combination)	15,339,761	16,281,795	16,425,520	16,177,343	15,931,795
Angiotensin Converting Enzyme Inhibitors+ Calcium Channel Blockers (Fixed-Dose Combination)	7,092,512	8,127,127	8,525,833	8,498,466	8,849,164
Angiotensin Converting Enzyme Inhibitors+ Calcium Channel Blockers+ Diuretics (Fixed-Dose Combination)	1,426,550	2,040,342	2,686,671	3,483,770	3,819,857
Angiotensin Receptor Blockers (mono)	9,005,003	10,246,494	9,860,478	11,158,966	10,803,069
Angiotensin Receptor Blockers+Diuretics (Fixed-Dose Combination)	34,036,946	37,138,626	35,273,668	35,867,229	35,394,639
Angiotensin Receptor Blockers+ Calcium Channel Blockers (Fixed-Dose Combination)	5,826,507	6,576,560	6,610,773	7,661,228	8,128,012
Angiotensin Receptor Blockers+ Calcium Channel Blockers+ Diuretics (Fixed-Dose Combination)	688,554	1,093,796	1,501,926	2,737,964	3,795,568
Angiotensin Receptor Blockers+ Neprilysin Inhibitors (Fixed-Dose Combination)	78,826	107,940	150,112	203,416	245,950
TOTAL	**176,453,254**	**192,852,380**	**193,937,261**	**199,893,727**	**203,690,099**

While antihypertensive drugs sold a total of 176,453,254 boxes in 2019, they increased by 15.44% and sold 203,690,099 boxes in 2023. The 3-month box sales data of antihypertensive drug groups between the first quarter of 2019 and the second quarter of 2024 are shared in Figure 1. The best-selling drug group in all quarters examined in the study of drugs that inhibit the Renin-Angiotensin System is the ARB-Diuretic fixed-dose combinations (Figure 1). The sales rate of ARB-Diuretic fixed-dose combination in all drug groups that inhibit the Renin-Angiotensin System was 38.85% in the first quarter, while it was 32.30% in the last quarter. In this

group, mono and fixed-dose combination pharmaceuticals of ACE inhibitor drugs were sold at a total rate of 43.54% in the first quarter and 43.80% in the last quarter.

In contrast, ARB mono and fixed-dose combination pharmaceuticals were sold at a rate of 56.46% in the first quarter and 56.20% in the last quarter. Investigations on the use of mono and fixed-dose combination medicines revealed that the sales of mono medications in this category (ARB+ACE inhibitors) were 25.98% in the first quarter and 25.35% in the last. In the first quarter, the fixed-dose combination pharmaceutical sales rates of ACE inhibitors and ARBs were 74.02%; in the last quarter, they were 74.65%. When the sales rates of fixed-dose combination pharmaceuticals were investigated among themselves, it was seen that the triple-drug fixed-dose combination pharmaceuticals of ACE inhibitors (ACE inhibitor + Calcium channel blocker + Diuretic combination) sold at a rate of 5.27% in the first quarter. In comparison, the sales rate increased to 15.74% in the last quarter. Similarly, it is seen that the triple-drug fixed-dose combination pharmaceuticals of ARBs (ARB + Calcium channel blocker + Diuretic combination) sold at a rate of 1.51% in the first quarter, while the sales rate increased to 11.21% in the last quarter. The usage rates of two and triple-drug fixed-dose combination pharmaceuticals of ACE inhibitors and ARBs between 2019-2023 are shared in Figure 2.

