Pharmacy Discounts and Profit Maximizing Pharmacy and Manufacturer Decisions in Turkey

by

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This is to certify that I have examined this copy of a master's thesis by

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ABSTRACT

Pharmacists play an important role in Turkish pharmaceutical market as well as some other countries such as United Kingdom. In Turkey, they can dispense most drugs without prescription to cash patients; and for patients reimbursed by the government they can substitute the prescribed drugs with cheaper bioequivalent alternatives. While the physician and -to some extent- patient directed marketing activities of pharmaceuticals have been modeled in the literature, there is a gap in understanding the profit maximizing decision of the pharmacist as a function of the discounting activities of the pharmaceutical manufacturers. We develop a mathematic model of the profit maximizing pharmacist, deciding on drug substitutions within equivalence class for patients with a prescription, and drug choice for patients without a prescription. We derive the optimal pharmacy decisions for both reimbursed and cash segment drugs as a function of the pharmacy discounts and physician detailing activities by the pharmaceutical companies. We then analyze the impact of pharmaceutical firm’s actions on pharmacy decisions and in return on firm’s sales in each segment. Results suggest that the drug substitution decision of the pharmacy is directly influenced by the pharmacy discounts of the pharmaceutical firms relative to each other, suggesting a discount war, as well as detailing. On the other hand, the drug choice for patient without a prescription is only affected by pharmacy discounts but not detailing spending.

We also study the manufacturer’s optimal discounting decision to pharmacies. The game theoretical approach that we employed in our analysis enables us to figure out the rational discounting decisions of pharmaceutical companies. Here, we derive potential Nash equilibria of pharmacy discounts for both reimbursed and cash segment drugs. Finally, we conduct sensitivity analysis in order to reveal the effect of parameters controlled by relevant players on the equilibrium pharmacy discount levels. The results suggest that when the relative power of the firms is such that one of the firms (say firm 2) captures some portion of the prescribed drugs of the other firm and is favored by pharmacist while advising in cash segment, then the equilibrium discount level maximizing firm 1’s profit decreases with increasing own detailing. Further, if the compulsory discounts given to government by pharmaceutical manufacturers are raised, equilibrium discount levels of both firms will decrease in reimbursed segment. The analytical results derived in this study can be utilized by pharmacist and pharmaceutical companies to maximize their profits, and at the highest level by regulators to maximize social welfare of the society.

ÖZETÇE

Britanya gibi bazı ülkelerde olduğu gibi Türk ilaç sektöründe de eczacılar önemli bir rol oynamaktadır. Eczacılar, çoğu ilacı reçete olmaksızın tüm ücreti cebinden ödeyen hastalara verdikleri gibi, ilaç bedeli devlet tarafından karşılanacak olan hastalara da reçetede yazan ilacın daha ucuz ikamesini verebilmektedirler. Literatürde doktor ve -bir dereceye kadar- hasta odaklı pazarlama aktiviteleri modellenirken, ilaç üreticilerinin indirim kararlarında eczacıların kar maksimizasyonunu dikkate alması hususunda eksiklik göze çarpmaktadır. Bu çalışmada, reçeteyle gelen hastaya ilaç ikamesi yapmak ve eczacının tavsiyesine başvuran reçetesiz hasta için ilaç tercih etmek üzerine kurulu matematiksel bir eczacı kar maksimizasyonu modeli geliştirilmiştir. Bu model; eczacının vermesi gereken en iyi kararı, hem devlet destekli hem de tüm ücreti hastadan alınacak ilaç sınıfları için, üretici şirketlerin eczacı indirimi ve ilaç tanıtım çalışmalarının fonksiyonu olarak ortaya koymaktadır. Sonrasında, ilaç şirketlerince alınan eczacı indirimi ve ilaç tanıtım kararlarının eczacının karına ve her bir segmandaki ilaç satışlarına olan etkisi analiz edilmiştir. Sonuçlar gösteriyor ki, eczacıların ilaç ikamesi kararları, şirketleri indirim savaşlarına iten eczacı indirim oranlarından ve doktora tanıtım çalışmalarından direkt olarak etkilenmektedir. Diğer yandan; eczacının tavsiyesine başvuran reçetesiz hastalar için ilaç tercihleri, tanıtım harcamalarından değil sadece eczacı indirimlerinden etkilenmektedir.

Aynı zamanda, üreticilerin eczanelere yaptıkları optimum indirim kararlarını da bu çalışmada ele alınmıştır. Analizlerimizde kullandığımız oyun teorisi yaklaşımı, ilaç üreticilerinin rasyonel indirim kararlarını ortaya çıkarmamıza olanak sağlamıştır. Ayrıca, yine hem devletçe bedeline ortak olunan hem de tüm ücreti hastadan tahsis edilen ilaç grupları için eczacı indirimlerinin olası Nash dengeleri elde edilmiştir. Son olarak da; ilaç endüstrisindeki oyuncular tarafında kontrol edilen parametrelerin, eczane indirim oranlarına etkilerini ortaya çıkarmak için duyarlılık analizi yapılmıştır. Elde edilen sonuçlara göre; firmalardan birinin (örneğin Firma 2), eczacının tavsiyesini soran reçetesiz hastalara ilaç sağlanırken tercih edildiği ve hatta diğer firmanın reçeteli ilaçlarından pay aldığı bir denge ortamında, Firma 1 tanıtım harcamasını arttırırsa kendi karını maksimize eden eczacı indirimini düşürür. Bunun yanında, üretici firmaların zorunlu olarak devlete verdiği indirimler yükseltildiğinde, devletçe bedeline ortak olunan ilaçların dengedeki eczacı indirimleri düşüş gösterecektir. Bu çalışma sonucunda elde edilen analitik sonuçlar; eczacılar ve ilaç firmaları tarafından kar

maksimizasyonunda, en üst seviyede ise düzenleyici kurumlar tarafından toplumun sosyal refahının yükseltilmesinde kullanılabilir.

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Nomenclature

i, j	drug (firm) indices
k	segment index
$\Pr ice_i$	Retail price of drug i
OOP_{ik}	out-of-pocket expenditure of a patient from segment k purchasing drug i
p_{vis}	the fraction of cash paying patients who choose to visit the physician, given that they are taking an action
p_{req}	the fraction of cash paying patients who choose to request a medication at the pharmacy, given that they are taking an action
p_{adv}	the fraction of cash paying patients who choose to ask for pharmacist's advice, given that they are taking an action
pr_i	the fraction of patients directly requesting drug i, given that they have requested a drug
pa_i	the fraction of patients being advised drug i, given that they have asked for pharmacist's advice
p_{ik}	the fraction of segment k patients visiting the physician, who prescribed drug i
$psubs_{ijk}$	the fraction of segment k patients, who are dispensed drug i by pharmacist instead of prescribed drug j
$psubs_{iik}$	the fraction of segment k patients, who are dispensed drug i as written in the prescription
$pfill_{ik}$	the fraction of patients from segment k filling the drug i
N_k	the total number of sufferers who take action in segment k
n_{ik}	the number of patients from segment k, who are (ultimately) treated with drug i
Det_i	detailing expenditures of firm i
Q_i	quality of drug i
$\xi(Det_i, Q_i, OOP_{ik})$	an increasing function of Q_i and Det_i, and decreasing function OOP_{ik}
R_{ik}	the expected number of refills by a patient of segment k who filled the first prescription for drug i

CC_i	the complaint cost of drug *I* resulting from pharmacy substitution
C_{comp}	the future revenue loss of a single complaint by a patient or her doctor caused by the substitution
$Nsubsfill_{ik}$	the number of segment *k* patients subject to substitution of drug *i*
$pcomp_{ik}$	the probability of complaint about drug *i*'s substitution in segment *k*
$\psi(Det_i)$	an increasing function Det_i
α_{lin}	the coefficient for linear component of the complaint cost
α_{quad}	the coefficient for quadratic component of the complaint cost
pm_{ik}	the profit margin of pharmacies for drug *i* regulated by the government
$disc_{ik}$	the effective discount rate offered to the pharmacist as "*mal fazlası*" by manufacturer *i* which sells its drugs to segment *k* patients
PP	
Pow_{ik}	the expected profit of the pharmacist from introducing a segment *k* patient to drug *i*.
X_{ik}	a parametrical expression of $psubs_{ijk}$
$sales_{ik}$	the sales of drug *i* in segment *k*
$Govdisc_i$	the mandatory discount off of the drug *i*'s retail price that the manufacturer *i* has to give to the government
MP_{ik}	firm *i*'s profit in segment *k*
BRC_{ik}	the best response correspondence of firm *i* in segment *k*
$Pow_{ik}^{\min}$	the minimum Pow_{ik} value when $disc_{ik}$ equals to 0
$Pow_{ik}^{\max}$	the maximum Pow_{ik} value when $disc_{ik}$ equals to 1

Chapter 1

INTRODUCTION

Turkish Healthcare System is currently at the threshold of a radical reform known as *"Transformation in Health" Programme*. The main objective of the programme is to improve the health status of the Turkish society by ensuring equity, increasing productivity, improving the quality of services provided and guaranteeing patient satisfaction [1]. In order to achieve this aim, one of the crucial aspects of the heath care system that needs improvement is pharmaceuticals [2].

Expenditure on pharmaceuticals constitutes a growing share of the total health expenditures in OECD countries. The real annual growth in pharmaceutical expenditures across OECD countries from year 1997 to 2003 was 5.6% whereas the real annual growth in total health expenditures was 4.4%. [3] This situation indicates that in OECD countries pharmaceuticals as a share of total health expenditures has been growing with each passing year. Turkish pharmaceutical spending as a percentage of total health expenditure is even higher than that of OECD countries. The share of pharmaceuticals of the health expenditures in Turkey was 10.2% in 1980 [4] whereas it reaches 40% in year 2000 [5] as a result of huge increase in drug expenditure per capita. On the other hand, the average share of pharmaceuticals in OECD countries was 17.5% according to 2003 statistics [3]. Furthermore, the major portion of pharmaceutical spendings is undertaken by government in Turkey where 78% of drug expenditures are reimbursed. [6], versus only %66 on average in EU countries [7] and 18.7% in US [8].

Reports also suggest that pharmaceuticals constitute one of the important components of Turkish health system that require improving measures ([1] and [4]). A better understanding of the motives of parties involved in the transactions will be instrumental in foreseeing effects of different measures that modify the system. This study is the first attempt, to our knowledge, to model the role of the pharmacies in drug choice and the pharmacy discounts offered by manufacturers in the Turkish pharmaceutical market. In first part of this thesis we model the commercial concerns of the pharmacists and analyze how their profit maximizing substitution and dispensing decisions are affected by the discounting and detailing by the pharmaceutical companies. In the second part, we construct a model for manufacturers' profit with respect to their pharmacy discount offers and find the steady-state equilibria of pharmacy discounts concerning profit maximizing substitution and dispensing decisions of pharmacy. We, then, analyze how pharmacy discount decisions of manufacturers are affected by the parameters controlled by exogenous players involved like government, patient and physician.

The rest of this study is structured as follows: Chapter 2 gives a brief literature related with our study. Chapter 3 describes Turkish pharmaceutical industry and lays out a discussion of governmental policies and decision makers (pharmacy and manufacturers) in our study. It also provides a comparison of prescription drug market in Turkey and United States. Chapter 4 follows with the description of the mathematical model quantifying the objective function and decision variables of the pharmacist. Then, we derive the analytical result for the pharmacist's optimal decision in response to the manufacturer's marketing decisions while complying with government regulations. In Chapter 5, we lay out the optimal discounting decision of manufacturer. This chapter also presents sensitivity analysis revealing the effect of various parameters on equilibrium discounting levels. Chapter 6 concludes with a summary of the findings, their possible implications and further research directions.

Chapter 2

LITERATURE REVIEW

Pharmaceutical industry has always presented great research opportunity for academicians due to abundance of players involved in pharmaceutical market, strong relations between them and availability of data. For this reason, pharmaceutical marketing has been a popular academic research area. In a great majority of these papers, authors focus on patient and physician directed marketing activities. Also, most of the papers about pharmaceutical industry concentrate on the US market and perform analysis according to US health care system. Even if in some cases it is not possible to adapt the results of these papers in different countries' system, they can help researchers to gain a better insight about their problems. Huskamp et al. (2005) [9], Rector et al. (2003) [10], Goldman et al. (2004) [11] are some remarkable empirical studies that clarify the impact of co-payment on drug demand. On the other hand, works of Gonul et al. (2001) [12], Manchanda et al. (2005) [13], Mizik and Jacobson (2004) [14], Narayan et al. (2004) [15], Wosinska (2002) [16], Wosinska (2005) [17] deal with patient and physician directed marketing models, empirical estimation of parameters in these models and their optimization.

Especially, papers of Wosinska in 2002 [16] and 2005 [17] deserve close attention since they try to explain the relation among marketing activities (DTC and detailing) of drug manufacturers, prescribing behavior of physicians, demand and compliance of patients *under the assumption of the presence of formularies and co-pay*. Available literature except the ones by Wosinska ([16] and [17]) has not included dissimilarities between "covered" (reimbursed by government or an insurer) and "cash" (paying whole price out of pocket) segment patients. Her empirical analyses depend on the database of a large health insurer. In Wosinska (2002) [16], she states that 1) detailing promotions affect prescription choice much more than promotions aimed at consumers, 2) DTC advertising affects treatment probability thereby benefiting all brands and 3) DTC advertising affects demand only for drugs that have preferred status with the patient's insurer. Furthermore, Wosinska (2005) [17] claims that the impact of DTC advertising on patient's therapy compliance is small in economic terms, the effect spills over to other brands and, in some certain cases, the effect may even decrease average compliance.

The remaining literature related with our research can be grouped in four distinct clusters. The first one is the report that is prepared by Kanavos et al. (2005) [4] for "Sağlıkta Umut Vakfı (SUVAK)", which describes the Turkish pharmaceutical system and the reimbursement policies. We reinforced this understanding by informal interviews with individual pharmacists and pharmaceutical company officials. The second set of studies such as the paper by Ess et al. (2003) [18] discuss the European healthcare policies for controlling drug expenditures, and summarize studies about their impact. The third set contains mathematical models of the rational behavior of the players in the pharmaceutical system, e.g., the theoretical paper by Brekke et al. (2006) [19] studies the effects of direct-to-consumer advertising in a prescription drug market with two differentiated original drugs. Gür Ali et al. (2006) [20] studies the rational decision of the Pharmacy Benefit Manager in the US system and the effect of the rebates, detailing and direct to consumer advertising on the decision. A review of US pharmaceutical marketing literature can be found in Manchanda et al. (2005) [21]. The final set consists of the paper by Blattberg (1987) [32] which provides a complete discussion of trade promotions in retail market.

The study by Brekke et al. (2006) [19] presents an economic point of view for the marketing activities of pharmaceutical manufacturers. It considers the public welfare implications of DTCA. The model is a duopoly of differentiated products where companies decide about detailing, DTCA and price (if not regulated) and where manufacturers' maximized profits and resulting social welfare are evaluated. Then the relations among DTCA, detailing, drug price, demand, manufacturer's profit, social welfare and parameters of the model (like co-payment etc.) are considered theoretically. This approach sometimes fails to clarify the relations between some parameters and variables because of the complexity of the model. In such cases, instead of deriving comparative statistics theoretically, they use numerical illustrations, which ease the presentation of results. However, choice of some parameters for numerical illustrations seems a bit arbitrary which necessitates the results of these numeric analyses to be verified by checking with different combinations of parameters. It is also an interesting work since it introduces a clear function for social welfare gained by pharmaceuticals. In this paper, two different kinds of welfare function are presented, one includes and the other excludes pharmaceutical firms' profit. When firm profits included, social welfare is represented as patient utility plus profits of the firms minus governmental reimbursement. Here, patient utility is also a function of drug quality, out of pocket (OOP) payment and mismatch cost (can be interpreted as side effect of the drug). Firm profits are also identified as a function of price, share of patients informed about drug via DTCA and share of physicians informed via detailing. On the other hand, welfare function excluding firm profits simply drops the profits from the function. The reason for forming two distinct welfare functions is that most countries with insignificant R&D and production of pharmaceuticals practice cannot regain the profits of pharma companies and as a result the contribution of these firms on social welfare becomes very limited. On the other hand, countries where firms invest heavily on R&D can benefit from the financial well-being of these firms and this situation reflects to society as increased welfare. The most interesting results of this study can be enumerated as follows: 1) DTCA, detailing and price (if not regulated by government) are complementary strategies for the firms. Thus, allowing DTCA causes more detailing and higher prices. 2) Firms benefit from DTCA if investing in detailing is sufficiently costly. Otherwise, manufacturers are better off with a ban on DTCA. 3) DTCA tends to lower social welfare if co-pay is low and/or price regulation is lenient.

