

## Pharmacoeco-economic study: A cost variation analysis of AKT drugs available in Indian market

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### Abstract

**Introduction:** The cost of drug play important role in practice of medicine and disease outcome. In Indian market numerous brand available of generic drug. Tuberculosis is curable disease but if proper treatment not taken by patients then lead to development of drug resistance or pulmonary disability. AKT drugs used for the management of tuberculosis.

**Objective:** To compare and analysed cost variation in AKT drugs with different brand name for same dosage form & same active compound.

**Materials and Methods:** The price of the drug with same formulation and same strength (Dosage) was review from Indian drug review issue 3, 2017 (IDR) & CIMS (Apr- Jul 2017). Percentage of cost price variation and Cost ratio is analysed.

**Result:** High percentage of cost variation among first line AKT drugs seen with Ethambutol (474.51%) followed by Isoniazid (432.60%). Least percentage of cost variation seen with streptomycin (1.01%) followed by rifampicin (1.33%). Maximum cost ratio of first line drugs seen with Ethambutol (5.74). Among 2<sup>nd</sup> line AKT drug Maximum and least percentage of cost variation are seen with levofloxacin 500 mg tablet formulations (1550.84%) and Ofloxacin 400 mg sustained Releases - tablet (1.57%) respectively. Higher percentage of cost variation seen with more manufacture company/ no. of brand.

**Conclusion:** The wide percentage of cost variation is seen with AKT drugs available in Indian market. Regulation of drug price by concerned agencies and by government is needed. Rational drug prescription with low cost is important for treatment adherence and disease outcome.

**Keywords:** Pharmacoeconomics, Cost variation, Cost ratio, AKT drugs.

### Introduction

Pharmacoeconomics identifies, measure and compare the cost and consequences of drug therapy to healthcare system and play important role in practices of medicine.<sup>1,2</sup> Cost of drugs is important factor for the good patient's compliances with treatment. In Indian market AKT drugs (antitubercular) drugs available are available with brand name.

Tuberculosis is cause by mycobacterium tuberculosis and it is treatable and curable disease. Globally, the best estimate is that 10.0 million people (range, 9.0–11.1 million) developed TB disease in 2017. Drug-resistant TB continues to be a public health crisis. The best estimate is that, worldwide in 2017, 558 000 people (range, 483 000–639 000) developed TB that was resistant to rifampicin (RR-TB), the most effective first line drug, and of these, 82% had multidrug-resistant TB (MDR-TB). TB is one of the top 10 causes of death and the leading cause from a single infectious agent.<sup>3,4</sup> AKT drugs /\*is also known as antitubercular drugs use for the treatment of tuberculosis. Antitubercular drug divided into first line drugs and second line drug according to clinical utility. Tuberculosis patient divided into newly diagnosed and previously treated patient. First line drugs

having high therapeutic efficacy and low toxicity used for newly diagnosed and previously treated patients. Second line drugs have a either low antitubercular efficacy or higher toxicity or both used for drug resistant tuberculosis. So, 2<sup>nd</sup> line drugs are reserve drugs.<sup>5</sup> treatment failure have higher morbidity and mortality compared with those who are cured as well as high rates of multidrug-resistant TB have been found among treatment failure cases especially in developing countries.<sup>6</sup> Obstructive ventilatory disorder is the commonly found disorder in patients with pulmonary TB.<sup>7</sup>

This study was planned to compare cost of various AKT drugs with same active compound (drug) and evaluate the difference in cost of various brand of same active compound (drug) with same formulations.

### Materials and Methods

For this study price of the drug was review from Indian drug review issue 3, 2017 (IDR) & CIMS (Apr- Jul 2017). Difference between maximum and minimum price of the same drug (same generic name) manufactured by different company was calculated from these percentage of price variation was calculated. By using following formula percentage of price variation was calculated.<sup>2</sup>

$$\text{Percentage of cost variation} = \frac{\text{Price of the most expensive brand} - \text{Price of least expensive brand}}{\text{Price of least expensive}} \times 100$$

Cost ratio was calculated by the ratio of the most expensive brand to least expensive brand of the same drug.<sup>2</sup> Cost ration and percentage of variation was calculated by entered data in Microsoft excel 2013. Permission was taken from institutional ethical committee of the American

international institute of the medical sciences. Udaipur, Rajasthan.

**Inclusion Criteria**

1. All single molecules, Fixed drug combinations of AKT drugs manufactured by more than one company

**Exclusion Criteria**

1. Drug formulation manufactured by only one company.
2. Drug formulations with no price information.

In present study cost of first line drug Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, Streptomycin (total number of drugs five) and second line drugs ofloxacin, levofloxacin, ciprofloxacin, moxifloxacin, ethionamide, cyclosporine, amikacin, capriomycin, prothioemide (total number of drugs nine) were analysed.

