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Access to medicine: Induction of novel drugs in the post era of new patent regulation in Pakistan

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Access to novel medicines was a disputed issue during the formation of Trade-Related Aspects of Intellectual Property Rights (TRIPs) agreement as developing countries had concerns that the patent rights on pharmaceutical products may produce negative implications on the induction of novel drugs. After a decade of TRIPs agreement, this study aims to evaluate the trends of novel drugs induction in Pakistan. The results of this study indicate a marked and consistent decline in the entries of novel drugs in the post era of TRIPs agreement which shows that the access to novel medicines issue likely amplified rather improved by giving the incentive of patent rights on the pharmaceutical products. Stakeholders should make cohesive policies to ensure the early induction of novel drugs to make them affordable in Pakistan.

Keywords: access to medicine; public health; pharmaceuticals; health policy; drugs; healthcare; health regulation

INTRODUCTION

Pakistan ranks sixth in the population index with approximately 200 million people and its Gross National Product (GNP) per capita (purchasing power parity) ranking was 158 out of 216 countries in 2016 (The World Bank, 2016).

The domestic pharmaceutical industry has exceeded over $3 billion with a growth rate of 15% annually (Pakistan Pharmaceuticals Manufacturers' Association. Pakistan's Pharmaceutical Industry, 2017).

Local pharmaceutical industry is limited to the manufacturing of generic drugs and largely depends upon the import of active pharmaceutical ingredients from abroad such as India, China, USA, and Europe for manufacturing of pharmaceutical products (European Commission Report. Trade-Related Technical Assistance Program, 2007).

The poor progress of local Pakistani pharmaceutical towards the manufacturing of novel expensive drugs has likely deprived a significant portion of the population from the access of advanced drugs due to affordability issues. In several developing countries, the essential medicines are not sufficiently available to patients, as around two (2) billion people have no power to purchase basic medicines (World Health Organization. Ten years in public health 2007-2017; 2017).

Access to medicines is a pervasive and rising concern as major gaps exist in the access of essential medicine in Pakistan (Zaidi et al., 2013) which requires comprehensive trans-disciplinary studies on various components of the health regulatory system.

TRIPs agreement was made in 1995 to harmonize the intellectual property rights protection and enforcement worldwide to spur the research and development activities and to encourage the global pharmaceutical industries to launch their new innovated products in the

developing countries thereby giving them incentive of patent rights on pharmaceutical products.

Pakistan is a member of TRIPs agreement since its creation and upgraded its local patent law in conformity with the provisions of TRIPs agreement which came into force on January 1st 2005 after completion of the transitional period of ten (10) years from 1995 to 2004 which was provided to members of developing countries under TRIPs agreement (Article 65(4)) that did not have pharmaceutical product patenting system. The purpose of transitional period was to assist the member countries to upgrade their laws and equip their local industries with the needed research and development facilities and organizational reforms so that they can subsequently compete and adopt viable technologies. In the new regulation, the patent rights particularly allowed on pharmaceutical products which were previously only permitted for the process of preparation of drugs and increased patent term from sixteen (16) to twenty (20) years.

Ironically, the pharmaceutical product patents have implications on the access to novel drugs as patented drugs are approximately three times more costly in comparison to generic drugs (Melly, 2011) which ultimately can produce a negative impact on the access of advanced drugs for low-income people. During the creation of TRIPs Agreement, the pharmaceutical patents on products was a disputed issue as developing countries shown concerns that the protection of pharmaceutical product patents may surge the novel drugs access issue in the domestic markets thereby restraining the induction of novel generic drugs as pharmaceutical patents on minor improvements covering novel drugs can be used strategically to block the entries of new generic drugs (Correa, 2011) which reduce drugs prices and makes novel drugs accessible for poor public. This study aims to empirically evaluate the trends of induction of novel drugs i.e. new molecular entities and generic drugs in post era of new patent regulation made in view of the TRIPs agreement in Pakistan.

MATERIALS AND METHODS

We collected a data of new drug products registered between May 2007 and February 2016 from the Pharma Guide book which publishes annually and provides a list of new drug products (including new drugs which launched first time in Pakistan and new brands of old available generic drugs) approved during every previous year.