As discussed before, a great majority of studies about pharma industry are US-centric. However, until Gür et al. (2006) [20] there did not exist a work focusing on the link between marketing strategies of pharmaceutical manufacturers and Pharmacy Benefit Manager (PBM), a unique agent in US responsible for managing the pharmacy benefits of patients on behalf of the final payer. In this paper, an integrated management view of the effects of pharma company's detailing and DTC marketing efforts along with rebate offers on PBM response is presented without ignoring formulary effect and differentiation between "covered" and "cash" segment patients. A high level model of pharmaceutical marketing and sales that incorporates two original and one generic drug producers, PBM, patient, physician and their relations is built. Theoretical results about the profit maximizing PBM formulary decision are derived: The PBM formulary tier decisions affect brand prescriptions (Rxs) substantially, especially the brand's share of patients and the patient's compliance and persistence. Especially PBMs that do not push generic use by physicians but discourage them against using non-preferred brands attract high discounts. Further, other things being equal, the rebate-maximizing PBM assigns a more favorable formulary tier position to a brand not only when it offers a higher percent discount but also when it is the higher- priced brand and/or has the greater pull marketing effort (detailing and DTC ad spending). The parameters of this model are estimated based on literature and surveys and then the model is used as a simulator to identify the relations among pull (detailing and DTCA) & push (rebate offers) marketing strategies of pharma companies and PBM's rational decisions. Consequently, the paper sheds light on how detailing and DTC efforts impact PBM response and provide directions for the allocation of pharmaceutical company's marketing efforts between patients (via DTCA), physicians (via detailing) and PBMs (via rebates).

In this thesis, we focus on pharmaceutical market and especially the interaction between two key players of this market, pharmacy and pharmaceutical companies. One can argue that there exist plenty of studies in literature concerning retail markets and the trade promotions offered to retailers by manufacturers. Besides, it might be claimed that these previous works can readily be applied to the pharmaceutical market since the same retail-manufacturer relation exists between pharmacies and pharmaceutical companies. The paper by Blattberg et al. (1987) [32] is a famous article that models the effectiveness and profitability of trade promotions in retail market. Offering trade promotions in the form of direct discounts and free case offers, manufacturers expect retailers to push the product through the pipeline by offering financial and merchandising incentives. In this paper, hence, trade promotions by manufacturers are transferable to the final consumer through retailers. The lack of this transferability to patients through pharmacies is the first reason that urges us to model a specialized version of studies in literature. Another characteristic that distinguish pharmaceutical market from a regular retail market is the fact that patients are not often the agent who makes the product choice. In pharmaceutical transactions, although, physician is the *gatekeeper* who decides which drug is more convenient to the patient, consumer is the final decision maker deciding on whether to purchase the product or not. This separation of drug choice and purchasing decision differentiates our study from retail market analysis. Finally, government's role as both payer and regulator is a unique characteristic of pharmaceutical market. Unlike retail market, pharmaceutical transaction is subject to strict audit and regulation of governmental agencies. To sum up, all these three distinguishing features necessitate a discrete study of pharmaceutical marketing.

Chapter 3

TURKISH PHARMACEUTICAL MARKET

3.1 Pharmaceutical Industry

3.1.1 Submarkets

Drugs used for therapeutic purposes can be classified in three main submarket categories:

1 the over-the-counter (OTC)

2 hospital submarket

3 prescription submarket

This study focuses on the prescription submarket but a brief discussion about OTC is given below in order to clarify the differences in Turkey and other countries in this submarket.

At this point before proceeding, it will be beneficial to mention an interesting characteristic of generic drugs in Turkey. In EU countries and US, generic versions are only bioequivalent of original drugs and they do not bear a brand name on their package. However, in Turkey generics also have brand names as their original versions and they engage in direct-to-physician (DTP) detailing activities unlike in the US. This causes an environment in which consumers are not informed whether their medication is an original patent holder or not.

Another important characteristic of the Turkish pharmaceutical market that is important in positioning the thesis work is the place of OTCs in Turkey. In Turkey, OTCs are classified as drugs that do not necessitate a prescription [4]. However, the sale of any drug (whether it requires a prescription or not) is in retailers other than pharmacies. In Turkey OTC drugs mainly fall into therapy classes like cough & cold preparations, pain killers and vitamins. Until very recently, almost all OTCs could be reimbursed in Turkey by governmental social security organizations if they were prescribed by the physician; however they are gradually being taken out of reimbursable drug lists. Only cough & cold preparations and vitamins constitute 15% of whole pharmaceutical consumption in Turkish market. It is estimated that 42% of all OTC market is covered by out of pocket expenditures where as the remaining portion is reimbursed by public sector. [4]

On the other hand, the situation for EU market is totally different than Turkey. The OTC market has a market share of 6-10% in most EU countries. In European countries OTCs are characterized by well known, low priced drugs and the consumers of these drugs pay out of pocket. As a result of this condition, consumers are cost conscious and they consider the price in their purchase decisions. [18]

The above statistics show the burden of OTC expenditures for the public budget in Turkey. There has been a prolonged debate among government, doctors and pharmacists in Turkey about the content of the list which categorizes drugs as OTC and prescription drugs. However, fresh regulations have incrementally started to remove the OTC drugs from reimbursement (positive) list of the government. For instance a recent regulation about the status of vitamins exacerbated this debate one more time. Pharmacists showed big negative reaction to the decision of the government that suggests excluding some of the vitamins from the positive list since they are classified as OTC and are not reimbursed in other countries [22].

The other important issue about the OTC, which will be probably put on the agenda of the government after OTC drugs and their reimbursement status are certainly defined, is the authorized institutions responsible in the supply of these drugs to the patients. In some OECD countries like Netherlands or the USA, OTC drugs can be sold in retailers like supermarkets having medical departments. Therefore, the pharmacists in Turkey worries about the introduction of direct competition from supermarkets and other non-pharmacy retail chains in future. The strong opposition of pharmacists to the decision about vitamins mentioned above partially arises from this worry.

3.1.2 Stakeholders

In Turkey, main stakeholders of pharmaceutical transactions are:

- Patients, as taxpayers and direct payers of the out of pocket pharmaceutical expenditures
- Government and its agencies; and private health insurance agencies
- Physicians
- Pharmaceutical manufacturers
- Wholesalers and retailers (pharmacies)

Figure 3.1 summarizes the cash flow in public reimbursement system. Although the parties involved in pharmaceutical transaction differ in United States, they are very similar to those in the European countries (Ess et al., 2003). Generic and original drug manufacturers sell their products to consumers (patients) via wholesalers and retail pharmacies.

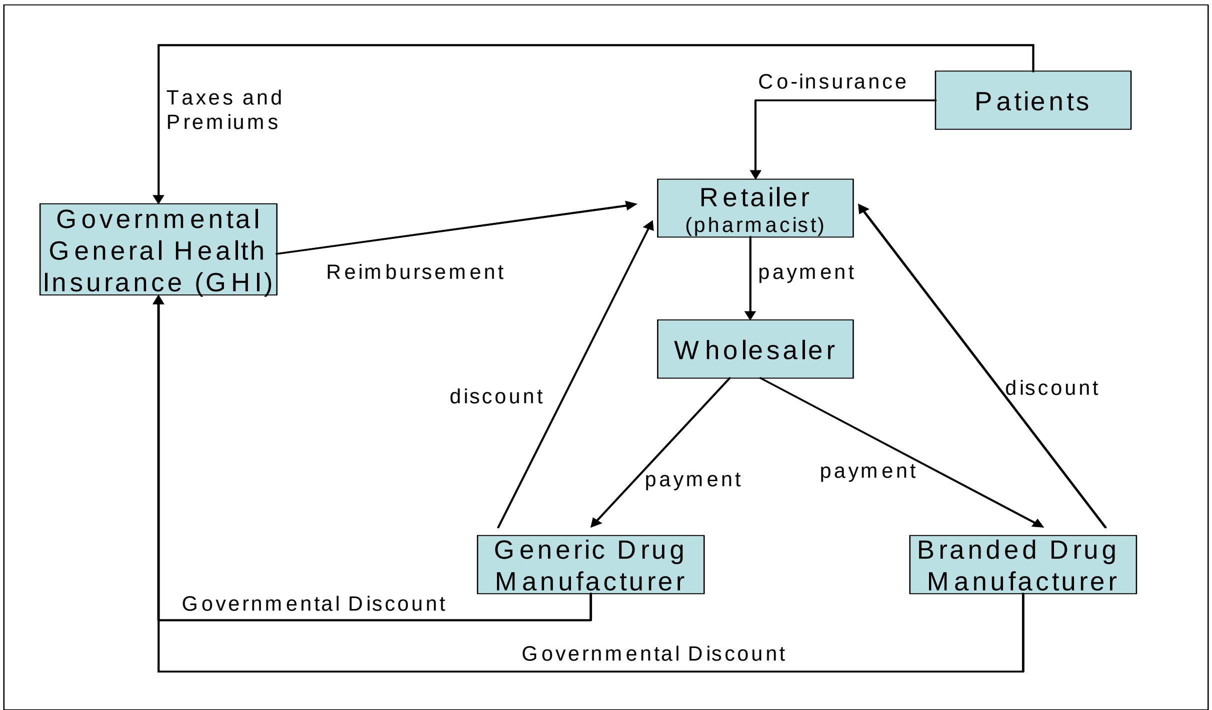


Figure 3.1 – Cash Flow in Public Reimbursement System in Turkish Market

Turkey has a number of social security institutions (SSK, Bağ-Kur, Emekli Sandığı, Consolidated Fund), which are currently in the process of a merger under the name "General Health Insurance" (GSS). The unified positive list guarantees the reimbursement of drugs by the social security institutions in most of the therapeutic classes. The beneficiaries of the social security system contribute to the drug that they receive by paying a coinsurance amount where the rate varies between 10% to 20% based on the social security system. Another consideration in determining the out-of-pocket (OOP) expenditure is the reference price which is currently defined as "the least expensive drug in an equivalence class plus 30%" by the GSS; i.e., if the drug's price is higher than the reference price, the patient pays the excess amount out of pocket (Kanavos et al., 2005).

In the US and most of the European countries, bioequivalent versions of original drugs are not branded. As mentioned earlier, however, in Turkey "generics" also have brand names and promote to physicians and pharmacists. Consequently, consumers and potentially physicians may not know which drug has the original patent. In Turkey, promotions directly targeting final consumers of pharmaceutical is restricted and branded ads are not allowed; hence direct to consumer advertising is at a negligible level, with few exceptions of public awareness campaigns for categories. The most common promotion form directed at physicians is "detailing", where sales representatives of pharmaceutical manufacturers pay a visit to physicians to provide information about their products. The detailing activities are supplemented by meetings and events, sponsorships and other activities directed toward the physician, which we collectively refer to as "detailing" in the rest of the paper. Detailing serves to increase the share of the drug among physician prescriptions and the proportion of patients who get treated with medication therapy. Further, detailing also tries to generate resistance to substitution of the prescribed drug by the equivalents in the pharmacy. Both generic and original drug manufacturers invest on detailing activities.

3.2 Governmental Policies for Controlling Drug Expenditures

All governments pay considerable effort to regulate the pharmaceutical industry to provide a better and cost efficient health care system. While doing these regulations, governments should take into account various factors conflicting with each other. The main purposes of the healthcare policies for drugs are to provide the best possible healthcare services for all society and to maintain the expenditures at a reasonable level. For the sake of these purposes, while regulating pharmaceutical industry policy makers consider three main dimensions of the system: the *quality* of the pharmaceuticals, the *equity* for all citizens and the *cost* of the pharmaceutical expenditures [4]. A policy only concentrated on cost containment strategies and ignoring the quality of the treatment cannot be a successful policy since the overall social welfare is not a parameter that could simply be omitted. While deciding on cost containment policies for drug expenditures the government should also keep in mind the integrity of the healthcare system. For instance, a regulation aiming to decrease the drug expenditures should not overlook the extra burden for healthcare system coming with poor medication leading to inpatient treatments at the hospital.

Policies for regulating pharmaceuticals and to what extent they are administrated differ from country to country. In the remainder of this section, the cost containment policies for drug expenditures in Turkey are summarized and the corresponding practices in EU and US are also provided. Comparative international analysis may contribute to a better understanding of policies in different countries. One needs to keep in mind, though, that there are significant differences between the political, social and economic structure of this countries. Moreover, there might be some significant limitations in the transferability of some policies form one country to another because of the above structural differences. Therefore, any policy ensuring a considerable benefit in a country may not cause the same effect in others even resulting in worse consequences.

In the following 4 sections the governmental cost containment policies affecting the stakeholders of pharmaceutical transactions are listed as follows:

3.2.1 Policies Affecting the Pharmaceutical Manufacturers

In Turkey, Head Office of Pharmaceuticals and Pharmacy, a unit working under Ministry of Health, is responsible for the licensing of all drugs before the sale in the market. In EU countries, there exists an independent institution giving the license to new drugs. Although in some of them this independent institution works under ministry of health, these institutions make their decision without any intervention coming from ministry of health. However, the report of Kanavos et al. (2005) [4] emphasizes the difference between the criteria followed in the licensing procedure in Turkey, EU and US related with the price of the drug. In EU and US; safety, efficiency and quality are the key criteria affecting the licensing decisions. However, price of the drug is also stands as a criterion in the licensing activities of Turkish agencies. This means that in Turkey pricing is an inseparable stage of licensing procedure and licensing is not possible without price setting.

A new regulation for patent protection similar to the one implemented in EU countries has come into effect since 1999. This regulation provides protection for the patent of the drugs introduced to the market after 1995. Although there still exist some problems in the implementation stage of the relevant laws, it is supposed that in a few years the patent and intellectual property right protection in Turkey will be at the level of EU countries.

Since the portion of the pharmaceutical expenditure publicly reimbursed in Turkey is really high, it is expected that pharmaceuticals to be subject to strict pricing policies. (In EU countries, on average, 66% of drug expenditures are reimbursed while in Turkey this percentage is 78% [7]). In Turkey the basic method used in price establishment of original drugs is comparing the price of the pharmaceuticals in other countries. The price of the original drug is chosen to the lowest price among 5 EU countries (Greece, Spain, Portugal, Italy and France). On the other hand, the price for the generic drugs is identified as the 80% of the original drug's price (the cheapest amount in the above 5 EU countries). In EU, criteria other than country comparison usually apply including assessing the medical value of the product, its conditions of use, examining the prices and sales volumes with other bioequivalent drugs. Also in most of the OECD countries, the process of price setting is separated from the process of reimbursement negotiations.