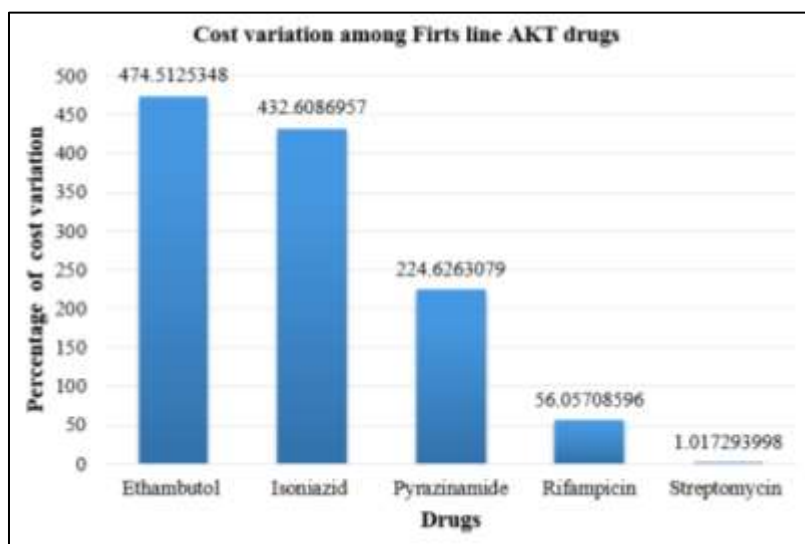
Five fixed drug combinations of first line drugs with different formulation were analysed. Second line drug like terizidone, para- aminosalicylic acid (PAS), rifabutin, thiacetazone, cyclosporine were not match with our inclusion criteria so not included in analysis.

**Result**

**Table 1: Cost variation analysis of the 1<sup>st</sup> line AKT drugs**

Drug	Strength	Formulation	MC	Minimum Price (INR)	Maximum price (INR)	Cost variation (%)	Cost ratio
Isoniazid	300 mg	Tab	2	2.76	14.7	432.60	5.32
Rifampicin	150 mg	Cap	2	17.74	21.78	22.77	1.22
	300 mg	Cap	4	30.13	47.02	56.05	1.56
	450 mg	Cap	6	44.31	68.93	55.56	1.55
		Tab	2	47.02	47.65	1.33	1.01
	600 mg	Cap	4	54.26	68.93	27.03	1.27
Pyrazinamide	500mg	Tab	5	35.3	52.54	48.83	1.48
	750 mg	Tab	7	26.76	86.87	224.62	3.24
	1000 mg	Tab	5	35.42	105.5	197.85	2.97
Ethambutol	200 mg	Tab	4	3.92	11.11	183.41	2.83
	400mg	Tab	6	7.18	41.25	474.51	5.74
	800mg	Tab	9	13.69	57.75	321.84	4.21
	1000 mg	Tab	2	55.68	72	29.31	1.29
	600 mg	Tab	3	25.05	39.84	59.04	1.59
Streptomycin	0.75 g	Inj	2	8.17	8.25	0.97	1.00
	1 g	Inj	2	9.83	9.93	1.01	1.01

MC: Manufacture Company, Tab: tablet, Cap: capsule, Inj: injection



**Fig. 1: Percentage of cost variation among first line drugs**

The cost variation of first line AKT drug are shown in Table 1 & figure 1. There is wide variation in price of Anti tubercular drugs. More manufacture company more price variation seen. Among first line drugs maximum percentage cost variation seen with Ethambutol (474.51%) followed by

Isoniazide (432.60 %). Least percentage cost variation seen with streptomycin (1.01 %) followed by rifampicin (1.33%). Maximum cost ratio of first line drugs seen with Ethambutol (5.74) followed by Isoniazid (5.32).

**Table 2: Cost variation analysis of first generation fluoroquinolone (2<sup>nd</sup> line AKT drugs)**

Drug	Strength	Formulation	MC	Minimum Price (INR)	Maximum price (INR)	Cost variation (%)	Cost ratio
Ofloxacin	100 mg	Tab	5	24.9	37	48.59	1.48
		DIS- tab	15	19.5	36	84.61	1.84
		FC- tab	2	16	34.65	116.56	2.16
	200 mg	Tablet	90	28	310	1007.14	11.07
		FC- tab	4	28.5	87.5	207.01	3.07
	400 Mg	Tablet	47	59.26	531.4	796.72	8.96
		FC- tab	4	53.26	112	110.28	2.10
		SR- tab	2	94	95.48	1.57	1.01
50 mg/5 ml	Suspension	26	19.5	48	146.15	2.46	
100mg/5ml	Suspension	4	31	78.5	153.22	2.53	
Ciprofloxacin	100 mg	Tab	2	13.95	20.33	45.73	1.45
		FC- tab	2	22.19	23.35	5.22	1.05
	250 mg	Tab	47	17.01	49.46	190.77	2.90
		FC- tab	4	30.66	59.8	95.04	1.95
	500 mg	Tab	59	34	156	358.82	4.58
		FC-tab	6	58	99.5	71.55	1.71
	750 mg	Tab	3	55	101.6	84.72	1.84
		FC tab	2	129.95	139.75	7.54	1.07
1000 mg	Tab	2	79.35	150	89.03	1.89	
2mg/ml	Inf	5	18.37	51.1	178.17	2.78	

