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GENERIC MEDICINES:- HISTORY, APPROVAL PROCESS, ECONOMIC AND CURRENT CHALLENGE

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ABSTRACT

The cost of pharmaceuticals, as a percentage of total healthcare spending, has been rising worldwide. This has resulted in strained national budgets and a high proportion of people without access to essential medications. Though India has become a global hub of generic drug manufacturing, the expected benefits of cheaper drugs are not translating into savings for ordinary people. This is in part due to the rise of branded generics, which are marketed at a price point close to the innovator brands. Considerable emphasis is presently being placed on usage of generic medicines by governments focussed on the potential economic benefits associated with their use. Unbranded generic medicines are not finding their way into prescriptions due to issues of confidence and perception, though they are proven to be much cheaper and comparable in efficacy to branded medicines. The drug inventory of unbranded generic manufacturers fares reasonably when reviewed using the World Health Organization- Health Action International (WHO-HAI) tool for analysing drug availability. Also, unbranded generic medicines are much cheaper when compared to the most selling brands and they can bring down the treatment costs in primary care and family practice.

KEYWORDS: Generic medicines, generic drugs, economic competition, drug industry, India, unbranded generic, systematic review, perceptions, opinions.

INTRODUCTION

The World Health Organization (WHO) estimates that almost 30% of the world population lacks access to essential medicines and that the figure will rise to more than 50% in some countries. The cost of the pharmaceuticals is the main factor that hampers access to medicines and the governments in poor countries seem to be doing very little to counter this problem. The public sector availability of essential medicines was less than 50% in most of the countries.

The situation in India is not very different than that of other developing nations. Healthcare expenditures have been growing in India, both in real terms and also when considered as a proportion of the Gross Domestic Product (GDP). The cost of medicines and pharmaceuticals as a percentage of total healthcare spending has also been rising worldwide. It is the fastest-growing item in the healthcare budgets worldwide and it varies between 20-60% in various healthcare budgets of countries.

Fig. 1:

Fig. 2:

Generic Drug Review

The availability and utilization of generic alternatives to brand-name drugs have had a significant effect on cost savings for health care consumers. In 2008, generic drugs accounted for more than 63% of total prescriptions filled in the United States. Although generics are used to fill the majority of prescriptions, the actual costs associated with these medications are less than 13% compared with their branded counterparts. While direct cost savings are a significant advantage for generic drug products, studies have also shown improvements in indirect costs such as therapy adherence and compliance.

Despite the benefits associated with the use of a more cost-effective drug, the generic drug industry has had its share of challenges. To understand these challenges and what the industry faces, it is important to examine the modest history of generic drug products and review the approval process.

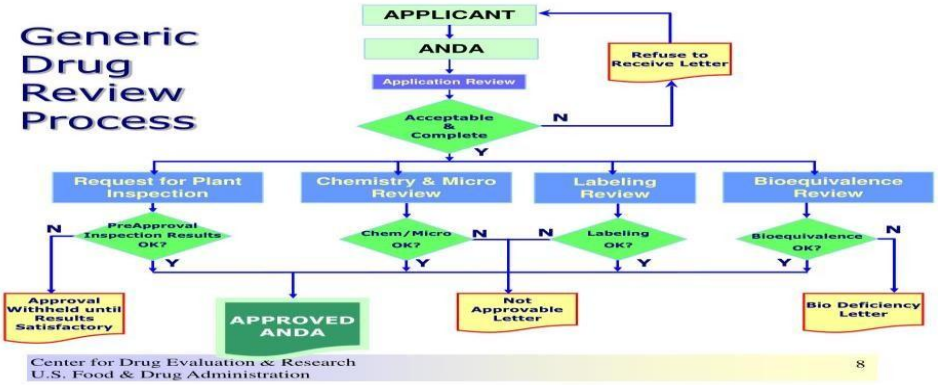

Fig. 3:

The Approval Process

Unlike the approval process for new chemical entities, that for generic drugs allows use of the ANDA, which does not require the submission of clinical data regarding safety and efficacy since this information was already provided for the pioneer product. Since the original active ingredient was already proven safe and effective, the manufacturer must now prove bioequivalence for the pharmaceutically equivalent generic drug product.

