Original Research Paper

Volume -10 | Issue - 4 | April - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Pharmacology

AN ANALYSIS OF DRUG APPROVALS IN INDIA OVER PAST 10 YEARS

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ABSTRACT **Background -** Drug development is a tedious process and takes a long time for approval by regulatory authorities. With time, India has revised rules and regulations for conducting clinical trials as well as for marketing of drug. This can impact the number of drugs been approved.

Objective - To analyse trends of drug approvals by CDSCO in India from 2009-2019.

Methods - List of drugs approved by CDSCO for human use over past 10 years was obtained from cdsco.gov.in. The drugs were analysed according to the type of drug approval.

Results - The total number of drugs approved were 853. Total drug approvals in 2009 and 2019 were 210 and 19 respectively. Maximum drugs were approved in the year 2010 (224) and minimum in 2019 (19) with median of 42. Maximum approvals were seen in oncology(108), CVS(102), and pain(115). With regards to the type of drugs approvals, maximum were FDDC(247) but with no FDDC approved in last 5 years

Conclusion - There is a decline in number of approvals of drugs over last 10 years and it coincides with the implementation of new rules and regulations. With strict vigilance on FDDC being approved, the number has declined tremendously.

KEYWORDS : CDSCO, drug development, new drug.

INTRODUCTION

The drug development and its approval involve various processes from target identification to manufacturing, testing and marketing of drugs. This takes around 12 years or more.[1] All these processes are governed by regulatory authorities specific to the region or country. These regulatory authorities ensure that the drug manufactures follow various rules and regulations of that country.

In India, these regulations fall under New drugs and clinical trial rules 2019. The regulation is divided among state and central authorities in India.[2]The regulations are enforced by central authorities whereby they regulate approval of new drugs and conduct of clinical trials in India. It lays down the standards for drugs, controls the quality of imported drugs. The state authorities regulate manufacture, sale and distribution of drugs. The central authorities coordinate the activities of state drug control organizations and provide expert advice to bring uniformity in enforcement of regulations. Central Drugs Standard Control Organization (CDSCO) is the central license approving authority that works under the Drugs Controller General of India. It regulates the import of drugs, approval of new drugs and clinical trial.

The rules and regulations are modified from time to time to incorporate the various changes in conduct of clinical trials and other processes involved in drug development. In India, the drugs and cosmetics act 1940 and Rule 1945 was amended multiple times along with schedule Y, the important amendments being in the years 2008 and 2013.[4]

In 2013 the various changes in Drugs and Cosmetics rule included registration of ethics committees with CTRI (Clinical Trials Registry India) before it can review or approve clinical trial, mandatory audio-visual recording of informed consent. It also restricted role of independent ethics committees registered with local authorities to review and approval of BA/BE studies only. The other changes mandated submission of annual reports and authorized CDSCO to inspect the trial site.[5]

In February 2019, there was a major amendment after which it is now called as the new drugs and cosmetics act. According to this ethics committees registered with CDSCO can review and approvenew drugs and trials of bioavailability and bioequivalence. The other researches like biomedical and health research would require separate ethics committee. In addition, various preclinical studies that are required before conduct of clinical trial, can be waived by regulator. Also, regulator can waive need for conduct of clinical trial in India if a drug has already been approved in certain developed countries.[2,3]

These constant amendments in rules and regulations regarding drug approval processes could affect the Indian pharmaceutical sector and the drug development. With the objective of studying the impact of such amendments, we reviewed the drug approvals in India from 2009 to 2019.

MATERIALS AND METHODS

The data of drug approval were obtained from CDSCO website. (as accessed on 13 October 2019)[6] The drugs approved from 2009 to 2019(August 2019) that were intended for human use were included. The data captured comprise of approvals for new drugs, additional strength, fixed dose combinations (of previously approved drugs), new indications, new dosage forms and new drug delivery systems. These data were entered and analysed using Microsoft Excel 2019. The values were expressed as total, percentage, mean ± standard deviation, median and range.

