

## Cost minimization analysis of generic and innovator formulations of antihypertensive drugs

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### ABSTRACT

**Background:** Hypertension, a chronic condition requiring lifelong care, affects approximately 25.3% Indian population. Average annual hypertension management cost which also includes medication cost varies from Rs. 4042 to 7621, amounting up to 40% of total household income of few families. Selection of a different brand or generic formulation may have an immense impact on total expenditure for treatment of hypertension. Present study aims at determining cost variability and cost analysis of various single drug antihypertensive formulations available in Indian market.

**Methods:** One most prescribed drug, each from Joint National Committee recommended antihypertensive- thiazide diuretics, calcium channel blockers, angiotensin converting enzyme inhibitors, angiotensin-receptor blockers and  $\beta$  blockers were selected for cost analysis. Cheapest, costliest and median priced formulations were searched for individual drugs and were compared to the price of their generic counterparts.

**Results:** Generic formulations of hydrochlorothiazide, amlodipine, enalapril, losartan and atenolol were cheaper even than their respective cheapest innovator formulations. Costliest innovator formulation of amlodipine was 1750% expensive than generic one. Costliest counterparts of generic formulations were many folds overpriced. Similarly, innovator formulation of losartan was up to 953.89% costly than generic one. Innovator formulations of hydrochlorothiazide were the least costly than its generic counterpart, yet being at least 150% more expensive. Also, there exists considerable broad range of price among similar innovator formulations.

**Conclusions:** By prescribing generic antihypertensive drug, we can reduce treatment expenditure by many folds. Same feat can be marginally achieved by using lower cost innovator formulations.

**Keywords:** Cost minimization, Antihypertensive, Generic, Innovator, Hypertension

### INTRODUCTION

Hypertension or high blood pressure, is when force of blood flowing through one's blood vessels is consistently too high. According to WHO, hypertension is diagnosed if, when it is measured on two different days, the systolic blood pressure readings on both days is  $\geq 140$  mmHg and/or the diastolic blood pressure readings on both days is  $\geq 90$  mmHg.<sup>1</sup> Hypertension is classified in two different types which are essential hypertension and secondary hypertension. Essential hypertension, most commonly

occurring of two, has no known cause and can be associated with a multitude of pathophysiological factors. Hyperactive sympathetic nervous system, certain dietary habits like high sodium intake, long standing uncontrolled diabetes mellitus, lack of regular physical exercise leading to obesity are few probable causes of essential hypertension.<sup>2</sup> While, separate pathophysiological conditions like renal disease, primary hyperaldosteronism, and obstructive sleep apnea often results in secondary hypertension.<sup>3</sup> Overall, hypertension occurs in an estimated 26 percent of world's population

(972 million people), and the incidence is expected to rise to 29 percent by 2025, driven largely by low and middle income countries.<sup>4</sup> In India, fourth district level household survey, reported higher prevalence of hypertension in men (27.4%) than women (20.0%) at 25.3 percent (age >18 years).<sup>5</sup>

Hypertension, a chronic disorder requiring lifelong treatment in majority of patients. In this scenario, treatment of hypertension would consume significant fraction of income of a household. Globally, monthly cost for hypertension treatment is around \$22.<sup>6</sup> While, an Indian study reported that, Rs. 7154 was the average total annual cost of hypertension and related disorders. For government and private hospital facilities, the average annual out of pocket expenditure was Rs. 4042 and Rs. 7621 respectively. Fifteen percent of households were catastrophically spending 40 percent of household income in management of hypertension.<sup>7</sup> This scenario warrants need of cost reduction for the treatment of hypertension.

Hypertension's economic costs include direct medical costs as well as indirect costs such as loss of productivity. Direct medical costs are the costs of medical products and services used for the prevention, diagnosis and treatment of a disease and its complications. These costs include hospitalization expenses, emergency room visits, doctor visits, laboratory and imaging tests, home health care, and prescription drugs. Among this, cost of prescription drugs, a monthly recurring expense, often for a lifetime is an important contributing factor in determining total expenditure behind treatment of hypertension. Cost of medicines varies among various company brands, generic formulations as well as government supplied or subsidized drugs. Generic formulations; defined as a medication created to be the same as an already marketed brand-name drug in dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use; are perceived as cheaper formulations.<sup>8</sup> But, cost comparison data of generic formulations to their innovator counterparts is not readily available, which may lead to selection of a particular brand or supplied drug over generic formulation. This decision has potential to immensely impact total expenditure on treatment of hypertension. Therefore, to aid treating physicians and patients in properly selecting generic or innovator formulations, present study was directed to carry out cost comparison by determining cost variability and doing cost analysis of various single drug antihypertensive formulations available in Indian market.

