REVIEW ARTICLE

Evergreening: A Deceiving Strategy in Pharmaceutical Market

Bharti Latwal, Amrish Chandra*

Department of Drug Regulatory Affairs, Amity Institute of Pharmacy, Amity University, Noida, Uttar Pradesh, India

ABSTRACT

Patent is an exclusive right given to the innovators to prevent the use of their invention from the 3rd parties. It is given for a specific period of time, that is, 20 years during which the innovators recover their investments made during the development of their innovation. To extend this monopoly right, many strategies are used by today's pharmaceutical companies. Evergreening of patents is one of the widely used strategies in the pharmaceutical industry. There are many ways by which this strategy can be used to extend the monopoly right given over drugs. However, currently, due to an increase in competition in the pharmaceutical market, this strategy is mainly misused to prevent generic drugs from entering the market. This article describes the different ways by which evergreening can be used and how its use affects the life of the consumers, generic drug manufacturers, and the pharmaceutical industries. Hence, to prevent the exploitation of this strategy, appropriate measure needs to be taken by the government.

Key words: Evergreening strategies, evergreening, Hatch-Waxman Act, intellectual property rights, patent

INTRODUCTION

Intellectual property rights are a tool used by many pharmaceutical companies for the protection of their pharmaceutical products. At present, they are playing a very crucial role in the life of big pharma companies. These rights help them in the protection of their products from unauthorized use by other organizations. The government has provided them with many IPRs such as patents, copyright, geographical indications, trademarks, and industrial design.

Intellectual property is defined as a property created using human intelligence which has both moral and economic values. The main objective of IPR is to boost the pharmaceutical companies to engage in more and more R&D for the creation of intellectual property. It allows them to prevent others from making, using, and selling their product without their consent for a specific period of time. During this time, they can use their property to regain the investments made by them in the creation of their intellectual property. The extent of protection granted on IP will decide the contribution of innovative companies in innovation.

More protection to IP means more and more investments which lead to more R&D.

PATENT

A patent is one of the mostly used IPR in the pharmaceutical market. It is an exclusive right that prevents others apart from inventor from making, using, and selling their innovation without their consent for a specified period of time, that is, 20 years. It is a monopoly right granted by the government to the innovator which helps the innovator in retrieving all the expenses invested in the development of that product. The requirements for patents are as follows:

- The innovation should be novel
- It should be non-obvious
- It should have an industrial application.[1]

To stimulate knowledge and innovation, a patentee is duty-bound to disclose some valuable information about his property in the public domain.

In the pharmaceutical market, a patent can be granted for a product's primary properties such as an active ingredient, formulation, process, and primary indication, and at the end of the patent expiry, the patent is extended by filing an application to authorities for patenting the secondary properties of the product such as new dosages, new combinations, and new forms of release. This is called evergreening of patents.[2]

EVERGREENING

Intellectual property rights have been given for a specified period of time. After the expiry of that period, the innovator product gets deprived of that protection and can be manufactured, used, sold, and transferred by any other manufacturing company. After the patent expiry of the product, many generic companies make use of the innovator's data to manufacture the generic drug. A generic drug is a copycat version of a brand name drug and is bioequivalent to that drug. After the introduction

***Corresponding author:**
Email: chandra.amrish@gmail.com

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of generics in the market, the sale of brand name drugs starts decreasing and their price gets declined by one-fifth of its original price. It also increases the competition for brand name drugs in the market because now the same drug is available at a very cheap price. Hence, to remain in the market and to prolong the lifecycle of brand name drugs, the pharmaceutical companies adopt life cycle management strategies. One such strategy is evergreening of patents. In evergreening, just before the expiry of the patent term of the original drug, the pharma companies apply to the patent office for patenting the secondary properties of the drug. The idea behind using this strategy is to extend the patent term beyond 20 years. Here, instead of discovering another drug, the pharma companies focus on modifying the properties of their patented drug and bring it into the market as a secondary patent.

