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Prices of combination medicines and single-molecule antihypertensive medicines in India's private health care sector

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Abstract

More than half of patients with hypertension require two or more medicines to control blood pressure. Combinations of anti-hypertensive medicines are available as Single Pill Combinations (SPCs) or Single Agent Pills (SAPs). SPCs of two or more antihypertensive medicines facilitate simpler dosing schedules, decrease pill burden, increase adherence to medicine, and simplify procurement and distribution. Despite this, equivalent combinations of separate pills (SAPs) are often prescribed instead of SPCs under the assumption that SAPs are priced lower. This study compared prices of anti-hypertensive SPCs and equivalent SAPs in the private health care sector of India. High sales volume anti-hypertensive SPCs and SAPs were selected from 2018 private sector pharmaceutical sales data. SPCs and SAPs price information was collected from online pharmacy websites between November 2019 and January 2020. Antihypertensive SPCs represent approximately 39.1% of India's private sector anti-hypertensive drug market. Multiple manufacturers produce the same top-selling SPCs, suggesting a viable and competitive market. A comparison of SPCs and SAPs across different manufacturers showed that the lowest prices of both SPCs and the sum of component SAPs were nearly identical across different manufacturers. An analysis of dual-drug SPCs and SAPs by the same manufacturer showed that most manufacturers (five of six) had priced their SPCs higher than SAPs. These observations suggest that the price of SPCs could be lowered to match the combined price of the component SAPs, and manufacturing costs and market forces do not present a barrier to the implementation of anti-hypertensive SPCs.

1 | INTRODUCTION

High blood pressure increases the risk of ischemic heart disease, stroke, and acute myocardial infarction.¹ India has a hypertension prevalence of 25.3% among adults (18+ years) which translates to 207 million persons.² Among a nationally representative sample of

individuals aged 15–49 years, 76% had been screened for hypertension, 45% were aware that they had hypertension, 13% were on treatment, and 8% had their hypertension under control.³ Long-term therapies for chronic conditions such as hypertension are associated with low treatment compliance, a contributor of uncontrolled blood pressure in more than two-thirds of patients.¹ While most patients

This is an open access article under the terms of the Creative Commons Attribution NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes. © 2020 The Authors. The Journal of Clinical Hypertension published by Wiley Periodicals LLC. with hypertension require two or more medicines to control their blood pressure,⁴⁻⁶ research has shown that each additional pill added to the treatment plan tends to lower adherence.⁷ Medicines for hypertension are available as single molecules or a combination of two or more single molecules. For the purpose of this paper, single-molecule medicines are referred to as Single Agent Pills (SAPs) and combination molecule medicines are referred to as Single Pill Combinations (SPCs). SPCs can improve adherence and blood pressure control^{8,9} by facilitating simpler dosing schedules and decreasing the pill burden. SPCs may also help simplify and streamline the processes related to procurement and distribution of medicines.¹⁰

Patients in India access medicines through government health facilities or private health facilities. States procure medicines to distribute through the government health facilities.¹¹ However, a large proportion of patients seek care in the private health sector.¹² In India, 70% of out-patient visits take place in the private sector.¹³ Patients' out-of-pocket payments account for over three-fourths of all health care payments.¹⁴ Medicines are the single largest component of these payments.¹⁵ Private pharmacies are often utilized more than public facilities due to ease of access, shorter waiting times, convenient opening hours, availability of medicines, and availability of credit.^{15,16}

India is home to a large pharmaceutical manufacturing industry; pricing patterns observed in India's private sector market have implications for pharmaceuticals supplies around the world. Low-cost generic medicines manufactured in India are seen as a competitive force for determining the market pricing. We conducted this study to analyze the prices of top-selling SPCs and compare the prices of these SPCs with the sums of their SAPs in the Indian private sector. We also surveyed data by individual manufacturers to compare prices between equivalent SPCs and SAPs in their own portfolios.

2 | METHODS

Sales data of anti-hypertensive medicines in India were analyzed using the private sector pharmaceutical sales dataset from IQVIA Consulting and Information Services (IQVIA), a private consulting firm that collects and maintains data on India's private sector pharmaceutical sales.¹⁷ IQVIA collects the drug sales data from a nationally representative sample of stockists and super-stockists on a monthly basis. For purpose of this study, national level sales data from January 2018 to December 2018 were considered and measured using number of units sold (quantity). Based on the 2018 data for total sales of anti-hypertensive SPCs, medicines (classes and molecules), their strengths (5, 10 mg etc), and brands (company name) were selected using the principles of ABC analysis in operations management.¹⁸ The criteria used were as follows: SPCs that contributed to 70% of annual sales of all SPCs in 2018 (quantity number of pills); strengths of the select SPC that contributed to 70% of annual sales of that SPC; brands that contributed to 70% of annual sales (in 2018) for the select strength of the chosen SPCs. This

criteria were also used for SAPs. Additionally, price data were collected specifically for those companies that manufactured both the SPCs and their component SAPs.