## METHODS

Generic medicines are well-tested pharmaceutical products of proven high quality. They are strictly regulated by the competent national and only through a comprehensive quality control process; they are given authorization. This procedure ensures that the generic

medicines available in the market are sufficiently safe and effective.<sup>9</sup> Hence, generic drugs and innovator drugs are considered as of similar efficacy and only their direct to patient cost were taken in to consideration for analysis in present study.

Prices of generic formulations of selected medicines were obtained from local generic medicine drug dispensing stores of different district of Gujarat. While prices of innovator formulations of selected medicines were obtained from CIMS and database.<sup>10,11</sup>

Thiazide diuretics, calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin-receptor blockers are recommended first line drugs for the treatment of various types of hypertension by Joint National Committee-8 (JNC-8).<sup>12</sup> In India, among thiazide diuretics, calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin-receptor blockers; hydrochlorothiazide, amlodipine, enalapril and losartan are most prescribed drugs among respective groups and hence their single drug oral formulations were selected for cost analysis in present study.<sup>13,14</sup>  $\beta$  blockers, which were considered as first line antihypertensive drug by JNC 7, and still one of the most commonly prescribed antihypertensive drugs in India were also included in the present study. Atenolol was selected from the  $\beta$  blockers group for cost comparison and analysis.

Present study was carried out at pharmacology departments of government medical college, Bhavnagar, Gujarat and medical college, Baroda, Gujarat, during September, 2019 to November, 2019.

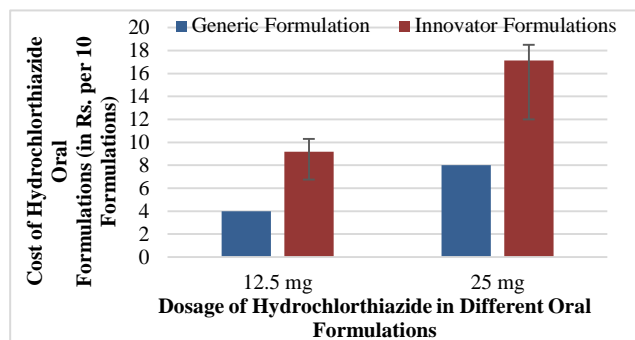
Drugs' prices were analyzed and cheapest and costliest and median priced formulations were searched for individual drugs and were compared to the price of their generic counterparts. Data is presented as absolute numbers as well as percentage cost difference between individual drugs formulations. They were also presented with their cost difference to median priced drug formulation of respective drugs.

Microsoft Excel (version 15.0) was used for data management and calculation.

## RESULTS

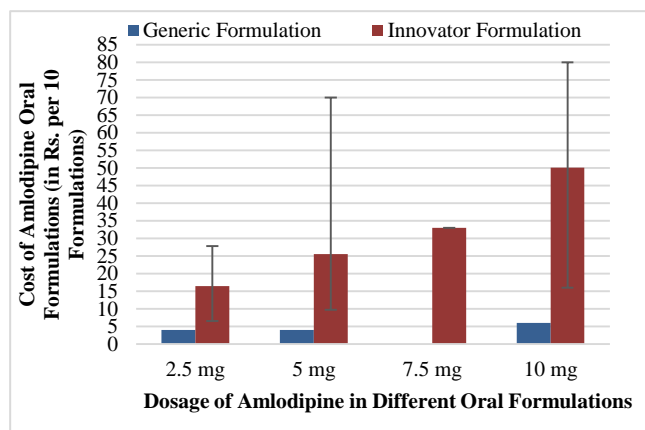
For hydrochlorothiazide, cost of generic 12.5 mg and 25 mg single drug oral formulations were Rs. 4 and Rs. 8, respectively. Cost of their innovator counterparts varied from Rs. 6.75-10.3 with many formulation nearing price of Rs. 9.17 for 12.5 mg dose, while for 25 mg dose cost varied from Rs. 12-18 with many falling near price of Rs. 17.14. These findings suggests that cost of innovator medicine are overpriced at least 168.75% to generic formulation and price goes all the way higher up to 257.5% for 12.5 mg dose. Same with 25 mg dose, cost of innovator formulations was higher from 150-231.25% than their generic counterparts. Even among innovator

formulations price varied from 1.53 to 1.54 fold between cheapest and costliest formulations (Table 1, Figure 1).



