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TO ASSESS THE IMPACT OF DPCO 2013 ON AVAILABILITY AND ACCESSIBILITY OF MEDICINES IN THE INDIAN PHARMACEUTICAL MARKET

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1. EXECUTIVE SUMMARY

This report analyzes the impact of DPCO 2013 and NLEM 2015 on the affordability and accessability of the listed medicines in India.

We employ two approaches to investigate whether DPCO 2013 and NLEM 2015 increased the level of access and affordability of the selected medicines in the Indian market. We use monthly molecule level and SKU level IQVIA data and bi-monthly Rx data from SMSRC for the investigation. We also provide a macro analysis of the context of the results.

What are the macro-contextual factor and firm related factors that underlie the results of this study when a price decrease may be expected to an increase in the volumes of the drugs as per classical economics? These factors can be summarized as under.

1. Competition in the Indian Pharmaceutical Industry
2. Impact of Imported API Prices on Indian Pharma Prices
3. Cost Based Pricing vs. Market Based Pricing in Price Control
4. Firm Related Factors
5. Experience of Other Industries

Given the high levels of competition in pharmaceutical industry in India (the HH Index – a measure of competition is less than 0.15 for 7 of the 9 NLEM categories indicating very high competition), there is an automatic downward pressure on price and downward pressure on profits. To be noted that prices in India are already amongst the lowest in the world – recent study suggests the 2nd lowest. The research literature also suggests that market related prices (based on reference prices) are likely to be better than cost related prices; cost related price controls tend to provide higher incentives for leakages in the system. When one put this together with the increase in the API prices by as much as 30% in the duration of the data that has been analyzed for this study, it seems logical to think that firms would be under higher pressure to maintain margins (which are among the lowest in the world for profitable innovating pharmaceutical firms). An earlier study in 2016 provides preliminary evidence that firms tend to pay a lower level of attention to molecules that are under price control and where input costs are rising (it is the logical thing to do) which would provide an impetus for lower volumes. The experience of other industries (fertilizer, sugar, etc. detailed in Section 6 of this report) also suggests that price controls over a period of time lead to an increase in subsidies and sub-scale manufacturing units and a lack of new investment.

The approach used is that of event study analysis and interrupted time series / regression discontinuity. In event study, we estimate a trend line of sales for the molecules and SKUs before the policy announcement and the trend line after the announcement and see if these are significantly different from one another. In regression discontinuity, we estimate a regression with a break in the data and look at the coefficients before and after the policy change to see if there is a significant change in the sales levels after the policy change as compared to before.

Our findings can be summarized as follows.

- The trend growth in volume of NLEM molecules
  - Is NOT significantly different from before DPCO 2013 – as compared to after DPCO
  - Is NOT significantly different from that of non-NLEM molecules in comparable periods before and after DPCO 2013
- A similar result applies after the change in NLEM in 2015.

At a more detailed level:

1. *There was a significant **increase** in sales volume of 24%-29% of NLEM SKUs and 30%-34% of NLEM molecules.*
2. *But there was also a significant **decrease** in sales volume of 18%-30% of NLEM SKUs and 21-22% of NLEM molecules. And **no significant change** in the rest (40%-55%).*
3. *At aggregate level there was no significant increase in sales volume of NLEM SKU and molecules post DPCO 2013.*

Overall, therefore, DPCO 2013 would appear not have achieved its objective of expanding affordability and accessability at the aggregate level, though there is success in selected categories**.**

At the prescription level, a significant increase in prescriptions was observed in only 10% - 12% of NLEM samples. Further, at the aggregate level, there was no significant positive difference in percentage sales growth of scheduled formulation and percentage sales growth of non-scheduled formulation post DPCO or % sales growth of scheduled formulation post and prior to DPCO. The same aggregate results were observed in important therapeutic areas as well.

Other findings are:

1. the prices of the Scheduled Formulations at the aggregate level did influence the prices of Non-Scheduled Formulations
2. sales of specified dosages and strengths of scheduled formulations have not grown (by volume) at a higher rate than others or at a higher rate than before DPCO.

2. DPCO 2013 and NLEM 2015

The Indian Government introduced Drug Cost control order (DCCO) in 1995 in the context of liberalization of the economy to increase the penetration of health care among population by increasing the accessibility and affordability of drugs. The DCCO 1995 calculated the ceiling prices of scheduled formulation on cost-based approach. The National List of Essential Medicines of India list was released in 1996 and subsequently updated in 2003 and 2011. In 2013, Indian government introduced Drug Price control order (DPCO) with market-based pricing mechanism to calculate the ceiling prices. This is in line with National pharmaceuticals pricing policy 2012 whose goal is to enable the Indian pharmaceutical industry growth along with balancing with the objective of making availability of essential medicines at affordable prices to all. The ceiling prices and MRP of the scheduled formulations i.e. 348 medicines in 27 Therapeutic areas as per NLEM 2011 list was subsequently calculated and announced based on DPCO 2013. Further DPCO 2013 also restricted the price increase in MRP of non-scheduled formulation to a maximum of 10% during preceding 12 months. The NLEM list was subsequently updated on 2015 with addition of 106 medicines and deletion of 80 medicines from NLEM 2011 resulting in total of 376 medicines in 30 therapeutic categories.

The performance of the Indian Pharmaceutical Market as a whole since the introduction of DPCO 2013 is given in figure 2.1 and the value and unit share of NLEM and non-NLEM medicines for important therapeutic areas based on IQVIA TA for MAT July 2018 is given in figure 2.2.

	Value Growth (MAT July)					
	2014	2015	2016	2017	2018	2019
IPM	**8%**	**15%**	**11%**	**8%**	**7%**	**9%**
NLEM	-9%	10%	5%	-6%	3%	6%
Non NLEM	11%	16%	12%	10%	7%	10%

Figure 2.1 Value Growth of Indian Pharmaceutical Market (IPM), MAT July Ref (PwC API Paper)

IQVIA Supergroup / TA	NLEM Category		Non NLEM Category		Total		NLEM Category		Non NLEM Category		Total	
	INR cr	Share	INR cr	Share	INR cr	Share	Units '000	Share	Units '000	Share	Units '000	Share
Anti Diabetic	718	0.57%	11084	8.71%	11802	9.28%	233528	0.95%	1168251	4.76%	1401779	5.71%
Anti malarials	274	0.22%	237	0.19%	511	0.40%	36730	0.15%	87203	0.36%	123934	0.50%
Anti-infectives	5486	4.31%	10381	8.16%	15867	12.47%	1169361	4.76%	1547793	6.31%	2717154	11.07%
Anti-Parasitic	189	0.15%	180	0.14%	369	0.29%	206327	0.84%	84524	0.34%	290851	1.19%
Anti-TB	97	0.08%	287	0.23%	384	0.30%	25831	0.11%	123229	0.50%	149060	0.61%
Antivirals	440	0.35%	610	0.48%	1050	0.82%	11757	0.05%	12244	0.05%	24001	0.10%
Blood Related	293	0.23%	891	0.70%	1184	0.93%	33855	0.14%	73074	0.30%	106928	0.44%
Cardiac Related	3344	2.63%	11605	9.12%	14950	11.75%	889607	3.62%	1705745	6.95%	2595352	10.57%
Dermatology	444	0.35%	9341	7.34%	9785	7.69%	194809	0.79%	1470152	5.99%	1664962	6.78%
Gastro Intestinal	1439	1.13%	11943	9.39%	13382	10.52%	903843	3.68%	2891965	11.78%	3795808	15.47%
Gynaecology	488	0.38%	5716	4.49%	6204	4.88%	122001	0.50%	474799	1.93%	596800	2.43%
Hormones	1132	0.89%	909	0.71%	2041	1.60%	660205	2.69%	290166	1.18%	950371	3.87%
Neuro / CNS	1850	1.45%	5504	4.33%	7354	5.78%	497888	2.03%	845612	3.45%	1343500	5.47%
Oncology	806	0.63%	1141	0.90%	1947	1.53%	28917	0.12%	10720	0.04%	39638	0.16%
Ophthal / Otologicals	96	0.08%	2373	1.86%	2469	1.94%	60629	0.25%	367466	1.50%	428095	1.74%
Others	67	0.05%	1180	0.93%	1248	0.98%	3336	0.01%	147220	0.60%	150556	0.61%
Pain / Analgesics	1286	1.01%	8581	6.74%	9867	7.75%	753572	3.07%	1900377	7.74%	2653949	10.81%
Parenteral	57	0.04%	139	0.11%	196	0.15%	30171	0.12%	21919	0.09%	52090	0.21%
Respiratory	1141	0.90%	8915	7.01%	10057	7.90%	442716	1.80%	2332728	9.50%	2775444	11.31%
Urology	2	0.00%	2192	1.72%	2193	1.72%	4	0.00%	198137	0.81%	198141	0.81%
Vaccines	440	0.35%	2028	1.59%	2468	1.94%	96400	0.39%	22890	0.09%	119290	0.49%
Vitamins / Minerals	203	0.16%	9784	7.69%	9987	7.85%	74219	0.30%	2054233	8.37%	2128452	8.67%
Other Items			1938	1.52%	1938	1.52%			237379	0.97%	237379	0.97%
Total	20292	15.96%	106961	84.05%	127253	100.0%	6475707	26.38%	18067826	73.62%	24543533	100.00%

Figure 2.2 Value and Unit share of NLEM & non NLEM medicines of IPM, MAT July 2018 Ref (IQVIA)

3. PURPOSE OF THE STUDY

The purpose of this study is to ascertain if the DPCO 2013 achieved its objectives. The primary objective of NLEM introduced by Indian government is to promote rational use of medicines considering the three important aspects i.e. cost, safety and efficacy. Similarly, the objective of DPCO 2013, which replaced DPCO 1995, is to ensure the growth of pharmaceutical industry while balancing the objective of Drug price control.

The objective of the proposed study is to measure the impact of DPCO 2013

- on availability of and access to scheduled formulations;
- on availability of and access to similar non-scheduled formulations; and
- on promoting standard treatment guidelines and rational use of medicine.

The research questions which this study attempts to answer are

1) What has been the impact of price controls (specifically DPCO 2013) on the sales of and availability of formulations that came under price control?

2) Have the sales and availability increased / decreased or remained about the same at the SKU level?

a. By sale volume of Scheduled Formulations, and

b. By Therapeutic Category (TC)

3) Have the sales of specified dosages and strengths have grown (by volume) at a higher rate than before (Prior to DPCO 2013), thereby promoting rational use of medicines?

4) What has been the impact of price controls on the price and sales of Non-Scheduled Formulations?

To answer these research questions, we formulated the following hypothesis with the apriori aggregate level hypotheses being that the Price control has achieved its objectives.