Although Turkish government basically concentrates on direct price control (pricing), in Europe pharmaceuticals are subject to a wide range of pricing policies like profit control and indirect control via reference pricing and generic substitution. In reference pricing control patients are required to pay the amount of the price above the reference price set for a certain therapeutic class. Also by generic substitution method pharmacists are allowed to substitute the generic drugs for original drugs. Especially UK had used this method effectively causing the generic usage to increase from 16% in 1977 to 54% in 1994. [18] Reference pricing application in Turkey will be based on "The cheapest plus 30%" rule with the introduction of General Health Insurance (GHI). In other words the patients will be required to pay the amount of the drug's price that is above 130% of the cheapest drug in the same therapeutic class. This procedure has already taken into effect in current transition period. Generic substitution is also another problematic issue in Turkish system because of the commercial concerns of pharmacists that will be discussed in proceeding sections. Profit control, a precaution used in lesser extend, aims to ensure that the profits of pharma companies are at reasonable levels. UK also used this approach to control the drug expenditures.

3.2.2 Policies Affecting Consumers

Until 2005, Turkey had a separate social security system for the employees and retired citizens relying on premium payment system. SSK, operating under Ministry of Labor and Social Security, served the private and public sector employees. Bağ-Kur served the self-employed citizens. Emekli Sandığı (Government Pension Fund), on the other hand, served retired government officers. Actively working governmental officers are subject to another social security source called consolidated fund. In February 1, 2005 all these social security agents are merged under the name "General Health Insurance" (GHI). Before the merger, SSK, Bağkur, Emekli Sandığı and consolidated fund had carried out its own reimbursement and cost containment policy. For instance even the positive list, the list of drugs showing the brand names of the drugs reimbursed, differs in each social security agent. However, new healthcare reform brings in a centralized structure in healthcare services. GHI covers all the members of SSK, Bağ-Kur and Emekli Sandığı. A unified positive list is introduced that guarantees the reimbursement of drugs contained in the formulary of the government. In the current transitional period, GHI sets the reference price as "the cheapest drug in an equivalence class plus 30%". This means that if a drug above the reference price is prescribed than the patient is required to pay the excess amount out of pocket. The co-insurance that a covered person should pay for the drugs below reference price is decided to be 10%. Also an explicit healthcare service is provided for the citizens, whose income level is below a certain point, without demanding any premiums. These people given green cards to document their circumstances and they are also subject to the same formulary identified for GHI and their co-share is set to be 20%.

According to Ess et al. (2003) [18], In EU countries patient cost-sharing levels can be identified in several ways: proportion of the total price, fixed charge per Rx or annual deductible. The reimbursement policies in Europe show great diversity from country to country. Combinations of three methods above are used in different countries. For instance, in Italy there is a prescription charge plus a percentage of the price, depending on the class of drug (Class A, B and C requires patient cost-sharing of 0%, 50% and 100% of retail price respectively.)

3.2.3 Policies Affecting Wholesalers and Retailers

In most of the European countries governments have defined the profit margins for wholesalers and retailers. Even if in Turkey the profit margin of each party involved the pharmaceutical transaction is strictly defined, some deviations occur in actual profit margins due to informal discounts given to wholesalers and retailers. Generic substitution of pharmacists is allowed by government in Turkey only if the price of the drug given is less than the price of the prescribed drug and it is listed as a generic substitute in the positive list. Although government allows the generic substitution as a cost containment strategy, the principal factor affecting the decision of the pharmacist about substitution is purely commercial. In other words, pharmacists are inclined to substitute the drug prescribed with its generic if the manufacturer of this generic offers the best profit via rebate to the pharmacists. This may result in a decrease in the welfare of patients since in some cases the physician prescribes a certain drug because of the side effects of its substitute. Moreover, pharmacist's generic substitution does not always result in a more cost effective situation for covered patients or government as the payer.

Furthermore, when the patient is willing to pay whole retailer price of the drug out of pocket, most of the drugs, including the ones requiring prescription, are supplied to the patient by the pharmacist without prescription unofficially. Also most of the patients trust the pharmacist's advice about their health problems. (For instance they ask pharmacists for the convenient antibiotics without consulting a physician.)

The above two points demonstrate how pharmacists are key players in healthcare system which is not the case in most of the European countries and US.

In EU countries, most governments have defined profit margins for drug wholesalers and retailers as a means of facilitating the control of costs. Also in Turkey as a regulative action of profit margins, the new healthcare system implemented with "Transformation in Health Programme" foresees specific discounts covered by wholesalers and retailers. These are listed as follows [4]:

- Social security agencies merged under GHI will take a discount of 14.5% for generic drugs. 3.5% of this rebate will be covered by pharmacists and the remaining will be covered by manufacturer or importer.
- For original drugs that have not completed 6 years in Turkish market, government will take a discount of 7.5%. (3.5% from pharmacists and 4% from manufacturer or importer)
- For original drugs that have completed 6 years in Turkish market, government will take a discount of 14.5%. (3.5% from pharmacists and 11% from manufacturer or importer)
- For drugs having a price lower than 3 YTL, government will take a discount of 7.5%. (3.5% from pharmacists and 4% from manufacturer or importer)

The main purpose of this rebate scheme is to reduce the huge amount of informal discounts that manufacturers offer to pharmacies via wholesalers. This approach resembles the clawback system in UK, a way to take money back from pharmacists that they were given by pharma manufacturers.

The wholesalers in Turkey have a concentrated structure. Only two of them (Hedef and Selcuk) represent 70% of the whole market. As the consequence of strict pricing activities of the government and enhanced distribution standards, the competition will be tougher and the number of the wholesalers will probably decrease in the following years [4].

3.2.4 Policies Affecting Physicians

In Turkey, physicians always fill the prescription with brand names whether the drug is original or generic. Turkish government does not stipulate any ceiling price for the drugs prescribed by the doctors. There does not exist any incentive for the prescription of specific drugs except positive lists. Meanwhile there is no sanction for over-prescribing. One of the restrictions on prescribing activity of the physician in Turkey is related to the number of drugs in a single prescription. The other limitation is about the area of specialization of physicians. This regulation necessitates that certain specialists can only prescribe certain drugs. In the light of this data it can be easily concluded that very few governmental regulations exist concerning the prescribing pattern of the physicians. Without a systematic regulation, physicians identify the drug to prescribe by relying on the commercially available sources. According to Kanavos et al. (2005) [4], direct to physician promotions (detailing) of manufacturers are not subject to any constraint. On the other hand, The Association of Research-Based Pharmaceutical Companies in Turkey published the code of ethical promotion practices for medical products [23]. All members of this community agree to obey the ethical rules of this document, however it is not independently verified that the manufacturers stick to these rules.

However, current government administration plans to implement some tough limitations on the prescribing behavior of the physicians. A very fresh regulation about the cholesterol drugs is a good example for this kind of regulations. According to new formulation, all publicly covered cholesterol drugs can be prescribed for only patients whose cholesterol level is above a certain level.

On the other hand, in EU instruments such as guidelines, drug utilization reviews and penalty for expenditures exceeding the budget, target cost containment by influencing the prescribing behavior of physicians. Guidelines are defined as “systematically developed treatment pathways which assist physicians in making decisions about appropriate treatment for specific conditions” [18]. UK, France, Germany and Sweden, some EU countries which introduced guidelines, did not show strong evidence that guidelines are cost efficient. Also Hıfzı Sıha Mektebi published guidelines in 2003 for Turkish physicians which have not been put into practice as yet. [4] Drug utilization reviews are the records of prescribing statistics to prescribers to increase their awareness of prescription volumes and costs. UK, Netherlands and several other EU countries provides information feedback systems for their physicians and this application works fine as a cost containment policy. [18] Unfortunately, there is no drug utilization review executed by any of the insurance funds. However, the new healthcare program suggests monitoring of prescriptions with computerized systems.

3.3 Pharmaceutical Companies

Drug manufacturers are definitely one of the most crucial players of the health care system. They should be thought as not only profit maximizing, commercial corporations both also vital institutions for the sustainability of the well being of the society. Pharmaceutical companies operating or marketing in Turkey can be classified with respect to their drug profiles. Some focus their efforts on innovative drug inventions whereas the others choose to specialize in generic production of drugs whose patent has expired. From now on, drug companies investing in R&D and contributing to welfare of society by introducing innovative drugs will be referred as “original manufacturers”. On the other hand, the manufacturers experienced in generic drug production will be named as “generic manufacturers”. Surely, there also exist foreign and domestic pharma firms in Turkey manufacturing both original and generic drugs. However; in this study it is assumed that when a generic manufacturer and a original manufacturer are mentioned, they are two different rival companies competing for the same patient segment.

Table 3.1 demonstrates the basic marketing strategies of original and generic drug manufacturers. The number of pluses designates the intensity of marketing expenditure on corresponding agent.

	DTC	Physician	Pharmacist	Wholesaler
Generic manufacturer	⊥	+++	++++	++++
Original manufacturer	+	++++	++	++

Table 3.1: Marketing expenditures on various agents by original and generic manufacturers

3.3.1 Direct to consumer advertising (DTCA)

Promotions directly targeting final consumers in Turkey are not as intense as the promotions in US. This is obviously because of the restrictions on DTC activities of pharma companies. However some indirect promotion activities still take place in Turkish market. Most common ones can be categorized as follows:

Indirect advertising without declaring company name or product:

In TV programs like talk shows, "healthy living" programmes or even TV series the customer awareness is increased by giving informative massages. Although these promotions are sponsored by drug manufacturers, they never use brand names. The ultimate purpose here is to make people realize their symptoms and present to the doctor. Indirect advertisements are interesting in a way that they have potential of expanding market size and increasing demand for all drugs (even including generics) in the therapeutic class.

Sponsorship to the campaigns increasing social awareness:

Civil non-profit organizations often organize social awareness campaigns to increase the public awareness about some critic health issues in Turkey like cholesterol, hypertension etc. Original manufacturers think these campaigns as a good opportunity of promoting their company or brand names. Hence, they provide required financial assistance to civil non-profit organizations for their campaigns and show up their name.

Free screening & diagnosis services:

It is very unlikely that you have never come across a stand (bench) providing free measure of blood pressure in a hospital. Actually, this free service is also a part of pharma companies' DTCA activities. By providing this hand service for free before the visit to the doctor, drug manufacturer aims to plant a positive image in the patient's memory about the company and its products.

Advertisement in pharmacies:

Another common DTCA activity is conducted by means of pharmacies. Representatives of manufacturers distribute brochures and posters of their new drugs and ask pharmacies to display them in the pharmacy. The primary target of these advertisements is patients paying whole price out of pocket (OOP). Also other patients are kept informed about the drug for the future probable needs.

DTC expenditures are rarely perceived as a marketing weapon by generic manufacturers. Instead, they usually prefer to leave original manufacturers alone in public awareness efforts. But as discussed before, this does not mean that they do not benefit from increase in demand.

3.3.2 Promotions directed to physician

Fundamental physician directed efforts are listed below:

Personal communication:

Personal communication with doctors is the most effective way of presenting a new drug to the physicians who has the potential of prescribing it. Pharmaceutical manufacturers introduce their products to the physicians by their sales representatives. Personal communication via sales representatives are designated by the term "detailing". Sales representative promotes the drug to the physician by proposing its superior specifications. They also try to influence the physician by talking about the clinical study and R&D investments of the company. Both generic and original drug manufacturers invest on detailing activities. Moreover, typically, these promotions constitute the largest proportion of their marketing expenditures.

Although the term "detailing" is used to designate personal communication via sales representatives, we used the term detailing to cover all physician directed efforts in this study.

Providing professional education and growth to physicians:

To increase the motivation to prescribe their drug, pharma companies sponsor professional meetings, seminars and health conferences. By attending these occupational events, physicians increase knowledge about their own area of specialization.

Providing personal development opportunities to physicians:

Additional to professional opportunities, pharma companies present invitations for personal development seminars etc.

Sponsorship:

Besides sending doctors to professional activities, pharma companies also provide the required financial support for these events.

Clinical Study

Even performing clinical study with universities and doctors are also an indirect way of informing physicians about manufacturer's activities contributing the literature. Physicians working in a clinical study organized by a specific company are persuaded that this firm is really investing in R&D activities. So, they become inclined to prescribe the drugs of this company to respond its goodwill in healthcare.

Infrastructure:

Drug manufacturers sometimes undertake the financial burden of infrastructure (refurbishment, library, air condition etc.) of governmental hospitals, dispensary or clinics. Hence they plan to cultivate an image of a company who cares about wellbeing of the society.

3.3.3 Promotions directed to pharmacists

Generic drug manufacturers focus their marketing effort on pharmacists more frequently than original manufacturers. The main reason is that they try to use substitution power of pharmacists. As discussed before, pharmacists are allowed to make a substitution in Turkey if the price of the equivalent drug to be substituted is less than the price of the prescribed drug. Manufacturers offer attractive discounts to the pharmacists in the hope of getting substitutions in their favor or to prevent substitutions away from their drug..

Since the profit margins of pharmacists are strictly defined by Turkish government, pharmacy discounts are not given as direct percent rebates. Instead of this, manufacturers offer their discounts as “mal fazlası”. Namely, they declare that they will give an extra amount of product for each specific amount of purchase. They are completely legal offers and no governmental restriction exists on these marketing activities. Another expenditure of manufacturers about pharmacists is related with representatives. Similar to the physician directed efforts, pharmacists are informed by the representatives about the drugs recently introduced in the market. Representatives also distribute brochures and posters of new drugs supplied by their companies and ask pharmacists to display them in the pharmacy. By doing this, manufacturers try to influence the decision of patients in cash segment. A patient meeting his/her expense fully out of pocket can be directed to the intended drug by these brochures while he/she is waiting for his/her turn in the pharmacy.

The strategy of the manufacturers for the wholesaler is very similar with the strategy for the pharmacists. In some cases, manufacturers give discount directly to wholesalers instead of pharmacies and these discounts are partially reflected to pharmacists by wholesalers. Wholesalers negotiate with manufacturers for the amount of discount in return for access to pharmacies working with these wholesalers. After that, wholesalers pass on part of the discount to the pharmacist so as to get the maximum possible profit.

3.4 Pharmacies

Pharmacies are key institutions that enable public access to medication. In Turkey, pharmaceuticals are only sold in pharmacies under the supervision of a licensed pharmacist. Apart from their social role in the society, pharmacies are operated with commercial motives. The main revenue of the pharmacies come from pharmaceuticals, with 78% of payments coming from government reimbursement, and coinsurance and payments from the patients making up the rest with a small contribution from private health insurance (Kızıltan et al., 2004). The pharmacy profit margin is regulated by the government, like the profit margins of other players in the supply chain. The retail prices of drugs are determined during the licensing process and are fixed apart from exchange rate related changes (Kanavos et al., 2005). Therefore, it is not very much likely for pharmacist to change the profit coming from a drug drastically. Table 3.2 gives the profit margins of both pharmacist and wholesaler predetermined by Turkish government in 2004.

Factory Price (YTL)	Wholesaler (%)	Pharmacy (%)
<10	9	25
10-50	8	24
50-100	7	23
100-200	4	16
>200	2	10

Table 3.2: Regulated profit margins for pharmacies and wholesalers

When the patient is willing to pay whole retailer price of the drug out of pocket, almost any drug, can be supplied by the pharmacist without a prescription. Patients can take pharmacist's advice without visiting the physician. Thus, Turkish pharmacists arguably play a more important role in the pharmaceutical system than their colleagues in most of the European countries and the US. Further, they can substitute the prescribed drugs of patients reimbursed by the government with cheaper bioequivalent alternatives. The substitutions can result in objections from physicians and patients who feel that the generic drug is not a perfect substitute for the prescribed original. Manufacturers offer attractive discounts to the pharmacists to encourage substitution of competitor and discourage own substitution. As mentioned in the previous section, because of the strictly regulated pharmacy profit margins, manufacturers offer discounts by providing free goods with purchase of a certain quantity, which is known as "*mal fazlası*". Substitution typically occurs from original drug to its generic alternate, and it is called "Generic substitution".