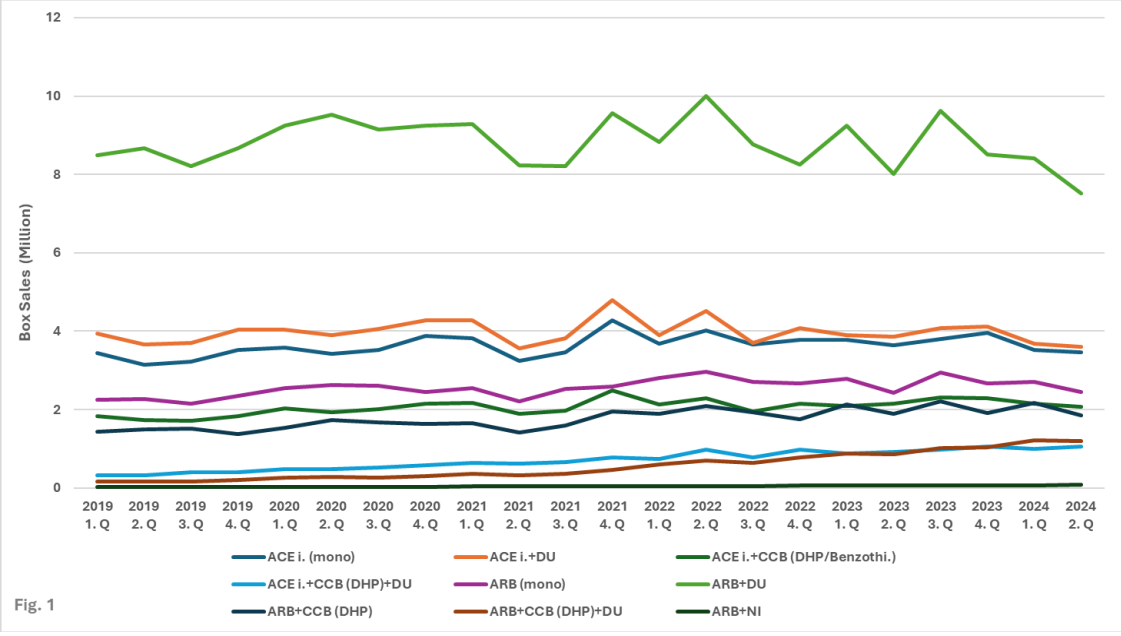

Figure 1. Box Sales of Drugs Acting on the Renin-Angiotensin System (Both Mono and Fixed-dose Combinations)

