Pharmacoeconomic Analysis of Cardiovascular Treatments in Romania - Original Vs. Generic Drugs

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Abstract

Pharmacoeconomic evaluations serve as pivotal tools in healthcare decision-making, particularly in the realm of cardiovascular treatments where efficacy, safety, and cost considerations intersect. This article presents a comprehensive analysis comparing the pharmacoeconomic profiles of original and generic drugs in cardiovascular care. The article delves into the intricate interplay of pricing dynamics, market competition, and regulatory policies shaping the accessibility and affordability of original and generic cardiovascular medications. Moreover, through case studies and comparative effectiveness research, the article provides insights into the real-world utilization patterns and economic outcomes associated with the adoption of generic cardiovascular drugs within clinical practice settings. It highlights the potential cost savings, budgetary implications, and patient outcomes stemming from the utilization of generic medications, while also acknowledging the importance of ensuring therapeutic continuity and medication adherence.

Keywords: cardiovascular, generic medications, accessibility, affordability, medication adherence

Introduction

Cardiovascular disease (CVD) has a major impact on people's lives. Cardiovascular disease is the leading cause of premature death worldwide. Health-EU Newsletter 257 states that non-communicable diseases, such as cardiovascular diseases and cancer, are the leading cause of disability, ill health, ill-health retirement and premature death in the EU, resulting in significant social and economic costs [1]. According to the Organisation for Economic Cooperation and Development, around 550,000 people of working age in the EU die prematurely each year from these diseases. [2]. Derose D. et al. in 2023, show that heart attacks and strokes are the cause of death for hundreds

of thousands of people worldwide, every year and that high blood pressure is one of the most important preventable risk factors for these diseases [3].

Pharmaceutical Market in Romania

The pharmaceutical market in Romania is experiencing a continuous growth which is reflected both in the volume of pharmaceuticals distributed and in the growth of the total market value for the reporting period January-December 2023. The growth in volume, was 2.4% higher than in January-December 2022 reporting period, and amounted to 722.6 million packs, compared to 705.8 million packs. Market value in the reporting period is thus 16.2% higher than in the reference period, i.e. RON 29.96 billion (EUR 6.1 billion) compared to RON 25.78 billion (EUR 5.23 billion) [4,5].

Cardiovascular Diseases

Cardiovascular diseases can have different causes. In particular, the change in lifestyle, the shift from physically active occupations to office work or sedentary work, longer working hours and less leisure time, explains the increase in cardiovascular disease. At the same time, a lifestyle associated with a high-calorie diet and the consumption of sugar and saturated fats favours the development of atherosclerosis and other metabolic disorders, diabetes mellitus and hypertension, which are common in people with cardiovascular disease [6-9].

There are numerous and varied problems that occur throughout the cardiovascular system, such as endocarditis, conduction system abnormalities and cardiovascular disease, which essentially relate to the following diseases (see Fig. 1) [10]:

Coronary heart disease is the result of reduced blood flow to the heart muscle, leading to angina pectoris, heart attack and/or heart failure. This disease is responsible for up to half of all cases of cardiovascular disease;

Cerebrovascular diseases including stroke and ischemic attack;

Peripheral arterial disease, in particular, arterial disease with limb involvement leading to claudication;

Atherosclerosis includes thoracic and abdominal aneurysms;

Arterial hypertension.