We obtained a data of registered drugs including 94 new drug products and 6962 new brands of old available generic drugs from the seven printed versions of the PharmaGuide editions 20th to 24th in an attempt to get the maximum data. We further verified the data related to new drug products from the documents issued by the registration board of Ministry of health/drug regulatory authority of Pakistan (DRAP). Afterward, we carefully analyzed each newly registered drug products which launched first time in Pakistan and coded them into new molecular entity drugs and new generic drugs in the light of information attained from the internet and official drug regulatory websites such as Food and Drug Administration (FDA), European Medicines Agency (EMA). In this respect, we considered a new molecular entity to an advance therapeutic drug registered in the recent era and considered a new generic drug which was available worldwide but registered first time in Pakistan. We counted a single entry of new generic drug when more than one brand of same new generic drug registered simultaneously and the other concurrent registered generic drugs were added in the category of new brands of old generic drugs. We analyzed the therapeutic classes of new drug products according to the classification system provided by the European Pharmaceutical Market Research Association (EphMRA) and World Health Organization (WHO). Lastly, we statistically analyzed the data in terms of (1) the shares of the coded categories of new registered drugs, and (2) the graphical illustrations of the coded categories of new registered drugs.

RESULTS AND DISCUSSION

The results of this study indicate that the induction of novel drugs i.e. new molecular entities and new generic drugs consistently and markedly declined in the post era of new patent regulation in Pakistan as shown in Figure 1. We found a very small ratio of new molecular entities registered with share 0.4% (n=27) and new generic drugs 0.9% (n=67) between 2007 and 2016 in Pakistan presented in Table 1. In contrast to the declining rates of new molecular entities induction in Pakistan, the new molecular entities approval rates remained high in the developed countries, for example, the FDA of USA approved two ninety three (293) new molecular entities between 2008 and 2015 with an average of twenty eight (28) novel drug approval per year (U.S. Food and Drug Administration. Novel Drugs Summary Report, 2015).

Table 1. Trends of new drugs registration

Category	Mean	SD	Numbers (%)
New molecular entity drugs	5.4	5.46	27 (0.4%)
Generic drugs	13.4	15	67 (0.9%)
Brands of old generic drugs	1392	219	6962 (98%)

Legend**:** Results are based on the data of 7056 new drugs registered between May 2007 and February 2016.