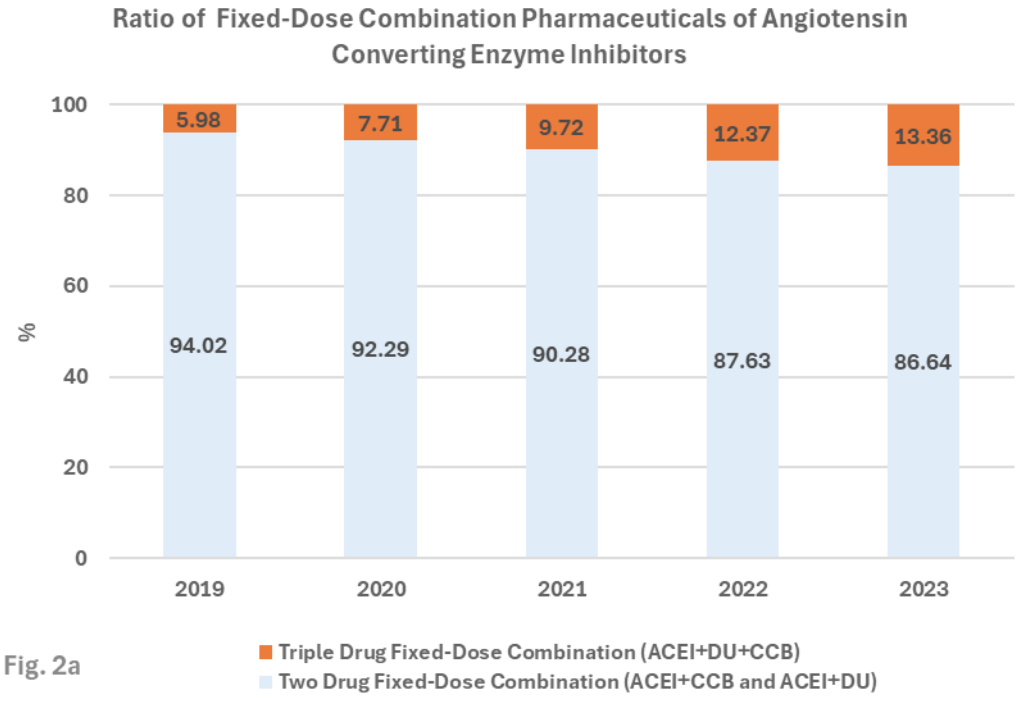

Fig. 2a

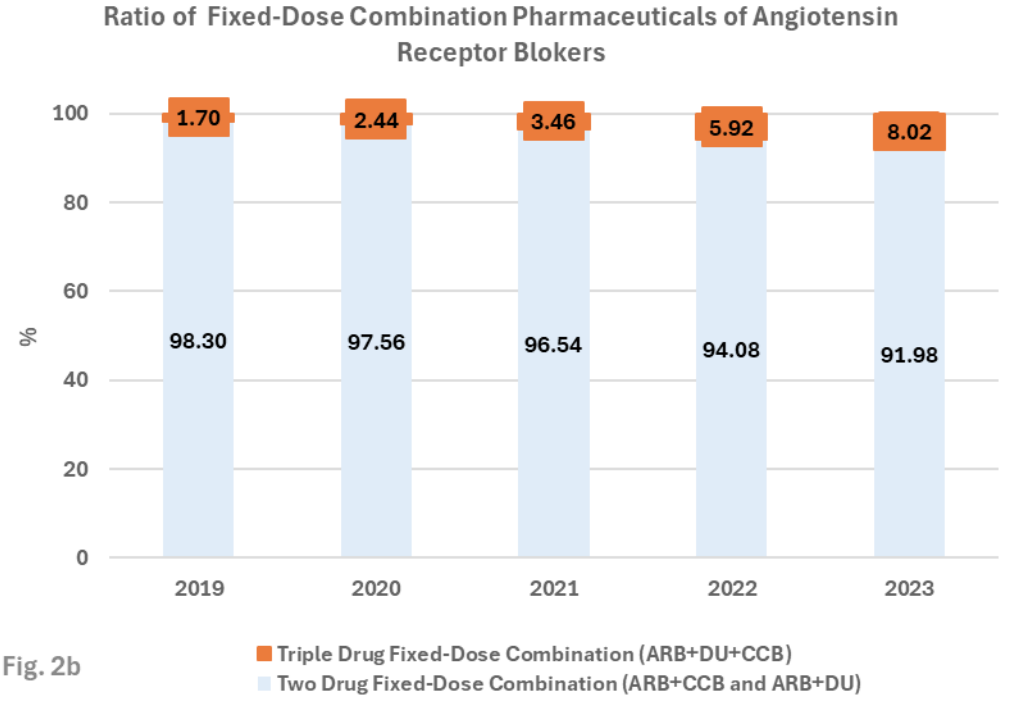

Fig. 2b

Figure 2a. Ratio of Fixed-Dose Combination Pharmaceuticals of Angiotensin Converting Enzyme Inhibitors

Figure 2b. Ratio of Fixed-Dose Combination Pharmaceuticals of Angiotensin Receptor Blockers

Dihydropyridine derivative medications were the best-selling mono calcium channel blocker pharmaceuticals across all research quarters (Figure 3). While the sales rate of mono dihydropyridine derivative calcium channel blockers in all calcium channel blocker groups was 45.18% in the first quarter, it was 36.89% in the last quarter. This group's overall sales rate for mono and fixed-dose combination medications containing dihydropyridine derivatives was 82.73% in the first quarter and 89.00% in the last. In contrast, sales of benzothiazepine mono and fixed-dose combination medications were 15.61% in the first quarter and 10.15% in the last. Phenylalkylamine derivatives, on the other hand, sold at a rate of 0.85% in the most recent quarter and 1.66% in the first. According to calculations, the overall sales rates of calcium channel blocker fixed-dose combination medications were 43.15% in the first quarter and 56.11% in the last. When the sales rates of fixed-dose combination pharmaceuticals were examined among themselves, it was seen that the triple-drug fixed-dose combination pharmaceuticals of dihydropyridine derivative calcium channel blockers (ACE inhibitor + Calcium Channel Blocker + Diuretic Combination and ARB + Calcium Channel Blocker) sold at a rate of 12.58% in the first quarter. In comparison, the sales rate increased to 36.35% in the last quarter.

Among diuretic pharmaceuticals, thiazides were the best-selling drug group in all quarters investigated (Figure 4). When all the fixed-dose combinations and mono forms were analyzed, ARB-Diuretic fixed-dose combinations were the best-selling drug subgroup. In the first quarter, the sales rate of ARB-Diuretic fixed-dose combinations across all diuretic medication groups was 57.71%; however, in the final quarter, it dropped to 49.84%. It was determined that the overall sales rate of diuretic fixed-dose combination medications was 93.64% in the first quarter and 94.98% in the last. When the sales rates of fixed-dose combination drugs are examined among themselves, it was seen that the triple-drug fixed-dose combinations of diuretics (ACE inhibitor + Calcium Channel Blocker + Diuretic Combination and ARB + Calcium Channel Blocker + Diuretic Combination) sold at a rate of 3.54% in the first quarter. In comparison, the sales rate increased to 16.43% in the last quarter.

Cardioselective beta-blockers are the best-selling class of beta-blocker medications throughout all study quarters (Figure 5). Cardioselective beta-blockers were sold at a rate of 78.85% in the first quarter and 81.71% in the last quarter across all beta-blocker medication categories. According to calculations, the overall sales rate of beta-blocker fixed-dose combinations was 2.96% in the first quarter and 3.64% in the last quarter.