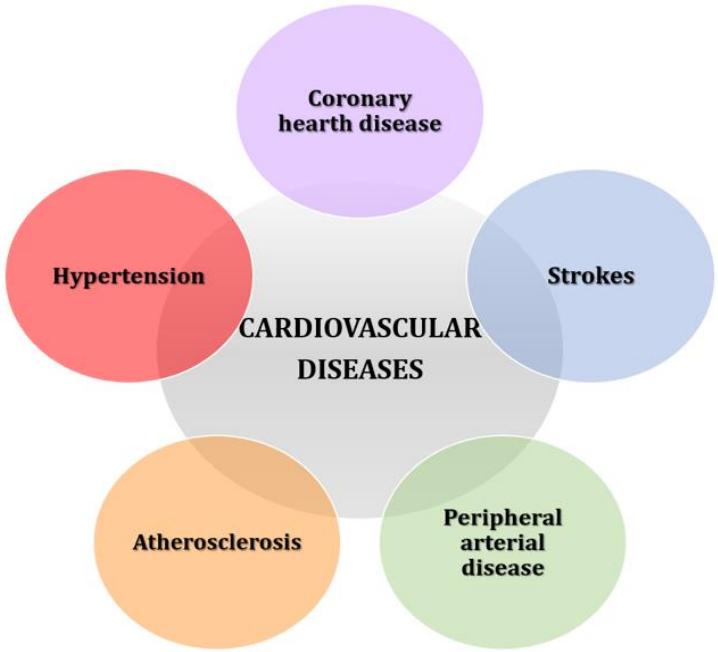

Figure 1. Cardiovascular diseases

Hypertension and Its Complications

Blood pressure can be defined as the force transmitted through the arteries after the blood has left the heart. Basically, human blood pressure is indicated by two numerical values. The lower number refers to the diastolic blood pressure and the higher value stands for the systolic blood pressure.

Systolic blood pressure is the highest pressure registered by the arteries during each cardiac cycle. In other words, systolic pressure is the measurement of the highest pressure in the arteries when the left ventricle contracts. Diastolic is the lowest value of blood pressure in the arteries when the heart fills with blood for another beat. Hypertension is the tension in the arteries that is so elevated that it causes problems for the tissues through which the blood flows. Table 1 lists the target organs and the complications that high blood pressure can cause.

Table 1. Target organs and complications that high blood pressure can produce

Target organs	Complications
Brain	Stroke Dementia Hypertensive encephalopathy (confusion, lethargy, seizures, coma)
Hearth	Heart attack

	Heart enlargement Increased risk of heart rhythm problems
Blood vessel	Aneurysm Atherosclerosis (narrowed, hardened arteries)
Kidneys	Kidney diseases Kidney failure Dialysis
Eyes	Retinal damage Blindness
Prostate (for men)	Weak urinary stream Problem of urinating

High blood pressure can have devastating effects on the brain. In 2018, Moroni et al. showed that high blood pressure accelerates brain ageing [11]. Song et al. showed in 2020 that hypertension in middle-aged adults is associated with cognitive decline and dementia, with elevated systolic levels causing the most damage [12]. Tarumi et al. showed in 2010 that high blood pressure leads to impairment of various brain functions: Memory, reaction time, attention, concentration, reasoning, task flexibility, problem solving, planning execution and cognitive processing speed [13].

High blood pressure is associated with the occurrence of heart attacks, heart enlargement and an increased risk of cardiac arrhythmia. High blood pressure also affects the risk of aneurysms, a condition in which the walls of blood vessels become weakened and stretched, often posing a risk of rupture of a blood vessel, such as the abdominal aorta, which poses an 88% risk of sudden death. High blood pressure is also involved in atherosclerosis, the narrowing and hardening of the arteries [14].

In relation to kidney disease, high blood pressure can lead to complications of kidney failure and dialysis. In addition, hypertension, together with diabetes, contributes to most cases of blindness due to retinal damage. Another common complication is the link between hypertension and symptoms associated with prostate enlargement. Vallianou et al. showed in 2019 that the higher a man's blood pressure, the greater the risk of prostate-related symptoms such as bleeding, erectile dysfunction, urethral stricture, urinary retention and urinary incontinence [15].

ORIGINAL VS. GENERIC DRUGS IN CARDIOVASCULAR DISEASES

The original drug is the product that was first developed by a pharmaceutical company, and the generic drug is the copy of the original drug that can only be marketed after the patent of the first product has expired [16]. Drug therapies are used in the treatment of heart disease, including both originals and generic drugs. In this study, we present an analysis comparing the pharmacoeconomic profiles of original and generic drugs in cardiovascular disease. Table 2 shows the brand name,

manufacturer and maximum price for each drug selected, with the status - original or generic - indicated.