For example, an XYZ company developed a new chemical entity, that is, A which is useful for the treatment of a particular disease. The company had filed for a patent for A on March 25, 2000. The patent will expire on March 2020. The company again filed a second patent for its new dosage form in April, 2005. The application was again approved and now the patent will expire on April 2025. In this way, the company was successful in extending the market exclusivity for 5 more years.

EVERGREENING STRATEGIES

Introduction of Redundant Variations in the Drug

To extend the monopoly right beyond 20 years, many pharmaceutical companies file applications for secondary properties of their product, that is, by introducing modifications or variations in an already patented product. This strategy is applied just before the expiry of the main patent so that generic drug entry can be delayed for some period of time.

Case study

In 1991 and 1992, Pfizer was granted patent for phosphodiesterase inhibitors. Their patented product was Viagra (Sildenafil Citrate) which was very useful in the treatment of angina and hypertension. In 1992 and 1993, many research articles were published claiming that phosphodiesterase inhibitors could be useful in the treatment of impotence and erectile dysfunction also.[3] So after knowing this, Pfizer filed patent application for this new indication of its patented product Viagra. They also claimed that it can be administered orally since the previous one was needed to be injected.

However, this secondary patent was challenged by Lily Icos stating that the invention was obvious because its new use was published in the research article. Pfizer justified this by stating that the article did not publish about its oral use and state it as inventive.

In November 2000, the judge found that the only difference between the prior patent and the claim was only of oral use, which did not make it inventive also and the patent was denied and declared invalid.

Switching from Prescription to Over the Counter (OTC)

During the 20-year period of the patented drug, the pharmaceutical companies gather more and more scientific data related to that drug. Just before the expiry of the patent term, they file another new drug application to market the drug as an OTC. The OTC drugs can be easily advertised to the patients and can be sold without prescription.

Application of Competitive Strategies

To get the attention of patients, pharmaceutical companies sometimes introduce their drugs at cheap prices or they introduce an improved version of their off-patented drug. For example, authorized generics introduced by the pharmaceutical companies are exactly similar to brand name drugs but cheaper than their branded counterparts.

Subsidiary Units Establishment in Generic Domain

Many big pharmaceutical companies are now showing their interest in generic domains so that they can get benefit from generics also. They have started manufacturing authorized generics, branded generics, and unbranded generics to compete with generic manufacturers.[4]

For example, in 2009, GSK made an agreement with India's Dr. Reddy Laboratories under which Dr. Reddy Laboratories will manufacture and supply drugs to GSK.

Brand Migration

In this process, when the patent term of one drug is nearly going to expire, the innovator drug company shifts the patient's attention to the company's other drug which is heavily advertised to patients and physicians.

For example, AstraZeneca shifted the attention of patients from Prilosec to Nexium before the patent expiry of Prilosec by heavily advertising it to the patients and physicians.[5]

30-month Extension

Under Hatch-Waxman Act, if a generic drug applicant files Para IV ANDA for a drug, then he or she has to notify about this to the patent holder. The patent holder is given 45 days to bring an infringement suit against the manufacturer if

IPR is violated. If the patent holder sues the generic drug applicant, then ANDA cannot be approved by the FDA for the next 30 months or until the litigation is resolved.[6] Hence, companies misuse this provision to block or to delay the entry of generics in the market.

Case study

In the 1960s, National Cancer Institute developed paclitaxel which was non-patentable. Hence, they came in an agreement with Bristol-Myers Squibb for commercializing it. The drug was approved by FDA for marketing it as Taxol in 1992. Bristol received 5-year market exclusivity for this up to 1997. At that time, Taxol was the top-selling product with a sale of more than $ 1 billion a year. Before the expiry of market exclusivity, Bristol obtained two patents on Taxol and used these to block generics entry. After the expiry of market exclusivity, many generic applicants tried to enter the market. However, Bristol-Myers Squibb challenged them based on the violation of its patents listed in the orange book. As a result, Bristol-Myers Squibb got 30-month extension (as per Hatch-Waxman Act) during which the FDA cannot approve generics of Taxol till 2000. However, the court found that Bristol-Myers Squibb patents were invalid. In June 2002, Attorneys general from 29 states charged Bristol-Myers Squibb of using these strategies to avoid generic companies from entering the market in spite of knowing the fact that Taxol could not be patented. One strategy involved was acting in collusion with American Bioscience (a California-based company). According to lawsuit, they filed a sham court action with the intention of further delaying the entry of generics into the market with the help of 30-month extension.[7]