MC: Manufacture Company, Tab: tablet, DIS-tab: Dispersible tablet, FC-Tab: Film coated tablet, Inf: Infusion

**Table 3: Cost variation analysis of second generation fluoroquinolone (2<sup>nd</sup> line AKT drugs)**

Drug	Strength	Formulation	MC	Minimum Price (INR)	Maximum price (INR)	Cost variation (%)	Cost ratio
Levofloxacin	250 mg	Tab	35	29.5	74	150.84	2.50
		FC- tab	7	30.04	102	239.54	3.39
	500mg	Tab	81	59	974	1550.84	16.50
		FC- tab	8	45	174	286.66	3.86
	750 mg	Tab	27	37.5	136	262.66	3.62
		FC -tab	7	73.02	123.5	69.13	1.69
	125/5 ml 30 ml	Suspension	2	32	54	68.75	1.68
	500 mg/m100 ml	Inf	11	35	279	697.14	7.97
Moxifloxacin	400 mg	Tab	2	750.2	800	6.63	1.06

MC: Manufacture Company, Tab: tablet, FC-Tab: Film coated tablet, Inf: Infusion

Fluoroquinolones are 2<sup>nd</sup> line AKT drugs. They are divided into first generation and second generation drugs. Ofloxacin and Ciprofloxacin are first generation fluoroquinolones and levofloxacin and moxifloxacin are second generation fluoroquinolones. The cost variation among fluoroquinolones are shown in Table 2 and Table 3. Fluoroquinolones have different type of formulation available in market. Maximum percentage of cost variation is seen with levofloxacin 500 mg tablet formulations (1550.84%)

followed by Ofloxacin 200 mg tablet formulation (1007.74%). While least percentage of cost variation seen with the Ofloxacin 400 mg sustained Releases - tablet (1.57%). Maximum cost ratio seen with levofloxacin 16.50 and minimum seen with Ofloxacin (1.01). The cost variation of Second line AKT drugs other than fluoroquinolones are shown in table 4. Maximum price variation seen with amikacin (119.71%) and least cost variation seen with prothionemide so among all 2<sup>nd</sup> line AKT

drug maximum price variation seen with levofloxacin and least cost variation seen with ofloxacin.

**Table 4: Cost variation analysis of other 2<sup>nd</sup> line AKT drugs**

Drug	Strength	Formulation	MC	Minimum Price (INR)	Maximum price (INR)	Cost variation (%)	Cost ratio
Amikacin	100 g/2ml	inj	22	15	29	93.33	1.93
	250mg/2ml	inj	21	24.9	95	281.52	3.81
	500 mg/ml	inj	22	38.55	84.7	119.7147	2.19
Prothionemide	250 mg	tab	2	99.9	126.2	26.32633	1.26
Capriomycin	1g	inj	2	236.1	428	81.27912	1.81

MC: Manufacture Company, Tab: tablet, Inj: injection

**Table 5: Cost variation among fixed dose combination**

Drug	Strength	Formulation	MC	Minimum Price (INR)	Maximum-price (INR)	Cost variation (%)	Cost ratio
Rifampicin(R) + Isoniazid(H)	R(450),H(300))	FC tab	2	52.35	52.58	0.43	1.00
		Tab	8	51.5	67.74	31.53	1.31
	R(600),H(300))	Tab	4	50.2	77.83	55.03	1.55
	R(100),H(100))	Tab(p)	2	12.12	14.76	21.78	1.21
Rifampicin (R) +Isoniazid (H) + Ethambutol (E)	R (150), H(75), E(275)	Tab	3	28.73	34.73	20.88	1.20
		Fc tab	2	30.78	39.9	29.62	1.29
Rifampicin(R) +Isoniazid(H) +Pyrazinamide (Z)	R (225), H(150), Z (750)	Tab	2	49.4	51.76	4.77	1.04
	R(120), H(80), Z (250)	Tab	2	29.9	30.09	0.63	1.00
Rifampicin (R) +Isoniazid(H)+ Ethambutol (E) +Pyrazinamide (Z)	R(150), H(75), Z(400) E(275)	Tab	4	29.23	47.08	61.06	1.61
		FC tab	2	45.96	49.9	8.57	1.08
	R(450), H(100) Z(750), E(800)	Tab	2	44.45	48.02	8.0314	1.08

MC: Manufacture Company, Tab: tablet, FC-Tab: Film coated tablet,

Fixed drug combination available with different formulations and different dosage form, among them FDCs which match our criteria they are analysed. The cost variation analysis is given in table 5. Maximum cost variation seen with isoniazid and ethambutol combinations (1984.69 %). Least cost variation seen with isoniazid and rifampicin(R 450+ H 300) combination (0.43%).