Data on price to consumers were collected for selected medicines using a publicly available website called "1mg" between November 2019 and January 2020¹⁹ and validated with the maximum retail price (MRP) reflected on other online pharmacy websites. Price data are reported in 2019–2020 India rupees (INR).

Price to consumers has been expressed as median values and a range of minimum and maximum values. Price ratio is calculated by dividing maximum price to the minimum price which interprets that Maximum MRP is "x" times higher than minimum MRP. Lower price ratio means that the drug has a narrow price range, and hence, the difference in maximum and minimum price will be lower, whereas higher price ratio means that the drug price varies with a large difference in minimum and maximum MRP.²⁰

3 | RESULTS

3.1 | Sales shares of SPCs and SAPs in the Indian private sector

In 2018, over eight billion units of anti-hypertensive SPCs were sold in the Indian private sector, representing 39.1% of the total private sector anti-hypertensive drug market. The remainder of the 21 billion anti-hypertensive medicines were sold as single-drug pills in 2018 and are classified as SAPs (Table 1).

3.2 | Price of SPCs in the Indian private sector

For the ten top-selling dual-drug SPCs sold in 2018 (70% of the overall sales of each type), seven were sold by five or more distinct pharmaceutical manufacturing companies (Table 2). The highest median prices per pill were for SPCs that included the angiotensin II receptor blocker (ARB) telmisartan as one of the two drugs. Sales by a larger number of manufacturers were associated with a higher price ratio for a given SPC, indicating a diverse and competitive market for those SPCs. There were fewer manufacturers of triple-drug SPCs (two or three manufacturers each), leading to a narrower price range for these triple-drug combinations (reflected in a price ratio < 2. 0; Table 3).

TABLE 1 Sales volume (quantities) and market shares of antihypertensive single pill combinations (SPCs) and single agent pills (SAPs) in the Indian private sector pharmaceuticals market, 2018

Medicine category	Volume (millions)	Market share (%)
SPCs	8241.20	39.1
SAPs	12,825.20	60.9
SPCs + SAPs	21,066.40	100

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SPC (contributing upto 70% of total 2 drug SPC sale)	Strength (contributing upto 70% of the select SPC)	Class	No. of brands considered (contributing upto 70% of the SPC-strength)	Median in INR (USD)	MRP range of the molecule in INR (USD)	Price ratio in INR (USD)
Amlodipine + Atenolol	5 MG/50 MG	CCB + BB	6	4.99 (0.07)	1.27-10.03 (0.02-0.14)	7.9 (7)
Hydrochlorothiazide + Telmisartan	12.5 MG/40 MG	Diuretic + ARB	12	9.08 (0.12)	3.53-15.48 (0.05-0.21)	4.39 (4.2)
Amlodipine + Telmisartan	5MG/40 MG	CCB + ARB	13	10.7 (0.14)	3.35-14.30 (0.05-0.19)	4.27 (3.8)
Hydrochlorothiazide + Losartan	12.5 MG/50 MG	Diuretic + ARB	7	6.38 (0.09)	3.00-11.95 (0.04-0.16)	3.98 (4)
Chlortalidone + Telmisartan	12.5 MG/40 MG	Diuretic + ARB	10	10.28 (0.14)	3.75-14.62 (0.05-0.19)	3.9 (3.8)
Chlortalidone + Telmisartan	6.25 MG/40 MG	Diuretic + ARB	4	11.89 (0.16)	4.34-13.63 (0.06-0.19)	3.14 (3.16)
Amlodipine + Metoprolol	5 MG/50 MG	CCB + BB	10	10.7 (0.14)	2.77-12.57 (0.04-0.17)	4.54 (4.25)
Furosemide + Spironolactone	20 MG/50 MG	Diuretic + Diuretic	5	3.77 (0.05)	2.5-6.12 (0.03-0.08)	2.45 (2.67)
Spironolactone + Torasemide	25 MG/10 MG	Diuretic + Diuretic	2	3.13 (0.04)	3.13 (0.04)	1
Spironolactone + Torasemide	50 MG/10 MG	Diuretic + Diuretic	1	4.92 (0.07)	4.92 (0.07)	1
<i>Note:</i> Exchange rate USD:INR 1:74. Prices are in 2019–2020 India rupees (INR).	INR).					