1. H1: Access and availability of Scheduled Formulations have improved (by volume) under the DPCO 2013.

2. H2: Post DPCO 2013, the prices of Scheduled Formulations had an influence on the prices of Non-Scheduled Formulations;

3. H3: Post DPCO, 2013, sales of specified dosages and strengths have grown (by volume) at a higher rate than *others*, thereby promoting standard treatment guidelines;

4. H4: Post DPCO, 2013, sales of specified dosages and strengths have grown (by volume) at a higher rate than *before* (Prior to DPCO 2013), thereby promoting rational use of medicines;

4. STUDY METHODOLOGY AND DATA

We used Event Study Method and Interrupted Study Analysis methods to test the above hypothesis on the monthly unit sales data from IQVIA and bimonthly RX data from SMSRC.

4.1 Event Study Method

Event study method is the first method we used to examine the impact of DPCO 2013 on sales units of both NLEM and non NLEM sample medicines. Event studies are commonly used in finance area to estimate the impact of an event on stock returns of target companies. In this study, we adapt the event study methodology to estimate the impact of event i.e. DPCO 2013 on the sales return of each molecule and SKU. The event study used in this paper consists of three stages: estimating a SARIMA forecast function (with or without drift) for each molecule and SKU based on their corresponding historic sales volume data, creating a baseline sales forecast based on forecast function developed in stage 1 for the period immediately following DPCO 2013 (termed the event window) and comparing the actual sales volume with the baseline to isolate the impact of the event during event window. The difference between hypothetical forecasted sales that would have happened in the absence of the event and actual sales is termed as abnormal return. We then test the significance of the abnormal return i.e. whether it is significant from 0 and collate the data for all the samples to determine the impact of DCPO on medicine sales.

The estimation period is from August 2010 to April 2013, a total of 33 months. We used the IQVIA monthly unit sales data for the above period to fit a forecast function for each individual NLEM and non NLEM molecule/SKU. The announcement of DPCO in May 2013 is the event whose impact this study is estimating. The event is followed by event window where the impact

of the event is felt the most. In this study we proposed July 2013 to June 2014 as event window. The firms were given a period of 45 days to implement the price change as per regulation and the enforcement of NLEM 2013 was expected to be complete by end of June 2013. Hence the event window is taken as the one-year period from July 2013.

We use the forecast function part of the in R and the estimated forecast models in stage 1 to estimate point forecasts for each month between July 2013 to June 2014. These point forecasts indicate the sales volume that would have been attained in the case of non-event (i.e., DPCO not being enacted). Hence the difference between the actual sales volume and the forecasted volume may be attributed to the event, DPCO 2013. We compute the difference for each of the sample NLEM & non NLEM molecule/SKU for the 12-month period. The differences over the 12-month period is then added for each molecule to arrive at "cumulative abnormal change" (CAC) for that molecule/SKU. This value denotes the impact of DPCO on that molecule/SKU sales volume in the 1-year period. The estimated model and cumulative abnormal change for the 109 sample molecules and 186 sample SKU for the event "DPCO 2103" is presented in Appendix A. The results of all individual NLEM/non NLEM samples were collated and a t-test was conducted to test whether there is significant difference in impact of DCPO 2013 on the NLEM and non-NLEM samples. The same exercise was repeated for the next event i.e. announcement of NLEM 2015 scheduled formulation list (Forecast model development period Jan 2014 – Dec 2105 & Event Window Mar 2016 – Feb 2107). We repeated the analysis for both the two events for RX data to study the impact of DCPO 2013 and NLEM 2015 on the prescriptions issued by doctors. The results will be discussed in detail in Results section.

4.1 Interrupted Time Series / Regression Discontinuity (ITS)

Event study is traditionally used to study the short-term impact of an event. In this study we measure the impact of the event i.e. 2013 over a short time horizon of 12 months. The limitation is mainly due to using forecasted sales based on prior sales figure. The forecast become more error as we move away from the estimation period and hence, they are typically limited to a shorter time period where there are no significant forecast errors. However, this limitation is overcome by Interrupted Time Series / Regression Discontinuity approach which uses the actual sales both before and after the event to study the impact of an event. Further another advantage of ITS is it can measure both the short-term impact (discontinuity at the time of an event characterized by sudden increase /decrease in sales) and long-term impact (significant difference in the long-term sales trend before and after event) of the event.

Interrupted time series is the strongest, quasi- experimental design to evaluate longitudinal effects of time- delimited interventions (Wagner et al. 2006). Wagner et al showed that by using

segmented regression analysis of interrupted time series data we can estimate dynamic changes in various processes and outcomes following interventions intended to change medication use, while controlling for secular changes that may have occurred in the absence of the intervention. ITS is similarly used to study the effect of several interventions both in medical context (Hye-Young Kwon et al., 2013, Fretheim et al. 2007, & Penfold et al 2013) as well as in the policy analysis context (Biglan et al.2000, & Pridemore et al. (2014)).

Interrupted time series is a segmented regression done by adding dummy variable for presence/absence of policy intervention and separate variable for time period after policy

implementation. In illustrative data example given in Fig 4.1 the rate is the dependent variable and the three dependent variables are T (Time from first data point), X (Dummy variable for intervention) and XT (time after interruption). The regression coefficients of T, X and XT will give pre intervention trend, post intervention level change (regression discontinuity) and post intervention level change.

Year	Rate	*T*	*X*	*XT*
2001	31.67	1	0	0
2002	30.19	2	0	0
2003	32.44	3	0	0
2004	31.50	4	0	0
2005	29.62	5	0	0
2006	30.18	6	0	0
2007	29.76	7	0	0
2008	29.89	8	0	0
2009	25.42	9	1	1
2010	24.26	10	1	2
2011	25.11	11	1	3
2012	24.07	12	1	4
2013	23.95	13	1	5
2014	22.78	14	1	6
2015	21.12	15	1	7

Fig 4.1 Example data for illustration of ITS (Ref www.sas.com)

In our study the sales units or RX, as case may be, is the dependent variable. If the DPCO 2103 has positively impacted the sales of molecules/SKU we expect the coefficients of post intervention level and/or trend to be positively significant.

The ITS was conducted on the data for the period between Aug 2010 -Nov 2105 i.e. 29 months after the introduction of DPCO 2013. As it can be noted ITS helps us understand the impact of DPCO 2103 over a long-time horizon (29 months) viz a viz short-time horizon of Event study analysis (12 months). We estimated both the level change (regression discontinuity – short term impact) and post intervention trend change (long term impact) which gives us the total impact of DPCO 2103 on sales units / RX of sample NLEM/non NLEM molecules/SKU. The ITS analysis is once again conducted at each molecule/SKU level and once again the results are

collated for the study of overall impact of DPCO 2103. The results of ITS analysis is given for in Appendix B.

Data: The sample data selected for this study was at two levels of aggregation. The first is at molecule level which is the aggregated sales of all SKUs under the selected molecule and the second aggregation is at SKU level. We selected randomly 47 NLEM molecules and 62 non NLEM molecules such that they are evenly distributed among the important therapeutic categories. We chose 127 NLEM SKUs under the chosen NLEM molecules and 59 non NLEM SKUs for analysis of impact of DCPO 2013 at SKU level. However, 18 molecules and 37 SKUs which were not under NLEM 2011 were subsequently added to NLEM 2015 list. Thus, the above molecules/SKU were part of non NLEM sample for DPCO 2013 analysis and part of NLEM ample for NLEM 2015 analysis. SMSRC provided bimonthly RX data for all the above selected sample of molecules/SKU which is used to study the impact of DCPO 2103 and NLEM 2015 on prescriptions issued by doctors.

The sample selected was not sufficient to infer decisions at therapeutic areas described by IQVIA. To further understand the impact of DPCO 2013 at therapeutic level we aggregated the sample in eight broad therapeutic areas mapping both DPCO categories and IQVIA therapeutic areas. The Annexure C list the eight therapeutic categories along with mapped DPCO and IQVIA categories.

The Fig 4.2 shows the category wise split of the samples selected along with their corresponding sales in terms of volume and revenue based on MAT July 2018 (IQVIA Database).

S.No	IPA Study Therapeutic Categories	MAT July 2018				NLEM Samples		Non NLEM Samples	
		INR cr	INR Share	Units '000	Units Share	Molecules	SKU	Molecules	SKU
1	Anti-Infectives	27966	22.0%	4969961	20.2%	19	48	16	12
2	Gastro Intestinal	21780	17.1%	4590749	18.7%	8	17	8	5
3	Others	18306	14.4%	3115863	12.7%	1	5	11	8
4	Neuro / Analgesics	17221	13.5%	3997449	16.3%	4	13	7	10
5	Cardiac and Blood Related	16134	12.7%	2702280	11.0%	7	21	6	7
6	Hormones	13843	10.9%	2352149	9.6%	6	16	5	4
7	Respiratory	10057	7.9%	2775444	11.3%	2	7	5	10
8	Oncology	1947	1.5%	39638	0.2%	0	0	4	3
	Total	127253	100%	24543533	100%	47	127	62	59

Fig 4.3 – Category wise Sample Selection

5. HYPOTHESIS TESTING AND RESULTS

H1: Access and availability of Scheduled Formulations have improved (by volume) under the DPCO 2013.

The Hypothesis 1 is tested using both the sales volume data and RX data. If the objective of DPCO 2103 is met then the access and availability of Scheduled formulations should have increased significantly than the average increase prior to the introduction of the DPCO 2013. We measure the increase in availability and accessibility through the proxy variables of increase in both the sales volume of the Scheduled formulations and prescriptions generated post DPCO 2013. As described above we conducted the Event study and Interrupted Time Series analysis on each and every Molecule/SKU samples. The results are given in the following tables.

DPCO 2013 IMPACT (EVENT STUDY) - SALES VOLUME							
	NEGATIVE IMPACT (Nos)	POSITIVE IMPACT (Nos)	NON-SIGNIFICANT (Nos)	TOTAL (Nos)	NEGATIVE IMPACT %	POSITIVE IMPACT %	NON-SIGNIFICANT %
	SKU LEVEL ANALYSIS						
NLEM SKU	38	30	59	127	29.92%	23.62%	46.46%
NON NLEM SKU	22	17	20	59	37.29%	28.81%	33.90%
	MOLECULE LEVEL ANALYSIS						
NLEM MOLECULE	10	14	23	47	21.28%	29.79%	48.94%
NON NLEM MOLECULE	14	23	25	62	22.58%	37.10%	40.32%

TABLE 5.1

The results as shown in Table 5.1 shows that DPCO 2013 has significantly increase the sales volume of 23.62 % of sample NLEM SKU and 29.79 % of sample NLEM molecules. Based on t-test we reject the hypothesis that DPCO 2013 has increased the sales volume of the Scheduled formulations. On the same sample, as discussed in methodology section, we conducted the Interrupted Time Series (ITS) analysis and the results are given in TABLE 5.2.

