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EMERGING INCLINATION IN GENERIC DRUGS

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ABSTRACT
Today, about half of all the prescriptions are filled with a generic equivalent of a brand-name drug. Because of the decrease in price, we are now switching from branded drugs to generic drugs and there is a steep inclination towards generic drugs by both patients and health care professionals without compromising the efficacy and safety of the drug. Any drug identified as a generic drug is the bioequivalent of the brand-name drug and is typically sold at substantially low cost from the branded one, hence, easily affordable by common man.

The present review encompasses the comprehensive portfolio of generic drugs comprising description, evolvement, approval, pharmaco-economics, demand, current scenario and future perspective of the generic drugs. It also throws some light on the position of Indian pharma sector in generics market.

Keywords: *Generics, FDA, ANDA.*

INTRODUCTION

World Health Organization (WHO) suggests that a generic drug (generics) is a pharmaceutical product usually intended to be interchangeable with an innovator product, that is manufactured without a licence from the innovator company and marketed under a non-proprietary or approved name rather than a proprietary or brand name after the expiry date of the patent or other exclusive rights.[1] U.S. Food and Drug Administration (FDA) suggests that a generic drug is identical or bioequivalent to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use.[2]

FDA GUIDELINES FOR GENERICS

Generic drugs must contain the same active ingredients as the innovator drug (inactive ingredients may vary); generic drug must be identical in strength, dosage form and route of administration; generic drug must have the same use indications; generic drug must be bioequivalent to brand name drug; generic drug must meet the same batch requirements for identity, strength, purity, and quality; generic drug must be manufactured under the same strict standards of FDA's good manufacturing practice regulations required for innovator products.[2]

HISTORY AND DEVELOPMENT OF GENERIC DRUGS

Development of generic drugs had started in the United States. FDA regulation of pharmaceuticals came into existence in 1906 with a Pure Food and Drug Act that required somewhat more than labelling of ingredients on a product. Due to consequences of serious incidences involved with various drug products (such as in 1912, Mrs. Winslow's Soothing Syrup for teething and colicky babies, unlabeled yet laced with morphine, killed many infants; in 1937, **Elixir Sulfanilamide,** containing the poisonous solvent diethylene glycol, killed 107 persons, many of whom were children), U.S. government had to take initiative to remove such drug products from the market. In 1938, the FDA passed a new law, according to which a drug product have to be tested by a manufacturer and then cleared by the FDA for safety before it could be marketed. Products introduced to market after 1938 were designated "new drugs". When the patents on a pioneer drug product expired, and another sponsor wanted to market an identical or similar product, the FDA would make a "finding" that the product was not a "new drug" and therefore did not require approval. This had led some manufacturers to introduce copies of approved products to the market without FDA approval. Due to which the market contained a hodgepodge of pioneer products approved for safety and copies that had not been reviewed by the FDA, because of the finding that they were not new drugs and were simply put on the market. In 1962, the law of 1938 was amended to add the requirement of evidence of effectiveness and safety for all products that entered the market between 1938 and 1962. The products on the market new and identical, similar and related were all declared to be new drugs. Marketers of pioneer products had to submit evidence of effectiveness for their drug products to be evaluated by Panels at the National Academy of Sciences. The FDA also concluded that if the pioneer drug product was found to be ineffective, all identical, similar, and related products should come off the market along with the pioneer product. This conclusion

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was challenged in the U.S. Supreme Court in Weinberger v. Hynson, Wescott & Dunning, Inc. - 412 U.S. 609 (1973) but was eventually upheld on June 18, 1973.[3] Drug Price Competition and Patent Term Restoration Act 1984 (Waxman-Hatch Amendments) was an important milestone in the US drug regulation history under following titles:

Title I: Food and Drug Administration have statutory authority to accept abbreviated new drug applications (ANDA) for approval of marketing of generic drugs.

Title II: Law authorizes extension of patent terms for approved new drugs.

The two parts of the law are intended to maintain a harmonized balance between encouraging competition, research and innovation. The historic amendments were designed to: Speed up the federal approval process of generic drugs; make high quality and therapeutically equivalent generic drugs more widely available to consumers, thus reducing health care costs; eliminate the costly, unnecessary and ethically questionable requirement of animal and human clinical studies to support the safety and efficacy of duplicate versions of drugs approved since 1962; assure the continuing development of new drugs through special incentives which include periods of market exclusivity and patent term restoration. [4]

PATENT ISSUES REGARDING GENERICS DEVELOPMENT

New drugs are developed under patent protection. Most drug patents are protected for 20 years. The patent protects the investment in the drug's development by giving the innovator company, the sole right to sell the drug while the patent is in effect and doesn't allow anyone else to make and sell the drug in the market.[5] Generic drugs can be legally produced for drugs where: patent has expired; generic company certifies the brand company's patents are either invalid, unenforceable or will not be infringed; for drugs which have never held patents; in countries where a patent(s) is/are not in force.