TABLE 3 Price per pill of top-selling triple-drug single pill combination (SPC) anti-hypertensive medicines in the Indian private sector	ngle pill combination (SPC) anti	-hypertensive medicines	in the Indian private sector			
SPC (contributing upto 70% of total 3 drug SPC sale)	Strength (contributing upto 70% of the select SPC)	Class	No. of brands considered (contributing upto 70% of the SPC-strength)	Median in INR (USD)	MRP range of the molecule in INR (USD)	Price ratio INR (USD)
Amlodipine + Hydrochlorothiazide + Telmisartan	5MG/12.5MG/40 MG	CCB + Diuretic + ARB	2	9.85 (0.13)	9.85 (0.13) 7.86-11.85 (0.11-0.16)	1.51 (1.45)
Amlodipine + Hydrochlorothiazide + Telmisartan	5MG/12.5MG/80 MG	CCB + Diuretic + ARB	3	17.18 (0.23)	17.18 (0.23) 12.40-21.33 (0.17-0.29) 1.72 (1.71)	1.72 (1.71)
Amlodipine + Hydrochlorothiazide + Olmesartan Medoxomil	5MG/12.5MG/20 MG	CCB + Diuretic + ARB	2	13.45 (0.18)	13.45 (0.18) 13.40-13.50 (0.18-0.18) 1.00	1.00
Amlodipine + Hydrochlorothiazide + Olmesartan Medoxomil	5MG/12.5MG/40 MG	CCB + Diuretic + ARB	2	21.35 (0.29)	20.95-21.75 (0.28-0.29) 1.04 (1.03)	1.04 (1.03)

Prices are in 2019-2020 India rupees (INR). Note: Exchange rate USD:INR 1:74.

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SPC						SAP 1			SAP 2			MRP range comparison	arison
2 Drug SPC	Strengths	Drug classes	No. of brands analyzed	Median in INR (USD)	Median MRP range in INR in INR (USD) (USD)	No. of brands analyzed*	Median in INR (USD)	No. of MRP range brands in INR (USD) analyzed*	No. of brands analy zed*	Median in INR (USD)	Median MRP range in INR in INR (USD) (USD)	MRP range as single mol (SAP1+SAP2) in INR (USD)	Range comparison as combination drug in INR (USD)
Amlodipine + Atenolol 5 MG/50 MG	I 5 MG/50 MG	CCB + BB	6	4.99 (0.07)	1.27-10.03 (0.02-0.14)	10	2.80 (0.04)	2.80 (0.04) 0.68-2.86 (0.01-0.03)	4	1.96 (0.03)	0.71-1.96 (0.01-0.03)	1.39-4.82 (0.02-0.07)	1.27-10.03 (0.02-0.14)
Hydrochlorothiazide + Telmisartan	12.5 MG/40 Diuretic + 12 MG ARB	Diuretic + ARB	12	9.08 (0.12)	3.53-15.48 (0.05-0.21)	8	1.02 (0.01)	0.87-1.09 (0.01-0.01)	12	7.19 (0.1)	3.40-7.33 (0.05-0.1)	4.27-8.42 (0.06-0.11)	3.53-15.48 (0.05-0.21)
Amlodipine + Telmisartan	5MG/40 MG CCB + AR	CCB + ARB	13	10.7 (0.14)	3.35-14.30 (0.05-0.19)	10	2.80 (0.04)	0.68-2.86 (0.01-0.04)	12	7.19 (0.1)	3.40-7.33 (0.05-0.1)	4.08–10.19 (0.06–0.14)	3.35-14.30 (0.05-0.19)
Hydrochlorothiazide + Losartan	12.5 MG/50 Diuretic + MG ARB	Diuretic + ARB	7	6.38 (0.09)	3.00-11.95 (0.04-0.16)	Ø	1.02 (0.01)	0.87-1.09 (0.01-0.01)	10	4.60 (0.06)	2.16-6.6 (0.03-0.09)	3.03-7.69 (0.04-0.10)	3.00-11.95 (0.04-0.16)
Amlodipine + Metoprolol	5 MG/50 MG	CCB + BB 10	10	10.7 (0.14)	2.77-12.57 (0.04-0.17)	10	2.80 (0.04)	0.68-2.86 (0.01-0.04)	7	6.31 (0.09)	6.14-6.33 (0.08-0.09)	6.82-9.19 (0.09-0.12)	2.77-12.57 (0.04-0.17)
Chlortalidone + Telmisartan	12.5 MG/40 Diuretic + 10 MG ARB	Diuretic + ARB	10	10.28 (0.14)	3.75-14.62 (0.05-0.19)	7	5.79 (0.08)	2-6.86 (0.02-0.09)	12	7.19 (0.1)	3.40-7.33 (0.05-0.1)	5.40–14.19 (0.07–0.19)	3.75-14.62 (0.05-0.2)
Note: SDCs/SDC strengths that had more than five hrands contributing to 70% of their sale only were considered for mice commarison with combined arise of the SADs to avoid skewing of data due to	the that had m	ore than five	e hrande con	trihuting t	o 70% of thei	w vlao eles r	vere consider	ed for price co	im accircum	th combin	ed price of th	SADe to avoid ek	ewing of data due to