DPCO 2013 (ITS) - SALES VOLUME							
	NEGATIVE IMPACT (Nos)	POSITIVE IMPACT (Nos)	NON-SIGNIFICANT (Nos)	TOTAL (Nos)	NEGATIVE IMPACT %	POSITIVE IMPACT %	NON-SIGNIFICANT %
	SKU LEVEL ANALYSIS						
NLEM SKU	22	37	68	127	17.32%	29.13%	53.54%
NON NLEM SKU	8	22	29	59	13.56%	37.29%	49.15%
	MOLECULE LEVEL ANALYSIS						
NLEM MOLECULE	10	16	21	47	21.28%	34.04%	44.68%
NON NLEM MOLECULE	8	17	36	61	13.11%	27.87%	59.02%

TABLE 5.2

The results in Table 5.2 validates the result obtained in earlier analysis. Once again, we reject the hypothesis 1 i.e. there is no significant increase in sales in scheduled formulations.

Having tested the sales volume of scheduled formulations we proceed to analyze the impact of DPCO 2013 on the other component of accessibility and availability of medicine i.e. prescriptions issued by doctors. Using the bimonthly SMSRC RX data we conducted ITS analysis to check whether the DPCO 2013 has increased the number of prescriptions of scheduled formulations. The results are given in Table 5.3.

DPCO 2013 (ITS) – RX							
	NEGATIVE IMPACT (Nos)	POSITIVE IMPACT (Nos)	NON-SIGNIFICANT (Nos)	TOTAL (Nos)	NEGATIVE IMPACT %	POSITIVE IMPACT %	NON-SIGNIFICANT %
	SKU LEVEL ANALYSIS						
NLEM SKU	10	11	92	113	8.85%	9.73%	81.42%
NON NLEM SKU	7	4	45	56	12.50%	7.14%	80.36%
	MOLECULE LEVEL ANALYSIS						
NLEM MOLECULE	4	5	34	43	9.30%	11.63%	79.07%
NON NLEM MOLECULE	6	4	47	57	10.53%	7.02%	82.46%

TABLE 5.3

The % of NLEM sample which had a significant increase in prescriptions post DPCO 2013 is in the range of 7% -12 %. The proportion of sample with positive impact is less than those observed for the positive increase in sales units. Similarly, the negative impact post DPCO 2103 is also limited in the range of 9% - 12% which is less than proportion of samples which felt negative impact post DPCO 2013. More than 80% of samples doesn't have any significant impact in prescription numbers post DPCO 2103. Once again, the Hypothesis 1 get rejected. That is, DPCO and NLEM have not not significantly increased sales volumes in the categories tested.

A further detailed analysis was done on the individual samples which had a positive and negative impact due to DPCO 2013. The Table 5.4 give the list of molecules which at aggregate level has significant increase in sales post DPCO 2013.

NLEM MOLECULE SAMPLE - POSITIVE IMPACT SALES POST DPCO

S.No	NLEM Molecule	IQVIA TA	IPA Study Cat
1	**Ampicillin**	Anti-infectives	Anti-Infectives
2	**Albendazole**	Anti-Parasitic	Anti-Infectives
3	**Acyclovir**	Antivirals	Anti-Infectives
4	**Acyclovir**	Antivirals	Anti-Infectives
5	**Clotrimazole**	Derma	Anti-Infectives
6	**Fluconazole**	Derma	Anti-Infectives
7	**Salicylic acid**	Derma	Anti-Infectives
8	**Povidone iodine**	Derma	Anti-Infectives
9	**Atorvastatin**	Cardiac	Cardiac and Blood Related
10	**Ondansetron**	Gastro Intestinal	Gastro Intestinal
11	**Nitrofurantoin**	Gynaec.	Gastro Intestinal
12	**Prednisolone**	Hormones	Hormones
13	**Levothyroxine**	Hormones	Hormones
14	**Paracetamol**	Pain / Analgesics	Neuro / Analgesics
15	**Cetirizine**	Respiratory	Respiratory

TABLE 5.4

Similarly, the Table 5.5 give the list of non NLEM molecules which has positive impact post DPCO 2103.

NON NLEM MOLECULE SAMPLE - POSITIVE IMPACT SALES POST DPCO 2103

S.No	NLEM Molecule	IQVIA TA	IPA Study Cat
1	**MEROPENEM TRIHYDRATE**	Anti-infectives	Anti-Infectives
2	**ALBENDAZOLE + IVERMECTIN**	Anti-Parasitic	Anti-Infectives
3	**ORNIDAZOLE**	Anti-Parasitic	Anti-Infectives
4	**ITRACONAZOLE**	Derma	Anti-Infectives
5	**LULICONAZOLE**	Derma	Anti-Infectives
6	**DARBEPOETIN ALFA RECOMBINANT**	Blood Related	Cardiac and Blood Related
7	**Lactulose**	Gastro Intestinal	Gastro Intestinal
8	**DOMPERIDONE + PANTOPRAZOLE SODIUM SALT**	Gastro Intestinal	Gastro Intestinal
9	**SILDENAFIL CITRATE**	Urology	Gastro Intestinal
10	**GLIMEPIRIDE + METFORMIN HYDROCHLORIDE**	Anti-Diabetic	Hormones
11	**Bicalutamide**	Oncology	Oncology
12	**MYCOPHENOLIC ACID SODIUM SALT**	Oncology	Oncology
13	**Letrozole**	Oncology	Oncology
14	**BRIMONIDINE TARTRATE + TIMOLOL MALEATE**	Ophthal / Otologicals	Others

TABLE 5.5

The Table 5.6 and 5.7 give the list of samples of NLEM and non NLEM molecules which has shown significant negative impact post DPCO 2013.

NLEM MOLECULE SAMPLE - NEGATIVE IMPACT SALES POST DPCO 2103

S.No	NLEM Molecule	IQVIA TA	IPA Study Cat
1	**Ceftriaxone**	Anti-infectives	Anti-Infectives
2	**Metronidazole**	Anti-infectives	Anti-Infectives
3	**Cefixime**	Anti-infectives	Anti-Infectives
4	**Metoprolol**	Cardiac	Cardiac and Blood Related
5	**Propranolol**	Cardiac	Cardiac and Blood Related
6	**Ranitidine**	Gastro Intestinal	Gastro Intestinal
7	**Dexamethasone**	Hormones	Hormones

8	**Trihexyphenidyl**	Neuro / CNS	Neuro / Analgesics

TABLE 5.5

NON NLEM MOLECULE SAMPLE - NEGATIVE IMPACT SALES POST DPCO 2103

S.No	NLEM Molecule	IQVIA TA	IPA Study Cat
1	**ALBENDAZOLE + IVERMECTIN**	Anti-infectives	Anti-Infectives
2	**LULICONAZOLE**	Anti-infectives	Anti-Infectives
3	**DARBEPOETIN ALFA RECOMBINANT**	Antivirals	Anti-Infectives
4	**ORNIDAZOLE**	Gastro Intestinal	Gastro Intestinal
5	**MEROPENEM TRIHYDRATE**	Anti-Diabetic	Hormones
6	**ITRACONAZOLE**	Neuro / CNS	Neuro / Analgesics

TABLE 5.6

The sample molecules which significantly show increase or decrease in sales post DPCO is shown on therapeutic area wise in Table 5.7.

S.No	IPA Study Therapeutic Categories	NLEM Molecules			Non NLEM Molecules		
		Sample (Nos)	Positive Impact %	Negative Impact %	Sample (Nos)	Positive Impact %	Negative Impact %
1	Anti-Infectives	19	42%	16%	16	31%	19%
2	Gastro Intestinal	8	25%	13%	8	38%	13%
3	Others	1	0%	0%	11	27%	0%
4	Neuro / Analgesics	4	25%	25%	7	0%	14%
5	Cardiac and Blood Related	7	14%	29%	6	17%	0%
6	Hormones	6	33%	17%	5	20%	20%
7	Respiratory	2	50%	0%	5	0%	0%
8	Oncology	0	0%	0%	4	75%	0%
	Total	47	32%	17%	62	26%	10%

TABLE 5.7

From the above table it can be inferred that samples from Oncology and Anti-Infectives has higher proportion of sample molecules with positive impact post DPCO. Still more than half of the sample in NLEM molecules doesn't significantly increase in sales post DPCO. Thus, a closer look at the sample molecules at Therapeutic Area level is similar to the general pattern observed till now. Based on all the above analysis we reject the null hypothesis 1 i.e. Access

and availability of Scheduled Formulations have not increased significantly (by volume) under the DPCO 2013.

Hypothesis 2: Post DPCO 2013, the prices of Scheduled Formulations had an influence on the prices of Non-Scheduled Formulations

The DPCO 2013 is expected to negatively impact the trend of prices of scheduled formulation. Since DPCO 2013 is market-based pricing mechanism any negative impact in scheduled formulation is expected to impact negatively the prices of non-scheduled formulation. DPCO 2013 also introduced a cap of 10% on increase in MRP over preceding 12 months for non-scheduled formulation. We hypothesize that the cap on MRP increase and negative impact on price trend of scheduled formulation will result in negative impact on price trend of non-scheduled formulation. This will be in line with the objective of DPCO i.e. increasing the affordability and availability of medicines.

We conducted ITS analysis on pricing of each and every NLEM/non-NLEM samples of molecules/SKU and the result is given in Table 5.8

DPCO 2013 (ITS) - PRICE							
	NEGATIVE IMPACT (Nos)	POSITIVE IMPACT (Nos)	NON-SIGNIFICANT (Nos)	TOTAL (Nos)	NEGATIVE IMPACT %	POSITIVE IMPACT %	NON-SIGNIFICANT %
	SKU LEVEL ANALYSIS						
NLEM SKU	54	22	46	122	44.26%	18.03%	37.70%
NON NLEM SKU	9	20	27	56	16.07%	35.71%	48.21%
	MOLECULE LEVEL ANALYSIS						
NLEM MOLECULE	15	7	25	47	31.91%	14.89%	53.19%
NON NLEM MOLECULE	6	25	29	60	10.00%	41.67%	48.33%

TABLE 5.8

As expected, a higher proportion of NLEM sample has shown significant negative impact on price trends post DPCO 2103. On contrary, a higher proportion of non-NLEM sample of molecules/SKU has shown an increasing trend in price post DPCO 2103. Hence, we reject the

Hypothesis 2 i.e. the prices of the sample of Scheduled Formulations on total did not influence the prices of sample of Non-Scheduled Formulations.

Hypothesis 3: Post DPCO, 2013, sales of specified dosages and strengths have grown (by volume) at a higher rate than others, thereby promoting standard treatment guidelines.

Hypothesis 3 test the impact of DPCO 2103 on the standard treatment guidelines. It is proposed that due to DPCO 2013 the difference between the scheduled formulation growth % and the non-scheduled formulation growth % will be significantly greater than zero. The implication is that the increase in sales trend of scheduled formulation post DPCO will be significantly higher than the increase in sales trend of non- scheduled formulation.