In order to receive approval for marketing, a generic drug must meet the same batch requirements for identity, strength, purity, and quality and be therapeutically equivalent to the branded product. Additionally, the drug must be manufactured according to the same Good Manufacturing Practice regulations required by the FDA.[4] For the generic drug to be therapeutically equivalent, two clinical characteristics must apply: It must be pharmaceutically equivalent as well as bioequivalent. Pharmaceutical equivalence means that the active ingredient(s), dose form, route of administration, and strength are the same for both the branded product and the generic product. Bioequivalence is when both products have comparable bioavailability when studied under similar conditions.

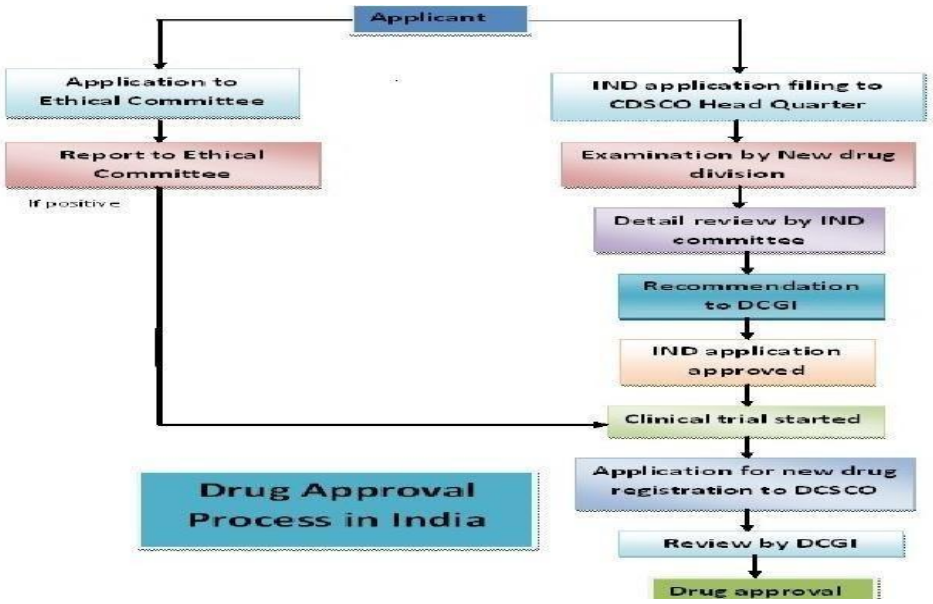

Fig. 4:

Rise of Generics

The role of generic medicines in reducing the healthcare expenditure has been recognised for a long time. Multiple studies have proven that saving through substitution of originator brands by cheaper generic medicines, savings in the range of 10-90% can be achieved. Most national governments have been encouraging the use of generic medicines worldwide and many healthcare systems have policies of substituting expensive branded original medications with generic medicines.

In India, the procurement price of essential medicines is generally lower than the mean International Reference Pricing (IRP) but availability of these drugs in the public sector has always been a problem. The exorbitant cost of some of the commonly used medications in private pharmacies makes it inaccessible to majority of the poor.[11] Also, the difference between procurement prices and retail prices in case of some of the generic medicines, were as high as 28 times, which shows a very high margin of profit-taking in view of limited price control mechanisms. It is in this light, that the government revised the National Pharmaceutical Pricing Policy in 2012. It gave methods to calculate ceiling prices for drugs which are under the National List of Essential Medicines (NLEM) which was modified in 2011. It gave a formula for deciding the ceiling prices for drugs under NLEM, using a market-based pricing (MBP) method, taking into account the prices of all manufacturers having a market share of more than 1% nationally. The Drug Price Control Order of 2013 was a follow-up to the National Pharmaceutical Pricing Policy and gave the price ceiling for 348 drugs and over 600 formulations. However, the action was considered inadequate by many activists lobbying for cheaper drugs and they termed it as a sell-out to international pharmaceutical companies.

