The Challenge of Patent Expiry: A Case Study of Pharmaceutical Industry

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Abstract

This paper investigates patterns of industrial dynamics and competition in the pharmaceutical industry, with particular reference to the consequences of patent expiry in different countries though out the world. The main focus is on the competition at the level of single chemical entities, distinguishing between original brands and generic products. All the products containing major molecules whose patent expiration date lies between 2013 to 2021 are included in our sample. This study shows that how challenging is the task of meeting the global competition at the expiration of patent rights and furthermore what losses the pharmaceutical companies can bear after wards. This empirical investigation shows that the dynamics of drug R&D and its ultimate effect on the prices, especially generics, varies a lot. This kind of phenomena drastically hurts the investment made by the pharmaceutical companies.

Keywords: *Pharmaceutical industry, Patent expiry, Generics, Drug development.*

1. Introduction

Pharmaceutical industry is a major driving force for global research and development (R&D) progress. Large pharmaceutical companies are investing in R&D, to discover innovative and exclusive drugs for the treatment of incurable diseases. Huge investments are made over a long period of time to discover new drugs. Billions of dollars are spent to discover new drugs. With patience, hard work and following certain stages of drug development, fewer are selected among thousands for proper marketing surveillance studies. The companies which get their products patented enjoy exclusive rights for specific time period, during which no other company can launch this molecule.

R&D investments are drastically decreasing due to less attractive returns on investments. Several patented molecules are going to be off-patented and will be facing intense generic war in the near future. Keeping in mind the generic war competition, several pharmaceutical companies are establishing their own generic version products just before exhaustion of patent monopoly period.

Edward et al (2004) reports that based on review of recent patent expiry data, that such rapid losses of revenue for

brand owners appear to be getting more common in recent times. Generic pharmaceutical companies are becoming and more sophisticated. The data also suggest that pharmaceutical brands (original molecules) are losing more share. The trade-off between promoting competition and protecting intellectual property has emerged as a principal issue not only in domestic but also in international policy in recent years (Arora et al; 2008). A few studies have used explicit models of consumer and firm behavior to simulate the welfare losses implied by patent protection in developing countries [e.g., Challu (1991), Fink (2000), Maskus and Konan (1994), Nogues (1993), Subramanian (1995), Watal (2000)].

2. Research Methodology and Results

This research was conducted on the secondary data collected from different resources. For this purpose, the different brands of pharmaceutical companies already available in the market in different countries of the world are selected. The enlisted molecules are selected irrespective of their individual properties. All are different and indicated for different kind of diseases. All these molecules are selected on the basis of two criteria; 1) date of expiration 2) expected global sales. The other criteria which was also considered as the expected loss that will be incurred after the patent expiration and what impact it make on the over all sales of the product.

2.1 Results

Due to new drugs discovery, morbidity and mortality has decreased. Life expectancy has increased multifold such as that human can live up to 30 years longer than they did a century ago. Reductions in mortality (e.g. in HIV/AIDS, many cancers, cardiovascular disease and TB in developing and poor countries) and significant progress in the quality of life are the results of some large and many small steps in biopharmaceutical research.

The key aspect of the pharmaceutical and medical research is to turn fundamental research into innovative and effective treatments that are widely available and accessible to patients on global basis. World citizens can expect not only to live longer, but to live longer and be healthier. High blood pressure and cardiovascular disease can be controlled with antihypertensive medicines and cholesterol-lowering medicines, knee or hip replacements prevent patients from immobility, and some cancers can be controlled or even cured thanks to newer targeted medicines. In case of free treatments (DOTS in developing countries) available for TB, a significant progress has been made to cure this deadly disease properly. Yet, there remain huge challenges in many disease areas such as Alzheimer, multiple sclerosis, many cancers and orphan diseases.