The above hypothesis was tested using t-test on aggregate NLEM and non NLEM sample SKUs growth rates on monthly basis from July 2013 to June 2015. However, t-test result showed that there is no significant difference in the growth rate of both scheduled formulation and non-scheduled formulations post DPCO 2103. The result was repeated once again at aggregated molecule level and once again the hypothesis is rejected.

Hypothesis 4: Post DPCO, 2013, sales of specified dosages and strengths have grown (by volume) at a higher rate than before (Prior to DPCO 2013), thereby promoting rational use of medicines

Hypothesis 4 test the impact of DPCO 2103 on rational use of the medicines. It is proposed that due to DPCO 2013 the difference in the growth % of scheduled formulation after introduction of DPCO 2013 and before introduction of DPCO 2103 will be significantly greater than zero. The implication is that the increase in sales trend of scheduled formulation post

DPCO will be significantly higher than the increase in sales trend of scheduled formulation before DPCO 2103.

The above hypothesis was tested using t-test on aggregate NLEM sample SKUs growth rates on monthly basis from July 2012 to June 2013 and the growth rates from July 2013 to June 2104. However, t-test result showed that there is no significant difference in the growth rate of scheduled formulation prior and post DPCO 2103. The result was repeated once again at aggregated molecule level and once again the hypothesis is rejected.

RESULTS SUMMARY TABLE

Hypothesis No	Hypothesis	Supported / Not Supported
1	Access and availability of Scheduled Formulations have improved (by volume) under the DPCO 2013	Not Supported
2	Post DPCO 2013, the prices of Scheduled Formulations had an influence on the prices of Non-Scheduled Formulations	Not Supported
3	Post DPCO, 2013, sales of specified dosages and strengths have grown (by volume) at a higher rate than others, thereby promoting standard treatment guidelines	Not Supported
4	Post DPCO, 2013, sales of specified dosages and strengths have grown (by volume) at a higher rate than before (Prior to DPCO 2013), thereby promoting rational use of medicines	Not Supported

TABLE 5.9

6. CONTEXTUAL FACTORS INFLUENCING RESULTS

What are some contextual factors leading to the results that we obtain? These factors can be summarized as under.

1. Competition in the Indian Pharmaceutical Industry
2. Impact of Imported API Prices on Indian Pharma Prices
3. Cost Based Pricing vs. Market Based Pricing in Price Control
4. Firm Related Factors
5. Experience of Other Industries

Below we provide details of these factors.

Competition in Indian Pharmaceutical Industry:

The market structure of pharmaceutical industries around globe lies between the perfect competition and monopolistic competition due to the presence of generic molecules and R&D driven innovation in pharmaceutical industry. Standard economic theories suggest that in both perfect competition and monopolistically competition the consumer surplus is maximized at the expense of producer surplus. The firms have little market power and hence couldn't raise price to increase the profits. The price elasticity is very high in monopolistically competitive industry and in long run the economic profit of the firm reaches zero. However, on the downside there is a possibility of monopoly market structure in newly developed drugs until the competition catches up.

The Indian pharmaceutical industry is characterized by very high competition. The Herfindahl index is a measure of competitive intensity of an industry and measures the size of firms in relation to the industry. US Agencies generally classify market into three types based on the Herfindahl index: 1) Unconcentrated markets (Herfindahl index value < 0.15) 2) Moderately

concentrated markets (Herfindahl index Values between 0.15 and 0.25) and 3) highly concentrated markets (Herfindahl index Values > 0.25). (Ref: https://www.justice.gov/atr/horizontal-merger-guidelines-08192010).

We calculated the Herfindahl index for randomly selected NLEM SKU in top seven therapeutic categories from the molecules with an annual sale of at least Rs 100 crores. The results as shown in the below table confirm the presence of competitive intensity of Indian pharmaceutical industry. In 6 out of the 8 sample NLEM SKUs competition exist between products offered by more than 50 firms. The competitive intensity is validated by the Herfindahl index values with 5 of the sample having the Herfindahl index of less than 0.15 indicating unconcentrated markets with very high levels of competition. On the other hand, two of the sample NLEM SKUs have less than 11 firm competing resulting in higher Herfindahl index indicating concentrated markets for those molecules.

The Table below illustrates the calculated values of the HH Index for NLEM molecules in India.

On a whole the analysis of Indian pharmaceutical industry reveals a highly competitive industry structure and based on the standard economic theories, competitive market structure should lead to a market clearing prices and increased consumer surplus. With increased competition comes an automatic downward price pressure.

A AIOCD-AWACS MAT 2019 report shows that 11% of the formulations in India are under the price point of Rs. 5. There are studies that document that prices of Indian generic medicines are amongst the lowest in the world.[1]

[1] https://gh.bmj.com/content/3/1/e000571#block-system-main.

Table

Calculation of HH Index for NLEM molecules

S.No	TC	SKU	MAT July 2018 (INR cr)	Unit MAT July 2018 (in thousands)	% Value share in IPM - MAT July 2018	% Unit share in IPM - MAT July 2018	% Value share in Supergroup/TA - MAT July 2018	% Unit share in Supergroup/TA - MAT July 2018	No of Firms	**Herfindahl Index**
1	Anti-Diabetic	Metformin |Tablet 500 mg	231	132276	0.20%	0.50%	2.00%	9.40%	57	**0.144**
2	Anti-infectives	Amoxicillin (A) + Clavulanic acid (B) |Tablet 500 mg (A) + 125 mg (B)	1120	103086	0.90%	0.40%	7.20%	3.90%	73	**0.099**
3	Anti-infectives	Azithromycin |Tablet 500 mg	390	69815	0.30%	0.30%	2.50%	2.60%	103	**0.104**
4	Cardiac	Telmisartan |Tablet 40 mg	470	89041	0.40%	0.30%	3.10%	3.40%	72	**0.121**
5	Derma	Fluconazole |Tablet 150 mg	96	96608	0.10%	0.40%	1.00%	5.80%	76	**0.100**
6	Gastro Intestinal	Ranitidine |Tablet 150 mg	436	287898	0.30%	1.20%	3.30%	7.60%	11	**0.249**
7	Pain / Analgesics	Paracetamol |Tablet 650 mg	247	141630	0.20%	0.60%	2.50%	5.30%	52	**0.388**
8	Respiratory	Budesonide (A)+ Formoterol (B) |Inhalation (MDI/DPI) 200 mcg (A) + 6 mcg (B)	255	17115	0.20%	0.10%	2.50%	0.60%	8	**0.305**

Impact of API price on Indian Pharmaceutical Industry:

The drugs are made up of two basic ingredients 1) Activated pharmaceutical ingredients (API) which are active ingredients in drug providing therapeutic effect and 2) excipients which are chemically inactive substances that help in delivering the medication. Generally, the APIs represent the maximum contribution in COGS (in the range of 40%-60%) of any medicine. One of the key changes in DPCO 2013 is that annual increase in drugs price is linked to WPI changes. The margin of drug manufacturers will not be impacted as long as the increase in API prices are in line with increase in WPI. ***However, in past 6 years API prices, in most cases, has increased by 10% CAGR against the CAGR 2.9% increase of drug prices allowed under DPCO 2013 (Ref: PwC API Paper).*** One of the key reasons is the dependent on China for import of APIs and internal factors affecting the Chinese API industry. Indian industry imports around 85% of APIs from china (Ref: https://www.tpci.in/blogs/the-api-paradox-of-indias-pharmaceutical-industry/). However, in past 15-18 months more than 150 API manufacturers in China have been closed down due to crackdown on polluting industries resulting in increase of prices of APIs imported from china by 25-30%. On one hand this might provide an opportunity to Indian API manufacturers who are operating at far less capacity utilization than their Chinese counterparts. On the other hand, it creates a huge pressure on margins for drugs manufactured by Indian pharmaceutical industry and can make businesses unviable. ***One way of alleviating the issue is to include the global prices of corresponding APIs in pricing mechanism of Indian drugs.***

Cost Based Pricing vs Market Based Pricing:

The cost-based pricing was used among Asian countries as price control mechanism for drugs. In an unpublished work (Saif, 2011) has mentioned that cost-plus pricing methods has been identified as price control mechanism in 13 countries. The work hasn't fully identified all the

countries but mentioned India, China, Pakistan, Bangladesh and Iran as the countries which have used cost-plus pricing. The author also mentioned Colombia as the one of the 13 countries which however at that point of time has discontinued cost-plus pricing. The work mentioned the mixed results obtained by cost-plus pricing on the stated objective. In Bangladesh the cost-plus pricing has increased the sales of essential medicines but the growth has tapered off subsequently. With respect to china, the report concluded that the availability of medicines were low, prices are 5.6-8.8 times greater than international reference prices for originator brands and 1.2-2.0 times greater for generic products. In Iran the prices of medicine were at par with international reference prices. WHO on their guideline for pharmaceutical pricing policies suggested to avoid cost-plus as an overall pharma pricing policy. One of the reasons for pessimistic view by WHO on cost-plus pricing is lack of evaluative research or systematic reviews documenting the results of price control by cost-plus approach. The challenge for the cost-plus approach includes reliable determination of manufacturing cost, requirement of technical and human resources to validate component prices, opportunity for manipulation to the advantage of manufacturers, switching over to in appropriate price-controlled medicines and disadvantageous to local small manufacturers. In the case of using of cost-plus pricing policy, WHO suggest complimentary policies to determine what components to be included in pricing formulae and a transparent policy and verification of prices. (Rovira and Darba, 2001) in their paper on Pharmaceutical pricing and reimbursement in Spain has identified Spain using cost plus pricing based on 1964 formula to determine drug pricing. The paper also specified that the price determined by cost-plus pricing determined seldom become definitive price as they are costlier than the international reference prices. The neighbouring countries such as Italy, France, Portugal and Greece have lower price products which result in lower prices in Spain than prescribed by the cost-plus pricing formula.

(Kyle, M. K, 2007) in their work on Pharmaceutical price controls and entry strategies has suggested 15 pharma pricing regulations used by several European countries. The paper conclude that firms headquartered in price control countries reach fewer markets than the countries without price control. The paper conclude that price control affects the strategies of domestic firms. WHO (2003) suggested three ways by which price controls of medicine was done 1) cost-plus pricing 2) controlling profit margin of firms and 3) Reference pricing. There are two types of reference pricing 1) External reference pricing or International reference pricing where price of medicine is controlled in one country by comparing the price of the medicine of other reference countries 2) Internal reference pricing, where the price of one drug is compared to the domestic price of therapeutically related drugs. WHO on their supply-side policy options cite the both reference pricing strategies result in direct price control while the cost-plus pricing will result in regulating profits. The literature has studied about the effects of Internal reference pricing and the results are generally positive. The research on reference pricing showed 10-25% reduction in prices in Germany and decreased the price of generic statins in Hungary. A study by Kanavos et al (2008) (80) concluded that reference pricing resulted in decrease of lowest generic prices by up to 47%, and, on an average, generic prices showed a significantly lower price decline over time. Portela, 2009 showed that Internal reference pricing has increased the market share for both generics and brands in Portugal. However, Drummond et al (2011) suggested that reference pricing supported by (Health Technology Assessment) HTA is most viable approach. Based on the above literature market-based pricing followed in DPCO 2013 in line with the Internal reference pricing appears to be better pricing strategy.