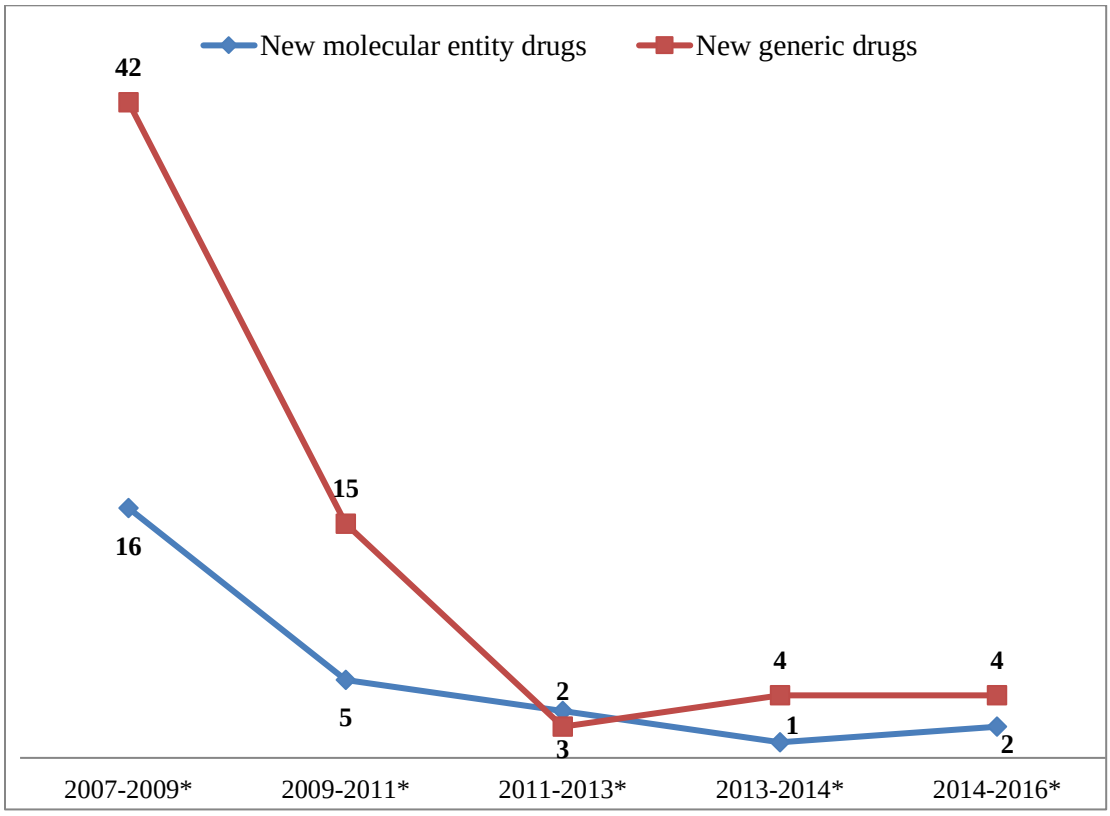

Figure 1. Showing declining trends of new molecular entities and new generic drugs induction in Pakistan.
Results are based on the data of 7056 new drugs registered between May 2007 and February 2016. The horizontal axis represents years. The vertical axis represents registration numbers of new molecular entities and new generic drugs.
Note: 2007-2009*: May 2007 to May 2009 (25 months)
2009-2011*: June 2009 to August 2011 (27 months)
2011-2013*: September 2011 to January 2013 (17 months)
2013-2014*: February 2013 to July 2014 (18 months)
2014-2016*: August 2014 to February 2016 (19 months)