GENERICS APPROVAL PROCESS

Drug Price Competition and Patent Term Restoration Act, 1984 or "Hatch-Waxman Act" standardized U.S. procedures for recognition of generic drugs. When the patent or other periods of exclusivity expires drug sponsors files an Abbreviated New Drug Application (or ANDA) with the Food and Drug Administration (FDA) and seeks to demonstrate therapeutic equivalence to a specified, previously approved "reference listed drug" for approval to market a generic version of brand name product. The ANDA process does not require the drug sponsor to repeat costly animal and clinical research on ingredients or dosage forms already approved for safety and effectiveness.[5] When an ANDA is approved, the FDA adds the drug to its Approved Drug Products list, also known as the "Orange Book". [6] On October 4, 2007, FDA launched the Generic Initiative for Value and Efficiency (GIVE). The initiative will use existing resources to help FDA modernize and streamline the generic drug approval process. GIVE aims to increase the number and variety of generic drug products available in the U.S. Generic drug substances are named through review and recommendation of the United States Adopted Names (USAN) Council.

PHARMACO-ECONOMICS OF GENERICS

Generic drugs are chemically identical to their branded counterparts and are typically sold at substantial low cost as compared to the branded price. The first generic version of a brand-name drug lowers the price of the drug dramatically, but the largest price reduction occurs when the second generic version hits the market. Generic drugs cost average about 80 to 85% lower than the brand name product because they generally do not engage in costly advertising, marketing and promotion, or significant research and development. According to the Congressional Budget Office, generic drugs save consumers an estimated $ 8 to $ 10 billion a year at retail pharmacies. Once the generic version of brand name drug is approved, market competition grows, which keeps the price of generics down.[2, 7]

GENERICS IN DEMAND

Rising health care costs have become a major public concern in recent years and prescription drugs represents a significant component of such costs, with shares ranging from 4% in the United States to nearly 18 % in France and Italy. So to reduce health related expenditures, branded molecules are substituted with lower priced generic versions. Now a days, nearly 8 in 10 prescriptions filled in the United States are for generic drugs. The use of generic drugs is expected to grow over the next few years as a number of popular drugs come off patent through 2015[7]. FDA approved generic drug products have met the same rigid standards as the innovator drug possessing same high quality, strength, purity and stability as brand-name drugs at substantial low cost. So, due to their less cost generic drugs are easily affordable by common man.[8]

CURRENT SCENARIO OF GENERICS

The imminent arrival of the dreaded "patent cliff" has been haunting the pharmaceutical industry for years, and it's finally here. Over the past decade, drug companies have become increasingly dependent on blockbuster drugs-patented specialty drugs that generate more than $1 billion in sales annually. However, when a major blockbuster loses patent protection, generic competition leaves a gaping hole in the top line, abruptly changing a company's greatest strength into its greatest liability. Top 5 Blockbuster

drugs i.e. Copaxone (Teva), Nexium (AstraZeneca), Sandostatin (Novartis), Exforge (Novartis) and Evista (Eli Lilly) are facing patent expiration in 2014 (Table 1).[9]

Table 1: *Top 5 Blockbuster drugs loosing patent in 2014.*

S.No.	Brand Name	Used in Condition	Company	Patent Expiry	2012 U.S. Sales
1	Copaxone	Multiple Sclerosis	Teva	May 2014	$4.0 billion
2	Nexium	Heartburn & acid reflux	AstraZeneca	May 2014	$3.9 billion
3	Sandostatin	Acromegaly	Novartis	June 2014	$1.5 billion
4	Exforge	Hypertension	Novartis	October 2014	$1.35 billion
5	Evista	Osteoporosis	Eli Lily	March 2014	$1.01 billion

INDIAN PHARMA SECTOR IN GENERICS MARKET

The Indian pharma sector was only $6 billion in 2005, has whiz up to $18 billion market in 2012, clocking a CAGR of 17%. The sector is expected to grow to $45 billion by 2020. Even in the gloomiest scenario, the sector is expected to be the 6th largest in the world in terms of absolute size by 2020 and will be amongst the top 3 global markets in terms of incremental growth by 2020. The sector had registered a strong double-digit growth of 13-14 per cent in 2013 on back of increasing sales of generic medicines. Currently, India's share of the US generic market is 24% in terms of volume and 40% of the new product approvals granted by the US-FDA to Indian companies (YTD 2013).[10] India has established a strong reputation in the global space for being a high quality supplier of affordable generics.

FUTURE PERSPECTIVE

Greater admittance to generic drugs will reduce health care costs because the price of generic drugs is typically much lower than the brand-name drug product. Reducing expensive lawsuits over drug patents and making the approval process more efficient will also help to lower national health care cost by reducing the cost of bringing safe and effective generic drugs to market. Throughout the years since enactment of Hatch-Waxman, the US patent and regulatory systems continued to evolve. The Hatch-Waxman Act has well encouraged the growth of the generic industry.[11]

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