Firm Related Factors

As economic actors, firms will respond to regulation with a view to continue their optimization problems with a newer set of constraints. For Indian pharma firms, typically, the constraint is that with prices that are amongst the lowest in the world, there is a need to achieve a decent level of profitability to be able to innovate. Compared to innovator pharma firms in the west where profit margins are in the range of 18-24%, Indian pharma firms have lower profit margins in the range of 9-14%. Innovation and new molecules requires at the very least, this level of profits. Lower prices in price control may act as an incentive to decrease a firm's focus on the drugs that are priced at levels where margins may be below internal benchmarks.

Experience of other Industries:

A] Indian Fertilizer Industry: Fertilizer industry is the highly regulated industry in India with Indian government allocating Rs 70000 crores as subsidy for the fertilizer industry (Ref: https://www.alphainvesco.com/blog/fertilizer-industry-landscape-subsidy-scene-government-policies/). There is leakage in administering the subsidy scheme like diversion of urea to industrial uses resulting in government initiating several measures such as soil health card scheme to contain the diversion. The manufacturers are paid on cost-plus basis resulting in little incentive to improve efficiency (Ravinutala, 2016). (Soumita, 2017) estimated that Indian fertilizer industry runs at 57% technical efficiency on an average with scope for further improvement. The increased efficiency of Indian fertilizer units will reduce the import burden of the country. The price of Urea is being controlled and phosphorus and potash fertilizers have been decontrolled in 1992. This has resulted in farmers to use urea in place of the P and K fertilizers resulting in consumption of N: P: K in ratio of 8:3:1 against the optimal ratio of 4:2:1. This uneven consumption lead to diminishing crop yields and increased soil toxicity. The investment has also been relatively mute in comparison with the completely deregularised industries. The distortions due to price control of urea include 1) 51% of Indian farmers buy

urea at above-MRP due to black marketing 2) black market prices are 61% higher than the stipulated prices 3) Black market hurts small and marginal farmers more than the large farm holders (17% extra expenditure on an average) (Economic Survey 2015-16).

B] Sugar Industry: India is the second largest producer of sugar in the world with Indian sugar industry being Rs 80000 crore industry. Indian sugar industry face dual cane pricing from both central and state governments. The central government fixes a uniform FRP (fair and remunerative price) for sugar which is the minimum price the sugar mills have to pay to the farmers for their sugarcane. Several state governments fix State advised price which generally will be higher than the FRP. These dual pricing results in pricing distortions leading to price arrears and cyclicality in production-consumption disparity. The price distortions also resulted in Indian sugarcane prices being among the highest in the world and Indian sugar price being among the lowest in the world and also result in high production cost (Ref: https://www.indiansugar.com/uploads/presentation_before_rangarajan_committee.pdf). Unlike the major sugar producers, there is no relationship between sugarcane price and sugar price in India. The price distortion resulted in India being dragged to WTO by brazil and Australia. The price distortion resulted in high sugar surplus with sugar surplus in 2018-19 expected to be 48% of annual consumption (Ref; **Error! Hyperlink reference not valid.**). The sugar surplus result in delayed payments to farmers and mounting arrears for the sugar mills. The sugar mills could not export the excess sugar due to high sugarcane price and high production cost resulting in unviability of the sugar mills

7. CONCLUSIONS

The objective of this study was to evaluate the impact of introduction of DPCO 2103 on the affordability and availability of scheduled formulations, reducing the cost of purchase of medicines, promoting standard treatment guidelines and rational use of medicines. The testing of hypothesis in this study showed that on aggregate level DPCO 2103 hasn't significantly increased the affordability and access. The DPCO 2103 also didn't significantly negatively impact access, either. There are some external factors beyond DPCO 2103 and NLEM 2015 that also would have played a key role in impacting the stated objectives – such as marketing effort of the companies in relation to the affected molecules, the GP growth rates in particular areas, the split between urban and rural areas and so on. But these are beyond the scope of the study.

8. REFERENCES

Biglan, A., Ary, D. & Wagenaar, The Value of Interrupted Time-Series Experiments for Community Intervention Research, A.C. Prev Sci (2000) 1, pp 31-49

Cost-Containment Mechanisms for Essential Medicines, Including Antiretrovirals, in China - Health Economics and Drugs Series No. 013, https://apps.who.int/medicinedocs /en/d/Js4907e/3.8.html

Fretheim A, Havelsrud K, MacLennan G, Kristoffersen D, Oxman A (2007) The effects of mandatory prescribing of thiazides for newly treated, uncomplicated hypertension: interrupted time-series analysis. PLOS Med 4: e232

https://www.sas.com/content/dam/SAS/en_ca/User%20Group%20Presentations/Health-User-Groups/ITS_SAS.pdf

http://www.nppaindia.nic.in/wp-content/uploads/2018/08/national_pharmaceutical.pdf

http://www.nppaindia.nic.in/en/drugs-prices-control-order-2013/

https://mohfw.gov.in/sites/default/files/NLEM%2C%202015.pdf

https://www.hks.harvard.edu/sites/default/files/degree%20programs/MPAID/files/Redesigning%20India's%20Urea%20Policy_SYPA_Sid%20Ravinutala_2016.pdf.

http://www.isec.ac.in/WP%20396%20-%20Soumita%20Khan%20-%20Final.pdf

https://www.indiabudget.gov.in/budget2016-2017/es2015-16/echapvol1-09.pdf

Kyle, M. (2007). Pharmaceutical Price Controls and Entry Strategies. The Review of Economics and Statistics, 89(1), 88-99.

Hye-Young Kwon, Ji-Min Hong, Brian Godman, Bong-Min Yang, Price cuts and drug spending in South Korea: The case of antihyperlipidemic agents, Health Policy,Volume 112, Issue 3, 2013, Pages 217-226,

Penfold, Robert B. et al. (2013), Use of Interrupted Time Series Analysis in Evaluating Health Care Quality Improvements, Academic Pediatrics, Volume 13, Issue 6, S38 - S44

Pridemore, W.A., Chamlin, M.B., Kaylen, M.T. and Andreev, E. (2014), The Effects of the 2006 Russian Alcohol Policy on Alcohol- Related Mortality: An Interrupted Time Series Analysis. Alcohol Clin Exp Res, 38: 257-266

Rovira, J., & Darbà, J. (2001). Pharmaceutical Pricing and Reimbursement in Spain. The European Journal of Health Economics, 2(1), 39-43

Sahay, A & Jaikumar, S (2016), Does Pharmaceutical Price Regulation Result in Greater Access to Essential Medicines?, IIMA Working paper

Saif A. Cost-plus price setting – WHO/HAI review series on pharmaceutical pricing policies and interventions. Unpublished

Vogler, Sabine (2019). "Pharmaceutical Pricing Policies". Encyclopedia of Pharmacy Practice and Clinical Pharmacy. Academic Press. pp. 188–201

Wagner, A.K., Soumerai, S.B., Zhang, F. and Ross- Degnan, D. (2002), Segmented regression analysis of interrupted time series studies in medication use research. Journal of Clinical Pharmacy and Therapeutics, 27: 299-309.

WHO GUIDELINE ON COUNTRY PHARMACEUTICAL PRICING POLICIES

APPENDIX A

EVENT STUDY ANALYSIS RESULTS - IMPACT OF DPCO 2013

NLEM SKU Samples: * - Significant Abnormal change in Sales, NS – Non significant

S.No	NLEM Medicine SKU| Dosage form & Strength	Seasonal ARIMA Model	% Abnormal Change in Sales Volume	Significance at 5%
1	**Metformin |Tablet 1000 mg (Immediate and controlled release)**	ARIMA(0,1,1) with drift	-2.10%	NS
2	**Metformin |Tablet 500 mg**	ARIMA(0,1,1)(0,1,0)[12]	3.43%	NS
3	**Metformin |Tablet 750 mg**	ARIMA(0,0,0) with non-zero mean		NS
4	**Amoxicillin (A) + Clavulanic acid (B) |Dry Syrup 125 mg (A) + 31.25 (B)/5 ml**	ARIMA(0,0,0) with non-zero mean	46.03%	NS
5	**Amoxicillin (A) + Clavulanic acid (B) |Oral liquid 200 mg (A) + 28.5 mg (B)/5 ml**	ARIMA(2,0,1)(0,1,0)[12] with drift	8.04%	*
6	**Amoxicillin (A) + Clavulanic acid (B) |Powder for Injection 1 g (A) + 200 mg (B)**	ARIMA(2,0,0) with non-zero mean	7.52%	*
7	**Amoxicillin (A) + Clavulanic acid (B) |Powder for Injection 500 mg (A) + 100 mg (B)**	ARIMA(0,0,0)(0,1,0)[12] with drift	-2.54%	NS
8	**Amoxicillin (A) + Clavulanic acid (B) |Tablet 500 mg (A) + 125 mg (B)**	ARIMA(0,0,0)(0,1,0)[12] with drift	2.60%	NS
9	**Amoxicillin |Capsule 250 mg**	ARIMA(0,0,1)(0,1,0)[12] with drift	21.79%	*
10	**Amoxicillin |Capsule 500 mg**	ARIMA(1,0,0) with non-zero mean	21.03%	*
11	**Amoxicillin |Oral liquid 250 mg/5 ml**	ARIMA(0,0,1)(0,1,0)[12] with drift	-7.60%	NS
12	**Ampicillin |Powder for Injection 1 g**	ARIMA(0,0,1) with non-zero mean	-85.13%	*
13	**Ampicillin |Powder for Injection 500 mg**	ARIMA(0,1,1)(0,1,0)[12]	20.30%	*
14	**Azithromycin |Oral liquid 200 mg/5ml**	ARIMA(0,0,2)(0,1,0)[12] with drift	11.89%	*
15	**Azithromycin |Powder for Injection 500 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	19.90%	*
16	**Azithromycin |Tablet 250 mg**	ARIMA(0,0,1)(0,1,0)[12]	5.41%	NS
17	**Azithromycin |Tablet 500 mg**	ARIMA(0,0,0)(0,1,0)[12]	5.23%	NS
18	**Cefixime |Oral liquid 100 mg/5 ml**	ARIMA(0,0,1)(0,1,0)[12] with drift	-1.03%	NS