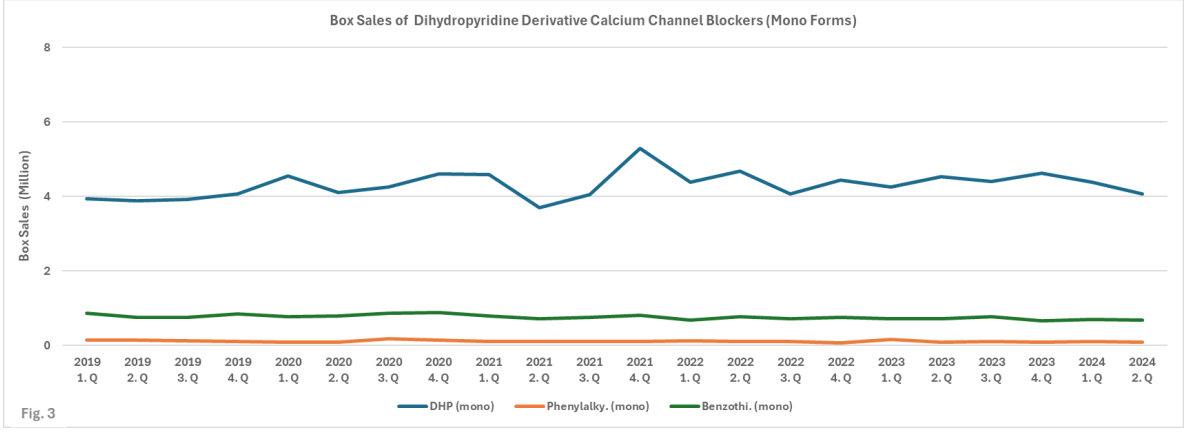

Figure 3. Box Sales of Dihydropyridine Derivative Calcium Channel Blockers (Both Mono and Fixed-dose Combinations)

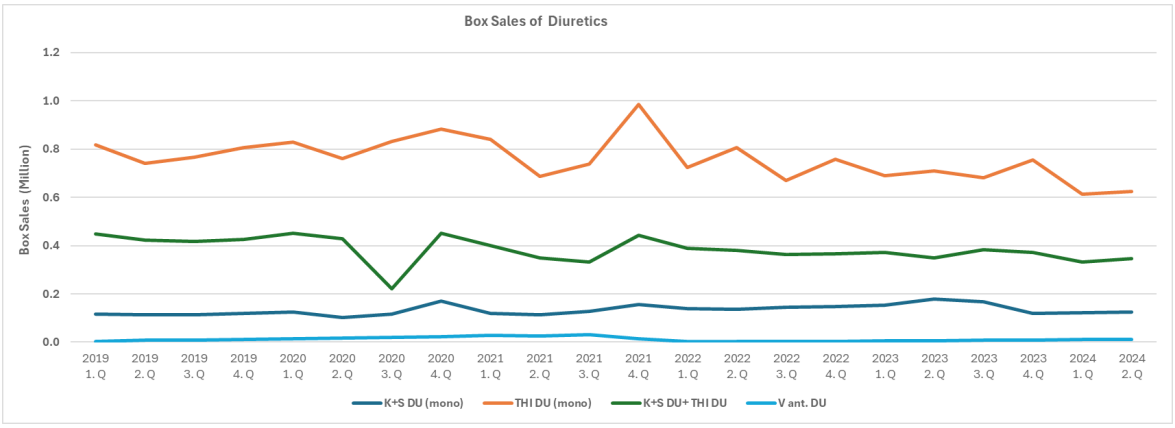

Figure 4. Box Sales of Diuretics

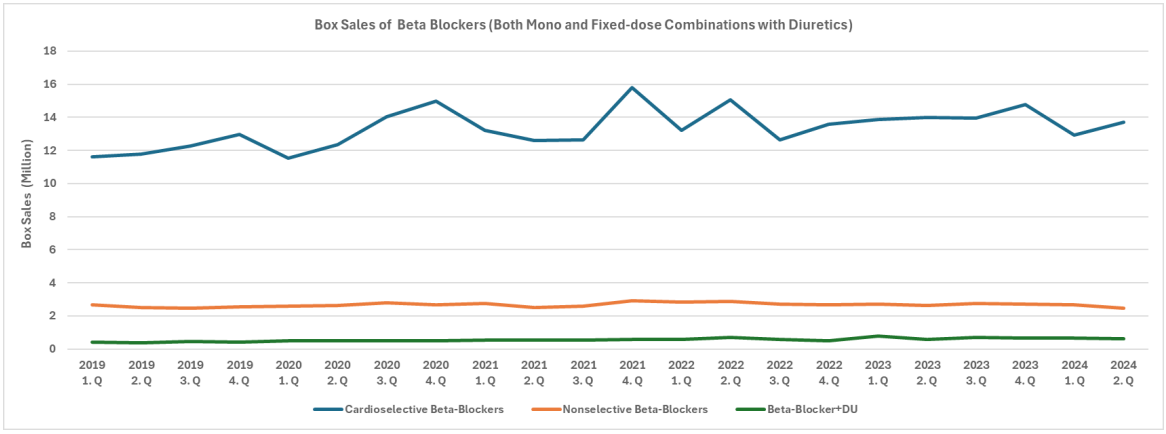

Figure 5. Box Sales of Beta Blockers (Both Mono and Fixed-dose Combinations with Diuretics)

WHO estimates that approximately 1.28 billion adults aged 30-79 suffer from hypertension worldwide. It is also stated that the number of adults with hypertension increased from 594 million to 1.13 billion between 1975 and 2015 and that this increase was seen mainly in low- and middle-income countries (WHO, 2023). In Türkiye, various studies have demonstrated the prevalence of hypertension. In the Turkish Hypertension Prevalence Study PatenT1 the prevalence of hypertension adjusted for age and gender was determined 31.8% in 2003 (Altun et al., 2005). In a recent study, Bayram et al. showed that 36.5% of adults in Türkiye had hypertension in 2021 (Bayram et al., 2021). Common chronic diseases, including hypertension, are shifting the disease burden of countries from acute diseases to chronic diseases. Chronic diseases, especially hypertension, and diabetes, cause significant economic and moral burdens also in our country (Sağlık Teknolojileri Değerlendirme Raporu 3). The Ministry of Health's Health Statistics report indicated that the sales volume of cardiovascular medicines increased by approximately 28% from 225.9 million boxes in 2017 to 291 million boxes in 2022 (Health Statistics Yearbook 2022). In this study, we determined that the total sales volume of antihypertensive drugs recommended in the guidelines increased by 15.44% between 2019 and 2023 in the Turkish market.