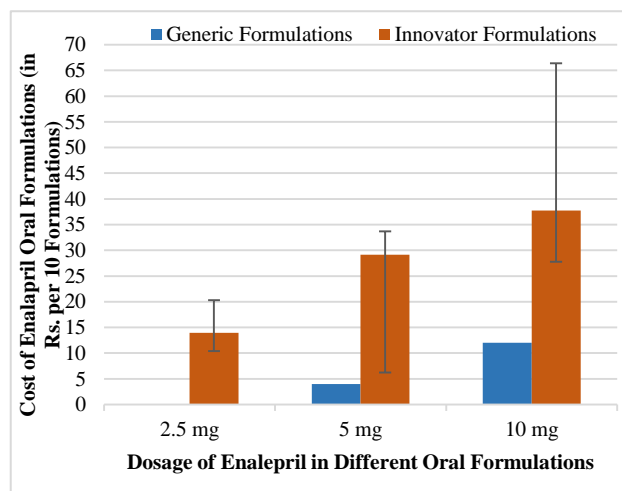
**Figure 1: Price variability of hydrochlorothiazide for various therapeutically used doses and their individual comparison with their generic counter parts (cost in Rs. per 10 formulations).**

The price of generic 2.5 mg, 5 mg and 10 mg of single oral drug formulations of amlodipine was Rs. 4, Rs. 4 Rs. 6, respectively. The cost of their innovator counterparts ranged from Rs. 6.5-27.7 with many formulations close to Rs. 16.38 for 2.5 mg dose, while the price of 5 mg dose varied from Rs. 9.71-70 with many falling close to Rs. 25.5, while the cost of 10 mg dose varied from Rs. 16-79.97 with many falling close to Rs. 50.04. This findings suggest that the value of innovator formulation is at least 162.5% overpriced and that the price may rise up to 693.75% for dose of 2.5 mg. Same with 5 mg dose, cost of innovator formulations were higher from 242.75-1750% than their generic counterparts. Price of innovator formulations were from 200-999.62% higher as compared to 10 mg generic formulations. The most expensive formulations for 2.5 mg, 5 mg and 10 mg are up to 4.27, 7.21 and 5 fold higher than their respectively cheapest formulations among innovative formulations (Table 1, Figure 2).

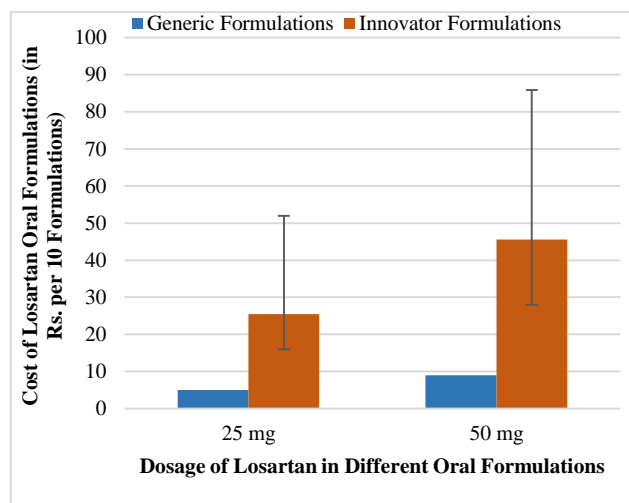


**Figure 2: Price variability of amlodipine for various therapeutically used doses and their individual comparison with their generic counter parts (cost in Rs. per 10 formulations).**

For enalapril, cost of generic 5 mg and 10 mg single drug oral formulations were Rs. 4 and Rs. 12, respectively. Cost of their innovator counterparts varied from Rs. 6.25-33.71; with many formulation nearing price of Rs. 29.15 for 5 mg dose, while for 10 mg dose, cost varied from Rs. 27.75-66.4 with many falling near price of Rs. 37.75. Such results suggest that innovator formulations' prices are overpriced for a generic formulation at least 156.25% and price may further increase by up to 842.75% for a dosage of 5 mg. Same with 10 mg dose, cost of innovator formulations were higher from 231.25-553.33% than their generic counterparts. The cost of the most expensive 2.5 mg, 5 mg and 10 mg formulations was even higher up to 1.95, 5.39 and 2,39 fold than those of their respective cheapest innovative formulations (Table 1, Figure 3).



