

Opportunities for Generic Drugs in India

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Abstract

Branded drugs play an important role in medications, but generics are their cost effective alternatives. Generics are similar to branded drugs in terms of purity, efficacy and are perceived to be safer as compared to new drug molecules, as they tend to be older and time tested. Indian pharmaceutical market of generic drugs is increasing day by day. The present communication describes various aspects and prospects of generic drugs in Indian Pharmaceutical Sector.

INTRODUCTION

According to U.S. Food and Drug Administration (US FDA), any substance intended for use in the diagnosis, cure, relief, treatment or prevention of disease is called as a drug¹. The drug which is protected by patent is a branded drug and the drug which is a copy of branded drug and is equivalent in terms of safety, efficacy, dosage and use is called a generic drug². Indian pharmaceutical industry has become an important hub in production of generic drugs from last some decades. Total global generic drugs market constituted USD 92 billion and is expected to grow at 11% to reach USD 155 billion in 2012. India is the 4th largest market in terms of production and ranks 13th in terms of consumption value³. Moreover, India accounts for 22% of the world market of generic drugs⁴. Indian pharmaceutical market was USD 13 billion in financial year 2007 but is expected to grow USD 34 billion in financial year 2012³. Today 95% of the country's medical needs are served by Indian Pharmaceutical industry. Indian pharma sector exports 32%, of which 90% is generic and marketing growth is about 20% per annum. More than 1/3rd volume of total market is covered by top 10 companies^{3,5}. There are several multinational pharmaceutical companies like Pfizer, Aventis, Medley, GlaxoSmithKline etc. which have set up operations in India and are expanding their existing business. Market value and percentage growth of generic drugs in world market is depicted in table 1.

Figure 1

Table 1. World Generic Drugs Market Value (2001 - 2005)

Year	US\$ (Billion)	Percentage Growth
2001	29.6	-
2002	36.7	23.7
2003	41.2	12.4
2004	47.8	16.0
2005	57.8	20.9
Compound Annual Growth Rate (CAGR) 2001-2005:		18.2

BRANDED DRUG

A branded drug is protected by a patent, has a trade name and the drug is manufactured by a well established pharmaceutical company. The drug cannot be produced or sold by any other company^{2,7}. Example of some brand name drugs are 'Paxil from GlaxoSmithKline', 'Norvasc from Pfizer', 'Zocor from Merck', 'Amaryl from Aventis' etc⁹.

GENERIC DRUG

Generic drug is a substitute or a copy of branded drug that satisfies the pharmacokinetic and pharmacodynamic standards¹⁰. Generic drugs are equivalent in terms of safety, dosage, strength, quality and performance. They are produced and distributed without any patent protection^{2,7}. According to US FDA, generic drugs are identical or bioequivalent to the brand name counterpart with respect to pharmacokinetic and pharmacodynamic properties². The therapeutic activity of a generic product is similar to that of innovators brand, for that they must be pharmaceutically equivalent as well as bioequivalent¹¹. The generic drugs are cost effective as no large amount is invested in research, development, marketing and promotion like in branded drugs⁷.

BRANDED GENERICS

Several medium and large sized companies market their products as branded generics. These branded generics are usually given a brand name but the generic name is primarily focused. Due to privilege of some duty exemptions, these branded generics are generally sold in a manner similar to that of generics. Prices offered to the end users are similar to usual branded drugs but prices offered to wholesalers are phenomenally very less¹². Branded generics have proprietary name, such as Pyrimide, Pyrestat, Cisachem, Cetral etc¹².

Similarities between branded and generic drugs^{2, 7, 10, 13}

Generics are copy of branded drugs and are almost similar in nature and use. The other similarities in branded and generics are:

Generic drugs have the same quality and strength as that of branded drugs.

The purity and dosage of generics are similar as branded drug.

Both generic and branded drugs are safe and effective for use.

All generics have same risks and benefits as their brand name counterparts.

Generics have the same mechanism of action and pharmacological action as branded drugs.

Both generic and branded drugs meet the same standards of good manufacturing practices.

Both of them have the same active ingredients.

The generic products must be bioequivalent to the branded product.

Comparison between branded drug and generic drugs^{2, 7, 13}

Both are similar in terms of safety, efficacy, use and pharmacology, but still there are some basic differences with which these can be compared. Pondering points are as follows:

Branded drugs are protected by a patent, usually patent protection are given for 20 years from the date of submission of the patent. This provides protection to the innovator of such drugs to generate revenue and make good initial cost incurred by the organization in research, development and

marketing expenses, to develop new drug. Generic drugs are not protected by patent because companies start manufacturing generic drugs once the patent license expires for a branded drug.

Branded drugs are costlier than generic drugs as there is a lot of investment in research, development, marketing and promotion of new drugs. But on other hand, generic manufacturers do not have investment costs for developing a new drug.

The cost of generic drugs generally averages 40-60% below the cost of the innovator or brand name drugs.

Benefits of generic drugs^{2, 7, 8, 13}

Some advantages of generic drugs are enlisted below:

Generic drugs reduce the monopoly and oligopoly power of patent holders.

The cost of generics is less than branded ones. Once the patent expires, the drug price falls substantially if there are generic producers. When more generic producers invade the market, more is the competition, leading to fall in prices.

Generic drugs do not have unfavorable effects on an individual.

The potency and safety are comparable to that of branded drugs.

The use of generic drugs can add up to marked savings for the elderly who generally take more medication than the young and may have less available income.

Bioequivalence and bioequivalence testing

Bioequivalence means that the generic drug and the branded drug demonstrate essentially the same rate and extent of availability of drug in the systemic circulation. The Central Drugs Standard Control Organisation (CDSCO) has defined; bioequivalence of a drug product is achieved if its extent and rate of absorption are not statistically significantly different from those of the reference product when administered in the same molar dose¹⁴.