Hypertension treatment includes lifestyle changes such as achieving an ideal body weight, healthy diet,

salt restriction, quitting smoking, alcohol restriction, being active, and managing stress, as well as pharmacotherapy. The Turkish Hypertension Consensus report prepared in 2015 recommended drugs from the diuretic, beta-blocker, calcium channel blocker, angiotensin-converting enzyme (ACE) inhibitor, and angiotensin receptor blocker (ARB) groups for use in hypertension pharmacotherapy (Arıcı et al., 2015). Again, in the guide prepared by the Turkish Endocrinology and Metabolism Association, thiazide group diuretics, calcium channel blockers, ACE inhibitors, and ARBs are the four major antihypertensive drug groups (Hipertansiyon Tani Ve Tedavi Kılavuzu, 2022). In the guideline published by the World Health Organization in 2021, thiazide diuretics, ACE inhibitors, ARBs, and long-acting dihydropyridine derivative calcium channel blockers were recommended in pharmacotherapy as first-line hypertension treatment. At the same time, it was stated that beta-blockers should be evaluated in patients with ischemic heart disease (Guideline for the pharmacological treatment of hypertension in adults, 2021). In the guideline prepared by the American College of Cardiology and the American Heart Association published in the United States (US) in 2017, ACE inhibitors, ARBs, dihydropyridine-derivative and non-dihydropyridine-derivative calcium channel blockers, and thiazide group diuretics were recommended in the first-line hypertension treatment (Whelton et al., 2018). In the latest guideline published by the European Society of Cardiology, ACE inhibitors, ARBs, dihydropyridine-derivative calcium channel blockers, thiazide group diuretics, and potassium-sparing diuretics are recommended in first-line hypertension treatment. Additionally, beta-blockers are advised as first-line therapy for individuals with heart failure or angina, following myocardial infarction, or for those seeking to regulate their heart rate (McEvoy et al., 2024). However, different publications criticize the use of beta-blockers in first-line therapy because of their slightly reducing effect on the risk of stroke (Messerli et al., 2023).

CONCLUSION

In this study, the last 66-month sales data of antihypertensive medication groups recommended by guidelines were analyzed separately. In 2019, ARB mono and combination preparations sold approximately 49.6 million boxes in Türkiye, while ACE inhibitors sold approximately 37.1 million boxes. It is observed that the market share between the two drug groups that inhibit the renin-angiotensin system, ACE inhibitors, and ARBs, did not change during the period examined in the study. These box sales reached approximately 58.3 million for ARBs and approximately 43.7 million for ACE inhibitors in 2023. In a different study examining the market distribution of hypertension drugs in Türkiye in 2020 and 2021, the highest box sales were in drugs that block angiotensin production or effect, followed by beta blockers. Among drugs that block angiotensin production or its effect, the highest box sales were in ARB and thiazide fixed-dose combinations (Tengiz et al., 2023). A prior study indicated that the consumption of ARB group antihypertensives increased by 175% from 2005 to 2010, and ACE inhibitors by 17% in Türkiye (Koçkaya et al., 2012). In a recent study ACE inhibitor and ARB sales in various European countries were examined using different parameters. Mono and fixed-dose combination pharmaceuticals of ACE inhibitors and ARBs were evaluated together, and the total sales of both pharmaceuticals were examined. When the amount of drug consumption per capita in 2016 was examined, the consumption of ARB and ACE inhibitors was close to each other in France and Spain, while ACE inhibitor consumption was determined to be dominant over ACE inhibitor consumption, especially in Poland, Hungary, Romania, and the UK. It was determined that the ARB consumption rate in the total consumption of these two drug groups was 1% in Poland, Hungary, and Romania in 2001, over 15% in 2009, and over 25% in 2016. The increase in ARB consumption in Eastern European countries was explained by the entry of generic medications in these markets. However, this increase was not detected in

other European countries, the Netherlands, England, and Italy. ARB sales data reached a certain plateau and remained at that level for a long time. It was stated that this situation shows that drug policies and regulations are essential factors affecting drug consumption at the country level (Kovács et al., 2021). Another study conducted in the Baltic countries (Estonia, Lithuania, and Latvia) found that the most commonly used medicine class was medications that block the action or synthesis of angiotensin and that the usage of antihypertensive agents has grown between 2008 and 2018. The mono forms of ACE inhibitors were determined as the most commonly used subgroup. Another critical data in that study is a remarkable increase in ARB use between 2008 and 2018 (Treciokiene et al., 2022). In a study in Bosnia and Herzegovina and Serbia, it was demonstrated that the use of antihypertensive drugs increased more than threefold between 2009 and 2019. ACE inhibitors were the most often used medication class during the years under review, followed by calcium channel blockers. The difference in use between the two groups is about 2-fold. It was found that the combination of ACE inhibitors with thiazide diuretics was close to calcium channel blockers in those years (Kalinić et al., 2022).