RESULTS:

Over last 10 years a total of 853 drugs have been approved by CDSCO. The maximum numbers of drug approvals were seen in the year 2010, i.e. 224. The median numbers of approvals were 42 with a range of 19-224. It was observed that the number of approvals has declined over the past years with least number of approvals in current year.

Table no:1- Drug approved year-wise:

Sr. no	Year	Total number of approvals	FDC	New molecule	New indication
1	2009	210	72	33	39
2	2010	224	107	33	24
3	2011	140	58	20	25
4	2012	42	7	17	6
5	2013	35	9	7	8
6	2014	49	2	9	18
7	2015	27	0	0	11
8	2016	23	0	1	7
9	2017	39	0	3	15
10	2018	45	0	1	23
11	2019	19	0	0	6

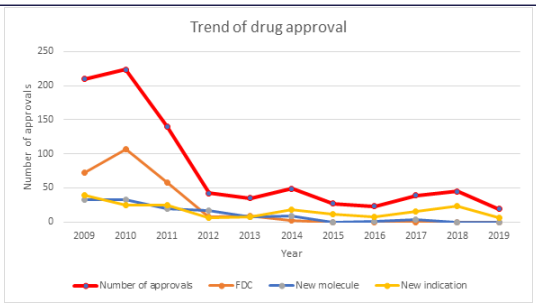
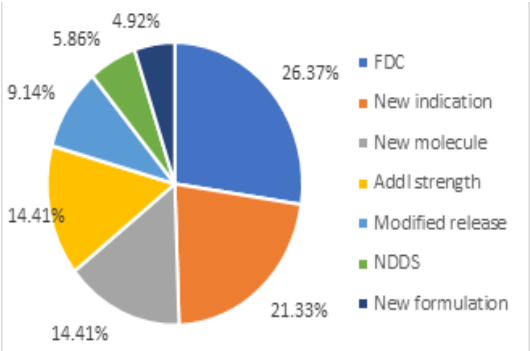


Figure 1.: Trends of drug approvals over past 10 years.

Of the drugs approved, majority were FDCs (26.37%), followed by new indication (21.22%), new molecule (14.41%), additional strength (14.41%), modified release (9.14%), new drug delivery system (5.86%) and new formulation (4.92%).[Figure 2] The approval of FDCs has declined tremendously with no approvals in past 5 years. Of the approvals for single agent, new molecule showed a decline in past 7 years with no new drug approval in the current year. Approvals for new indication has been steady with a mean of 16 10 approvals per year.



Of the total number of approvals, majority were drugs for pain management (116). Of these, 51 were FDCs. Amongst 116 single agents approved, 35 were of NSAIDs group of drugs.Oncology was the most common disease for which the drugs were approved. Various classes of drugs were approved, with tyrosine kinase inhibitors (36/108) the most common class. This was followed by CVS, infection, CNS etc.

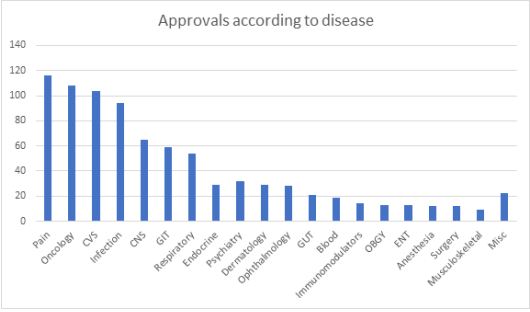


Figure 3.: Approval of drugs according to disease.

Amongst the drugs approved as new molecule, oncology(18/123) and infections(18/123) were the highest followed by CVS (15), CNS(10), GIT(12).

For new indications, majority were drugs used in oncology (58/181) followed by CVS (23/181), infections, CNS.

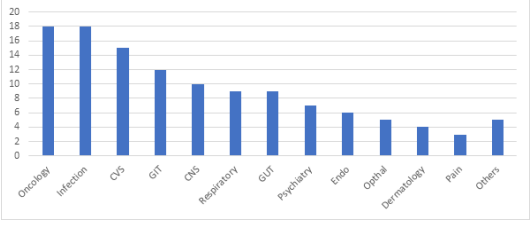


Figure 4.: Approval of new molecule according to disease.