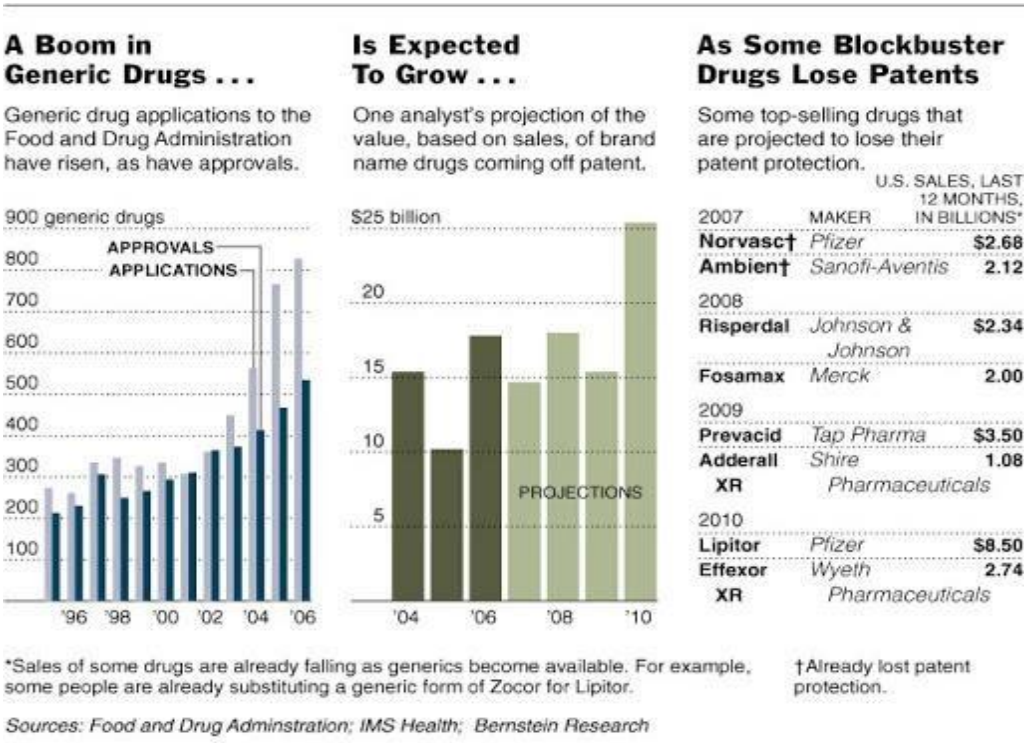

Fig. 5:

Economics

When a pharmaceutical company first markets a drug, it is usually under a patent that, until it expires, the company can use to exclude competitors by suing them for patent infringement. Pharmaceutical companies that develop new drugs generally only invest in drug candidates with strong patent protection as a strategy to recoup their costs of drug development (including the costs of the drug candidates that fail) and to make a profit. The average cost to a brand-name company of discovering, testing, and obtaining regulatory approval for a new drug, with a new chemical entity, was estimated to be as much as US$800 million in 2003[15] and US$2.6 billion in 2014. Drug companies that bring new products have several product line extension strategies they use to extend their exclusivity, some of which are seen as gaming the system and referred to by critics as "evergreening", but at some point there is no patent protection available. For as long as a drug patent lasts, a brand-name company enjoys a period of market exclusivity, or monopoly, in which the company is able to set the price of the drug at a level that maximizes profit. This profit often greatly exceeds the development and production costs of the drug, allowing the company to offset the cost of research and development of other drugs that are not profitable or do not pass clinical trials. Generic drugs are usually sold for significantly lower prices than their branded equivalents and at lower profit

margins. One reason for this is that competition increases among producers when a drug is no longer protected by patents. Generic companies incur fewer costs in creating generic drugs—only the cost of manufacturing, without the costs of drug discovery and drug development—and are therefore able to maintain profitability at a lower price. The prices are often low enough for users in less-prosperous countries to afford them.