3.5 Comparison of Pharmaceutical Industry between US and Turkey

The pharmaceutical industry in the United States was a large and important industry in 2002, whose size was estimated at $193 billion which has grown at a double-digit rate in the last two decades [24]. The US is ranked first in pharmaceutical expenditures per capita among all OECD countries. Therefore, the huge amount of monetary transactions among different parties of the industry necessitates a mediator agent for United States. Other than the end consumer, manufacturers, physicians, governments, private insurers, wholesalers and pharmacies, one of the main participants in US pharma industry is pharmacy benefit manager (PBM). Pharmacy benefit manager, a key player in the pharmaceutical marketing channel, manages the relationship between the pharmaceutical companies and the insurers (government or private insurance companies). They are compensated directly by insurers for this task. Like any other for-profit business, the PBM's objective is also to maximize profits. PBMs do this by securing drug price rebates from drug makers and discounts from pharmacists in exchange for a contract fee from insurers. The most common technique used by PBMs in order to put downward pressure on prescription drug prices is mediation between insurers and drug manufacturers with respect to large volume purchases of drugs. Drug makers agree to pay rebates in exchange for a better place for the purchased drugs on the formularies. These formularies are designed by PBMs for insurers. PBMs also design generic substitution plans for insurers to lower their costs. These plans indicate when it is appropriate for prescribers to substitute a generic version of a drug for a brand name.

PBMs subcontract with third-party payers such as government, health plans, health insurance companies or employers. At present, over 175 million people are served by PBMs in US. PBMs process over sixty percent of all retail drug prescriptions by third-party payers [25].

Although a structuring with the mediation of PBM does not exist in Turkey, pharmaceutical manufacturers still give discounts to make their products more preferable. However, in Turkey this rebate deals take place between manufacturers and vendors of the drugs (wholesalers and pharmacists). This attitude eliminates the interest of government which could have been as a share of the discount coming from manufacturers otherwise. One of the main problems, Turkish government encounters with in cost containment strategies, is the lack of a system that enables them receive discounts from manufacturers. As mentioned before, governments give authority to pharmacists for generic substitution if the price of the drug given is less than the price of the prescribed drug and it is listed as a generic substitute in the positive list. At the first glance this action seems reasonable to decrease public health expenditures. However; since the decision of the pharmacist about substitution is purely commercial in most cases, they substitute a prescribed drug for its generic only if the discount offered by the generic manufacturer justifies the substitution.

Actually, there exists a resemblance between PBM and pharmacists in terms of their bargaining power with manufacturers. In US system PBM takes the advantage of volume discount while negotiating for discounts. In Turkish system wholesalers and pharmacists use their generic substitution authority while receiving rebates from drug manufacturers. PBMs are only offered discounts from original drugs and they use their influence on physician for prescribing generics as a tool that increases their bargaining power. On the other hand, Turkish pharmacists mainly take their rebate deals from generic manufacturers (which are also drugs with brand names in Turkish market) and they use their direct power on substituting a prescribed drug with its generic [4]. The main distinction between two systems is the desire that they show to preserve the interest of the government. PBMs are compensated directly by insurers (government) and execute their rebate negotiation activities on behalf of their customers. However, wholesalers and pharmacists in Turkey negotiate for rebates coming from generic manufacturers without considering the interest of any agent except theirs. For this reason government are unable to take advantage of these rebates.

Figure 3.1 and Figure 3.2 summarize the cash flow in Turkish and US market respectively. As it can be seen in these tables, wholesalers and pharmacists in Figure 3.1 take the place of PBM in Figure 3.2 so that they become agents taking rebates from manufacturers. Also again in Figure 3.1 it can be observed that government cannot take any portion of these rebates offered to pharmacy.

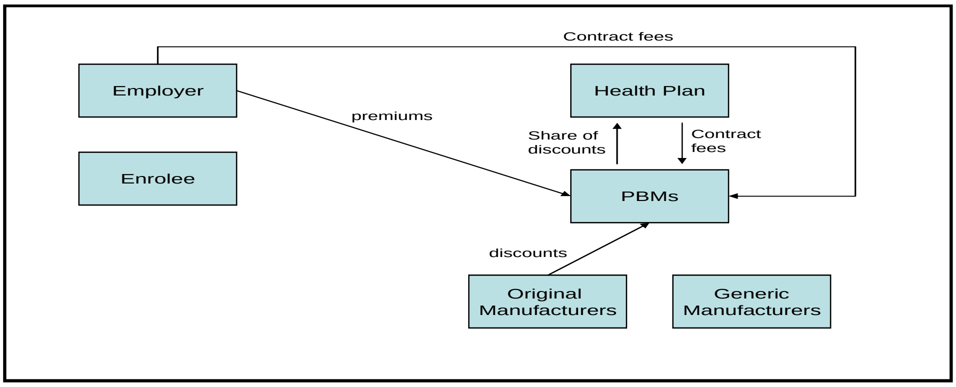


Figure 3.2: Cash Flow in US Pharma Industry (adapted from Cohen (2000) [25])

Chapter 4

OPTIMAL PHARMACY ACTION

4.1 The Model

As mentioned earlier; like all other retailers, pharmacies and pharmaceutical manufacturers would like to maximize profits. We construct a mathematical model of the pharmacist's drug substitution and recommendation decision, in order to gain insights into the incentives of the players. A similar model of the US system focusing on the pharmacy benefit managers (PBM) and the manufacturers' decisions was developed by Gür Ali et al. (2006) [20].

Since private sector companies can only cover 1% of total population in Turkey [4], we omit the patients enrolled in private health insurance programs at this study. We consider the remaining consumers of the prescription drugs in two segments: the reimbursed segment and the cash segment. The *reimbursed segment* contains patients covered by the government reimbursement system who pay a coinsurance. The remaining consumers who meet their drug expenses totally out of pocket constitute the *cash segment*. k = 1 (reimbursed) and = 2 (cash) denote the two segments.

We also consider a therapeutic drug market, comprised of two medications that can treat the same problem (e.g., high cholesterol). The two drugs in our analysis, the original (i = 1) and the generic (i = 2), are in the same equivalence class. The retail price of the original is higher than that of the generic ($Price_1 > Price_2$), as the generics are obliged in a lower retail price than the original during the licensing process. This relationship holds in all but very few extreme cases where the original manufacturer lowered its price to prevent substitution of its prescriptions by the generic. The out-of-pocket expenditure of a patient from segment k purchasing drug i (OOP_{ik}) is $Price_i$ times the co-insurance rate in segment k, plus $Price_i$ in excess of the reference price; i.e.; 130%*$Price_2$.

In our model we handle the maximization problem of both pharmacy and manufacturers in reimbursed and cash segment separately to mitigate the complexity of our analysis. Namely, we assumed that both drugs are consumed either by reimbursed patients or patients paying whole price out of pocket. The profit coming from reimbursed segment will be the focal point for the “reimbursed segment analysis” and the cash segment profits of both manufactures will be examined in our "cash segment analysis". Reimbursed segment analysis involves two focal reimbursed drugs contained in the reimbursement list of the government. We assumed that the majority of these drugs are consumed by publicly reimbursed patients so that the pharmacy and manufacturers concentrate their effort only on maximization of profits coming from this segment. We assume, on the other hand, cash segment analysis will investigate two drugs from a therapeutic class that is not covered by the government which means the cash segment revenues are the only matter of concern for pharmacy and manufacturers. Thus, the choice of only a specific segment for profit maximization would not damage the integrity of our analysis.

Figure 4.1 depicts the possible actions of cash patients, taking action to relieve their condition, leading to the purchase of a drug. These patients may choose to visit physician and potentially get a prescription; or go directly to the pharmacy and request a specific drug; or ask for pharmacist's advice for a treatment. The pharmacist has no influence on the patients requesting a specific drug.

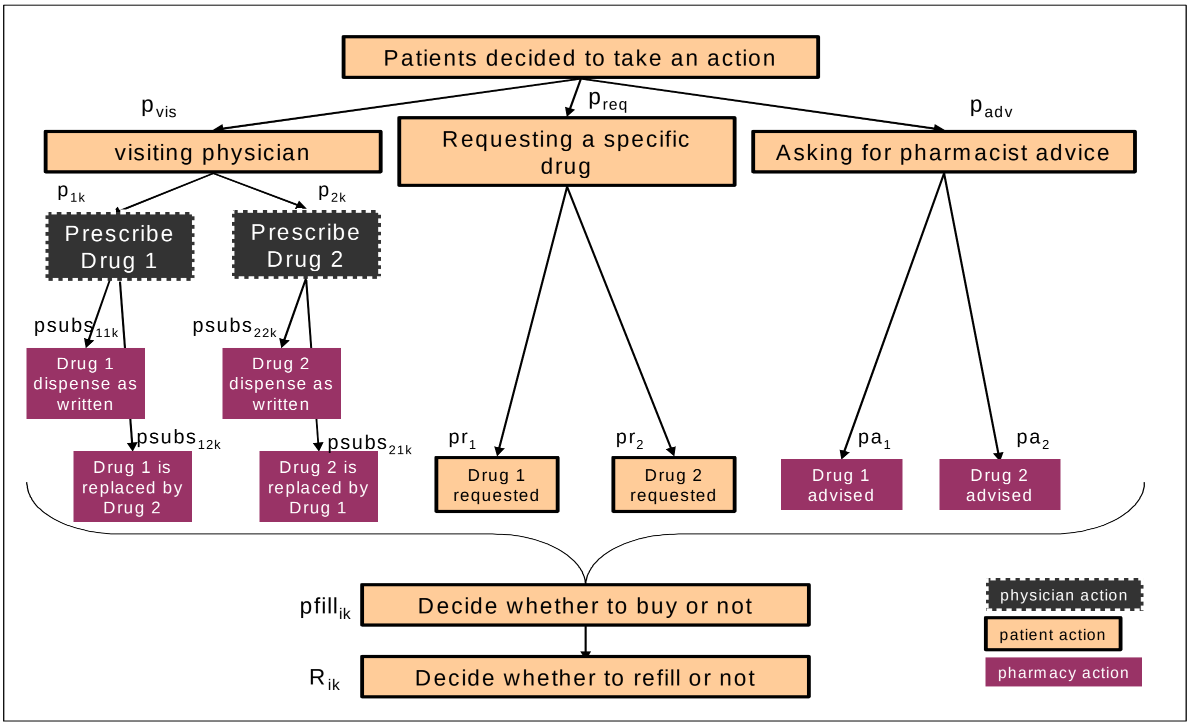


Figure 4.1: Drug Filling Process for cash segment patients

We let p_{vis}, p_{req}, p_{adv} denote the fraction of cash paying patients who choose to visit the physician, request a medication at the pharmacy, and ask for pharmacist's advice, given that they are taking an action, respectively. We also let pr_i, denote the fraction of patients directly requesting drug *i,* given that they have requested a drug; and pa_i denote the fraction of patients being advised drug *i,* given that they have asked for pharmacist's advice. Here, p_{vis} + p_{req} + p_{adv} = 1; $pr_1 + pr_2$ = 1. We assume that the pharmacist dispenses the patient one of the two drugs when asked for advice: $pa_1 + pa_2$ = 1. Since patients must visit a physician to obtain a prescription, all reimbursed segment patients follow the left-most path starting with the "visiting physician" box in Figure 4.1. The probability of each possible action for each segment can also be seen in Table 4.1.

	Prob. of visiting physician	**Prob. of asking for pharmacist's advice**	**Prob. of directly requesting a drug**
Reimbursed segment	1	0	0
Cash segment	p_{vis}	p_{adv}	p_{req}

Table 4.1: *The probability of each possible action in each segment*

For patients who visit the physician, the physician either prescribes one of the two drugs or recommends a different treatment. We denote the fraction of segment *k* patients visiting the physician, who get drug *i* prescribed by p_{ik} Є [0,1]. The pharmacist can substitute this prescribed drug in the same equivalence class with any other drug for cash patients but only with its less expensive alternative for reimbursed patients. This along with $Price_1 > Price_2$ implies that a reimbursed patient with the original prescription can get the generic dispensed by the pharmacy, but not the other way around. The fraction of segment *k* patients, who are dispensed drug *i* instead of prescribed drug *j,* is given by $psubs_{ijk}$ Є [0,1]. Here, $psubs_{iik}$ stands for the proportion of patients from segment k, who were dispensed drug *i* as written in the prescription. Therefore, $psubs_{i1k}$ + $psubs_{i2k}$ = 1 for each drug *i* and segment *k*. Notice that $psubs_{211}$ = 0, as explained earlier.

Turning to the patient, she might choose to fill the prescription by paying for her out-of-pocket payment or not purchasing the drug at all. Let $pfill_{ik}$ Є [0,1] denote the fraction of patients from segment *k* filling the drug *i*. Like any consumer, patients are price sensitive customers of the prescription drugs, so $pfill_{ik}$ is a decreasing function of out-of-pocket expenditure (OOP_{ik}).

Let n_{ik} denote the number of patients from segment *k*, who are (ultimately) treated with drug *i*, where N_k denotes the total number of sufferers who take action in segment *k*.

$$n_{i1} = N_1 * \left[\sum_{j=1}^{2} (p_{j1} * psubs_{ji1}) \right] * pfill_{i1} \quad \text{for } i=1,2 \qquad \textbf{(4.1)}$$

$$n_{i2} = N_2 * \left\{ \begin{array}{l} p_{vis} * \left[\sum_{j=1}^{2} (p_{j2} * psubs_{ji2}) \right] \\ + p_{adv} * pa_i + p_{req} * pr_i \end{array} \right\} * pfill_{i2} \quad \text{for } i=1,2 \qquad \textbf{(4.2)}$$

In (4.1) and (4.2), we assume the physician to be a perfect agent who is only concerned with the utility of his/her patient. The physician's choice is affected by the quality assessment of the drugs, the information he/she receives about the drugs in the form of detailing, and the concern about the patient's out-of-pocket expense. This choice (p_{ik}) is given by the ratio of drug i's attraction to the sum of the attractions of the two alternatives and the outside good option. The attraction of drug i , $\xi(Det_i, Q_i, OOP_{ik}) \geq 0$ for all i =1,2, is an increasing function of its intrinsic quality (Q_i), and own detailing effort (Det_i), and decreasing function of segment k patient's out-of-pocket expenditure to purchase drug i (OOP_{ik}); Finally, p_{ik} is increasing in own and decreasing in competitor attraction:

$$p_{ik} = \frac{\xi(Det_i, Q_i, OOP_{ik})}{\xi(Det_1, Q_1, OOP_{1k}) + \xi(Det_2, Q_2, OOP_{2k}) + 1} \qquad \textbf{(4.3)}$$

In equation 4.3; since physician may always choose an outside treatment instead of the prescription of either drug, we assumed $\sum_i p_{ik} < 1$ in each segment.

In equation 4.1 and 4.2, further, we assumed that no matter what is the process before pharmacy dispenses the drug -whether directly requesting the drug, dispensed by the advice of the physician or subject to pharmacy substitution- patient will choose to fill the drug with the same probability $pfill_{ik}$. Whether the patient complains about the substitution or not, the filling probability will only be the function of out-of-pocket expenditure of the drug which is ultimately dispensed by the pharmacy.

The expected number of refills by a patient of segment k who filled the first prescription for drug i (R_{ik}), captures the compliance and persistence behavior in chronic categories. Since same drivers are valid for both, we posit that R_{ik} is an increasing function of $pfill_{ik}$.

