Invited Article

Paradigm shift of Indian pharma industry during covid-19 pandemic and beyond

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Abstract

Indian pharmaceutical Industry is well developed and recognized as the "Pharmacy of the World" because of its contribution to the people of the major portion of the world. It exported drugs to over 300 countries and vaccines to more than 250 countries, but its contribution in the area of drug development and discovery is not satisfactory. During Covid pandemic India has proved its ability for drug/vaccine development using indigenous technology. It is also registered a new trend of developing new drug/vaccine jointly by private entrepreneurs and government laboratories like-ICMR, CSIR etc. In order to quick development of drugs, government of India has taken several steps like- framing of new legislation - New Drugs and Clinical trial Rules, making provision for quick approval of new Covid-19 vaccines developed and marketed by developed countries. On the other hand new provisions were made to increase production capacity to make India self reliant under "Atmanirvar Bharat" mission. These initiatives resulted a Paradigm shift of the Indian Pharma Industry during Covid-19 pandemic and beyond from manufacturing to innovation.

Keywords: Innovation, New Drugs, Covid-19, Atma Nirvar, repurposed

Introduction

Pharmaceutical industry being knowledge based industry showed tremendous development in the last few decades. Indian pharmaceutical industry is now one of the largest in developing countries having a yearly turnover of $43 billion1. India is now the 3rd largest by volume and 10th largest by value in case of production of drugs and Pharmaceuticals. Presently India is contributing 8 percent global production. India recorded its turnover of $43 billion in 2019-20201 and it is expected that it will cross 55 billion US$ by 2030. India exported $20 billion worth of drugs and Pharmaceuticals in 2019-2020 among 350 countries. Indian pharmaceutical Industry recorded a growth of 9.4 percent CAGR in 2018-2019, which is one of the highest among industries. India is producing almost 50 percent of vaccines consumed worldwide and exported vaccines to about 250 countries. India's medical devices market stood at US$ 10.36 billion in FY20. The market is expected to increase at a CAGR of 37% from 2020 to 2025 to reach US$ 50 billion. This showed the strength of Indian Pharmaceutical industries in case of pharmaceutical adds.

Paradigm shift:

Though India showed tremendous growth in pharma manufacturing since amendment of Indian Patent Act 1970 2. Very little success was noted in the area of drug discovery and development. Efforts were made in different sectors like- amendment of clinical trial regulation3, incentives from govt. and manufacturers increased R & D expenses during last few decades.

During this covid period Indian pharmaceutical industry showed much progress in drug development and innovation by way of getting emergency approval of several drugs and

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Table-I: Repurposed drugs developed by Indian Manufacturers.

S.N.	Drug	Inventor	Repurposed	Covid-19	Date of Approval
1.	Remdesivir 100 mg Injection	Gelad Sciences (USA), for Ebola	Gelad, Hetero and 19 more firm is manufacturing subsequently	For emergency use for hospitalized patients suffering from Co vid- 19. In these cases, informed consent of the patient or his /her representative in the prescribed form is mandatory before initiating the treatment.	01.06.2020 (Gelad) 20th June 2020 (Hetero)
2.	Favipiravir 200 mg Tablet	Favipiravir is an anti-influenza drug which was developed by FUJIFILM Toyama Chemical Co., Ltd, Japan	Glenmark etc.	Mild to moderate Covid-19 patients in I ndia. In both the cases, informed consent of the patient or his /her representative in the prescribed form is mandatory before initiating the treatment.	19th June 2020
3.	Itolizumab injection	Cuba Biocon (Psoriasis since 2013)	Biocon	Restricted Emergency Use of the drug for the treatment of Cytokine Release Syndrome (CRS) in moderate to severe Acute Respiratory Distress Syndrome (ADRS) patients due to COVID-19	11th July 2020
4.	Tocilizumab iv Injection	Roche Originally used for Arthritis	Cipla	Slow down the cytokine response in COVID-19 patients by modulating a protein called IL6	
5.	Dexamethasone	Old drug	Several manufacturers	For patients on ventilators, the treatment was shown to reduce mortality by about one third, and for patients requiring only oxygen, mortality was cut by about one fifth.	27th June 2020

vaccines for fighting Covid-19.

Indian firms conducted clinical trials of several drugs in Indian population and marketed after getting emergency approval for use in Covid-19 patients. The following drugs have got approval from Drugs Controller General of India (DCGI) and marketed for use in several conditions of Covid patients which are as presented in Table –I.

India has made notable progress in case of innovating vaccines for Covid-19 and its manufacturing. Bharat Biotech in collaboration with Indian Council for Medical Research (ICMR) - National Institute of Virology (NIV) has invented a Covid vaccine having brand name Covaxin and marketing for use after receiving approval from Drugs Controller General of India (DCGI) on 3rd January 2021. This Covid vaccine has been developed indigenously in India and now approved by more than 14 regulatory agencies. This is a unique occasion where a research laboratory in Government sector joined hand with a private entrepreneur for innovation of a vaccine. Covaxin developed by Bharat Biotech has been listed for Emergency Use by World Health Organization (WHO) 4 on 4th November 2021 made great recognition for Indian strength for vaccine development.