On the other hand, a study examining the antihypertensive drug market in India showed that the market grew by 6.9% between 2016 and 2018. In that study, it was demonstrated that the group with the highest market share among mono drugs was calcium channel blockers, while beta blockers and ARBs followed this group (Sahoo et al., 2021). We showed that mono forms of beta-blocker agents have sold over 60 million boxes annually since 2020, and cardioselective beta-blockers accounted for more than 80% of these sales. The point to remember here is that beta-blockers are also used in the treatment of other cardiovascular diseases. Therefore, it cannot be concluded from the data in our study that the group of drugs used as mono to treat hypertension in Turkey is cardioselective beta blockers. On the other hand, while mono forms of calcium channel blockers were sold around 20 million boxes annually during the five years, box sales of their fixed-dose combined forms increased by over 60% since 2019, approaching 25 million. When the data of calcium channel blockers are examined, it is seen that the group predominantly used in Türkiye is dihydropyridine derivatives under the guidelines.

Fixed-dose drug combinations have also been shown to increase patient compliance with antihypertensive drug treatment (Tsioufis et al., 2020). Fixed-dose drug combinations are recommended in terms of effectiveness and cost in the treatment of hypertension, and in recent years, WHO has added some of these drugs to the essential drug list (Salam et al., 2020). In our study, we showed that combinations of drugs used in the treatment of hypertension are widely used, and their use has increased over the years. In contrast to their mono formulations, we discovered that fixed-dose combinations of ACE inhibitors and ARBs are more often used. In recent years, fixed-dose calcium channel blockers have begun to outsell their combined formulations. In a study that investigated data from 75 countries between 2010 and 2021, it was stated that the use of fixed-dose combined antihypertensive drugs increased in low-income countries compared to middle- and high-income countries. However, it was found that antihypertensive drug consumption rates were significantly lower in these countries compared to middle- and high-income countries (Jayawardana et al., 2024). In a study in Germany, it was stated that, despite the recommendation of fixed-dose combination drugs in the joint guideline of the European Society of Cardiology and the European Society of Hypertension in 2018, fixed-dose combination drugs had a share of 15.4% in antihypertensive drug box sales in 2016. Still, this share decreased to 10.9% in 2020 (Mahfoud et al., 2023). In the study in India between 2016-2018, mentioned in the paragraph above, it was seen that fixed-dose combinations of two drugs had a share of 36% in the entire antihypertensive drug market (Sahoo et al., 2021). In the study in Bosnia and Herzegovina and Serbia be-

tween 2009 and 2019, as mentioned above, it was seen that the combination of ACE inhibitors and thiazide diuretics were the two most preferred antihypertensive drug groups after mono ACE inhibitors, together with calcium channel blockers (Kalinić et al., 2022). One of the essential results of this study is the demonstration that sales dates of triple fixed-dose drug combinations have been increasing over the years in Türkiye. It has been determined that triple fixed-dose combinations of ARBs and ACE inhibitors that suppress the renin-angiotensin system with calcium channel blockers and diuretics have been increasing regularly in the period examined in the study. We believe that these rising rates should be evaluated concerning the diagnosis, management, and treatment of hypertension in Türkiye.

In each country, the choice of antihypertensive drug group in the treatment is different. Generic formulations, pharmaceutical strategies, legal frameworks, and other variables in various nations contribute to this circumstance. As a result, according to the data in our study, we demonstrated that the drug groups that have the highest share in the antihypertensive drug market in Türkiye in recent years are the groups recommended in the guidelines. We found that the total box sales of these drugs increased by 15.44% between 2019 and 2024. However, it is not possible to conclude that this data only covers medicine sales for the treatment of hypertension, particularly beta blockers, because our analysis only includes wholesaler sales data without prescription and diagnosis information. It would be more beneficial for future studies to include clinical data such as diagnosis and the treatment step in which the drugs are used. As mentioned above, an essential finding of this study is that triple fixed-dose combination sales are increasing regularly. This data is essential for assessing the rational treatment of hypertension in our nation. Such studies are helpful because they contribute to the assessment of whether drugs used in the treatment of chronic diseases are used rationally following the guidelines, as well as to the status of access to drugs in countries. More detailed studies are needed on medications used in the treatment of all chronic diseases, especially hypertension, to evaluate health systems and public health.