19	**Cefixime |Oral liquid 50 mg/5 ml**	ARIMA(2,0,0)(0,1,0)[12] with drift	3.37%	NS
20	**Cefixime |Tablet 200 mg**	ARIMA(0,0,1)(0,1,0)[12] with drift	-7.88%	*
21	**Cefixime |Tablet 400 mg**	ARIMA(0,0,0)(0,1,0)[12]	-18.47%	*
22	**Ceftriaxone |Powder for Injection 1 g**	ARIMA(0,0,1)(0,1,0)[12] with drift	-6.85%	NS
23	**Ceftriaxone |Powder for Injection 2 g**	ARIMA(0,0,0)(0,1,0)[12] with drift	0.19%	NS
24	**Ceftriaxone |Powder for Injection 250 mg**	ARIMA(0,0,1) with non-zero mean	1.12%	NS
25	**Ceftriaxone |Powder for Injection 500 mg**	ARIMA(0,0,1)(0,1,0)[12] with drift	-14.41%	NS
26	**Ciprofloxacin |Injection 200 mg/100 ml**	ARIMA(0,0,0)(0,1,0)[12]	-22.62%	*
27	**Ciprofloxacin |Tablet 250 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	-3.67%	NS
28	**Ciprofloxacin |Tablet 500 mg**	ARIMA(2,0,0)(0,1,0)[12] with drift	-4.86%	NS
29	**Doxycycline |Capsule 100 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	-1.57%	NS
30	**Metronidazole |Injection 500 mg/100 ml**	ARIMA(0,0,0)(0,1,0)[12] with drift	-12.91%	*
31	**Albendazole |Oral liquid 200 mg/5 ml**	ARIMA(0,0,1)(0,1,0)[12]	17.81%	*
32	**Albendazole |Tablet 400 mg**	ARIMA(0,0,0)(0,1,0)[12]	4.40%	NS
33	**Metronidazole |Tablet 200 mg**	ARIMA(0,1,1)	-50.70%	*
34	**Metronidazole |Tablet 400 mg**	ARIMA(0,1,0)	-42.21%	*
35	**Acyclovir |Oral liquid 400 mg/5 ml**	ARIMA(0,0,1)(0,1,0)[12] with drift	-9.06%	NS
36	**Acyclovir |Powder for Injection 250 mg**	ARIMA(0,1,0)(0,1,0)[12]	-31.40%	*
37	**Acyclovir |Powder for Injection 500 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	31.08%	*
38	**Acyclovir |Tablet 200 mg**	ARIMA(0,0,0)(0,1,0)[12]	-4.84%	NS
39	**Acyclovir |Tablet 400 mg**	ARIMA(0,1,0)(0,1,0)[12]	37.56%	*
40	**Folic acid |Tablet 5 mg**	ARIMA(0,0,0)(0,1,0)[12]	-7.50%	NS
41	**Acetylsalicylic acid |Effervescent/ Dispersible/ Enteric coated Tablet 150 mg**	ARIMA(0,0,0)(0,1,0)[12]	1.91%	NS
42	**Acetylsalicylic acid |Effervescent/ Dispersible/ Enteric coated Tablet 300 mg to 500 mg**	ARIMA(0,0,0) with non-zero mean	-9.95%	*
43	**Acetylsalicylic acid |Effervescent/ Dispersible/ Enteric coated Tablet 75 mg**	ARIMA(2,1,0)	7.12%	*
44	**Acetylsalicylic acid |Tablet 100 mg**	ARIMA(0,1,0)	-94.19%	*
45	**Acetylsalicylic acid |Tablet 150 mg**	ARIMA(0,1,1)	-17.99%	*
46	**Acetylsalicylic acid |Tablet 75 mg**	ARIMA(0,0,0) with non-zero mean	-13.77%	*
47	**Amlodipine |Tablet 10 mg**	ARIMA(0,1,1)(0,1,0)[12]	-0.50%	NS

48	**Amlodipine |Tablet 2.5 mg**	ARIMA(0,1,1)(0,1,0)[12]	6.82%	*
49	**Amlodipine |Tablet 5 mg**	ARIMA(0,1,1)(0,1,0)[12]	-1.34%	NS
50	**Atorvastatin |Tablet 10 mg**	ARIMA(0,1,1)(0,1,0)[12]	8.60%	*
51	**Atorvastatin |Tablet 20 mg**	ARIMA(2,1,0) with drift	-3.07%	*
52	**Atorvastatin |Tablet 40 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	-3.12%	*
53	**Furosemide |Injection 10 mg/ ml**	ARIMA(0,1,1)	-2.37%	NS
54	**Furosemide |Oral liquid 10 mg/ml**	ARIMA(2,1,0) with drift	-1.06%	NS
55	**Furosemide |Tablet 40 mg**	ARIMA(1,1,0)(0,1,0)[12]	7.94%	NS
56	**Metoprolol |Tablet 25 mg**	ARIMA(0,1,1) with drift	-9.75%	*
57	**Metoprolol |Tablet 50 mg**	ARIMA(0,1,1) with drift	-12.44%	*
58	**Propranolol |Tablet 10 mg**	ARIMA(0,1,1) with drift	-5.38%	*
59	**Propranolol |Tablet 40 mg**	ARIMA(0,1,1)(0,1,0)[12]	-0.46%	NS
60	**Propranolol |Tablet 80 mg**	ARIMA(0,1,1)	-3.90%	NS
61	**Clotrimazole |Cream 1%**	ARIMA(0,0,0)(0,1,0)[12]	8.58%	*
62	**Clotrimazole |Drops 1%**	ARIMA(1,1,0)(0,1,0)[12]	10.52%	NS
63	**Clotrimazole |Pessary 100 mg**	ARIMA(0,0,0)(0,1,0)[12]	-9.96%	*
64	**Fluconazole |Injection 200 mg /100 ml**	ARIMA(0,1,1)	21.13%	*
65	**Fluconazole |Oral liquid 50 mg/5 ml**	ARIMA(0,1,0)	-106.85%	*
66	**Fluconazole |Tablet 100 mg**	ARIMA(0,1,1)(0,1,0)[12]	23.17%	*
67	**Fluconazole |Tablet 150 mg**	ARIMA(1,1,0)(0,1,0)[12]	9.22%	*
68	**Fluconazole |Tablet 200 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	29.39%	*
69	**Fluconazole |Tablet 400 mg**	ARIMA(0,1,1)(0,1,0)[12]	20.65%	*
70	**Povidone iodine |Solution 4% to 10%**	ARIMA(0,1,1)(0,1,0)[12]	1.78%	NS
71	**Salicylic acid |Ointment 6%**	ARIMA(0,1,1)	87.69%	*
72	**Silver sulphadiazine |Cream 1%**	ARIMA(0,0,0) with non-zero mean	-15.58%	NS
73	**Domperidone |Oral liquid 1 mg/ml**	ARIMA(1,0,0)(0,1,0)[12]	-1.21%	NS
74	**Domperidone |Tablet 10 mg**	ARIMA(0,0,0)(0,1,0)[12]	-4.88%	NS
75	**Ondansetron |Injection 2 mg/ml**	ARIMA(0,1,1)(0,1,0)[12]	3.45%	NS
76	**Ondansetron |Oral liquid 2 mg/5 ml**	ARIMA(0,0,1)(0,1,0)[12] with drift	-2.61%	NS
77	**Ondansetron |Tablet 4 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	1.27%	NS
78	**Ondansetron |Tablet 8 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	-1.37%	NS
79	**Ranitidine |Injection 25 mg/ml**	ARIMA(0,0,1)(0,1,0)[12]	-5.51%	NS
80	**Ranitidine |Oral liquid 75 mg/5 ml**	ARIMA(0,0,0) with non-zero mean	100.00%	*
81	**Ranitidine |Tablet 150 mg**	ARIMA(0,0,1)(0,1,0)[12] with drift	2.55%	NS
82	**Clomiphene |Tablet 100 mg**	ARIMA(0,1,0)	-12.78%	*
83	**Clomiphene |Tablet 50 mg**	ARIMA(0,1,0)	-28.51%	*

84	**Medroxyprogesteroneacetate |Tablet 10 mg**	ARIMA(0,1,0)	-11.86%	*
85	**Misoprostol |Tablet 100 mcg**	ARIMA(0,1,1)	-48.49%	*
86	**Misoprostol |Tablet 200 mcg**	ARIMA(0,0,0)(0,1,0)[12] with drift	-25.17%	*
87	**Nitrofurantoin |Oral liquid 25 mg/5 ml**	ARIMA(0,1,0)	75.52%	*
88	**Nitrofurantoin |Tablet 100 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	27.84%	*
89	**Norethisterone |Tablet 5 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	-1.49%	NS
90	**Dexamethasone |Injection 4 mg/ml**	ARIMA(0,0,0)(0,1,0)[12]	-8.41%	NS
91	**Dexamethasone |Tablet 0.5 mg**	ARIMA(0,1,2)	-33.38%	*
92	**Levothyroxine |Tablet 12.5 mcg to 150 mcg* (Several strengths are available in market such as 12.5, 25, 50, 62.5, 75, 88, 100, 112 mcg. Therefore it was considered to give a range of available strengths)**	ARIMA(0,1,0)(0,1,0)[12]	-1.03%	NS
93	**Methylprednisolone |Injection 40 mg/ml**	ARIMA(0,0,0)(0,1,0)[12] with drift	-1.65%	NS
94	**Methylprednisolone |Tablet 16 mg**	ARIMA(0,1,0)(0,1,0)[12]	9.41%	*
95	**Methylprednisolone |Tablet 8 mg**	ARIMA(0,1,0)	1.98%	NS
96	**Prednisolone |Injection 20 mg/2 ml**	ARIMA(0,1,0)	-350.00%	*
97	**Prednisolone |Oral liquid 15 mg/5 ml**	ARIMA(0,0,0)(0,1,0)[12] with drift	16.30%	*
98	**Prednisolone |Oral liquid 5 mg/5 ml**	ARIMA(0,0,1)(0,1,0)[12] with drift	25.38%	*
99	**Prednisolone |Tablet 10 mg**	ARIMA(0,1,1)(0,1,0)[12]	16.96%	*
100	**Prednisolone |Tablet 20 mg**	ARIMA(0,0,1) with non-zero mean	-9.03%	*
101	**Prednisolone |Tablet 40 mg**	ARIMA(0,1,1)	-1.18%	NS
102	**Prednisolone |Tablet 5 mg**	ARIMA(1,0,0) with non-zero mean	-5.74%	*
103	**Amitriptyline |Tablet 10 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	-2.16%	*
104	**Amitriptyline |Tablet 25 mg**	ARIMA(0,1,0)	-6.01%	*
105	**Amitriptyline |Tablet 50 mg**	ARIMA(0,0,0) with non-zero mean	-6.67%	NS
106	**Amitriptyline |Tablet 75 mg**	ARIMA(1,1,0)(0,1,0)[12]	-7.34%	*
107	**Trihexyphenidyl |Tablet 2 mg**	ARIMA(2,1,1) with drift	-23.78%	*
108	**Acyclovir |Ointment 3%**	ARIMA(0,0,0)(0,1,0)[12] with drift	16.06%	*
109	**Ciprofloxacin |Drops 0.3 %**	ARIMA(1,0,0) with non-zero mean	-0.18%	NS
110	**Ciprofloxacin |Ointment 0.3%**	ARIMA(0,0,0) with non-zero mean	-4.39%	*
111	**Prednisolone |Drops 1%**	ARIMA(0,1,0)	47.85%	NS
112	**Diclofenac |Injection 25 mg/ml**	ARIMA(0,1,1)(0,1,0)[12]	12.20%	NS