The other example of success made by Zydus in developing an rDNA Covid-19 vaccine for above 18 which has got Emergency Use Approval(EUA) from Central Drugs Standard Control Organizations (CDSCO) and is going to introduce in the Indian market.

In the meantime the Zydus has developed a version of the same for 12-18 years of age. Bharat Biotech has also developed a

Table-II: Covid-19 Vaccines available in India.

S.N.	Name	Vaccine Type	Primary Developed	Country of origin	Authorization/ Approval
1	Covaxine	Inactivated Vaccine	Bharat Biotech, ICMR	India	DCGI + 13 Countries
2	ZyCov D	rDNA vaccine	Zydus	India	DCGI
3	Covishield	Adenovirus Vaccine	BARDA, OWS	UK, Serum Institute	DCGI + 45 Countries
4	Sputnik V	Recombinant Adenovirus Vaccine (rAD26 and rAD5)	Gamaleya Research Institute, Acellena Contract Drug Research and Development	Russia	DCGI + 72 Countries
5	Moderna Covid-19 vaccine (mRNA-1273)	mRNA based Vaccine	Moderna, BRDA, NIAID	US	DCGI + 75 Countries
6	Jansen Ad26.COV2.5	Non-replicating viral vector	Jansen (Johnson & Johnson)	US	DCGI + 73 Countries
7	AZD1222	Adenovirus vaccine	Oxford/ Astra Zeneca	UK	DCGI + 123 Countries

version of their Covaxine (Covid-19 vaccine) for use for 2-18 years of age and got EUA from CDSCO.
Similarly Serum Institute of India has joined with AstraZeneca and developed technology for manufacturing another Covid vaccine and marketed with a Brand name Covishield which is being available in several countries throughout the world. Dr. Reddy's joined hand with RFID and Gamaleya National Research Center of Russia and conducted clinical trials of Sputnik-V in India and Sputnik V is in use in India. Details about the Covid-19 Vaccines are presented in Table-II.

Using these seven Covid-19 vaccines India delivered 108.9 crore doses and made full vaccination of 34.8 crore Indian people (25.2 % of population) till 8th November 2021.

Government policy change and amendment of Rule for improving access to essential medicines and vaccines:

Change in Government policies and amendment of Drug Rules have given opportunities for improving access to medicines and vaccines. The newly introduced New Drugs and Clinical trial Rules have provisions to market drugs and vaccines under rule 75 (7) without local clinical trials with prior permission of the Central licensing authority (DCGI) which states that- "(7) The local clinical trial may not be required to be submitted along with the application referred to in sub-rule
(1) if,_
(i) the new drug is approved and marketed in countries specified by the Central Licencing Authority under rule 101 and if no major unexpected serious adverse events have been reported; or
(ii) the application is for import of a new drug for which the Central Licencing Authority had already granted permission to conduct a global clinical trial which is ongoing in India and in the meantime such new drug has been approved for marketing in a country specified under rule 101; and
(iii) there is no probability or evidence, on the basis of existing knowledge, of difference in Indian population of the enzymes or gene involved in the metabolism of the new drug or any factor affecting pharmacokinetics and pharmacodynamics, safety and efficacy of the new drug; and
(iv) the applicant has given an undertaking in writing to conduct Phase IV clinical trial to establish safety and effectiveness of such new drug as per design approved by the Central Licencing Authority:
Provided that the Central Licencing Authority may relax this condition, where the drug is indicated in life threatening or serious diseases or diseases of special relevance to Indian health scenario or for a condition which is unmet need in India

such as XDR tuberculosis, hepatitis C, H1N1, dengue, malaria, HIV, or for the rare diseases for which drugs are not available or available at a high cost or if it is an orphan drug."

Thereafter CDSCO has published a guideline in this matter and the process of approving new vaccines becomes easier. This guidelines stated that no local clinical trials are required if a vaccine for Covid-19 already approved by USFDA, MHRA, PDMA Japan and listed by WHO for emergency use for Covid-19 5. These two steps helps quick approval for emergency use of vaccines already approved by USFDA, MHRA, PDMA Japan and WHO listed Covid-19 vaccines. Using these provisions Covid -19 vaccines developed by Moderna in US already got approval for import by Cipla limited and hope that some more vaccines will be available in India in future using these provisions.

New Government schemes under"Atmanirvar Bharat" mission:

This mission was launched by Government of India in the year 2020 to make Indian Industries self reliant. Aatmanirbhar Bharat will go beyond self-sufficiency to the pharmaceutical Industry of India, both in case of pharmaceutical products and Active Principal Ingredients (APIs). Along with accelerating domestic manufacturing, it will facilitate innovation and expand the global export base to create 'Brand India' in the global pharmaceutical space.
The government of India has taken active steps by releasing the Production Linked Incentive (PLI 1.0 and 2.0) schemes to take forward the Atmanirbhar mission for the pharmaceutical industry 6. These initiatives will be important to build on the strength of the Indian pharmaceutical industry to manufacture high quality affordable medicines and be a dependable supplier around the globe for the benefit of the patients.

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