For the determination of bioequivalence, pharmacokinetic studies are performed. In these studies, each of the generic and branded drugs is administered in a crossover study in usually healthy normal 24-36 adults. In 1977, the first bioequivalence criterion was set by the FDA. Currently, the determination of bioequivalence is done by assessing the

equivalence of the rate and extent of drug absorption. For single dose study, the area under curve (AUC) and the peak blood concentration (C_{max}) provides the rate and extent of drug absorption. According to FDA standards, the innovator and the generic (test) products whose rate and extent of absorption differ by -20/+25% or less are considered to be bioequivalent. The generic manufacturer establishes bioequivalence by using log-transformed data, for approval of Abbreviated New Drug Applications (ANDAs), by showing that the 90% confidence interval of the ratio of the mean response of its product to that of innovator is contained within the limits of 0.8 to 1.25^{14, 15}.

SCOPE OF GENERIC DRUGS

In today's era, the scope of generic drugs is increasing day by day specially in several ill health conditions such as diabetes, cardiovascular and in microbial diseases etc. When any patent expires, new generics are introduced into the market. The scope is also increased due to Para IV filings and Bolar provisions.

Recently, Para IV filing strategy has been adopted by leading Indian pharmaceutical companies to introduce generic drug of its own taking advantage of shortcoming in patent application of patent holders. According to this, a generic manufacturer challenges the original patented drug and claims that the generic version proposed to be launched by the manufacturer does not infringe the patent holder's version. In case a patent challenge is won, it entitles the first to file Para IV generic manufacturer a 180 days exclusivity, if company come up with an equivalent of the innovator's branded formulation¹⁷.

'Bolar provision' allows generic manufacturers to prepare and develop regulatory procedures before patent expires, so that, products are ready for market as soon as the patent ends. With these provisions, in India, the scope of generic drug manufacturing has also increased¹⁸.

SOME IMPORTANT CASES OF PARA IV FILINGS

Ranbaxy has 7-8 Para IV filings with first-to-file status in US market that includes 'Lipitor' of Pfizer, a blockbuster cholesterol lowering drug. The drug generated annual revenue of \$ 12.4 billion in 2008 for Pfizer¹⁹. In a recent Para IV filing war, Ranbaxy has lost against Pfizer for Lipitor. Ranbaxy has won only one patent Para IV filing case in US in the year 2000, wherein this pharma major challenged the GlaxoSmithKline's Ceftin- Cefuroxime

Axetil. As a result, the company launched its generic version of drug in March 2002, and generated annual revenue of around \$115 million in 1st year of launch^{5, 20}. Some important cases of Para IV filing are enlisted in table 2.

Figure 2

Table 2. Some important cases of Para IV filing

Para IV filed by	Against	Brand name	Molecule	Result
Ranbaxy	Pfizer	Accupril	Quinapril Hydrochloride	Lose
Dr.Reddy's	Pfizer	Norvasc	Amlodipine Besylate	Lose
Ranbaxy	GlaxoSmithKline	Ceftin	Cefuroxime Axetil	Won
Astra Zeneca	KV Pharmaceutical	Toprol XL	Metoprolol Succinate	Won
Dr.Reddy's	Eli Lilly	Zyprexa	Olanzapine	Lose
Ranbaxy	Pfizer	Lipitor	Atorvastatin Calcium	Lose

SOCIAL ASPECTS

In the third world countries, a large number of people are living below poverty line. They are not able to afford branded drugs because many a times these drugs are too much expensive. Therefore, generic drugs become the preferred alternatives. Generic drugs are as effective and safe as branded drugs, so physicians may also prefer generic drugs. Due to an increase in competition between domestic companies and multinational companies, the cost of generic drug gets reduced. Indian pharmaceutical companies are primarily generic based; they spend time and money on generic research. Generic market has now also increased due to expiry and shortcoming of patents. During period 2005-2010, patents of many drug molecules have been expired and many more are going to be expired (Table 3).

Figure 3

Table 3. Patent Expiry Schedule of Different Molecules

Innovatory Companies	Branded Drug	Pharmacological Category	Patent Expiry Schedule
Pfizer	Zithromax	Antibiotic	2005
Pfizer	Zoloft	Antidepressant	2005
Pfizer	Accupril	Hypertension	2005
Pfizer	Norvasc	Hypertension	2007
GlaxoSmithKline	Paxil	Antidepressant	2006
Bristol-Myers Squibb	Pravachol	Cholesterol	2005
Merck	Zocor	Cholesterol	2005
Aventis	Amaryl	Diabetes	2005
Novo Nordisk	Novolin	Diabetes	2005
Abbott Laboratories	Depakote	Epilepsy	2008
Tap Pharmaceutical Products	Prevacid	Gastrointestinal disorders	2009
Johnson & Johnson	Sporanox	Anti-fungal	2005
Johnson & Johnson	Risperdal	Schizophrenia	2010

CONCLUSION

Generic drugs are effective, safe and bioequivalent as branded drugs. The generic drug market is increased due to expiry of patents and also by winning of Para IV filing cases. Once the patent expires, there is a great competition in the market and therefore, the price of a particular molecule gets decreased. Due to this, generics become the preferred alternatives. The recent amendments in the Indian patent laws are also changing the paradigm of Indian pharmaceutical industry. In the light of these findings, India

is emerging as a preferred hub where various multinational pharmaceutical companies intend to invest and generate revenue due to its huge human resource at affordable cost along with a very potential domestic market as well. Thus the Indian pharmaceutical sector has tremendous opportunities for generic drugs in the times ahead.

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