2.1.1 The Pharmaceutical Industry: A Key Asset

Globally pharmaceutical industry is being considered as a key asset and a top performing high technology sectors in many developed and developing countries. The research-based pharmaceutical industry can play a critical role in restoring Europe to growth. In 2011 it invested an estimated € 27,500 million in R&D in Europe (1). It directly employs 660,000 people and generates three to four times more employment indirectly – upstream and downstream – than it does directly. In recent days the market and research environment in emerging economies such as Brazil, China and India, leading to a migration of economic and research activities outside of Europe to these fast-growing markets. In 2011 the Brazilian and Chinese markets grew by more than 20% (20.0% and 21.9% respectively) compared with an average market growth of 2.6% for the five major European markets and 3.6% for the US market (source: IMS). In 2011, North America accounted for 41.8% of world pharmaceutical sales compared with 26.8% for Europe. According to IMS data, 56% of sales of new medicines launched during the period 2006-2010 were on the US market, compared with 24% on the European market. The fragmentation of the EU pharmaceutical market has resulted in a lucrative parallel trade. This benefits neither social security nor patients and deprives the industry of additional resources to fund R&D. Parallel trade was estimated to amount to € 5,100 million (value at ex-factory prices) in 2010 (see, Table 1).

Table 1: Geographical breakdown (by main markets) of sales of new medicines launched during the period 2006-2010

USA	EUROPE	JAPAN	REST OF THE WORLD	PHAMERGING
56%	24%	12%	6%	2%

Note: New medicines cover all new active ingredients marketed for the fi rst time on the world market during the period 2006-2010 Pharmerging comprises 17 countries ranked by IMS Health as high-growth pharmaceutical markets (Argentina, Brazil, China, Egypt, India, Indonesia, Mexico, Pakistan, Poland, Romania, Russia, South Africa, Thailand, Turkey, Venezuela, Vietnam and The Ukraine)

The world pharmaceutical market worth an estimated € 614,583 million ($ 855,500 million) at ex-factory prices in 2011. The North American market (USA & Canada) remained the world's largest market with a 41.8% share, well ahead of Europe and Japan.1

2.1.2 Pharmaceutical Industry R&D

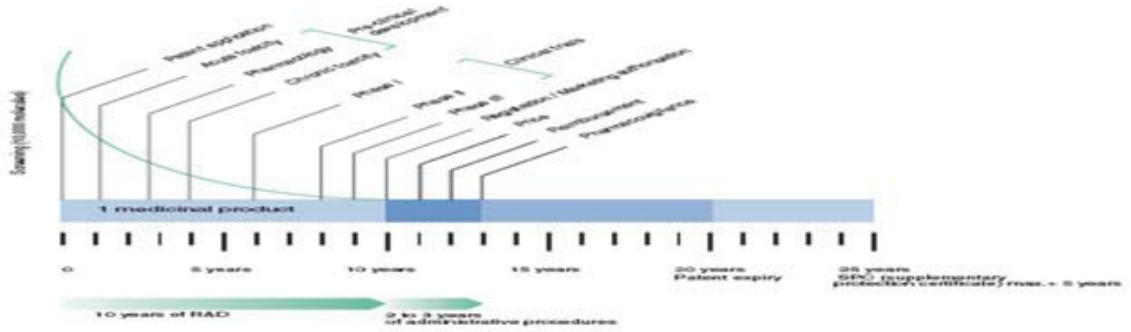
Table 2 shows that all new medicines to be ready to introduce into the market are the result of lengthy, costly and risky research and development (R&D) conducted by pharmaceutical companies. By the time a medicinal product reaches the market, an average of 12-13 years will have elapsed since the first synthesis of the new active substance. The cost of researching and developing a new chemical or biological entity was estimated at € 1,059 million ($ 1,318 million in year 2005). On average, only one or two of every 10,000 substances synthesized in laboratories, will successfully pass all the stages to become marketable medicines (see Figure 1).