CONCOR 10mg (Bisoprololum)

Bisoprolol, together with atenolol, metoprolol and nebivolol, belongs to the class of cardioselective β-blockers, which are considered the first choice for the treatment of indications following myocardial infarction or coronary heart disease. Numerous studies have shown that the risk of cardiovascular events is lower when β-blockers are used after a myocardial infarction, during an acute coronary syndrome or in patients with chronic angina pectoris with ischemic symptoms [17].

All β-blockers exert a membrane-stabilising effect on cardiac cells when administered in high doses. This effect is necessary when β-blockers are used as antiarrhythmics.

Bisoprolol works by altering some nerve impulse responses, particularly in the heart, which leads to a reduction in heart rate, thereby increasing the effectiveness of blood pumping through the heart. At the same time, the heart's demand for blood and oxygen is reduced. The most important areas of application for bisoprolol are the treatment of high blood pressure and angina pectoris [17,18].

SORTIS 10mg (Atorvastatinum)

The class of statins competitively inhibits the activity of HMG-CoA reductase, an enzyme that limits the rate of cholesterol synthesis. Inhibition of HMG-CoA reductase leads to a modest decrease in cellular cholesterol concentrations. Over the years, various clinical studies have been conducted on the effects of statins, which have concluded that the mortality rate after a heart attack could be significantly reduced.

However, some studies have also shown that lowering LDL cholesterol levels with statins can reduce mortality in the absence of overt cardiovascular disease. Statins have also been shown to be effective in patients at high risk of cardiovascular disease, such as diabetics [19].

The active substance atorvastatin is indicated as an adjunct to diet to reduce elevated plasma concentrations of total cholesterol, LDL cholesterol and triglycerides in individuals with hypercholesterolemia or mixed hyperlipidemia when diet and other non-pharmacologic measures do not have a satisfactory effect [19,20].

SPIRONOLACTONA 25mg (Spironolactonum)

Spironolactone belongs to the class of potassium-sparing diuretics, which increase the reabsorption of potassium by the nephron. The active substances in this class interrupt sodium reabsorption by the cells of the main collecting ducts via various

mechanisms. Spironolactone inhibits the biosynthesis of new sodium channels in the main cells [21-23].

The main indications of spironolactone are:

Congestive heart failure is characterised by impaired heart function, which manifests itself in signs such as swollen ankles or shortness of breath;

Ascites is an accumulation of fluid in the abdomen that is mainly caused by cirrhosis of the liver or certain types of cancer;

Nephrotic syndrome is a condition of the kidneys that causes fluid to accumulate [24];

Primary aldosteronism is manifested by the accumulation of excess fluid in the body, a consequence of excessive secretion of the hormone aldosterone.

Table 2. Differences between the maximal price of original and generic products

Brand name	Manufac-turer	Maximal price (RON)*	Brand name	Manufac-turer	Maximal price (RON)*	Brand name	Manufac-turer	Maximal price (RON)*	Brand name	Manufac-turer	Maximal price (RON)*	NAMMDR Status**
Concor 10mg x 60 film. tabl.	Merck Healthcare KGAA	54,44	Sortis 10 mg x 30 film. tabl.	Pfizer Manufacturing Deutschland GMBH	22,16				Triplixam 5/1.25/5 mg x 30 film. tabl.	Les Laboratoires Servier Industrie	46,70	ORIGINAL
Bisogamma 10mg x 100 film. tabl.	Worwag Pharma GMBH & Co. KG	29,03	Amicor 10 mg x 30 film. tabl.	Medochemie LTD	12,51	Spironolactona Terapia 25mg x 50 film. tabl.	Terapia S.A.	23,59				GENERIC
Bisotens 10mg x 30	Antibiotice S.A.	16,52	Atorvastatina Terapia	Terapia S.A.	13,28	Alspiron 25 mg x 20 film. tabl.		9,43				GENERIC

film. tabl.			10 mg x 30 film. tabl.					
Sobyc 10 mg x 30 film. tabl.	Krka D.D.	13,30	Atoris 10mg x 28 film. tabl.	Krka D.D.	12,14	Spironolactona Medreg 25 mg x 50 film. tabl.	23,59	GENERIC
Corsib 10mg x 30 film. tabl.	Saneca Pharmaceuticals A.S.	21,29	Torvacrd 10 mg x 30 film. tabl.	Zentiva K.S.	5,90			GENERIC

*the maximum price that can be used by the pharmacy for the sale of a medicinal product that has been approved and registered in CANAMED (National catalogue of prices for medicinal products for human use subject to medical prescription, authorized for marketing)

**NAMMDR – National Agency for Medicines and Medical Devices of Romania

TRIPLIXAM 5/1,25/5mg (combinations: perindoprilum/indapamidum/amlodipinum)

Perindopril belongs to the class of angiotensin-converting enzyme inhibitors (ACE inhibitors). It works primarily by dilating the blood vessels, which facilitates blood flow in the blood vessels [17].