Note: SPCs/SPC strengths that had more than five brands contributing to 70% of their sale only were considered for price comparison with combined price of the SAPs to avoid skewing of data due to limited sample. Brands for SAPs are also chosen based on top brands that contribute upto 70% sales of the particular SAP. Exchange rate USD:INR 1:74. Prices are in 2019-2020 Indian rupees. -WILEY

3.3 | Price of SPCs as compared with price of their component SAPs

Of six dual-drug SPCs analyzed, each were sold by six or more distinct pharmaceutical companies (Table 4). The lower-bound estimate of the dual-drug SPC MRP range was consistently similar to (and slightly lower than) the lower-bound estimate of the sum of the component SAPs. The upper-bound estimate of the SPC MRPs was consistently higher than the upper-bound of the sum of their component SAPs. Thus, though the MPR range was wider for the dual-drug SPCs compared with the MPR range of the sum of the component SAPs, the ranges broadly overlap. The lowest prices of both SPCs and the sum of component SAPs were nearly identical. A comparison of dual-drug SPCs and SAPs by the same manufacturer showed that for the six different dual-drug SPCs at least one company offered an SPC at a lower price than the sum of same company's component SAPs.

For the limited sample of the three different triple-drug SPCs (two with different doses of amlodipine/hydrochlorothiazide/telmisartan and one with amlodipine/hydrochlorothiazide/olmisartan), the prices were consistently higher than the sums of their component SAPs, and there was relatively less overlap in their MRP ranges.

4 | DISCUSSION

Our analysis found that, on average, SPCs are priced higher in the Indian private sector than the sum of their component SAPs, but the range of prices for dual-drug SPCs broadly overlaps the range of the sums for the component SAPs. In addition, some companies manufacture SPCs at a lower price than the sum of the component SAPs. This may indicate that the cost of manufacturing SPCs is not much higher than the combined cost of manufacturing each individual SAP. Alternatively, it could be that SPCs are a sold and marketed at a lower price, strategically and temporarily for the purpose of gaining a foothold in the market. If the latter strategy explains instances of equivalent SPC and SAP prices, with passage of time, prices of the company's SPC should rise faster than prices of their corresponding SAPs.

From a public health perspective, SPCs are considered advantageous as they improve patient's adherence to medicines, thus enhancing blood pressure treatment efficacy, and, through reduction in the numbers of pills, streamline large-volume procurements, and ease pressure on supply chains.¹⁰ Based on these considerations, some anti-hypertensive SPCs were added to the World Health Organization essential medicines list in 2019.²¹ Lowering SPC prices is a critical part of opening access and incentivizing use of these preferred SPC medicines. One way to lower SPC prices could be through centralized procurement of medicines by the government for patients regardless of whether they access services in public or private sector facilities. Standardized hypertension treatment protocols that feature preferred SPCs could be mandated for government health care facilities and then disseminated in the private sector. Distribution of these government-procured SPCs could also be channeled into private sector facilities.

The volume of private sector anti-hypertensive medicine sales in India is massive, topping more than 20 billion pills sold in 2018 alone. The molecules that dominate majority share of private sector anti-hypertensive medicine sales for some of these drug classes are those that come under price control by the Government of India (amlodipine, atenolol, and hydrochlorothiazide).²² This seems to suggest that this market is predominantly a low-retail-price high-volumes market that is competitive for many generic manufacturers and profitable despite the price control. The Government of India's control of dual-drug SPCs to match the equivalent prices at the lower-bound estimate of their component SAPs would accelerate the uptake of SPC anti-hypertensive medicines in India. At an equivalent price per patient, the superior efficacy and treatment efficiency of SPCs, along with streamlined procurement and supply chain impacts, could lead to greater health gains for the same financial investment from society.

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CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Sagri Negi, Anupam Khungar Pathni, Swagat Kumar Sahoo, and Bhawna Sharma contributed to the conception of the work. Sagri Negi, Swagat Kumar Sahoo, Kishan Swaroop, and Tanushree Mahajan contributed to the acquisition of the data. All authors contributed to the analysis and interpretation of the data. Sagri Negi developed the draft of the manuscript with all authors contributing to the revision of the manuscript. All authors gave the final approval of the version to be published.

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