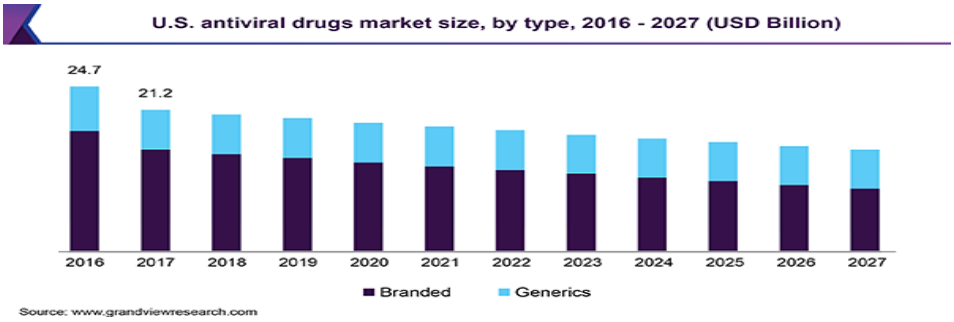

Fig. 6:

Indian Pharmaceutical Industry

The multiplicity of brands and manufacturers makes it difficult to decipher the actual market dynamics and the structural issues in the Indian pharmaceutical industry. The complexity of the market and the intensity of the competition between companies in India have made the country a hub for manufacture of generic medicines, earning a sobriquet "pharmacy of the developing world. This, along with a favorable governmental stance has made India a powerhouse in this field, bringing it into direct confrontation with certain developed nations where most of the big multinational pharmaceutical companies are located. here have been many instances when the Indian Patents Office and the Supreme Court of India effectively used certain flexibilities of the Trade Related Aspects of Intellectual Property Rights (TRIPS) agreement of the World Trade Organization and also the safeguards embedded in the Indian Patents Act.

Pharmacological Group	Brand-name (strength)	Brand name price per unit dose (LYD)	Generic (strength)	Generic price per unit dose (LYD)
Antibiotic	Cipro (750 mg)	0.70	Ciprofloxacin (750 mg)	0.65
Antibacterial	Flagyl (500 mg)	0.85	Amidazole (500 mg)	0.10
Heartburn/Ulcer	Zantac (150 mg)	0.45	Ranitidine	0.10
Hypertension	Renitic (20 mg)	0.25	Enalpril	0.25
	Zestril (10 mg)	0.55	Linopril (10 mg)	0.18

Fig. 7:

CONCLUSION

Today, the generic drug industry is driven by many stakeholders. Consumers demanding low- cost alternatives to expensive brand-name products are at the forefront. Federal and state programs, which were some of the original supporters of generic drug development, also lead the way in encouraging healthy competition and ensuring the safety and efficacy of generic drug products. Additionally, the professional services of medicine and pharmacy, despite having a somewhat conflicting relationship in the past, now jointly advocate the development of low-cost alternatives to serve the needs of their patients and have identified some common ground regarding pharmacotherapeutic decision-making and substitution. Regardless of who is involved and in spite of the controversies surrounding economics, professional interests, and drug development, the generic drug industry is and will continue to be an invaluable player in the health care field.

REFERENCES

1. The World Medicines Situation 2011. The World Health Organisation. [Last accessed on 2015 Mar 2]. Available from: http://apps.who.int/medicinedocs /documents/s18772en/s18772en.pdf.
2. Health Expenditure, Total (% of GDP) | Data | Table. [Last accessed on 2015 Mar 2]. Available from:http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS.
3. Hoffman JM, Li E, Doloresco F, Matusiak L, Hunkler RJ, Shah ND, et al. Projecting future drug expenditures--2012. Am J Health Syst Pharm. 2012; 69: 405– 21. [PubMed] [Google Scholar].
4. Daemmrich A, Mohanty A. Healthcare reform in the United States and China: Pharmaceutical market implications. J Pharm Policy Pract, 2014; 7: 9.