4.2 Pharmacist objective function

The pharmacist's objective function within this restricted situation becomes profit maximization with three components: the revenues from patients and the government reimbursements, the cost of goods sold, and the cost of dealing with patients and doctors complaining about the substitution made by pharmacist. In some cases, physicians and patients think that although generics are less expensive for most therapeutic classes, a saving acquired by the use of a generic can become a higher cost if switching from the original to generic results in a change in clinical course of the illness being treated [26].In equation (4.4), the complaint cost of drug *i* in segment *k* (CC_{ik}) quantifies the future revenue loss caused by this change in clinical course or the sufferer's (or physician's) objection to the substitution of drug *i*. We assume that a sufferer complains only when she would have filled prescribed drug if not substituted. We also assume that the higher the detailing for the prescribed drug, and he higher the number of substitutions, the higher the probability of a complaint. C_{comp} stands for the future revenue loss of a single complaint (or dissatisfaction) of a patient or her doctor about pharmacist's substitution.

$$CC_{ik} = C_{comp} * pcomp_{ik} * Nsubsfill_{ik} \qquad \textbf{(4.4)}$$

$Nsubsfill_{ik}$ stands for the number of segment *k* patients subject to substitution of drug *i*:

$$\begin{aligned} Nsubsfill_{11} &= N_1 * p_{11} * psubs_{121} * pfill_{11} \\ Nsubsfill_{21} &= 0 \\ Nsubsfill_{12} &= N_2 * p_{12} * psubs_{122} * pfill_{12} \\ Nsubsfill_{22} &= N_2 * p_{22} * psubs_{212} * pfill_{22} \end{aligned} \qquad \textbf{(4.5)}$$

Further, $pcomp_{ik}$ stands for the probability of complaint about drug *i*'s substitution in segment *k*, which is an increasing function of drug *i*'s detailing (Det_i) and drug *i* substitutions ($Nsubsfill_{ik}$):

$$pcomp_{ik} = \alpha_{lin} * \psi(Det_i) + \alpha_{quad} * \psi(Det_i) * Nsubsfill_{ik} \qquad \textbf{(4.6)}$$

Here, ψ is an increasing function of Det_i, and α_{lin} and α_{quad} are the coefficients for linear and quadratic components of the complaint cost, respectively.

Thus, we express the pharmacist's objective function for segment k drugs (PP_k) as follows:

$$PP_k = \sum_{i=1}^{2} n_{ik} * (1 + R_{ik}) * \Pr ice_i - \sum_{i=1}^{2} \left[n_{ik} * (1 + R_{ik}) * \frac{\Pr ice_i}{1 + pm_i} * (1 - disc_{ik}) \right] - \sum_{i=1}^{2} CC_{ik} \qquad \textbf{(4.7)}$$

In equation 4.7, pm_i stands for the profit margin of pharmacies regulated by the government, which differs by factory price intervals, hence we distinguish by the drug's index *i*. Finally, $disc_{ik}$ is the effective discount rate offered to the pharmacist as "*mal fazlası*" by manufacturer *i* which sells its drugs to segment *k* patients.

4.3 Pharmacy Optimal Decision

The pharmacist maximizes (4.7) with respect to $psubs_{ijk}$ and pa_i; anticipating the demand for drug i, as given by (4.1) and (4.2), the complaint cost, as given by (4.4), and considering cost of goods altered by the discounts $disc_i$. The solution to the problem follows from the Theorem of Karush-Kuhn-Tucker (KKT) sufficient optimality conditions [27].

Since the pharmacy decisions for a segment do not have any influence on the decisions of the other segment, we consider the segment optimizations independently. For the sake of brevity, we focus on the more complicated cash segment (k = 2) problem, and apply "KKT Sufficient Conditions" Theorem. The optimal decisions for (k = 1) become a special case of (k = 2) with p_{vis}=1 and p_{req} = 0, p_{adv} = 0, and $psubs_{211}$ = 0.

Let $x = \{psubs_{111}, psub_{121}, psubs_{212}, psubs_{222}, pa_1, pa_2\}$. Consider Problem P to

Maximize $f(x)$: the profit from only cash segment

Subject to $h_i\ (x) = 0$ for i = 1, 2

$g_{ij}\ (x) \geq 0$ for i, j = 1, 2 where

$$f(x)=\sum_{i=1}^{2} n_{i2} * pfill_{i2} * (1+R_{i2}) * \left[\Pr ice_i - \left(\frac{\Pr ice_i}{1+pm_i}\right) * \left(1-disc_i\right)\right]$$

$$-C_{comp} * \psi(Det_1) * \left(\alpha_{lin} * \left[N_2 * p_{vis} * p_{12} * psubs_{122} * pfill_{12}\right] + \alpha_{quad} * \left[N_2 * p_{12} * p_{vis} * psubs_{122} * pfill_{12}\right]^2\right)$$

$$-C_{comp} * \psi(Det_2) * \left(\alpha_{lin} * \left[N_2 * p_{vis} * p_{22} * psubs_{212} * pfill_{22}\right] + \alpha_{quad} * \left[N_2 * p_{22} * p_{vis} * psubs_{212} * pfill_{22}\right]^2\right)$$

$h_i(x) = 1 - psubs_{i12} + psubs_{i22}$ for i = 1, 2 ; $g_{ij}(x) = psubs_{ij2}$ for i, j = 1, 2

4.3.1 Karush Kuhn Tucker Theorem (KKT Sufficient Conditions)

Let $\bar{x}$ be a feasible solution and let I = {{i,j}: $g_{ij}\ (\bar{x})$ = 0}. Suppose that the KKT conditions hold at $\bar{x}$, that is, there exists scalars $\bar{u}_{ij} \geq 0$ for {i,j} Є I and $\bar{v}_i$ for i = 1, 2 such that

$$\nabla f(\bar{x}) - \sum_{\{i,j\}\in I} \bar{u}_{ij} \nabla g_{ij}(\bar{x}) - \sum_{i=1}^{2} \bar{v}_i \nabla h_i(\bar{x}) = 0 \quad \textbf{(4.8)}$$

Then, since f is a concave function, $\bar{x}$ is a global optimal solution to Problem P. The details related to the implication of "KKT Sufficient Conditions" theorem in our problem are provided in Appendix A.

After applying above theorem to various $psubs_{ij2}$ and pa_i combinations, the optimal pharmacy decision is found as follows. The pharmacist's optimal decisions for reimbursed segment (k = 1) and cash segment (k = 2) are given by 4.9 and 4.10 respectively.

$\{psubs_{111}, psubs_{121}\}$ =

D1: $\{0, 1\}$ if $Pow_{21} - Pow_{11} \geq A_{11} + B_{11}$

D2: $\{1\text{-}X_{11}, X_{11}\}$ if $A_{11} \leq Pow_{21} - Pow_{11} \leq A_{11} + B_{11}$ **(4.9)**

D3: $\{1, 0\}$ if $Pow_{21} - Pow_{11} \leq A_{11}$

$\{psubs_{112}, psubs_{122}, psubs_{212}, psubs_{222}, pa_1, pa_2\}$ =

D1: $\{0, 1, 0, 1, 0, 1\}$ if $Pow_{22} - Pow_{12} \geq A_{12} + B_{12}$

D2: $\{1\text{-}X_{12}, X_{12}, 0, 1, 0, 1\}$ if $A_{12} \leq Pow_{22} - Pow_{12} \leq A_{12} + B_{12}$

D3: $\{1, 0, 0, 1, 0, 1\}$ if $0 \leq Pow_{22} - Pow_{12} < A_{12}$

D4: $\{1, 0, 0, 1, Y, 1\text{-}Y\}$ if $Pow_{12} - Pow_{22} = 0$ **(4.10)**

D5: $\{1, 0, 0, 1, 1, 0\}$ if $0 \leq Pow_{12} - Pow_{22} \leq A_{22}$

D6: $\{1, 0, X_{22}, 1\text{-}X_{22}, 1, 0\}$ if $A_{22} \leq Pow_{12} - Pow_{22} \leq A_{22} + B_{22}$

D7: $\{1, 0, 1, 0, 1, 0\}$ if $Pow_{12} - Pow_{22} \geq A_{22} + B_{22}$

In Equations (4.9) and (4.10) for i = 1, 2 and k = 1, 2:

$$Pow_{ik} = pfill_{ik} * (1 + R_{ik}) * \left[\Pr ice_i - \left(\frac{\Pr ice_i}{1 + pm_i} \right) * \left(1 - disc_{ik}\right) \right] \quad \textbf{(4.11)}$$

$$A_{ik} = C_{comp} * \psi(Det_i) * \alpha_{lin} * pfill_{ik} \quad \textbf{(4.12)}$$

$$B_{i1} = C_{comp} * \psi(Det_i) * 2 * \alpha_{quad} * N_1 * p_{i1} * pfill_{i1}^2$$
$$B_{i2} = C_{comp} * \psi(Det_i) * 2 * \alpha_{quad} * N_2 * p_{vis} * p_{i2} * pfill_{i2}^2 \quad \textbf{(4.13)}$$

$$X_{1k} = \frac{Pow_{2k} - Pow_{1k} - A_{1k}}{B_{1k}} \quad , \quad X_{2k} = \frac{Pow_{1k} - Pow_{2k} - A_{2k}}{B_{2k}} \quad \textbf{(4.14)}$$

Y is any real number between 0 and 1.

Each optimal decision region, D1 to D3 in 4.9, and D1 to D7 in 4.10, is identified with respect to the power difference between two drugs. Pow_{ik} is the expected profit of the pharmacist from introducing a segment k patient to drug i. It depends on the probability to fill, the expected number of fills and the marginal profit from each fill, which is determined by government dictated margins, the retail price and the manufacturer discounts. As the power difference increases in favor of a drug, the pharmacist moves more patients toward the drug, starting with non-prescription cash patients. The non-prescription dispensing decisions are 0-1 functions except when there is no power difference between two drugs, when the pharmacist is indifferent in pa_i, as in D4 in 4.10. The substitution rate (X_{ik}) depends on the power difference as well as the complaint parameters, as in D2 at 4.9, and in regions D2 and D6 at 4.10. The A_{ik} and B_{ik} expressions give the thresholds for power difference implying the decision region boundaries. They are complaint parameters controlled by the patient and physician, and pharmaceutical manufacturers through detailing: ψ is an increasing function of Det_i while p_{ik} increases with own detailing and decreases with competitor's detailing. Figure 3 and 4 will provide a better understanding about the pharmacy decision. In Figure 3, the profit maximizing decision of pharmacy in reimbursed segment is demonstrated by optimal decision regions from D1 to D3. Likewise, Figure 4 gives the optimal decision regions of pharmacy where substituting ad non-prescription dispensing decisions are clearly identified.

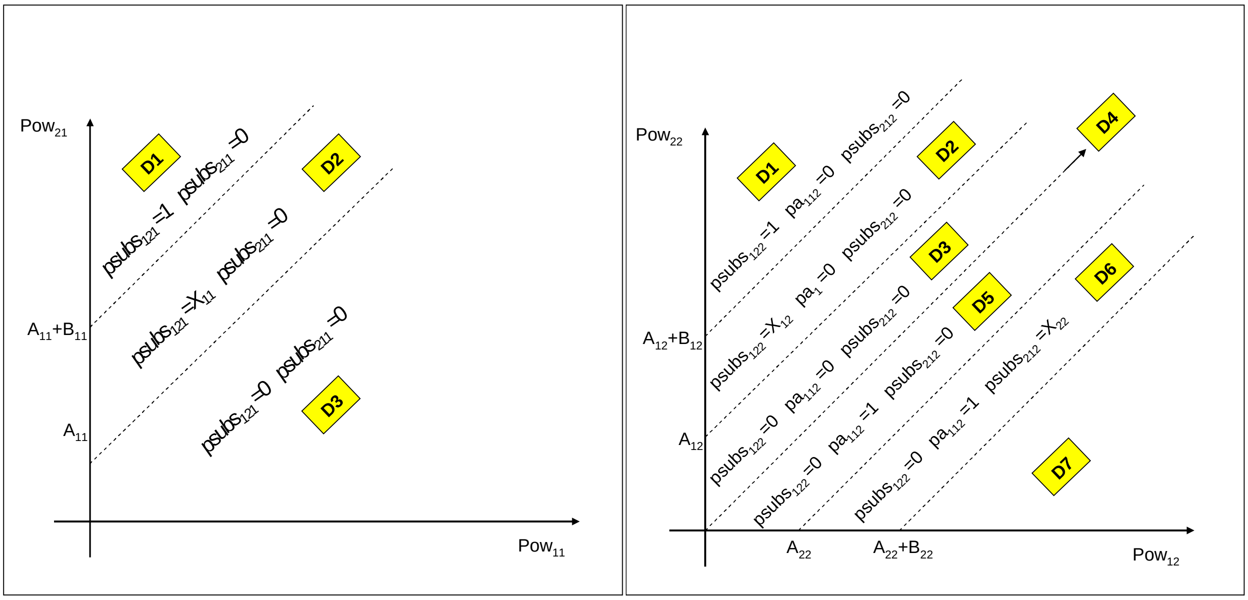


Figure 4.2 and Figure4.3: Pharmacy Optimal Decision in Reimbursed Segment; Pharmacy Optimal Decision in Cash Segment

4.4 The Effect of Manufacturer on Pharmacy Decision

We investigate each manufacturer firm separately due to the non-symmetric nature of substitution in the reimbursed segment. The sales of drug *i* in reimbursed and cash segments are defined with the expressions in 4.15 and 4.16 respectively.

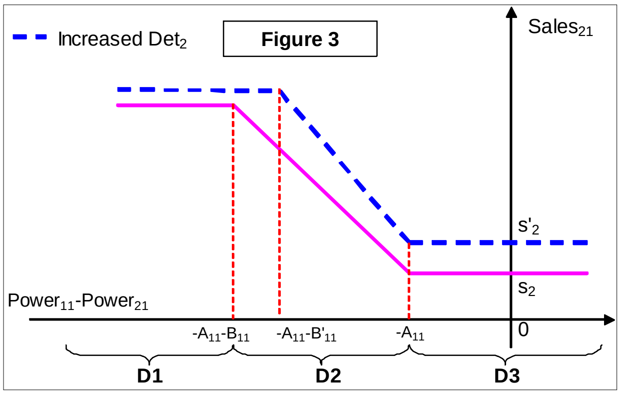
$$sales_{i1} = N_1 * (p_{11} * psubs_{1i1} + p_{21} * psubs_{2i1}) * pfill_{i1} * (1 + R_{i1}) \quad \textbf{(4.15)}$$

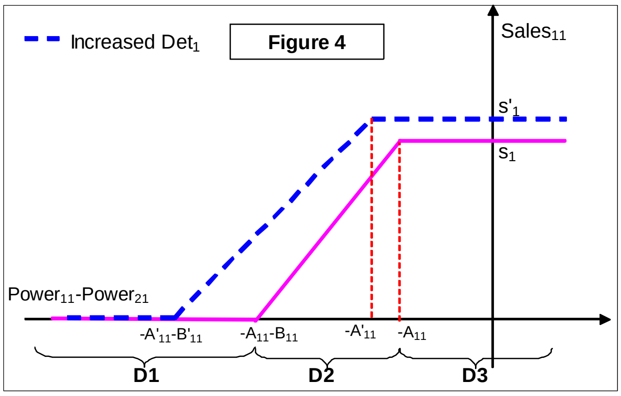
$$sales_{i2} = N_2 * \left[p_{vis} * (p_{12} * psubs_{1i2} + p_{22} * psubs_{2i2}) + p_{adv} * pa_i + p_{req} * pr_i \right] * pfill_{i2} * (1 + R_{i1}) \quad \textbf{(4.16)}$$

First, consider the reimbursed segment in which only substitution from the original more expensive drug 1 to the generic drug 2 is allowed. The generic manufacturer can use pharmacy discounts to substitute the prescribed original. The solid line in illustrative Figure 4.4 shows sales of the generic drug in the reimbursed segment, $Sales_{21,}$ as a function of the power difference of two drugs ($Pow_{11} - Pow_{21}$). It is obtained by substituting the optimal decision of the pharmacist 4.9 in the sales equation 4.15. When the generic manufacturer increases the discount ($disc_2$), the power difference decreases, and we move to the left in the graph. Based on Figure 4.4, $disc_2$ will have an effect on generic sales only if it is above a threshold, corresponding to the power difference $-A_{11}$ and the sales will increase with increasing discount until power difference reaches another threshold ($-A_{11}$ - B_{11}) after which there is no more benefit of additional discount.