Table 2: Ranking of Industrial Sectors by Overall Sectors R&D Intensity (R&D as percentage of net sales 2010)

INDUSTRY	R&D Investment of net sales (%)
Pharmaceutical & biotechnology	15.3
Software & computer services	9.6
Technology hardware & equipment	7.8
Leisure goods	6.2
Health care equipment & services	6.1
Electronic & electrical equipment	4.2
Automobiles & parts	4.1
Aerospace & defense	4.0
Chemicals	3.1
Industrial engineering	3.0
General industrials	2.4
Fixed line telecommunications	1.7
Food producers	1.7
Banks	1.5
Oil & gas producers	0.4

Source: EFPIA 2012

Figure 1: Phases of the R&D process



Source: EFPIA (2012)

2.1.3 Research and Development

The process of drug development has evolved with the passage of time. In recent times the emergence of biotechnology focuses on understanding the metabolic pathways related to a disease state or pathogen, and manipulating these pathways using molecular biology or biochemistry. All these recent developments have helped a lot in

understanding the true nature of incurable diseases.

Drug development passes through many stages to determine the appropriate formulation, dosing, safety, in vitro studies, in vivo studies, and clinical trials. This whole process of research and development is mainly carried out by larger pharmaceutical companies because of large budgetary requirements. Much expense is incurred in the early phases of development of compounds that will not become approved drugs. In addition, it takes about 7 to 10 years and only 3 out of every 20 approved drugs bring in sufficient revenue to cover their developmental costs, and only 1 out of every 3 approved drugs generates enough money to cover the development costs of previous failures. This means that for a drug company to survive, it needs to discover a blockbuster (billion-dollar drug) every few years.

In 2010 18 NMEs (New Molecular Entities) were approved and three biologics by the FDA, or 21 in total, which is down from 26 in 2009 and 24 in 2008. On the other hand, there were only 18 approvals in total in 2007 and 22 back in 2006. Since 2001, the Center for Drug Evaluation and Research has averaged 22.9 approvals a year. This approval comes only after heavy investment in pre-clinical development and clinical trials, as well as a commitment to ongoing safety monitoring. Drugs which fail part-way through this process often incur large costs, while generating no revenue in return. If the cost of these failed drugs is taken into account, the cost of developing a successful new drug (New chemical entity or NCE), has been estimated at about 1.3 billion USD (not including marketing expenses). According to Light and Lexchin (2012), the rate of approval for new drugs has been a relatively stable average rate of 15 to 25 for decades.

The opportunity cost of investing capital many years before revenues are realized in time value of money. As discussed earlier very long time needed for discovery, development, and approval of pharmaceuticals which cost nearly half of the total expense. On the other hand some approved drugs, such as those based on re-formulation of an existing active ingredient (also referred to as Line-extensions) are much less expensive to develop.

Pharmaceutical industry is heavily dependent on the discovery of innovative and exclusive drugs. As discussed earlier the industry has cut down its R&D spending $68 bn in 2010 vs $70 bln in 2009 after decades of relentless increases, and the pace of decline looks set to quicken further in coming years. This is because of declining returns on pharmaceutical R&D. Disappointing research productivity is arguably the biggest single factor behind the declining valuations of the sector over the past decade. Due to these declining trends pharmaceutical industry is faced with the loss of exclusivity and patent expiration of more than 110 products in the key U.S. market between 2012 and 2014, the industry has stepped up its drive to buy in promising experimental medicines from small biotech companies. Such kind of situation not only creates strong challenges for the developed counties but also for the developing countries to conduct any further research activities. But still there is hope that productivity in drug research may be improving, as evidenced by progress with breakthrough medicines like GlaxoSmithKline's new drug Benlysta for lupus and Bristol-Myers Squibb's melanoma treatment Yervoy (see Table 3).