113	**Diclofenac |Tablet 50 mg**	ARIMA(0,1,1)(0,1,0)[12]	12.20%	*
114	**Paracetamol |All licenced oral liquid dosage forms and strengths**	ARIMA(0,0,2)(0,1,0)[12] with drift	12.20%	NS
115	**Paracetamol |Injection 150 mg/ml**	ARIMA(0,0,0)(0,1,0)[12] with drift	12.20%	*
116	**Paracetamol |Suppository 170 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	12.20%	*
117	**Paracetamol |Suppository 80 mg**	ARIMA(0,1,1)(0,1,0)[12]	12.20%	*
118	**Paracetamol |Tablet 500 mg**	ARIMA(0,0,1)(0,1,0)[12]	12.20%	NS
119	**Paracetamol |Tablet 650 mg**	ARIMA(2,0,0)(0,1,0)[12] with drift	12.20%	NS
120	**Cetirizine |Oral liquid 5 mg/5 ml**	ARIMA(0,0,1)(0,1,0)[12] with drift	12.20%	NS
121	**Cetirizine |Tablet 10 mg**	ARIMA(1,0,0)(0,1,0)[12]	12.20%	*
122	**Salbutamol |Inhalation (MDI/DPI) 100 mcg/dose**	ARIMA(0,1,1)(0,1,0)[12]	12.20%	*
123	**Salbutamol |Oral liquid 2 mg/5 ml**	ARIMA(0,0,1)(0,1,0)[12]	12.20%	NS
124	**Salbutamol |Respirator solution for use in nebulizer 5mg/ml**	ARIMA(1,0,0)(0,1,0)[12]	12.20%	NS
125	**Salbutamol |Tablet 2 mg**	ARIMA(1,0,0)(0,1,0)[12]	12.20%	NS
126	**Salbutamol |Tablet 4 mg**	ARIMA(1,0,0)(0,1,0)[12]	12.20%	*
127	**Ascorbic acid (Vitamin C) |Tablet 500 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	12.20%	NS

Non NLEM SKU Sample: * - Significant Abnormal change in Sales, NS – Non significant

S.No	**Non NLEM Medicine SKU| Dosage form & Strength**	**Seasonal ARIMA Model**	**% Abnormal Change in Sales Volume**	**Significance at 5%**
1	**Glimepiride |Tablet 1 mg**	ARIMA(0,1,1)(0,1,0)[12]	-6.17%	*
2	**Glimepiride |Tablet 2 mg**	ARIMA(0,1,1)(0,1,0)[12]	-2.88%	*
3	**Levofloxacin |Tablet 250 mg**	ARIMA(0,0,1)(0,1,0)[12] with drift	2.78%	NS
4	**Levofloxacin |Tablet 500 mg**	ARIMA(0,0,0)(0,1,0)[12]	-16.52%	*
5	**Levofloxacin |Tablet 750 mg**	ARIMA(0,0,1)(0,1,0)[12]	-8.11%	*
6	**Linezolid |Tablet 600 mg**	ARIMA(0,1,1)(0,1,0)[12]	-10.01%	*
7	**Moxifloxacin |Tablet 400 mg**	ARIMA(0,1,1) with drift	1.23%	NS
8	**Tranexamic acid |Injection 100 mg/ml**	ARIMA(0,0,0)(0,1,0)[12] with drift	-4.82%	*
9	**Tranexamic acid |Tablet 500 mg**	ARIMA(0,1,1)(0,1,0)[12]	5.66%	*
10	**Telmisartan |Tablet 20 mg**	ARIMA(0,1,0)(0,1,0)[12]	-17.26%	*

11	**Telmisartan |Tablet 40 mg**	ARIMA(0,1,0)(0,1,0)[12]	-13.72%	*
12	**Telmisartan |Tablet 80 mg**	ARIMA(0,1,0)(0,1,0)[12]	-15.82%	*
13	**Fusidic acid |Cream 2%**	ARIMA(1,1,0)(0,1,0)[12]	1.48%	NS
14	**Lactulose |Oral liquid 10 g/15 ml**	ARIMA(0,0,0) with non-zero mean	100.00%	*
15	**Iron sucrose |Injection 20 mg/ml**	ARIMA(1,0,0)(0,1,0)[12] with drift	-5.61%	*
16	**Clonazepam |Tablet 0.25 mg**	ARIMA(0,1,2)(0,1,0)[12]	4.30%	*
17	**Clonazepam |Tablet 0.5 mg**	ARIMA(1,1,0)(0,1,0)[12]	0.62%	NS
18	**Clonazepam |Tablet 1 mg**	ARIMA(1,0,0)(0,1,0)[12] with drift	2.65%	NS
19	**Escitalopram |Tablet 10 mg**	ARIMA(0,1,1)(0,1,0)[12]	-3.01%	*
20	**Escitalopram |Tablet 20 mg**	ARIMA(0,1,1) with drift	-3.84%	*
21	**Escitalopram |Tablet 5 mg**	ARIMA(0,1,1)(0,1,0)[12]	1.11%	NS
22	**Flunarizine |Tablet 10 mg**	ARIMA(0,0,0)(0,1,0)[12] with drift	-7.06%	*
23	**Flunarizine |Tablet 5 mg**	ARIMA(0,0,1)(0,1,0)[12] with drift	-3.52%	*
24	**Bicalutamide |Tablet 50 mg**	ARIMA(0,1,1)	8.92%	*
25	**Letrozole |Tablet 2.5 mg**	ARIMA(0,1,1)	5.91%	NS
26	**Budesonide (A)+ Formoterol (B) |Inhalation (MDI/DPI) 100 mcg (A) + 6 mcg (B)**	ARIMA(0,1,1)(0,1,0)[12]	15.46%	*
27	**Budesonide (A)+ Formoterol (B) |Inhalation (MDI/DPI) 200 mcg (A) + 6 mcg (B)**	ARIMA(0,1,1)(0,1,0)[12]	3.16%	*
28	**Budesonide (A)+ Formoterol (B) |Inhalation (MDI/DPI) 400 mcg (A) + 6 mcg (B)**	ARIMA(0,0,0)(0,1,0)[12] with drift	4.77%	*
29	**Budesonide |Inhalation (MDI/DPI) 100 mcg/dose**	ARIMA(0,0,0)(0,1,0)[12] with drift	28.53%	*
30	**Budesonide |Inhalation (MDI/DPI) 200 mcg/dose**	ARIMA(0,1,1)(0,1,0)[12]	0.55%	NS
31	**Budesonide |Respirator solution for use in nebulizer 0.5 mg/ml**	ARIMA(0,0,1)(0,1,0)[12] with drift	9.81%	*
32	**Budesonide |Respirator solution for use in nebulizer 1 mg/ml**	ARIMA(0,1,1)(0,1,0)[12]	-13.21%	*
33	**Xylometazoline |Nasal drops 0.05 %**	ARIMA(0,0,0)(0,1,0)[12]	10.24%	*
34	**Xylometazoline |Nasal drops 0.1 %**	ARIMA(0,1,1)(0,1,0)[12]	12.64%	*
35	**Cholecalciferol |Oral liquid 400 IU/ml**	ARIMA(0,2,1)	-49.41%	*
36	**Cholecalciferol |Tablet 1000 IU**	ARIMA(0,2,1)	-43.66%	*
37	**Cholecalciferol |Tablet 60000 IU**	ARIMA(0,2,1)	-25.81%	*
38	**ACETYLCYSTEINE|ORAL SOLID ORDINARY EFFERVESCENT TABLETS|600 MG**	ARIMA(0,0,0)(0,1,0)[12] with drift	11.63%	*

39	**ACICLOVIR|ORAL SOLID ORDINARY SOLUBLE TABLETS|800 MG**	ARIMA(0,1,0)(0,1,0)[12]	10.90%	*
40	**ALBENDAZOLE|ORAL LIQUID ORDINARY SUSPENSIONS|400 MG**	ARIMA(0,0,0)(0,1,0)[12] with drift	1.57%	NS
41	**AMOXICILLIN TRIHYDRATE + CLAVULANIC ACID POTASSIUM SALT|ORAL LIQUID ORDINARY DRY SUSPENSIONS/SYRUPS/DROPS|228 MG**	ARIMA(2,0,0)(0,1,0)[12] with drift	4.44%	NS
42	**ATORVASTATIN CALCIUM SALT|ORAL SOLID ORDINARY FILM-COATED TABLETS|80 MG**	ARIMA(1,1,0)(0,1,0)[12]	2.11%	NS
43	**BETAMETHASONE DISODIUM PHOSPHATE|ORAL SOLID ORDINARY TABLETS|0.5 MG**	ARIMA(0,0,0)(0,1,0)[12] with drift	-5.67%	NS
44	**CHLOROQUINE PHOSPHATE|ORAL SOLID ORDINARY FILM-COATED TABLETS|250 MG**	ARIMA(0,0,0)(0,1,0)[12] with drift	18.38%	NS
45	**COLECALCIFEROL|ORAL SOLID ORDINARY CAPSULES|60 K**	ARIMA(1,2,0)	-57.36%	*
46	**DICLOFENAC SODIUM SALT|PARENTERAL ORDINARY AMPOULES|75 MG**	ARIMA(0,1,0)(0,1,0)[12]	36.54%	*
47	**EPOETIN ALFA RECOMBINANT|PARENTERAL ORDINARY PRE-FILLED SYRINGES|4000 IU**	ARIMA(0,1,1) with drift	-17.30%	*
48	**ETHAMBUTOL HYDROCHLORIDE|ORAL SOLID ORDINARY TABLETS|1 G**	ARIMA(0,1,0)(0,1,0)[12]	3.09%	NS
49	**FOLIC ACID + IRON FERROUS ASCORBATE|ORAL SOLID ORDINARY FILM-COATED TABLETS|1.1 MG**	ARIMA(0,0,0)(0,1,0)[12] with drift	-10.02%	*
50	**GLIMEPIRIDE|ORAL SOLID ORDINARY TABLETS|3 MG**	ARIMA(0,1,1)(0,1,0)[12]	16.65%	*
51	**GLUCOSE + SODIUM CHLORIDE|PARENTERAL ORDINARY INFUSION VIALS/BOTTLES|5 G**	ARIMA(0,1,0)	11.93%	NS
52	**HEPARIN SODIUM SALT|TOPICAL EXTERNAL OINTMENTS|50 IU**	ARIMA(0,1,1)	-0.55%	NS
53	**LEVETIRACETAM|ORAL SOLID ORDINARY FILM-COATED TABLETS|1000 MG**	ARIMA(0,1,0) with drift	2.79%	NS
54	**MOXIFLOXACIN HYDROCHLORIDE|OPHTHALMIC DROPS|0.5 %**	ARIMA(0,0,1)(0,1,0)[12] with drift	-6.70%	*
55	**PANTOPRAZOLE SODIUM SALT|ORAL SOLID ORDINARY ENTERIC-COATED TABLETS|40 MG**	ARIMA(0,1,1)(0,1,0)[12]	-0.51%	NS
56	**POVIDONE-IODINE|TOPICAL EXTERNAL OINTMENTS|10 %**	ARIMA(0,1,1)	99.72%	*