Indapamide belongs to the class of thiazide diuretics (sulphonamide derivatives with an indole ring). Indapamide leads to an inhibition of sodium and chloride reabsorption and thus to increased diuresis [17].

Amlodipine belongs to the class of calcium channel blockers (classes of drugs called dihydropyridines). It works by relaxing the blood vessels so that they can flow more easily through the vessels [25].

The main indication for Triplixam is the substitution treatment of essential hypertension.

Pharmacoeconomic Differences Between Original and Generic Medicines for a Selected Category of Medicines with Marketing Authorization in Romania.

The financial differences between the original product from Concor and the generics Bisogamma, Bisotens, Sobyc and Corsib are quite large for the active substance bisoprololum. Concor 10mg x 60 film. tabl. has a prescribed maximum price, which can be found in all pharmacies in Romania, of 54.44 RON, while the most expensive generic Bisogamma 10mg x 100 film. tabl. costs 29.03 RON, followed by Corsib 10mg x 30 film. tabl. with a maximum price of 21.29 RON, then Bisotens 10mg x 30 film. tabl. at 16.52 RON and Sobyc 10mg x 30 film. tabl. at 13.30 RON. Thus, the price differences can vary between 75.56% and 46.67% for generics on the Romanian market for the active ingredient bisoprolol 10mg.

Also, the active substance Atorvastatinum, in Romania, is available under the name of Sortis, as original drug, and as generic drugs under the names of Amicor, Atorvastatin Therapy, Atoris and Torvacard.

The differences between the maximum price of the original preparation Sortis 10mg x 30 Tabl. and the generics can vary between 73.37% and 40.07%. Thus, the original drug Sortis 10mg x 30 tabl. film has a maximum price of 22.16 RON, while the generics have a lower price, for example Atorvastatin Terapia 10mg x 30 tabl. film. a price of 13.28 RON, Amicor 10mg x 30 film. tabl. a price of 12.51 RON, Atoris 10mg x 28 film. tabl. a maximum price of 12.14 RON and Torvacard 10mg x 30 film. tabl. the lowest price of 5.90 RON.

For the active ingredient Sprionolactonum there is no original preparation on the market in Romania, only generics, where the price differences are not significant, except that they differ in the number of units per pack, e.g. Spironolactone Terapia 25mg x 50 film. tabl. and Spironolactone Medreg 25mg x 50 film. tabl. have a maximum price of 23.59 RON, while Alspiron 25mg x 20 film. tabl. has a maximum price of 9.43 RON.

In the case of Triplixam, which is also the original product, on the Romanian market, there is no generic drug version containing the same active substances and the same concentrations. Thus, for the combination perindopril/indapamide/amlodipine we do not have a difference in terms of maximum price, this being the only option listed in Romania.

Conclusion

Generic medicines are considered to be cheaper versions of the original drug. Our aim was to compare the costs of original and generic drugs in the category of products for the treatment of cardiovascular diseases. Thus, we can observe the situation of the two drugs where the original product was available, bisoprolol 10mg and atorvastatin 10mg. The price difference varies between 75.56% and 46.67% for the first active ingredient and for the second active ingredient the cost of the original product vs. the generic varies between 73.37% and 40.07%. The cost of the original drug is much

higher which can lead to issues with patient adherence to the treatment. In order to solve those issues pharmaceutical companies have created generic medicines with lower costs.

We can conclude that the differences in costs are visible, and in terms of accessibility and affordability of the patient to treatment, the doctor is the person who, following the consultation and diagnosis, chooses the best option for the patient in cause.

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