**Figure 3: Price variability of enalapril for various therapeutically used doses and their individual comparison with their generic counter parts (cost in Rs. per 10 formulations).**



**Figure 4: Price variability of losartan for various therapeutically used doses and their individual comparison with their generic counter parts (cost in Rs. per 10 formulations).**

**Table 1: Price variability of hydrochlorothiazide, amlodipine, enalapril, losartan and atenolol for various therapeutically used doses and their individual comparison with their generic counter parts (cost in Rs. per 10 formulations).**

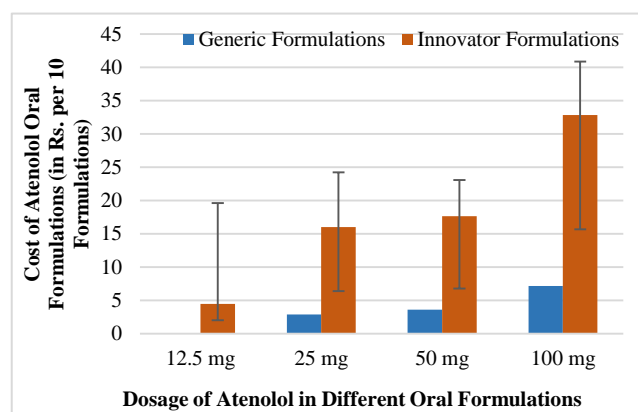
Name of drug and dosage of formulations	Cost of generic formulation	Cheapest innovator formulation	Median cost innovator formulation	Costliest innovator formulation	Fold increase in cost <sup>\$</sup>
		N (%)	N (%)	N (%)	
Hydrochlorothiazide 2.5 mg	4	6.75 (168.75)*	9.175 (229.37)*	10.3 (257.5)*	1.53
Hydrochlorothiazide 25 mg	8	12 (150)*	17.14 (214.25)*	18.5 (231.25)*	1.54
Amlodipine 2.5 mg	4	6.5 (162.5)*	16.38 (409.5)*	27.75 (693.75)*	4.27
Amlodipine 5 mg	4	9.71 (242.75)*	25.5 (637.5)*	70 (1750)*	7.21
Amlodipine 7.5 mg	N.A.	33	33	33	-
Amlodipine 10 mg	6	16 (200)*	50.04 (625.56)*	79.97 (999.62)*	5
Enalapril 2.5 mg	N.A.	10.4	13.95	20.27	1.95
Enalapril 5 mg	4	6.25 (156.25)*	29.15 (728.75)*	33.71 (842.75)*	5.39
Enalapril 10 mg	12	27.75 (231.25)*	37.75 (314.58)*	66.4 (553.33)*	2.39
Losartan 25 mg	5	15.95 (319)*	25.5 (510)*	52 (1040)*	3.26
Losartan 50 mg	9	28 (311.11)*	45.55 (506.11)*	85.85 (953.89)*	3.07
Atenolol 12.5 mg	N.A.	2	4.46	19.6	9.8
Atenolol 25 mg	2.86	6.39 (223.43)*	16 (559.44)*	24.22 (846.85)*	3.79
Atenolol 50 mg	3.57	6.77 (189.63)*	17.64 (494.12)*	23.07 (646.22)*	3.41
Atenolol 100 mg	7.14	15.64 (219.05)*	32.85 (460.08)*	40.88 (572.55)*	2.61

<sup>\$</sup>=Fold increase in cost between cheapest to costliest innovator formulations; \*=Price difference (in percentage) between individual innovator formulation to its generic counterpart; N.A.= Generic formulation not available.

For losartan, cost of generic 25 mg and 50 mg single drug oral formulations were Rs. 5 and Rs. 9, respectively. Cost of their innovator counterparts varied from Rs. 15.95 to Rs.52; with many formulation nearing price of Rs. 25.5 for 25 mg dose, while for 50 mg dose, cost varied from Rs. 28-85.85; with many falling near price of Rs. 45.55. These findings suggests that cost of innovator medicine are overpriced at least 319% to generic formulation and price goes all the way higher up to 1040% for 25 mg dose. Same with 50 mg dose, cost of innovator formulations were higher from 311.11 to 953.89% than their generic counterparts. Even among innovator formulations, costliest formulations' price for 25 mg and 50 mg were up to 3.26 and 3.07 fold higher than their respective cheapest innovator formulations (Table 1, Figure 4).