AUTHOR CONTRIBUTION STATEMENT

Concept: E.H.V., B.G; Design: E.H.V., B.G; Control: E.H.V., B.G; Sources: E.H.V., B.G; Materials: -.; Data Collection and/or Processing: E.H.V.,B.G.; Analysis and/or Interpretation: E.H.V.,; Literature Review: E.H.V., B.G.; Manuscript Writing: E.H.V., B.G.; Critical Review: E.H.V., B.G; Other:-

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

Altun, B., Arici, M., Nergizoğlu, G., Derici, U., Karatan, O., Turgan, C., Sindel, S., Erbay, B., Hasanoğlu, E., Cağlar, S., & Turkish Society of Hypertension and Renal Diseases (2005). Prevalence, awareness, treatment and control of hypertension in Turkey (the PatenT study) in 2003. *Journal of Hypertension*, *23*(10), 1817–1823. https://doi.org/10.1097/01.hjh.0000176789.89505.59

Arıcı, M., Birdane, A., Güler, K., Yıldız, B. O., Altun, B., Ertürk, Ş., Aydoğdu, S., Özbakkaloğlu, M., Ersöz, H. Ö., Süleymanlar, G., Tükek, T., Tokgözoğlu, L., Erdem, Y., Türk Kardiyoloji Derneği (TKD), Türk İç Hastalıkları Uzmanlık Derneği (TİHUD), Türkiye Endokrinoloji ve Metabolizma Derneği (TEMD), Türk Nefroloji Derneği (TND), & Türk Hipertansiyon ve Böbrek Hastalıkları Derneği (2015). Türk Hipertansiyon Uzlaşı Raporu [Turkish Hypertension Consensus Report]. *Turk Kardiyoloji Dernegi arsivi: Turk Kardiyoloji Derneginin yayin organidir, 43*(4), 402–409. https://doi.org/10.5543/tkda.2015.16243

ATC/DDD Toolkit. Anatomical Therapeutic Chemical (ATC) Classification. Retrieved from https://www.who.int/tools/atc-ddd-toolkit

Bayram, F., Demir, Ö., Sabuncu, T., Eren M.A., Gedik A.V., Çorapçıoğlu D, Kaya A. (2021). Prevalence and Awareness of Hypertension in Seven Distinct Geographic Regions of Turkey: The SEMT HT Study. *The Turkish Journal of Endocrinology and Metabolism, 25*(1), 1–10. https://doi.org/10.25179/tjem.2020-78532

Benowitz NL (2018). Antihypertensive Agents. B. Katzung (Ed.) *Basic and clinical Pharmacology* (pp.173-193) 14th Edition. USA: McGraw Hill Education.

Guideline for the pharmacological treatment of hypertension in adults. (2021) Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO. Retrieved from https://iris.who.int/bitstream/handle/10665/344424/9789240033986-eng.pdf?sequence=1

Health Statistics Yearbook (2022) T.C. Sağlık Bakanlığı, Ankara. Ministry of Health Publication no: 1280. ISBN: 978-975-590-901-1 Retrieved from https://dosyasb.saglik.gov.tr/Eklenti/48055/0/siy2022eng-050420241pdf.pdf

Hipertansiyon Tani Ve Tedavi Kılavuzu (2022). Türkiye Endokrinoloji ve Metabolizma Derneği. 6. Baskı ISBN: 978-605-66410-4-6. Retrieved from https://file.temd.org.tr/Uploads/publications/guides/documents/Hipertansiyon-Kilavuzu-2022.pdf

Jayawardana, S., Campbell, A., Aitken, M., Andersson, C. E., Mehra, M. R., & Mossialos, E. (2024). Global consumption patterns of combination hypertension medication: An analysis of pharmaceutical sales data from 2010-2021. *PLOS Global Public Health*, *4*(9), e0003698. https://doi.org/10.1371/journal.pgph.0003698

Kalinić, D., Škrbić, R., Vulić, D., Stojaković, N., Stoisavljević-Šatara, S., Stojiljković, M. P., Marković-Peković, V., Golić Jelić, A., Pilipović-Broćeta, N., Wong, N. D., & Godman, B. (2022). Trends in Antihypertensive Medicine Utilization in the Republic of Srpska, Bosnia and Herzegovina: An Eleven-Year Follow-Up. *Frontiers in Pharmacology, 13*, 889047. https://doi.org/10.3389/fphar.2022.889047

Koçkaya, G., Tanyeri, P., Kılıç, P., Vural, İ. M., Akbulat, A., Artıran, G., Kerman, S. (2012). Türkiye'de anjiyotensin reseptör blokerleri ve anjiyotensin dönüştürücü enzim inhibitörlerinin yıllar içerisinde tüketim, bütçe ve fiyat değişim analizi. *MN Kardiyoloji, 19*(3), 112 - 119.