The dashed line in Figure 4.4 shows the generic sales vs. the power difference at an increased level of generic detailing. The increase in generic manufacturer's detailing (Det_2) causes increase in generic prescribing probability (p_{21}) and decrease in original prescribing probability (p_{11}). Thus, A_{11} would stay unchanged while B_{11} decreases to B'_{11}. Meanwhile, the sales of drug 2 when there is no substitution increases from s_2 to s'_2 due to higher (p_{21}). Consequently; for all power difference values, the drug 2 sales in reimbursed segment increase with increasing Det_2.

The solid line in Figure 4.5 shows sales of the original drug in the reimbursed segment as a function of the power difference ($Pow_{11} - Pow_{21}$). Similar to generic manufacturer case, when the original drug increases the discount given to pharmacy ($disc_1$), increasing the power difference in favor of drug 1 we move to the right in the graph. The maximum sales the original manufacturer can capture in this segment are due to keeping of all its own prescriptions.





Figures 4.4 and 4.5: Sales of Drug 2 in Reimbursed Segment; Sales of Drug 1 in Reimbursed Segment

On the other hand, if original manufacturer becomes more aggressive in its detailing expenditures, the sales function shifts as shown with the dashed line in Figure 4.5. As discussed earlier, A_{11} and B_{11} are increasing functions of Det_1. Therefore A_{11}, $B_{11,}$ and s_1, (sales of drug 1 when there is no substitution) increase to A'_{11}, B'_{11}, and s'_1. Further, when the current decision of manufacturer implies a power difference between $-A'_{11}$ and $-A'_{11} - B'_{11}$ in Figure 4.5; a higher level of drug 1 detailing induces higher complaint probability and prescribing probability (p_{11}), which decreases the optimal substitution probability (X_{11}) for the same power difference. Therefore, detailing by the original increases its sales by increasing the amount of discounting needed by the generic to make substitution profitable and by decreasing substitution rates for a given level of power difference, as well as by increasing the un-substituted sales volume.

Let us now consider the cash segment where pharmacy is allowed to substitute any one of the drugs for the other one. Although we conduct the relevant analysis for only original manufacturer, one can easily infer similar results for generic manufacturer. Figure 4.6 is the drug 1 sales vs. power difference graph for cash segment. Since generic drug is also substitutable in cash segment, original manufacturer can incentivize the pharmacist to replace the generic with the original, by giving enough discounts to increase the power difference and eventually moving the pharmacist decision to the right, as seen in 4.6.

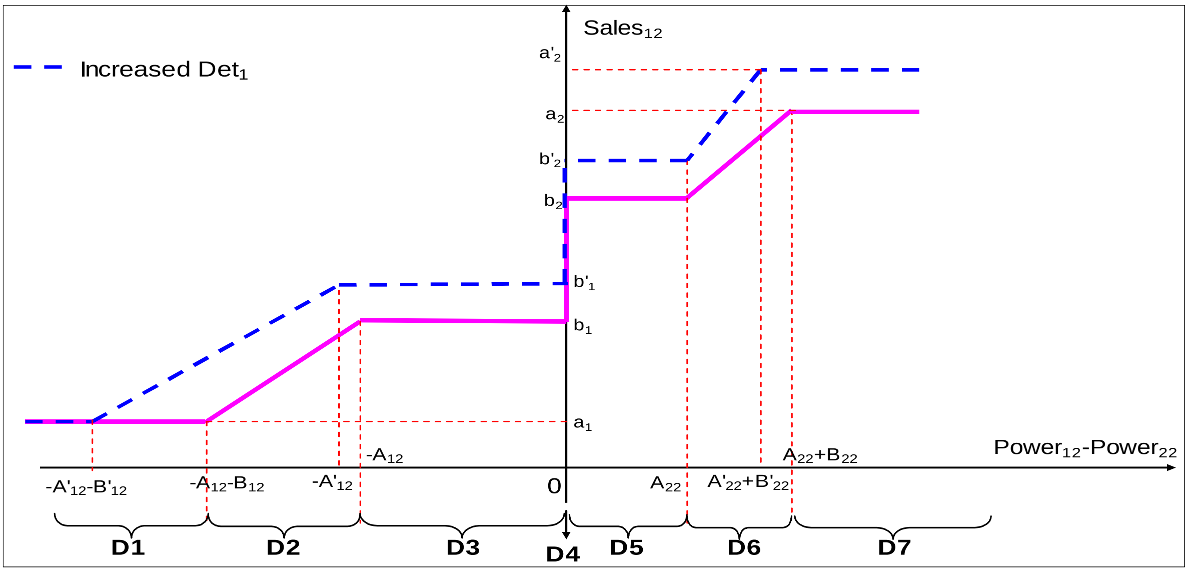


Figure 4.6: Sales of Drug 1 in Cash Segment

On the other hand; if original manufacturer starts to spend more aggressively on detailing (Det_1), the graph would become the dashed line in Figure 4.6. Here we can observe that as long as the power difference between drug 1 and 2 ($Pow_{11} - Pow_{21}$) remains less than a specific value ($-A'_{12} - B'_{12}$), drug 1 sales in cash segment ($sales_{12}$) remain unchanged with increasing Det_1. This means detailing does not help the original manufacturer if all of its drugs are replaced with the generics. Further; increasing Det_1 decreases ($A_{22}+B_{22}$), which is the threshold needed to capture all of generic drugs prescribed, and the original manufacturer captures all prescribed generic drugs in the cash segment. Furthermore; increasing Det_1 causes higher drug 1 sales in cash segment for all power difference levels higher than $-A'_{12} - B'_{12}$. Finally, in region D6 where some of the prescribed drugs of generic manufacturer are replaced with original drugs, it can be seen that the line becomes steeper. This means, in region D6, every incremental pharmacy discount offered by original firm will have a greater effect on original manufacturer's sales with increased original detailing. This outcome designates the *synergistic* effect of detailing and pharmacy discount. In region D6 substitution rate from generic to original ($psubs_{212}$) is given by equation 4.14. Increasing pharmacy discount will result in an increase in power level difference in favor of original firm (Pow_{12}-Pow_{22}). Further, a positive shift in original detailing will make p_{22} and in return B_{22} to decrease. Thus, simultaneous increase in detailing and pharmacy discount of original firm create a multiplicative effect in equation 4.14 and cause substitution from original to generic

($psubs_{212}$) to increase more than the total of that detailing and discount can do separately. ($\frac{\partial psubs_{212}}{\partial Det_1} > 0$ will verify this result.)

All the results stated in this section concentrate on the effect of manufacturer's actions on pharmacy decision and in return the ***sales*** of the corresponding manufacturer in a particular segment. However, it should be kept in mind that ***profitability*** is another issue. Profit maximizing manufacturers will look for a detailing and discounting combination that maximizes profit in corresponding segment rather than or in addition to the highest possible sales amount.

Chapter 5

OPTIMAL DISCOUNTING DECISIONS OF PHARMACEUTICAL COMPANIES

5.1 Pharmaceutical Companies

As discussed before, pharmaceutical manufacturers are the producers of both generic and original prescription drugs and the main source of their revenues is the sales of these drugs to pharmacies.

In our study we stated that three distinct variables controlled by manufacturers are the detailing activities, DTC advertising and the discounts given to pharmacies. We have mentioned the regulations about direct-to-customer advertising campaigns in Section 3.3.1. Because of their limited utilization by the manufacturers, we exclude these DTC expenditures from our analysis.

The most common detailing activities are listed in 3.3.2. Although pharmaceutical companies can invest in detailing by various means, the most preferred practice is the introduction of the drug and detailing of the medical specifications of the drug to the physicians via sales representatives of the company. All detailing expenditures relying on sales representative efforts require a comprehensive planning of the sales forces of the company. Recruitment process, training period and delayed effect of detailing on physician's prescription behavior designates a long term marketing plan.

On the other hand, the decision related to discount offered to pharmacies is not a consequence of such longer term strategy. A firm can decide on how much discount to propose and can instantly put this discount decision into effect in the form of "mal fazlası" as discussed in Chapter 3.

Keeping this crucial distinction between detailing and discounts in mind, we try to identify the rational decisions of both generic and original drug manufacturers in the proceeding sections. Although the amount of financial investment on detailing is a critical decision, we assumed that it is determined beforehand by the sales and marketing department of pharmaceutical companies. In this circumstance, the only short-term decision remaining for a producer turns to be the "discount to the pharmacy" ($disc_{ik}$).

The notion Pow_{ik}, first introduced in Chapter 4, is used to identify the decision variables of two firms in the model. Pow_{ik} is the expected profit of the pharmacist from introducing a segment k patient to drug i and it is an increasing function of $disc_{ik}$ as described before.

$$Pow_{ik} = pfill_{ik} * (1 + R_{ik}) * \left[Price_i - \left(\frac{Price_i}{1 + pm_i} \right) * \left(1 - disc_{ik}\right) \right] \quad \textbf{(5.1)}$$

The optimal decision of manufacturers will be represented in terms of Pow_{ik} rather than $disc_{ik}$ in order to ease the quantitative analysis. Keeping all other parameters fixed, Pow_{ik} is linear in $disc_{ik}$. Therefore, this temporary conversion of discounting decision into some other variable as given by Equation 5.1 does not alter the ultimate results. In the sensitivity analysis stage we will transform the optimal value of Pow_{ik} into discounting decision variable ($disc_{ik}$) by again employing the inverse of Equation 5.1 with respect to $disc_{ik}$.

The analysis are documented for cash segment in Section 5.3.2 and 5.3.3 and for reimbursed segment in Section 5.3.3.

5.2 Manufacturer Objective Function

All profit-making enterprises aim to maximize the monetary value remaining in their hand after all the operational, administrative and research oriented costs are deducted. The same motive definitely holds for the pharmaceutical companies too. However, unlike many other industries, the operational cost of pharmaceuticals is relatively low when compared with its revenue. In our analysis we also focus on two drugs that are already introduced in the market, so there is no point in including R&D cost in our model. Thus, we exclude the cost of goods sold (COGS) from the objective function of the manufacturer and approximate the profit to be the net revenue coming from the sales of drug to pharmacies.

The pharmaceutical industry is one of the industries that spend intensively on advertising activities. Even promotional expenditures sometimes exceed the spending on R&D [19]. Again according to Schweiter (1997) [28], the marketing expenses of Merck, Pfizer and Eli Lilly vary between 21% and 40% of annual sales. In pharmaceutical market, the biggest proportion of these marketing expenditures relies on detailing. For instance, in US almost one-third of whole marketing expenditure of prescription drugs is spent on the personal communication with doctors via pharmaceutical sales representatives. [29] Even if detailing is assumed not to be a decision tool for profit-maximization in our analysis, it takes place inside the manufacturer's profit function as a marketing cost item.

The above discussion makes it necessity to re-state the manufacturer objective function to be maximized. Each manufacturer's objective becomes profit maximization with the decision variable of discount given to pharmacy. The objective function (manufacturer's profit) subject to maximization has four main components: 1) the revenue from the sales of drugs to the pharmacies, 2) discounts given to pharmacies, 3) discount given to the government if the drug is included in reimbursement list and 4) spending on detailing

If the drugs are reimbursed by the government and the major part of the consumers are from reimbursed segment:

$$MP_{i1} = n_{i1} * (1 + R_{i1}) * \left[\frac{\Pr ice_i * (1 - disc_{i1})}{1 + pm_i} - \Pr ice_i * Govdisc_i \right] - Det_i \quad \textbf{(5.2)}$$

If the drugs are not reimbursed by the government:

$$MP_{i2} = n_{i2} * (1 + R_{i2}) * \frac{\Pr ice_i * (1 - disc_{i2})}{1 + pm_i} - Det_i \quad \textbf{(5.3)}$$

In equation 5.2, $GovDisc_i$ is the mandatory discount off of the drug *i*'s retail price that the manufacturer *i* has to give to the government, if it wants to be reimbursed by social security agents. The governmental discount is transferred to the government via pharmacies.

As mentioned before, the manufacturer's optimization problem will be solved for both reimbursed and cash segment patients. If the sales to the reimbursed segment patients are the main consideration then Equation 5.2 will be the objective function for manufacturers. On the other hand; if the drugs are only purchased by patients who pay the whole price of the drug out of pocket, Equation 5.3 should be used as the manufacturer's profit.

5.3 The Optimal Discounting Decision of Manufacturers

We assumed a *two-stage game* in our study. Anticipating the rational decision of the pharmacy, both original and generic manufacturers give their discounting decisions at the same time without knowing each other's decisions. A pharmacy knowing the discount offers from both generic and original manufacturers gives the most rational substituting and advising decisions. Applying backward induction method, the optimal decision of the follower firm (pharmacy) can be identified. We have already stated the optimal decision of the pharmacist by utilizing KKT Theorem in Section 4.3.1. Now it is time to compute the rational discounting decisions of the pharmaceutical firms given the rational decision of the pharmacist.

The game theoretical approach that we employed in our analysis enables us to figure out the rational discounting decisions of pharmaceutical companies. Since the action of one firm has an effect on the outcome of the other, we have to study the strategic interaction within these two pharmaceutical manufacturers. What makes pharma manufacturer's discount decision problem a strategic game is the fact that what is best for one firm depends upon other firm's actions [30].

To find the rational decisions of both manufacturers, one of the basic assumptions we have to maintain throughout the paper is that all parties (pharmacy, manufacturers) are rational. In other words, they take the best available action to pursue their profit maximization objectives.

5.3.1 Best Response Correspondence

Subgame Perfect Nash equilibrium is the steady state of this two-stage strategic game. If all the players are acting in accordance with the Nash equilibrium, no one has an incentive to deviate and take another action. Since each player's choice of action is a best response to the actions actually taken by his opponent in Nash equilibrium, the identification of Nash equilibrium can also be based on the concept of the best response correspondence.

Let A and B be subsets of $\mathbb{R}^l$ and $\mathbb{R}^n$ respectively. A correspondence f from A to B is a map that associates with each element $a \in A$ a nonempty subset $f(a) \subset B$ [31]. In other words, each element in A maps to a non-empty subset of B.

An example of a correspondence in this sense is the best response correspondence in game theory, which gives the optimal action for a player as a function of the strategies of other player. If there is always a unique best action given what the other player is doing, then this is a function. If for some opponent's strategy, there is a set of best responses that are equally good, then this is a correspondence.

For our analysis, we can define the best response correspondence of firm i in segment k as the correspondence $BRC_{ik} : [\mathrm{Pow}_{jk}^{\min}, \mathrm{Pow}_{jk}^{\max}] \rightarrow [\mathrm{Pow}_{ik}^{\min}, \mathrm{Pow}_{ik}^{\max}]$ given by

$$\begin{aligned} BRC_{ik}(Pow_{jk}) &= \left\{ x_i \in [\mathrm{Pow}_{ik}^{\min}, \mathrm{Pow}_{ik}^{\max}] : MP_i(x_i, Pow_{jk}) \geq MP_i(Pow_{ik}, Pow_{jk}) \quad for \quad \forall Pow_{ik} \in [\mathrm{Pow}_{ik}^{\min}, \mathrm{Pow}_{ik}^{\max}] \right\} \\ &= \underset{x_i \in [\mathrm{Pow}_{ik}^{\min}, \mathrm{Pow}_{ik}^{\max}]}{\arg\max} MP_i(x_i, Pow_{jk}) \end{aligned}$$

Best response correspondence characterizes the best possible discounting decision of each firm with respect to the every possible discounting decision of the competitor firm. Above *BRC* function of firm *i* depicts the optimum power level(s) (or discounting level(s)) ranging from Pow_{ik}^{min} to Pow_{ik}^{max} that gives the best outcome for firm *i* for every power level of the other firm between Pow_{jk}^{min} and Pow_{jk}^{max}.