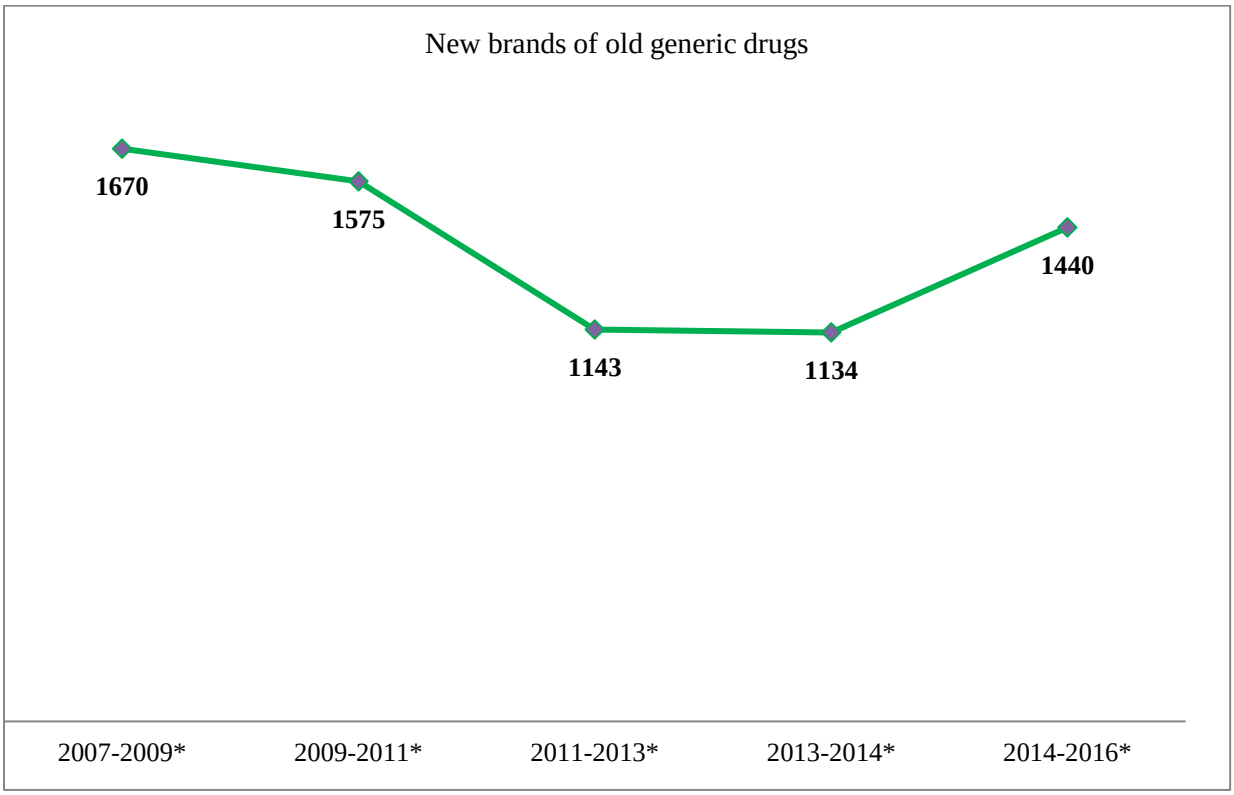

Figure 2. Showing inclining trends of new brands of old generic drugs induction in the recent years in Pakistan.
Results are based on the data of 7056 new drugs registered between May 2007 and February 2016. The horizontal axis represents years. The vertical axis represents registration numbers of new molecular entities and new generic drugs.
Note: 2007-2009*: May 2007 to May 2009 (25 months)
2009-2011*: June 2009 to August 2011 (27 months)
2011-2013*: September 2011 to January 2013 (17 months)
2013-2014*: February 2013 to July 2014 (18 months)
2014-2016*: August 2014 to February 2016 (19 months)

We further observed that the rate of novel drugs induction increased in the recent years in USA in contrast to the consistently declining trends of induction of novel drugs in Pakistan, for instance, the FDA approved forty one (41) and forty five (45) novel drugs in 2014 and 2015 respectively (U.S. Food and Drug Administration. Novel Drugs Summary Report, 2015).

We observed that the novel drugs registered mostly in the advance therapeutic classes shown in Table 2 such as anticancer drugs, central nervous system related drugs, antiviral; antifungal drugs, blood related drugs, cardiovascular drugs, anti-diabetics drugs. In contrast, the old generic drugs 99% (n=6962) largely registered in therapeutic classes in which generic drugs already abundantly available in the local market such as antibiotics 21% (n=1451), alimentary tract and metabolism 12% (n=874), and central nervous system 12% (n=839) presented in Table 2 which indicates the lack of drug manufacturing policy in Pakistan.

The patents on pharmaceutical products under TRIPs agreement may be a reason of decline of novel drugs in Pakistan as there is no substantial amendment or new regulation made in respect of pharmaceutical patents in the studied period and also in the longstanding drug laws of Pakistan. Although, it is possible that the novel drugs induction may be declined in Pakistan due to the influence of various external factors, but simultaneously increasing rates of old generic drugs shown in Figure 2 perhaps diminishing influence of such factors.

Table 2. Therapeutic categories of the new registered drugs

Therapeutic Category	Molecular entity drugs	Generic drugs	Brands of old generic drugs	Total (%)
Alimentary tract and Metabolism	2	2	870	874 (12%)
Anti-diabetics	1	7	129	137 (2%)
Nutritional supplements, Vitamins	-	1	360	361 (5%)
Blood and Blood forming drugs	2	8	425	435 (6%)
Cardiovascular	3	7	332	342 (5%)
Dermatological	-	3	293	296 (4%)
Genito-urinary, Hormones related drugs	1	4	150	155 (2%)
Antibiotics	1	3	1447	1451 (21%)
Antivirals, Antifungals, other infective	3	9	159	171 (2%)
Vaccines	-	2	45	47 (1%)
Cytostatic	6	4	99	109 (2%)
Musculo-skeletal system	-	3	722	725 (10%)
Central nervous system	4	5	830	839 (12%)
Parasitology	-	4	329	333 (5%)
Respiratory system	4	3	515	522 (7%)
Sensory organs		1	185	186 (3%)
Immunomodulators	-	1	11	12 (0.1%)
Hospital solutions	-	-	45	45 (1%)
Antidotes, Diagnostic aids, Test preparations	-	-	16	16 (0.2%)
Total	27	67	6962	7056

Legend: Results are based on the data of 7056 new drugs registered between May 2007 and February 2016.

CONCLUSION

Access to novel medicine issue likely amplified in the post era of new patent regulation made in view of the TRIPs agreement in Pakistan rather improved by giving the patent rights incentive in relation to the pharmaceutical products to research based pharmaceutical companies. Declining trends of novel drugs induction is an alarming condition in the health sector of Pakistan which urges stakeholders to make cohesive policies to ensure early induction of new molecular entities and generic drugs to improve the novel drugs access at affordable prices in Pakistan.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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