Kovács, B., Darida, M., & Simon, J. (2021). Drugs Becoming Generics-The Impact of Genericization on the Market Performance of Antihypertensive Active Pharmaceutical Ingredients. *International Journal of Environmental Research and Public Health*, *18*(18), 9429. https://doi.org/10.3390/ijerph18189429

Mahfoud, F., Kieble, M., Enners, S., Kintscher, U., Laufs, U., Böhm, M., & Schulz, M. (2023). Use of fixed-dose combination antihypertensives in Germany between 2016 and 2020: an example of guideline inertia. *Clinical Research in Cardiology: Official Journal of the German Cardiac Society*, *112*(2), 197–202. https://doi.org/10.1007/s00392-022-01993-5

McEvoy, J. W., McCarthy, C. P., Bruno, R. M., Brouwers, S., Canavan, M. D., Ceconi, C., Christodorescu, R. M., Daskalopoulou, S. S., Ferro, C. J., Gerdts, E., Hanssen, H., Harris, J., Lauder, L., McManus, R. J., Molloy, G. J., Rahimi, K., Regitz-Zagrosek, V., Rossi, G. P., Sandset, E. C., Scheenaerts, B., … ESC Scientific Document Group (2024). 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *European Heart Journal*, *45*(38), 3912–4018. https://doi.org/10.1093/eurheartj/ehae178

Messerli, F. H., Bangalore, S., & Mandrola, J. M. (2023). β blockers switched to first-line therapy in hypertension. *Lancet (London, England)*, *402*(10414), 1802–1804. https://doi.org/10.1016/S0140-6736(23)01733-6

Sahoo, S. K., Pathni, A. K., Krishna, A., Moran, A. E., Cohn, J., Bhatia, S., Maheshwari, N., & Sharma, B. (2021). Research Letter: Antihypertensive Drugs Market in India: An Insight on Size, Trends, and Prescribing Preferences in the Private Health Sector, 2016-2018. *Global heart*, *16*(1), 51. https://doi.org/10.5334/gh.999

Sağlık Teknolojileri Değerlendirme Raporu 3 (2016). Türkiye İlaç ve Tıbbi Cihaz Kurumu, Ankara/Türkiye. Retrieved from https://titck.gov.tr/Dosyalar/Ilac/SaglikTeknolojileriDegerlendirme/STDRaporu3.pdf

Salam, A., Huffman, M. D., Kanukula, R., Hari Prasad, E., Sharma, A., Heller, D. J., Vedanthan, R., Agarwal, A., Rodgers, A., Jaffe, M. G., R Frieden, T., & Kishore, S. P. (2020). Two-drug fixed-dose combinations of blood pressure-lowering drugs as WHO essential medicines: An overview of efficacy, safety, and cost. *Journal of Clinical Hypertension (Greenwich, Conn.)*, *22*(10), 1769–1779. https://doi.org/10.1111/jch.14009

Tengiz, I., Atila, D., & Ercan, E. (2023). Market Distributions and Pricing/Reimbursement Policies of Antihypertensive Drugs in Turkey. Türkiye'de Antihipertansif İlaçların Pazar Dağılımları ve Fiyatlandırma/Geri Ödeme Politikaları. *Turk Kardiyoloji Dernegi arsivi: Turk Kardiyoloji Derneginin yayin organidir*, *51*(5), 299–303. https://doi.org/10.5543/tkda.2023.84039

Treciokiene, I., Bratcikoviene, N., Gulbinovic, J., Wettermark, B., & Taxis, K. (2022). Trend of Antihypertensive Medicine Use in the Baltic States between 2008 and 2018: A Retrospective Cross-National Comparison. Pharmacoepidemiology, 1(1), 1-11. https://doi.org/10.3390/pharma1010001

Tsioufis, K., Kreutz, R., Sykara, G., van Vugt, J., & Hassan, T. (2020). Impact of single-pill combination therapy on adherence, blood pressure control, and clinical outcomes: a rapid evidence assessment of recent literature. *Journal of Hypertension*, *38*(6), 1016–1028. https://doi.org/10.1097/HJH.0000000000002381

Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E., Jr, Collins, K. J., Dennison Himmelfarb, C., DePalma, S. M., Gidding, S., Jamerson, K. A., Jones, D. W., MacLaughlin, E. J., Muntner, P., Ovbiagele, B., Smith, S. C., Jr, Spencer, C. C., Stafford, R. S., Taler, S. J., Thomas, R. J., Williams, K. A., Sr, Williamson, J. D., … Wright, J. T., Jr (2018). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension (Dallas, Tex.: 1979)*, *71*(6), 1269–1324. https://doi.org/10.1161/HYP.0000000000000066

World Health Organization (WHO) (2021). *Cardiovascular diseases (CVDs)*. Retrieved from https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

World Health Organization (WHO) (2023). *Hypertension*. Retrieved from https://www.who.int/news-room/fact-sheets/detail/hypertension