## Discussion

According to global tuberculosis report 2018, Tuberculosis is one of the top 10 causes of death and the leading cause from a single infectious agent & the proportion of people with TB who died from the disease was 16% in 2017.<sup>3</sup> According to various population-based studies there are numbers of risk factors associated with mortality following diagnosis of tuberculosis one of them is drug resistance.<sup>8</sup> MDR-TB is associated with an increased risk of death during treatment.<sup>9</sup> One of the reason for development of drug resistant TB is patient do not complete a full course

of treatment.<sup>10</sup> So, patient adherence to the treatment is import for cure of the disease and to stop drug resistant TB.

In this Pharmacoeconomic studies result shows wide variation in the pricing of AKT drugs. First line drug which is mainly used for the treatment of TB shows wide variation in cost. High percentage cost variation seen with drug have more brand. Cost of the drug is one of the important factor for the compliance of the patients or adherence to treatment because the patient feels that the cost of therapy is a financial burden, then the compliance with therapy will be compromised.<sup>11</sup> Cost of the prescription rise more during last several decades. In USA for single prescription average price was \$55 in 2004. The average charge over prescription was over \$80, with generic product being under \$40 per prescription and brand name product over \$140. Reason for this rise in cost is occasioned by new technology, marketing cost and stockholder expectations.<sup>12</sup> This may directly affect the adherence of the treatment which affect the success of treatment. Poor adherence to the treatment decreases optimum clinical benefits and therefore reduces the overall

effectiveness of health systems.<sup>13</sup> According study conducted by Indrajt Hazarika around half of the patient attended privet facility for tuberculosis although AKT drugs are available free of cost under RNTCP program in government sector. Thus Role of privet sector is also important for the control of tuberculosis.<sup>14</sup> Pharmaceutical are not affected as all cost incurred in developing a drug/ formulations is ultimately passed on poor patients who have no choice and have to accept the drug.<sup>15</sup> The patients are mainly depend upon the clinician for the treatment so, whatever is prescribed they have to use it. Thus the rational prescription by clinician is important, they should prescribed low cost drug to the patients.<sup>2</sup> If clinician do not prescribed the higher cost formulation of drug the drug automatic out of market. So, Clinicians has greater responsibility to promote or to discourage the drug on the basis of scientific justification and rationality without influence any of pharmaceutical companies.<sup>15</sup>

The DPCO (Drug price control order) list of price controlled drug includes rifampicin and streptomycin from first line AKT drugs.<sup>16</sup> Rifampicin having low cost variation about 1% to 56% among all first line AKT drugs. Cost ratio helps to know how many times the most expensive formulation is costlier then the least expensive formulation of the same drugs.<sup>2</sup> In present study cost ratio of rifampicin is ranges from 1.01 to 1.56 according to different formulations and dosage of the drug which suggest lower cost ratio then other first line drugs because rifampicin is controlled drug. Ofloxacin having both high and lest price variation, reason for this may be no. of brand available as in result shows more number of brand high cost variation.<sup>2</sup> High cost variation seen with 200 mg tablet which is manufactured by around 90 pharmaceutical companies & least percentage of cost variation seen with 400 mg SR which is manufactured by only 2 pharmaceutical companies. The DPCO fixed the price of the drug so, once medicine included as controlled drug under DPCO, drug cannot be sold at a price higher than that fixed by the government (DPCO).<sup>17</sup> Thus, first line drugs used for tuberculosis treatment should be include under DPCO as controlled drug.

This study provide cost variation among AKT drugs so, advantages of the study is to cross cut out of pocket expenditure of patients on AKT drugs and that will lead to more compliance for treatment and reduce economical burden among patients.

## Conclusion

The wide percentage of cost variation is seen with AKT drugs available in Indian market. High no. of brand or manufacture companies for single drug then high cost variation is seen. So, regulation of drug price by concerned agencies and by government is needed. The cost of drug is plays important role for the treatment adherence. Thus, low cost of prescription more treatment adherence. Clinician should aware about the different drug formulation with high cost variation which are available in Indian market. Privet sector also play important role in economics by rational prescribing with low cost.

**Conflict of Interest:** None.

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