Table 3: Break down of world pharmaceutical market in percentage (2011)

Country/region/continent	Market share (%)
North America (USA, Canada)	41.8
Europe	26.8
Japan	12.0
Africa, Asia (excluding Japan), Australia	13.7
Latin America	5.7

2.1.4 Generics

Besides the patent molecules, there also exist the generic products which are launched in the market after the expiry of the patent expiry. Generics are usually produced by a manufacturer who is not the inventor of the original product, and are marketed when intellectual property protection rights are exhausted. The market share of generics is significantly higher in many countries of the world with historically low levels of intellectual property protection. By definition, 'generic' means a medicine based on an active substance that is out of patent and which is marketed under a different name from that of the original branded medicine (generics data do not include those generics marketed by the originator). 1

2.1.5 Patents and Generics

Generally in pharmaceutical industry companies are granted exclusivity rights for about 20 years. Patent rights enable the

owner of the patent company to market and sell the products, and to recover the costs of research and development through high profit margins for the branded drug. At patent expiry, a generic drug is usually developed and sold at low price by a competing company. Besides this the owner of the branded drug by itself will introduce a generic version before the patent expires in order to get a head start in the generic market. Restructuring has therefore become routine, driven by the patent expiration of products launched during 1990s and companies' failure to develop sufficient new blockbuster products to replace lost revenues.

During 2013 and coming years many major drug companies are losing their patent protection. Several high profitable pharmaceutical companies will be compelled to share their massive profits with generic companies, which ultimately provide low priced versions of the previous exclusive drugs. Roughly calculated there will be $290 billion in sales at risk due to patent expiry between 2012 and 2018. Several pharmaceutical companies are experiencing dramatic sales drops in many exclusive drugs at this time, which can result in even more dramatic results in the coming years. Recently an article published in The New York Times, “Generic Drug Makers See a Drought Ahead” elaborated that there even grounds for the generic companies and mega companies. Patent expiry is a major concern for the major pharmaceutical companies, because generic companies will be able to convince the FDA (Food and Drug Administration) to sell the generic version exclusively, so to provide cheaper products to the customers at affordable price. Such kind of environment in the market no doubt is posing a great threat to the mega companies, but on the other hand it will enable the R&D pharmaceutical companies to focus on specialized and innovative drugs for the greater level of research (see Table 4).

Table 4: Top 15 drug patent losses for 2013

	Drug	Generic	Company	Patent expiration	Estimated global sales, 2012
1	Cymbalta	Duloxetine	Eli Lilly	Dec. 11, 2013	$4.9 billion
2	Avonex	Interferon beta1a	Biogen Idec	Dec. 31, 2013	$2.9 billion
3	Humalog	Insulin lispro	Eli Lilly	May 7, 2013	$2.52 billion
4	OxyContin	oxycodone	Purdue Pharma	August 31, 2013	$2.35 billion
5	Rebif	Interferon beta-1a	Merck KGaA	Dec. 31, 2013	$2.3 billion
6	Aciphex	Rabeprazole	Johnson & Johnson	May 8, 2013	$1.93 billion
7	Xeloda	Capecitabin	Roche	December 14, 2013	$1.62 billion
8	Procrit	Epoetin Alfa	Johnson & Johnson	Aug. 20, 2013	$1.41 billion
9	Neupogen	Filgrastim	Amgen, Kirin, Roche, Royalty Pharma	Roche, Royalty Pharma, March 12, 2013 / Amgen-Kirin Dec. 12, 2013	$1.29 billion
10	Zometa	Zoledronic Acid	Novartis	March 2, 2013	$1.26 billion
11	Lidoderm	Lidocaine patch 5%	Endo Health Solutions/ EpiCept	Sept. 15, 2013	$918 million
12	Temodar	Temozolomide	Merck /Bayer	August 31, 2013	$882 million
13	Asacol	Mesalamine	Warner Chilcott, UCB and Zeria Pharmaceutical	July 30, 2013	$891 million
14	Niaspan	Niacin	Abbott Laboratories , Teva Pharmaceutical Industries	Sept. 20, 2013	$835 million
15	Reclast	Zoledronic acid injection	Novartis	March 2, 2013	$612 million

To meet this challenge of the patent expiry in coming years several companies are going after difficult-to-make products like extended-release tablets, patches and creams in the hope that, with less competition, prices will not erode as quickly. This strategy is mainly adopted because the prices of many traditional pills drop sharply and the market is flooded with competitors.