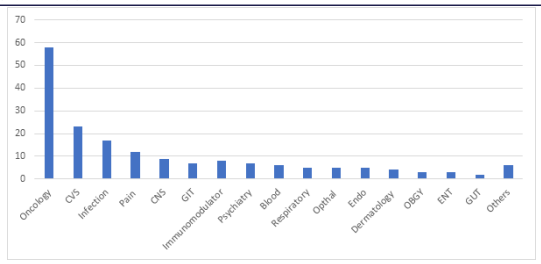


Figure 5.: Approval of drugs with new indications.

DISCUSSION:

We observed a total of 853 approvals over past 10 years with a decline in number of approvals over last few years. A drastic decline was observed in the year 2010 till 2013 and this decline has been consistent over past few years.

In India, the Ministry of Health and Family Welfare (MoHFW) and the Ministry of Chemicals and Fertilizers are the two main ministries that regulate drug approvals. On the other hand, CDSCO and MoHFW maintain licensing and quality control and distribution of drugs. There are various other regulatory bodies that were associated with drug regulation. As a result of incoordination between these regulatory bodies, 33 drugs were approved without any clinical trial between January 2008 and October 2010 as concluded by the 59th report of Parliamentary Standing Committee on Health and Family Welfare. Inspection of clinical trials was started by CDSCO in 2008 though actual onsite inspection started in 2010 by US-FDA trained Indian Inspectors and regulatory experts to uphold the quality of the trials.[7] We believe that because of the timing of the application of stringent laws in India matches with the decline of the drug approvals, it could be responsible for later.

A study by Chawan *et. al.* of drugs approved from 1999 to 2015 showed an increasing trend followed by a fall in the year 2010 was observed.[8] This study also reported a median of 57 approvals which was higher than that reported in our study (42).

There were only 123 new molecule/novel drug approvals in past ten years in India, an average of 12 per year and no new approvals in 2019. In contrast, FDA has approved an average of 33 novel drugs per year over past 10 years, with 59 drugs approved last year.

It is a known fact that the number drug approved is directly proportional to the incidence and prevalence of diseases in a particular r geographical area. And this evident from our study results as well. We observed that oncology was the most common therapeutic area for which maximum drugs were approved followed by CVS and infectious diseases. It is a known fact that the incidence of cancer is increasing in India. Also prevalence of infectious disease is high in India although no increase or fall has been seen in past.[9] While prevalence of CVS disease has increased considerably over past few years. These two are still among the leading causes of death.[10,11] Of all the drugs approved as new molecule, cancer and infection were highest followed by CVS. These diseases are also among the top causes of disease burden although not in the same order. Relative decreased number of approvals in cardiovascular drugs is due to less clinical trials contributed to lack of new targets.[12]Infections usually require antibiotic management for few days. Also, new breakthrough antibiotics are usually reserved as last resort for infection due to rise in antibiotic resistance. These factors account for low returns in antibiotic development which reflects in reduced interest by pharmaceutical sector.[13]

The trend in number of approvals for FDC has come down drastically with no new approvals in recent years. Chawan et. al reported an increasing trend followed by fall with a median approval of 11 drugs per year till 2015. In 2012, the 59th report of Parliamentary Standing Committee on Health and Family Welfare reported issues regarding manufacturing licences being granted by few states without CDSCO approval. It also noted that multiple FDCs that were available in India were banned in other well regulated countries. Subsequently, DCGI issued notice to manufacturers of these combination to prove safety and efficacy of the irrational combinations. CDSCO also setup committee to evaluate safety and rationality of these combinations following which 324 FDCs were finally banned in 2018. This probably led to the drastic fall in approval of FDCs in following years.[14]

Limitations: Biologicals (monoclonal antibodies) were not included in study as they were not included in drug approval lists by CDSCO.

CONCLUSION:

The number of approvals has declined drastically over years with amendments in rules related to drug approval. Though a well-regulated approval process ensures better quality of drugs in market it could have an adverse effect on the number new drug approvals in that region.

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