For atenolol, cost of generic 25 mg, 50 mg and 100 mg single drug oral formulations were Rs. 2.86, Rs. 3.57, Rs. 7.14, respectively. Cost of their innovator counterparts varied from Rs. 6.39 to Rs. 24.22 with many formulation nearing price of Rs. 16 for 25 mg dose, while for 50 mg dose cost varied from Rs. 6.77-23.07 with many falling near price of Rs. 17.64; for 100 mg dose cost varied from Rs. 15.64 to Rs. 40.88 with many falling near price of Rs. 32.85. These findings suggests that cost of innovator medicine are overpriced at least 223.43% to generic formulation and price goes all the way higher up to 846.85% for 25 mg dose. Same with 50 mg dose, cost of innovator formulations were higher from 189.63-646.22% than their generic counterparts. Price of innovator formulations were from 219.05-572.55% higher as

compared to 100 mg generic formulations. Even among innovator formulations, costliest formulations' price for 12.5 mg, 25 mg, 50 mg and 100 mg were up to 9.8, 3.79, 3.41 and 2.61 fold higher than their respective cheapest innovator formulations (Table 1, Figure 5).



**Figure 5: Price variability of atenolol for various therapeutically used doses and their individual comparison with their generic counter parts (cost in Rs. per 10 formulations).**

## DISCUSSION

Treatment of a life style disorder i.e., hypertension is a costly affair as it acquires regular recurring costs often for lifelong duration. It is necessary to encourage complete adherence to drug therapy for optimal control of hypertension. Yet, in real world scenario, compliance to

the treatment of hypertension is low. There are multiple reasons for non-adherence, but relative high cost of medicines, is one of few pertinent causes for non-adherence to treatment in India.<sup>15</sup> As a result, if patient is opted for the drug which is of higher cost than he can afford, his adherence to the treatment gets affected.<sup>16</sup> Even if the patient tries to cope with cost of medicine, his family income may get blunted resulting in poorer household conditions and lesser expenditure on essential modalities like nutrition and education. A study reported that fifteen percent households were incurring catastrophic expenditure at highest threshold of 40% of their household income, leading to impoverishment of 34.2% households.<sup>7</sup> Hence, price of medicine remains one of the important factor which can be minimized to provide affordable treatment options to patient.

Hence, selection of proper drug formulations becomes an important aspect in improving adherence to treatment protocols for chronic lifestyle disorders. Cumulative cost imparted by costliest formulation as compared to cheapest formulation or generic formulation may be many fold in long run. If, instead of generic formulation of hydrochlorothiazide, its innovator formulations are prescribed, cost of daily therapy may increase anywhere between 1.69 to 2.57 fold (168.75-257.5% difference between costs). Most commonly utilized maintenance doses of amlodipine are 5 mg and 10 mg OD. If innovator formulations of amlodipine are selected, they will increase cost burden for medicines up to 2.42 to staggering 17 fold per day (242.75-1750% difference between cost) and 2 to 10 fold (200-999.62% difference between costs) in case of 5 mg and 10 mg OD therapy, respectively. Similarly, if innovator formulations of enalapril are selected over generic, patient will be spending 1.5 to 8.4 fold higher amount for 5 mg dose (156.25-842.75% difference between cost of formulations) and 2.3 to 5.53 fold higher amount, daily for 10 mg dose (formulation cost difference of 231.25-553.33%). These situation becomes dreadful in case of losartan if patient is prescribed with costliest innovator formulation for 25 mg daily dose; expenditure increases to 10 fold over generic one as cost of this innovator formulation is 1040% high than its generic counterpart. Similar higher expenditure can be anticipated in case of 50 mg innovator formulations. Coming to one of the most prescribed antihypertensive agent atenolol, its generic formulations are up to 8.46, 6.46 and 5.72 fold cheaper than their counterpart innovator formulations of 25 mg, 50 mg and 100 mg, respectively.

Dilemma between selecting generic formulations and innovator formulations are perceived by many physicians and patients. In this scenario, even if one prefers innovator formulations and selects the cheapest available innovator formulation, one can save substantially. Like cost of cheapest innovator formulations were up to 1.5, 7.21, 5.39, 3.26 and 3.41 fold cheaper than their costliest counterparts in case of commonly prescribed doses of

hydrochlorothiazide, amlodipine, enalapril, losartan and atenolol.

Awareness regarding availability of various generic and innovator formulations or cheaper and costly ones; helps in proper selection of formulations for each patient. This information will also help patient in selecting a formulation according his willingness to spend and affordability. This in turn, will improve compliance and adherence to the treatment goals, leading to effective management of hypertension.

## CONCLUSION

Available data shows price of generic formulations are found to be less than all of their innovator counterpart formulations for selected antihypertensive drugs. Cost of costliest of innovator formulations is found to be many fold high in many antihypertensive drugs than their cheapest counterparts.

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