To avoid any dramatic set backs, as highlighted earlier, several companies are focusing on the new category of products, which are hard to copy, known as biologics. Biologics are protein made and are commonly used for the treatment of cancer (Avastin) and rheumatoid arthritis (Humira). FDA is still setting the guidelines for how generic versions of biologics — called biosimilars — will be approved (see, Table 5).

Table 5: List of products' patent expiration from Jan 2013 to August 2021.

Drug	Generic	Patent expiration	Sales in 2012 (millions)
Evista®	Raloxifene	2013 1Q (Jan)	$534
Zomig®	Zolmitriptan	2013 2Q (May)	Tablets: $165 ZMT: $34 Nasal: $25
Fosamax Plus D™	alendronate / cholecalciferol	2013 2Q (Jun)	$240
Eloxatin®	oxaliplatin injection	2013 4Q (Oct)	$6
Aciphex® (tablets approved but not launched 2/07)	Rabeprazole	2013 4Q (Nov)	$1,159
Fuzeon®	enfuvirtide injection	2013 4Q (Dec)	$43
Cymbalta®	Duloxetine	2013 4Q (Dec)	$2,294
Asacol®	mesalamine delayedrelease tablet	2014 1Q (Feb)	$494
Avodart®	Dutasteride	2014 1Q (Mar)	$389
Advicor®	lovastatin/niacin	2014 1Q (Mar)	$106
Viracept®	Nelfinavir	2014 2Q (Apr)	$71
Namenda®	Memantine	2014 2Q(Apr)	$606
Nexium®	Esomeprazole	2014 2Q (May)	$5,080
Celebrex®	Celecoxib	2014 2Q (May)	$1,634
Actonel®6	Risedronate	2014 2Q (Jun)	35 mg: $765 5mg: $12 75 mg: $28
Micardis®	Micardis® HCT telmisartan telmisartan/ hydrochlorothiazide	2014 3Q (Jul)	$163
Temodar®	Temozolomide	2014 3Q(Aug)	$224
Maxalt®	Rizatriptan	2014 3Q (Aug)	$235 (does not include MLT form)
Exelon®7	Rivastigmine	2014 3Q (Aug)	$203
Avelox®	Moxifloxacin	2014 3Q (Sep)	$514
Copaxone®	Glatiramer	2014 4Q (Nov)	injection $391
Cipro® HC	ciprofloxacin/ hydrocortisone otic suspension	2015 1Q (Jan)	$46
Lumigan®	bimatoprost ophthalmic solution	2015 1Q (Feb)	$253
Sustiva®	Efavirenz	2015 1Q (Mar)	$192
Renagel®	Sevelamer	2015 1Q (Mar)	$394
Welchol®	Colesevelam	2015 2Q (Jun)	$221
Travatan®	travoprost ophthalmic solution	2015 2Q (Jun)	$120
Patanol®	olopatadine solution	2015 4Q (Dec)	$256
Relpax®	Eletriptan	2017 2Q (May)	$231
Byetta®	exenatide injection	2017 3Q (Jul)	$627
Zetia®	Ezetimibe	2017 4Q(Oct)	$1,232
Vytorin®	ezetimibe/simvastatin	2017 4Q (Oct)	$1,635
Spiriva®	tiotropium powder for inhalation	2018 3Q (Jul)	$1,191
Nasonex®	mometasone nasal spray	2018 4Q (Oct)	$1,045
Lyrica®	Pregabalin	2019 3Q (Jul)	$1,492
Detrol® LA	Tolterodine	2020 2Q (May)	$729
Crixivan®	Indinavir	2021 3Q (Aug)	$12

3. Conclusion

To minimize the impact of patents' expiry, companies are trying to minimize the impact through various means. Many companies are releasing authorized generic versions of the drugs, which would reduce the companies' overhead costs and could result in more efficiency. Keeping with the same pace many companies are opting for cost control programs and also by making strategic investments in the fast growing emerging markets. Many companies are expanding their R&D in these emerging markets like China and Russia and also up to some extent in India. According to some top managers of mega companies, companies want to conduct medium-sized acquisitions to boost its growth and would probably not be engaged in any "mega takeovers" in the near future.

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