[PMC free article] [PubMed] [Google Scholar].
5. Savage C, Gatyas G. IMS Health reports annual global generics prescription sales growth of 3.6 percent, to $78 billion. December 10, 2008. www.imshealth.com/portal/site/imshealth/menuitem. a46c6d4df3db4b3d88f61101941 8c22a/?vgnextoid= 2943d52288d1e110VgnVCM100000ed152ca2RCR D&vgnextfmt=default.Accessed April 27, 2009.
6. Shrank WH, Cox ER, Fischer MA, et al. Patients' perceptions of generic medications. Health Aff (Millwood), 2009; 28: 546-556.
7. Shrank WH, Hoang T, Ettner SL, et al. The implications of choice: prescribing generic or preferred pharmaceuticals improves medication adherence forchronic conditions. Arch Intern Med.
8. FDA Center for Drug Evaluation and Research. Office of Generic Drugs. What are generic drugs? www.fda.gov/cder/ogd/#, 2006; 166: 332-337.Introduction. Accessed March 16, 2009.
9. FDA Center for Drug Evaluation and Research. Approved drug products with therapeutic equivalence evaluations. 29th ed. www.fda.gov/cder /orange/obannual.pdf. Accessed February 27, 2009.
10. Cameron A, Mantel-Teeuwisse AK, Leufkens HG, Laing RO. Switching from originator brand medicines to generic equivalents in selected developing countries: How much could be saved? Value Health, 2012; 15: 664–73. [PubMed] [Google Scholar].
11. Hassali MA, Alrasheedy AA, McLachlan A, Nguyen TA, Al-Tamimi SK, Ibrahim MI, et al. The experiences of implementing generic medicine policy in eight countries: A review and recommendations for a successful promotion of generic medicine use. Saudi Pharm, 2014; 22: 491–503. [PMC free article] [PubMed] [Google Scholar].
12. Kotwani A, Ewen M, Dey D, Iyer S, Lakshmi PK, Patel A, et al. Prices and availability of common medicines at six sites in India using a standard methodology. Indian J Med Res., 2007; 125: 645–54. [PubMed] [Google Scholar].
13. Copy of f1.pdf – NPPPNotification.pdf [Internet] [Cited 2015 Mar 2, Last accessed on 2015 Mar 2]. Available from: http://www.nppaindia.nic.in/NPPPNotification.pdf .
14. Paying the Price - The Hindu. [Last accessed on 2015 Mar 2]. Availablefrom: http://www.thehindu. com/opinion/op-ed/paying-the-price/article 4912732.ece .
15. Gupta, H; Kumar, S; Roy, SK; Gaud, RS (January). "Patent protection strategies". Journal of Pharmacy & Bioallied Sciences, 2010; 2(1): 2–7. doi:10.4103/0975- 7406.62694. PMC 3146086. PMID 21814422.
16. Frakt, Austin (28 September). "How Patent Law Can Block Even Lifesaving Drugs". The New York Times, 2015.
17. Tufts Center for the Study of Drug Development (November 18). "Cost to Develop and Win Marketing Approval for a New Drug Is $2.6 Billion". Tufts University. Archived from the original on 2014-11-21. Retrieved 2015-12-01, 2014.
18. "An insider's view of generic-drug pricing". Los Angeles Times. March 25, 2013.
19. "Savings From Generic Drugs Purchased at Retail Pharmacies". Food and Drug Administration. April 2004. Archived from *the original* on 2008-02-23. Retrieved, 2008-07-11.
20. "The role of reverse engineering in the development of generic formulations". www.clihouston.com. Retrieved 23 May, 2017.
21. Benson, Mike (February 20, 2015).
22. "Thailand to import generic version of heart drug Plavix from "What it takes to be called 'big pharma' – Market Realist". *Market* Realist.India". Forbes. 2007-08-22. Retrieved 2008-10-13.
23. Kapczynski A. Engineered in India--patent law 2.0. N Engl J Med, 2013; 369: 497–9. [PubMed] [Google Scholar].
24. Bhaumik S. India's rejection of Novartis's patent is but a small step in the right direction. BMJ, 2013; 346: f2412. [PubMed] [Google Scholar].
25. Lancet Oncology. Is India ready to lead the battle for fair access to medicines? Lancet Oncol, 2013; 14: 437. [PubMed] [Google Scholar].