57	**RITUXIMAB RECOMBINANT|PARENTERAL ORDINARY INFUSION VIALS/BOTTLES|500 MG**	ARIMA(0,0,0) with non-zero mean	100.00%	*
58	**SODIUM BICARBONATE|ORAL SOLID ORDINARY FILM-COATED TABLETS|1000 MG**	ARIMA(0,0,0) with non-zero mean		NS
59	**VACCINE, POLIOMYELITIS INACTIVATED|PARENTERAL ORDINARY PRE-FILLED SYRINGES|0**	ARIMA(1,1,0)	12.81%	NS

APPENDIX B

INTERRUPTED TIME SERIES ANALYSIS RESULTS - IMPACT OF DPCO 2013

NLEM Molecules Samples: NS – Non significant, Otherwise significant at 5%

S.No	NLEM Molecule	Pre DCPO trend (units)	Post DCPO Level change (units)	Post DCPO trend (units)
1	**Metformin**	59.03	NS	-42.16
2	**Amoxicillin (A) + Clavulanic acid (B)**	73.77	NS	NS
3	**Amoxicillin**	NS	458.10	NS
4	**Ampicillin**	NS	NS	NS
5	**Azithromycin**	22.47	NS	NS
6	**Cefixime**	52.81	NS	-39.95
7	**Ceftriaxone**	128.25	-1126.94	NS
8	**Ciprofloxacin**	-19.12	-583.82	51.31
9	**Doxycycline**	8.50	NS	NS
10	**Metronidazole**	NS	NS	NS
11	**Albendazole**	NS	NS	52.77
12	**Metronidazole**	45.12	NS	-43.06
13	**Acyclovir**	NS	NS	2.97
14	**Folic acid**	NS	NS	NS
15	**Acetylsalicylic acid**	NS	NS	NS
16	**Amlodipine**	30.09	NS	NS
17	**Atorvastatin**	NS	266.74	NS
18	**Furosemide**	10.60	NS	NS
19	**Metoprolol**	47.87	NS	-23.44
20	**Propranolol**	NS	NS	-8.68
21	**Clotrimazole**	NS	NS	2.35
22	**Fluconazole**	NS	319.58	38.44
23	**Povidone iodine**	NS	NS	2.05
24	**Salicylic acid**	NS	1.35	0.16
25	**Silver sulphadiazine**	NS	NS	NS
26	**Domperidone**	NS	NS	NS
27	**Ondansetron**	48.16	NS	45.27
28	**Ranitidine**	156.19	NS	-245.95
29	**Clomiphene**	NS	NS	NS
30	**Medroxyprogesteroneacetate**	1.82	NS	NS
31	**Misoprostol**	-3.70	NS	3.35

32	**Nitrofurantoin**	0.67	16.99	0.94
33	**Norethisterone**	5.41	NS	NS
34	**Dexamethasone**	123.85	-2269.70	-184.93
35	**Levothyroxine**	33.64	NS	31.15
36	**Methylprednisolone**	NS	NS	NS
37	**Prednisolone**	NS	NS	NS
38	**Amitriptyline**	NS	NS	NS
39	**Trihexyphenidyl**	NS	-119.31	NS
40	**Acyclovir**	-0.07	1.02	0.05
41	**Ciprofloxacin**	NS	NS	NS
42	**Prednisolone**	NS	NS	1.61
43	**Diclofenac**	NS	-651.65	96.39
44	**Paracetamol**	123.02	NS	80.30
45	**Cetirizine**	23.75	NS	29.91
46	**Salbutamol**	50.56	NS	-41.94
47	**Ascorbic acid (Vitamin C)**	NS	NS	NS

Non NLEM Molecules Samples: NS – Non significant, Otherwise significant at 5%

S.No	**non NLEM Molecule**	**Pre DCPO trend (units)**	**Post DCPO Level change (units)**	**Post DCPO trend (units)**
1	**Glimepiride**	NS	NS	-15.97
2	**Levofloxacin**	NS	-239.72	-11.74
3	**Linezolid**	NS	NS	NS
4	**Moxifloxacin**	6.166	33.467	-5.21
5	**Tranexamic acid**	2.894	NS	NS
6	**Telmisartan**	51.816	NS	NS
7	**Fusidic acid**	NS	NS	NS
8	**Lactulose**	NS	NS	0.01
9	**Iron sucrose**	0.986	NS	NS
10	**Clonazepam**	NS	NS	NS
11	**Escitalopram**	4.299	NS	NS
12	**Flunarizine**	4.415	NS	NS
13	**Bicalutamide**	NS	NS	0.20
14	**Letrozole**	-1.856	NS	2.12
15	**Budesonide (A)+ Formoterol (B)**	11.715	NS	NS
16	**Budesonide**	33.013	NS	NS
17	**Xylometazoline**	NS	NS	NS

18	**Cholecalciferol**	5.138	NS	NS
19	**ACECLOFENAC + PARACETAMOL + SERRAPEPTASE**	18.488	NS	8.91
20	**ALBENDAZOLE + IVERMECTIN**	NS	NS	3.49
21	**ARTEMOTIL**	NS	NS	NS
22	**ARTEROLANE MALEATE + PIPERAQUINE PHOSPHATE**	0.963	NS	-1.40
23	**CALCIUM CHLORIDE + DL-LACTIC ACID SODIUM SALT + POTASSIUM CHLORIDE + SODIUM CHLORIDE**	NS	NS	NS
24	**CALCIUM CHLORIDE + POLYGELINE + POTASSIUM CHLORIDE + SODIUM CHLORIDE**	NS	NS	NS
25	**CARMELLOSE SODIUM SALT**	16.186	NS	NS
26	**CEFPODOXIME PROXETIL**	77.913	NS	-56.90
27	**CHLORPHENAMINE MALEATE + PARACETAMOL + PHENYLEPHRINE HYDROCHLORIDE**	14.991	NS	NS
28	**CLONAZEPAM + ESCITALOPRAM OXALATE**	9.477	NS	NS
29	**DARBEPOETIN ALFA RECOMBINANT**	0.112	NS	0.36
30	**DEFLAZACORT**	NS	NS	NS
31	**DOMPERIDONE + PANTOPRAZOLE SODIUM SALT**	57.461	NS	22.62
32	**DOMPERIDONE + RABEPRAZOLE SODIUM SALT**	61.861	NS	-21.52
33	**DUTASTERIDE + TAMSULOSIN HYDROCHLORIDE**	NS	NS	NS
34	**EFAVIRENZ + EMTRICITABINE + TENOFOVIR DISOPROXIL FUMARATE**	0.26	NS	-0.20
35	**ETHAMBUTOL HYDROCHLORIDE + ISONIAZID + PYRAZINAMIDE + RIFAMPICIN**	-8.208	NS	NS
36	**GLUCOSE, BLOOD TESTS**	NS	NS	1.31
37	**HYDROCHLOROTHIAZIDE + TELMISARTAN**	NS	NS	NS
38	**IBUPROFEN + PARACETAMOL**	NS	NS	NS
39	**INSULIN HUMAN BASE RECOMBINANT + INSULIN HUMAN ISOPHANE RECOMBINANT**	11.126	NS	NS
40	**ISONIAZID + RIFAMPICIN**	-6.985	NS	NS
41	**ITRACONAZOLE**	NS	NS	7.02
42	**LEUPRORELIN ACETATE**	0.095	NS	-0.24
43	**LEVOCETIRIZINE HYDROCHLORIDE + MONTELUKAST SODIUM SALT**	38.458	NS	NS
44	**LULICONAZOLE**	0.57	NS	2.23
45	**MECOBALAMIN + PREGABALIN**	9.043	NS	-4.94
46	**MEFENAMIC ACID + TRANEXAMIC ACID**	1.333	NS	NS
47	**MEROPENEM TRIHYDRATE**	2.885	NS	1.43
48	**MIFEPRISTONE + MISOPROSTOL**	NS	NS	NS
49	**MYCOPHENOLIC ACID SODIUM SALT**	NS	NS	0.48
50	**NANDROLONE DECANOATE**	3.979	NS	NS
51	**ORNIDAZOLE**	-1.578	NS	1.06
52	**PREGNANCY TESTS**	NS	NS	10.85
53	**PROGESTERONE**	5.546	NS	NS

54	**ROSUVASTATIN CALCIUM SALT**	42.012	NS	NS
55	**SILDENAFIL CITRATE**	NS	NS	12.54
56	**VACCINE, PNEUMOCOCCAL CONJUGATE**	0.918	NS	NS

ANNEXURE C
CATEGORY MAPPING IPA STUDY, IQVIA TA, NLEM CATEGORIES

S.No	IPA Study Therapeutic Categories	IQVIA TA	NLEM Categories
1	Anti-Infectives	Anti-Infectives, Antivirals, Derma, Anti-malarials, Anti-TB, Anti-Parasitic	Anti-Infectives, Derma, Antiseptic
2	Gastro Intestinal	Gastro Intestinal, Gynaec, Urology	GI, Oxytocics & Antioxytocics, Hormones & Contraceptives (Hormonal Contraceptives, Estrogen, Progestrone & Androgen, Hypoglycemia, Ovulation Inducers)
3	Others	Vitamins / Minerals / Nutrients, Opthal/Otologicals,Parenteral,Vaccines, Others	Antidotes, Disinfectant, Diagnostics, Ophthalmology, Contraceptives, Parenteral, Immunologicals, Vitamins
4	Neuro / Analgesics	Neuro / CNS, Pain / Analgesics	Anesthesia, Analgesics, Antipyretics & Anti Inflammatory, Anticonvulsants, AntiMigraine, AntiParkinson, Dementia, Muscle Relaxants, Psychotherapeutic
5	Cardiac and Blood Related	Cardiac, Blood Related	Blood, Cardio, Diuretics, Plasma
6	Hormones	Anti-Diabetic, Hormones	Hormones & Contraceptives (Anti-diabetic, Thyroids,Adrenal hormones)
7	Respiratory	Respiratory	Respiratory, Anti-allergics, ENT
8	Oncology	Oncology	Cancer