Introduction of Combination Drugs

When drugs are given in combination, they provide a synergistic effect. Hence, for the drug going off-patent, the pharmaceutical companies combine their danger product with their other brand name product and introduce them as combination drugs that can be useful in treating two conditions.

NEGATIVE INFLUENCE OF EVERGREENING

Big Pharmaceutical Companies

Generic drugs entry into the market can be a problematic issue for brand name drug companies. Generic drug manufacturers sold their drugs at a very cheap price and shift the attention of consumers from brand name drugs to generic drugs. This decreases the sale of pharmaceutical companies that are dependent on the revenue generated by their blockbuster drugs. As their blockbuster drug goes off-patent, the competition in the pharmaceutical market increases. Due to this reason, pharmaceutical companies get triggered to adopt life cycle management strategies. These strategies help them in extending the market exclusivity of their blockbuster drugs. The pharmaceutical companies spend billions of dollars in developing a drug. Only four or five molecules enter the clinical phase and only one got selected. Their only way to recover the cost spends in R&D of the drug is the market exclusivity. During this market exclusivity period, they try to make maximum profit from their drugs and just before the patent expiry of their drug, they try to bring a modified or an alternative version of that drug. Bringing a modified version is also a very costly process and if they failed in proving the required safety and efficacy of their modified version again they will face the risk of losing a lot of money. Most of these evergreening strategies involve lengthy litigation. Many pharmaceutical companies face financial burden. Hence, these strategies will work well if they are well planned in advance.

Generic Drug Manufacturers

Generic drugs are priced at a very low cost (approx. 30% lesser than the brand name drugs) because they do not have conducted R&D where a huge amount of money is used. They enter the market by two ways:

Safe entry: They introduce their generic version after the expiry of all patents of the brand name drugs.

At-risk entry: Here, they enter the market even before the patent expiry of the brand name drug by filing Para IV ANDA.[8]

The entry of generics into the market causes the destruction of market share of brand name drugs. This triggers the big pharmaceutical companies to use strategies like evergreening of patents to extend their market exclusivity. They sometimes sue the generic manufacturers and the legal proceedings involve a huge cost. Small generic drug manufacturers are severely affected by these huge costs and they also face a further delay in the entry of generics in the market.

Consumers

The consumers have to face the consequences of this battle between generic drug manufacturers and brand name drug manufacturers. Generic drugs are very cheap as compared to branded drugs and can be afforded by all sections of the society. However, when the entry of generics gets delayed by the use of evergreening strategy, the consumers are only left with the option of buying the costly branded drugs. There are also many people who cannot afford these costly drugs and get deprived of the medical treatment they need.[9] The pharmaceutical companies use evergreening strategy to mislead people

who believe that branded drugs are safer than generics. Their attention is shifted from one branded drug to another modified branded drug which can barely be called improvement.

CONCLUSION

Pharmaceutical companies invest a large amount of money in the development of a drug and to continue the monopoly right given over the drug, they employ evergreening strategy. But currently, this strategy is mainly exploited by the pharmaceutical companies. Evergreening of patents is in the contravention of the interest of healthy competition, generic drug manufacturers, and consumers. We have to take necessary measures to put an end to this exploitation. A strong patent protection regime is required to distinguish between frivolous patents and actual inventions. Section 3(d) of the patents act is helpful in distinguishing patentable inventions from non-patentable inventions which states that "the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance" is non-patentable.[10] The loopholes in the laws and rules must be reviewed from time to time so that they cannot be exploited by big pharma companies.

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CONFLICTS OF INTEREST

The author declares that they have no conflicts of interest.

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