Here, Pow_{ik}^{min} and Pow_{ik}^{max} stand for the minimum and maximum power levels when $disc_{ik}$ equals to 0 and 1 respectively. Namely;

$$Pow_{ik}^{min} = pfill_{ik} * (1 + R_{ik}) * \left[Price_i - \left(\frac{Price_i}{1 + pm_i} \right) \right] \quad \textbf{(5.4)}$$

$$Pow_{ik}^{max} = pfill_{ik} * (1 + R_{ik}) * Price_i \quad \textbf{(5.5)}$$

Assuming rational pharmacy giving the profit maximizing decision about either reimbursed segment drugs or cash segment drugs; Figure 5.1 shows the feasible region where the best response correspondence of each firm can take place.

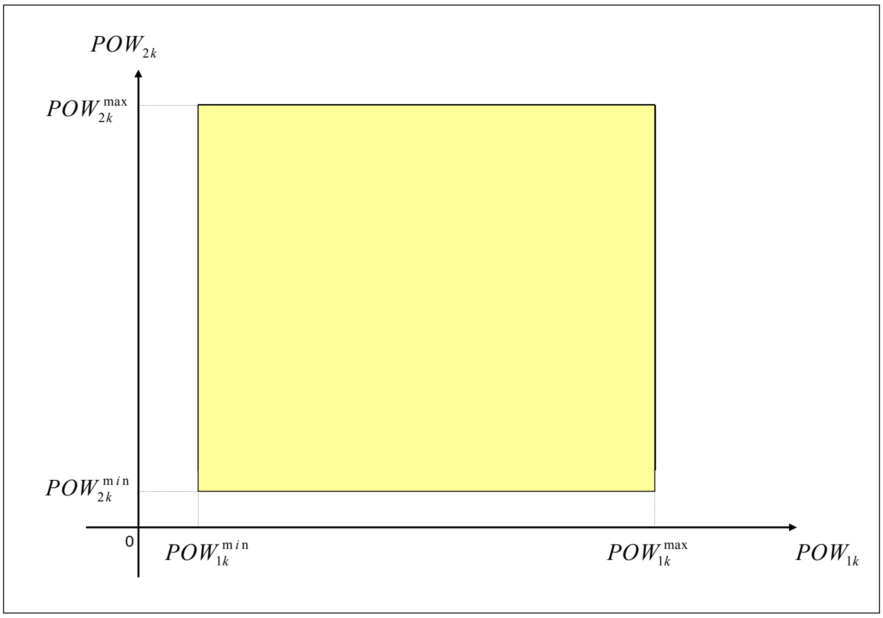


Figure 5.1: Feasible region where BRC of each firm can take place

The best response correspondence graph of neither firm 1 nor firm 2 can be outside the shaded region since co-domain of any drug *i*'s pharmacy discount rate is defined between Pow_{ik}^{min} and Pow_{ik}^{max}. As modeled in 4.3; pharmacy decides on substituting and advising probabilities for cash segment, and only substituting decisions in reimbursed segment. The pharmacist's decisions in both segments have been given in Figure 4.2 and 4.3. If we fit the pharmacist's optimum decision on Figure 5.1 above, the resulting graphs are given below.

Figure 5.2 indicates the optimal pharmacy decision for reimbursed segment drugs according to the feasible power levels of each manufacturer. Similarly, Figure 5.3 represents the pharmacy decision for cash segment. However; one should keep in mind that all Pow_{ik}^{min}, Pow_{ik}^{max}, A_{ik} and B_{ik} are parameters that are functions of other parameters. For this reason, the order of magnitude between these parameters can vary due to the parameters constituting them. We arbitrarily choose the order of magnitude as shown in Figure 5.2 and 5.3 (which means $Pow_{ik}^{min} < A_{ik} < A_{ik} + B_{ik} < Pow_{ik}^{max}$ where applicable) for illustration purposes.

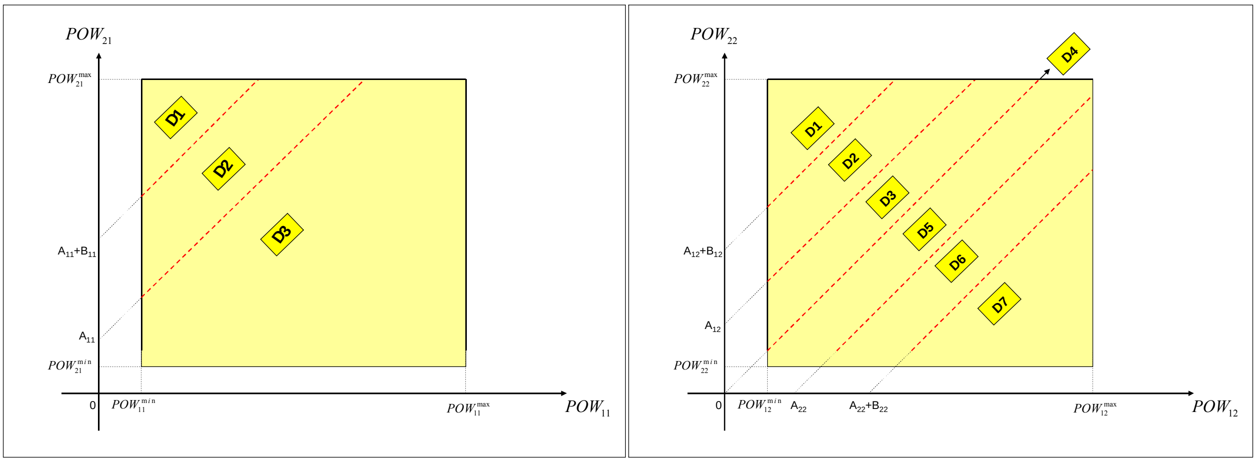


Figure 5.2 and 5.3: Feasible pharmacy decision for reimbursed segment; Feasible pharmacy decision for cash segment

In each decision region, say for cash segment from D1 to D7, the pharmacy gives a different substitution ($psubs_{ijk}$) and advising (pa_i) decision. We have given the profit function of the manufacturer in 5.3. According to this equation, manufacturer's profit is an increasing function of the number of patients treated with drug *i* sold in segment *k* (n_{ik}), which is also a function of $psubs_{ijk}$ and pa_i as given in 4.2. This situation means that the profit function of manufacturer changes with values of $psubs_{ijk}$ and pa_i in each pharmacy decision region. Different profit functions with respect to each Pow_{1k} and Pow_{2k} (i.e. $disc_{1k}$ and $disc_{2k}$) pair distinguishes our analysis from classical game theory problems (for instance Cournot Duopoly Model) in which the outcome function stays same for every pair of action.

Pharmacy chooses his optimum decision region according to the power difference between two drugs as summarized in 4.9 and 4.10 for reimbursed and cash segments respectively. Since each pharmacy decision region implies a different substitution and advising decision for pharmacy, we have to rewrite the manufacturer's profit for each decision region. For the sake of brevity, in cash segment, we only show how the best response correspondence of firm 1 is constructed. In the following 7 sub-sections we show the applicable profit function in every decision region and construct the best response correspondence corresponding every decision region's manufacturer profit.

Pharmacy Decision Region D1:

If the pharmacy decides to replace all prescribed drug 1's with drug 2 (i.e. $psubs_{122}=1$) and favors drug 2 for non-prescription dispensing decision (i.e. $pa_2 = 1$); this means that the pharmacy decision region is D1. Thus, the resulting profit function for firm 1 (MP_{12}) turns to be as follows:

$$MP_{12} \left| \left(Pow_{22} - Pow_{12} > A_{12} + B_{12} \right) = N_2 * (p_{req} * pr_1) * pfill_{12} * (1+R_{12}) * \frac{\Pr ice_1}{(1+pm_1)} * (1-disc_{12}) - Det_1 \right. \quad \textbf{(5.6)}$$

As it can be observed in 5.6; whatever firm 2 gives as a pharmacy discount firm 1 shouldn't give any discount to maximize the profit. Hence, firm 1's best response for power level is equal to $Pow_{12}^{\min}$.

$$BRC_{12}^{D1}(Pow_{22}) = Pow_{12}^{\min} \quad \textbf{(5.7)}$$

Pharmacy Decision Region D2:

If the pharmacy gives a decision in region D2, which means $pa_2 = 1$ and $psubs_{122} = X_{12} = \dfrac{Pow_{22} - Pow_{12} - A_{12}}{B_{12}}$ Thus,the resulting profit function will be as state in 5.8:

$$MP_{12} \left| \left(A_{12} \le Pow_{22} - Pow_{12} \le A_{12} + B_{12} \right) = N_2 * \left[p_{vis} * p_{12} * \left(1 - \frac{Pow_{22} - Pow_{12} - A_{12}}{B_{12}} \right) + p_{req} * pr_1) \right] \right.$$

$$*pfill_{12} * (1+R_{12}) * \frac{\Pr ice_1}{(1+pm_1)} * (1-disc_{12}) - Det_1 \quad \textbf{(5.8)}$$

In 5.8, firm 1's profit is a concave function of Pow_{12} (after replacing $disc_{12}$ with Pow_{12} in the equation by using 5.1) since $\dfrac{\partial^2 MP_{12}}{\partial Pow_{12}{}^2} < 0$. Therefore, solving $\dfrac{\delta MP_{12}}{\delta Pow_{12}} = 0$ with respect to Pow_{12} will give the best response correspondence for firm 1. However; we should always keep in mind that power difference Pow_{22}–Pow_{12} is between A_{12} and $A_{12}+B_{12}$.In 5.9 the best response correspondence of firm 1 in pharmacy decision region D2 is given.

$$BRC_{12}^{D2}(Pow_{22}) = \begin{cases} Pow_{22} - A_{12} & \text{if } Pow_{22} < \Pr ice_1 * pfill_{12} * (1+R_{12}) + A_{12} - B_{12} * \left(1 + \dfrac{p_{req} * pr_1}{p_{vis} * p_{12}}\right) \\ Pow_{22} - A_{12} - B_{12} & \text{if } Pow_{22} > \Pr ice_1 * pfill_{12} * (1+R_{12}) + A_{12} + B_{12} * \left(1 - \dfrac{p_{req} * pr_1}{p_{vis} * p_{12}}\right) \\ \dfrac{Pow_{22}}{2} - \dfrac{A_{12}}{2} + \dfrac{pfill_{12} * (1+R_{12}) * \Pr ice_1}{2} - \dfrac{B_{12}}{2} * \dfrac{p_{vis} * p_{12} + p_{req} * pr_1}{p_{vis} * p_{12}} & o/w \end{cases}$$

(5.9)

<u>Pharmacy Decision Region D3:</u>

If the pharmacy gives a decision in region D3, substitution does not occur but drug 2 is preferred in dispensing drug to non-prescribed patients asking for pharmacist's advice. (i.e. $pa_2 = 1$). The profit function is as stated in 5.10:

$$MP_{12} \Big| \left(0 < Pow_{22} - Pow_{12} < A_{12}\right) = N_2 * \left[p_{vis} * p_{12} + p_{req} * pr_1\right] * pfill_{12} * (1+R_{12}) * \frac{\Pr ice_1}{(1+pm_1)} * (1 - disc_{12}) - Det_1 \quad \textbf{(5.10)}$$

According to 5.10 there is no point in giving discount from the aspect of firm 1. Therefore the best response correspondence is given by:

$$BRC_{12}^{D3}(Pow_{22}) = Pow_{12}^{\min} \quad \textbf{(5.11)}$$

<u>Pharmacy Decision Region D4:</u>

In pharmacy decision region D4, where there is no substitution and both drugs are indifferent with respect to the advising decision of the pharmacy, the power level of both drugs are equal (i.e. $Pow_{12} = Pow_{22}$). Therefore the best response correspondence for firm 1 is Pow_{22} which is the only value that makes pharmacy choose decision region D4.

$$BRC_{12}^{D4}(Pow_{22}) = Pow_{22} \quad \textbf{(5.12)}$$

<u>Pharmacy Decision Region D5:</u>

Let the pharmacy give a decision in region D5, which means $pa_1 = 1$ and no substitution. Thus, the resulting profit function will be as stated in 5.13:

$$MP_{12} \Big| \left(0 < Pow_{12} - Pow_{22} \le A_{22}\right) = N_2 * \left[p_{vis} * p_{12} + p_{adv} + p_{req} * pr_1\right] * pfill_{12} * (1+R_{12}) * \frac{\Pr ice_1}{(1+pm_1)} * (1 - disc_{12}) - Det_1 \quad \textbf{(5.13)}$$

This profit function implies that firm 1 maximizes its profit by offering power level providing minimum possible discount in region D5 which is $Pow_{22}+\varepsilon$. Here, ε is a very small number which guarantees pharmacy to choose drug 1 for non-prescribed patients asking for pharmacist's advice. If $Pow_{12}^{\min}$ have a greater magnitude than $Pow_{22}^{\min}$ as seen in our example at Figure 5.3, firm 1's minimum possible power level for Pow_{22} values smaller than $Pow_{12}^{\min}$ is $Pow_{12}^{\min}$. Therefore;

$$BRC_{12}^{D5}(Pow_{22}) = \begin{cases} Pow_{22} + \varepsilon & \text{if } Pow_{22} \geq Pow_{12}^{\min} \\ Pow_{12}^{\min} & \text{if } Pow_{22} < Pow_{12}^{\min} \end{cases} \quad \textbf{(5.14)}$$

Pharmacy Decision Region D6:

Assume that the pharmacy decides to favor drug 1 while advising to non-prescribed patients and replace a specific portion of the prescribed drug 2's with drug 1. This decision is represented by pharmacy decision region D6. The proportion of the substituted drug 2's is given by $psubs_{232} = X_{22} = \dfrac{POWER_{12} - POWER_{22} - A_{22}}{B_{22}}$. According to that pharmacy decision, profit function will be as follows:

$$MP_{12} \Big| \left(A_{22} \leq Pow_{12} - Pow_{22} \leq A_{22} + B_{22} \right) = N_2 * \left[p_{vis} * p_{12} + p_{vis} * p_{22} * \left(1 - \frac{Pow_{12} - Pow_{22} - A_{22}}{B_{22}} \right) + p_{adv} + p_{req} * pr_1) \right]$$

$$* pfill_{12} * (1 + R_{12}) * \frac{\Pr ice_1}{(1 + pm_1)} * (1 - disc_{12}) - Det_1 \quad \textbf{(5.15)}$$

In 5.15, firm 1's profit is a concave function of Pow_{12} (after replacing $disc_{12}$ with Pow_{12} in the equation by using 5.1) since $\dfrac{\partial^2 MP_{12}}{\partial Pow_{12}{}^2} < 0$. Therefore, solving $\dfrac{\delta MP_{12}}{\delta Pow_{12}} = 0$ with respect to Pow_{12} will give the best response correspondence for firm 1. However; we should not overlook that power difference Pow_{22}–Pow_{12} is between A_{22} and A_{22}+B_{22}. In 5.16 the best response correspondence of firm 1 in pharmacy decision Region D6 is given:

$$BRC_{12}^{D6}(Pow_{22}) = \begin{cases} Pow_{22} - A_{12} & \text{if } Pow_{22} < \Pr ice_1 * pfill_{12} * (1 + R_{12}) + A_{22} - B_{22} * \left(2 + \dfrac{p_{vis} * p_{22} + p_{adv} + p_{req} * pr_1}{p_{vis} * p_{22}} \right) \\ Pow_{22} - A_{12} - B_{12} & \text{if } Pow_{22} > \Pr ice_1 * pfill_{12} * (1 + R_{12}) + A_{22} - B_{22} * \left(\dfrac{p_{vis} * p_{22} + p_{adv} + p_{req} * pr_1}{p_{vis} * p_{22}} \right) \\ \dfrac{Pow_{22}}{2} + \dfrac{pfill_{12} * (1 + R_{12}) * \Pr ice_1}{2} + \dfrac{A_{22}}{2} - \dfrac{B_{22}}{2} * \dfrac{p_{vis} * p_{12} + p_{adv} + p_{req} * pr_1}{p_{vis} * p_{22}} & o/w \end{cases}$$

(5.16)

Pharmacy Decision Region D7:

Finally; if the decision of the pharmacy is the one denoted by pharmacy decision region D7, all the prescribed drugs of firm 2 are replaced with drug 1 ($psubs_{122} = 1$) and pharmacy favors drug 1 while advising patients without prescription. Firm 1's profit in decision region D7 is designated by 5.17:

$$MP_{12} \Big| \left(Pow_{12} - Pow_{22} \geq A_{22} + B_{22} \right) = N_2 * \left[p_{vis} * (p_{12} + p_{22}) + p_{adv} + p_{req} * pr_1) \right] * pfill_{12} * (1 + R_{12}) * \frac{\Pr ice_1}{(1 + pm_1)} * (1 - disc_{12}) - Det_1$$

(5.17)

This profit function implies that firm 1 maximizes its profit by offering minimum possible discount in region D5 which is $Pow_{22}+A_{22}+B_{22}+\varepsilon$. Here, ε is a very small number which guarantees pharmacy decision to take place inside decision region D7.

$$BRC_{12}^{D7}(Pow_{22}) = Pow_{22} + A_{22} + B_{22} + \varepsilon \quad \textbf{(5.18)}$$

We have defined the best response correspondence of firm 1 in each pharmacy decision region (ranging between D1 and D7) assuming that manufacturers can only offer discount rates restricted by corresponding decision region. Best response correspondence lines for each decision region are given in 5.7, 9, 11, 12, 14, 16 and 18. If we draw all of them on a single graph, the resulting figure will be the one as shown in Figure 5.4.

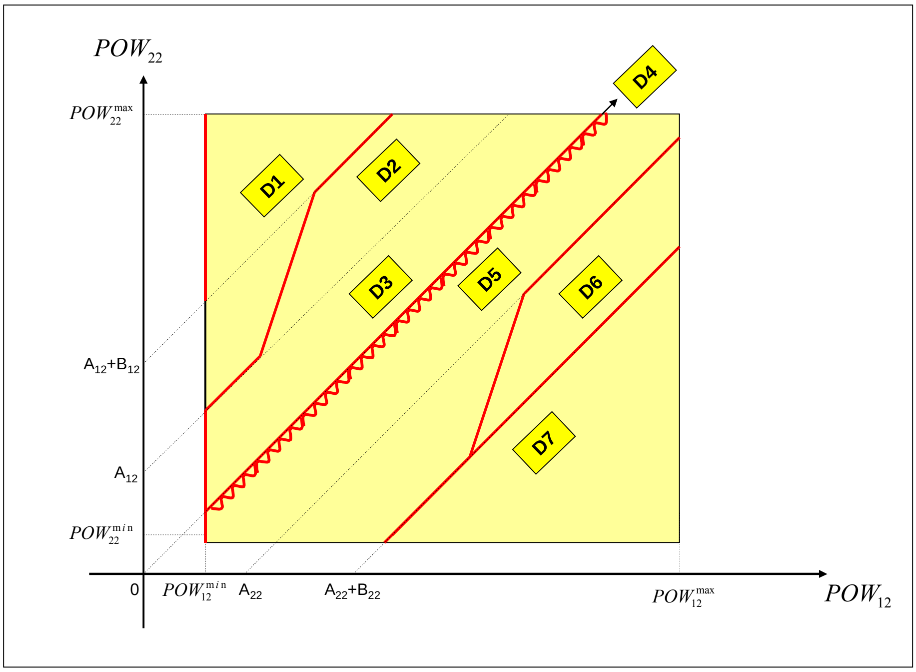


Figure 5.4: "Best response correspondence of firm 1 in cash segment for each decision region" in one graph

The wavy line in the graph is utilized to show that the line has an equation of $Pow_{12}=Pow_{22}+\varepsilon$ where ε is an infinitesimal ensuring the acquisition of pharmacist's advice to non-prescribed patients.

We have constructed each best response line according to the profit function of the region where the corresponding best response line takes place. We have not compared the best response lines in each region yet in order to find the best possible choice of firm 1 for each power level of firm 2. In other words, we have not combined whole regions yet to make a unified optimal decision for firm 1. The next step is to eliminate the best response lines (or portions of best response lines) that are inferior. In Figure 5.4, some of the lines do not have the chance of being a part of ultimate best response correspondence, since they are dominated by some other best response lines. For instance, BRC_{12}^{D5} is always superior to BRC_{12}^{D4} since giving a discount rate higher than the component's discount offer by an infinitesimal number (say ε) will bring in the profit resulting from non-prescribed patients who are asking for pharmacy advice. On the other hand, BRC_{12}^{D6} dominates BRC_{12}^{D4} for every Pow_{22} level. After eliminating BRC_{12}^{D4} and BRC_{12}^{D4} best response correspondence lines from the graph, we obtain the following graph:

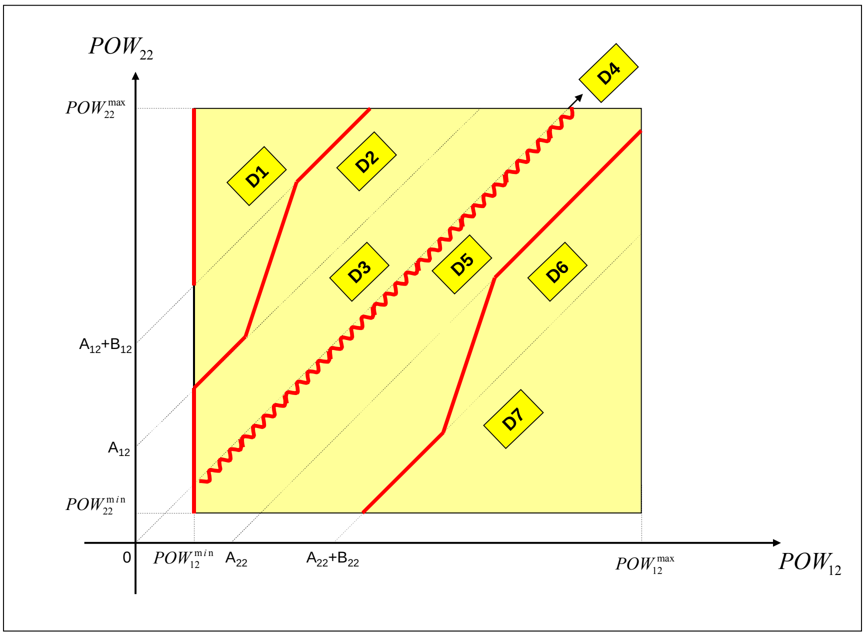


Figure 5.5: "Best response Correspondence of firm 1 in cash segment for each decision region" in one graph after dominated best response lines are eliminated

After that point, the final unified best response correspondence varies due to different values of parameters like $Price_i$, C_{comp}, Det_i, p_{vis}, p_{req}, p_{1k}, p_{2k} etc. If we also include the best response choice of firm 2, some reasonable best response correspondence graphs can be formed as seen in Figure 5.6. In this figure best response correspondence for firm 2 is shown with the blue line.

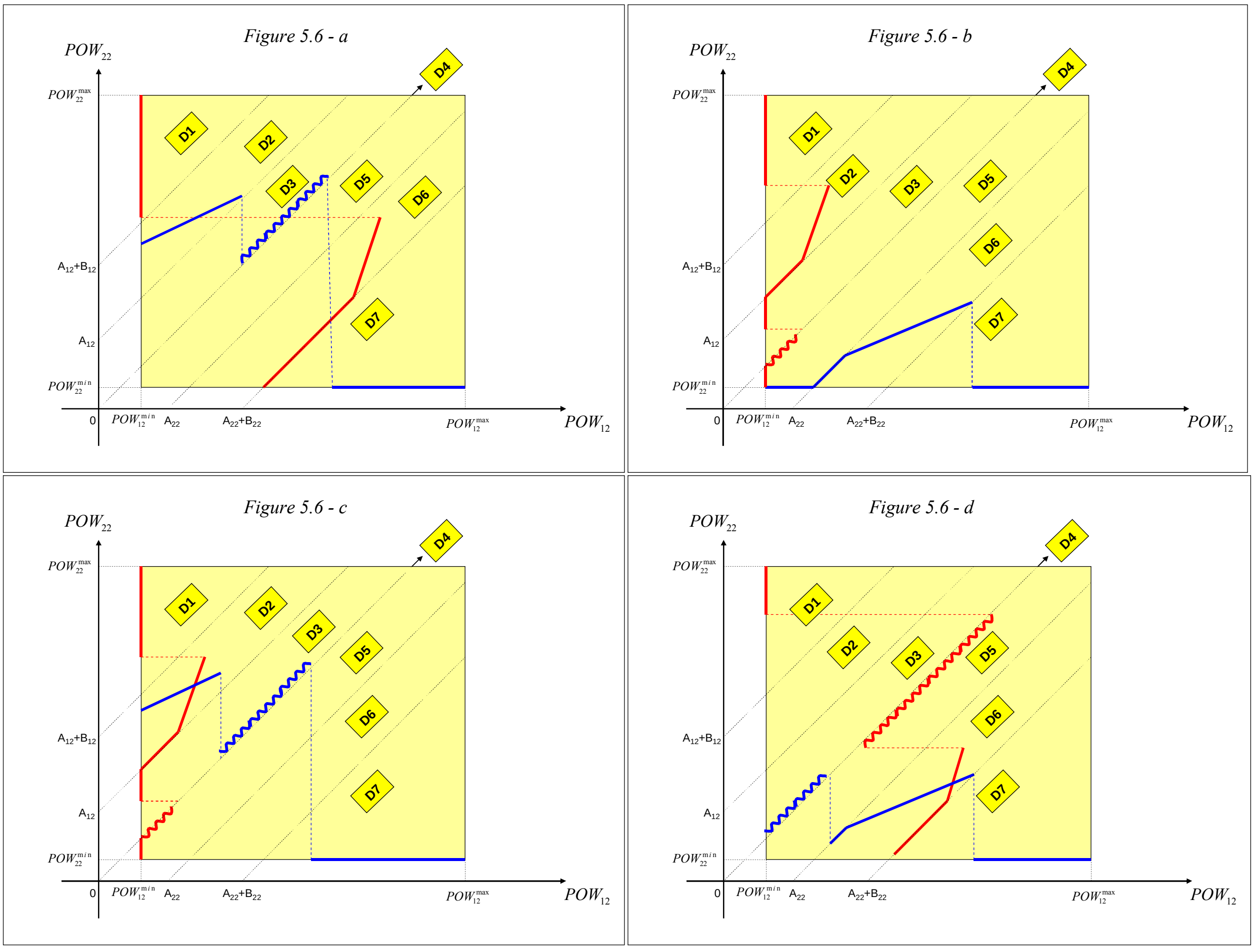


Figure 5.6: Four possible best response correspondence graphs in cash segment

5.3.2 Nash Equilibrium

In our 2-firm game in strategic form G, we have $(Pow_{1k}^{*}, Pow_{2k}^{*}) \in N(G)$ if and only if,

$Pow_{1k}^{*} \in BRC_{1k}(Pow_{2k}^{*})$ and $Pow_{2k}^{*} \in BRC_{2k}(Pow_{1k}^{*})$

Namely, the intersection of best response correspondences of firm 1 (original) and firm 2 (generic) will give the Nash equilibrium of strategic discounting game. If best response lines of the two firms do not intersect, then we can conclude that there is no equilibrium for this game (Figure 5.6-a). For cash segment drugs, firms can have equilibrium either at minimum power levels $(Pow_{12}^{\min}, Pow_{22}^{\min})$ (Figure 5.6-b) or at the intersection of best response lines in region D2 (Figure 5.6-c) or region D6 (Figure 5.6-d).

We are particularly interested in discount equilibria which cause substitution of one firm's drugs for the other firm's drugs. In further sections, we also would like to see the effect of interventions caused by manipulating parameters in the model on Nash equilibrium where some of the drugs are substituted for other brands.

For cash segment drugs, let us now try to find Nash equilibriums formed inside region D2 where a specific portion of the prescribed drugs of firm 1 is replaced with drug 2. We have already found the best response correspondence of firm 1 in 5.9 which is:

$$BRC_{12}^{D2}(Pow_{22}) = \frac{Pow_{22}}{2} + \frac{pfill_{12} * (1+R_{12}) * \Pr ice_1}{2} - \frac{A_{12}}{2} - \frac{B_{12}}{2} * \frac{p_{vis} * p_{12} + p_{req} * pr_1}{p_{vis} * p_{12}}$$

We should also define the best response correspondence of firm 2 inside region D2. Given that firm 1 propose $Pow_{12} \in [\mathrm{POW}_{12}^{\min}, \mathrm{POW}_{12}^{\min}]$ dependent of its discount offer, the best response of firm 2 inside region D2 is found by solving the first order condition:

$$\frac{dMP_{22} \Big| \left(A_{12} \le Pow_{22} - Pow_{12} \le A_{12} + B_{12} \right)}{dPow_{22}} = 0$$

which yields $BRC_{22}^{D2}(Pow_{12}) = \frac{Pow_{12}}{2} + \frac{pfill_{22} * (1+R_{22}) * \Pr ice_2}{2} + \frac{A_{12}}{2} - \frac{B_{12}}{2} * \frac{p_{vis} * p_{22} + p_{adv} + p_{req} * pr_2}{p_{vis} * p_{12}}$

(Second order condition checks since $\frac{\partial^2 MP_{22} \Big| \left(A_{12} \le Pow_{22} - Pow_{12} \le A_{12} + B_{12} \right)}{\partial Pow_{22}^{\;2}} < 0$).

Therefore, by proposition given at the beginning of Section 5.3.2, to compute the Nash equilibrium all we need to do is to solve the following two equations:

$$Pow_{12}^* = \frac{Pow_{22}^*}{2} + \frac{pfill_{12} * (1+R_{12}) * \Pr ice_1}{2} - \frac{A_{12}}{2} - \frac{B_{12}}{2} * \frac{p_{vis} * p_{12} + p_{req} * pr_1}{p_{vis} * p_{12}} \quad \textbf{(5.19)}$$

$$Pow_{22}^* = \frac{Pow_{12}^*}{2} + \frac{pfill_{22} * (1+R_{22}) * \Pr ice_2}{2} + \frac{A_{12}}{2} - \frac{B_{12}}{2} * \frac{p_{vis} * p_{22} + p_{adv} + p_{req} * pr_2}{p_{vis} * p_{12}} \quad \textbf{(5.20)}$$

Doing this, we find that the unique Nash equilibrium of this game inside region D2 is

$$(Pow_{12}^*, Pow_{22}^*) =$$

$$\left(\begin{array}{l} \frac{2 * pfill_{12} * (1+R_{12}) * \Pr ice_1}{3} + \frac{pfill_{22} * (1+R_{22}) * \Pr ice_2}{3} - \frac{A_{12}}{3} - \frac{B_{12}}{3} * \frac{1 + p_{vis} * p_{12} + p_{req} * pr_1}{p_{vis} * p_{12}}, \\ \frac{pfill_{12} * (1+R_{12}) * \Pr ice_1}{3} + \frac{2 * pfill_{22} * (1+R_{22}) * \Pr ice_2}{3} + \frac{A_{12}}{3} - \frac{B_{12}}{3} * \frac{1 + p_{vis} * p_{22} + p_{adv} + p_{req} * pr_2}{p_{vis} * p_{12}} \end{array} \right)$$

(5.21)

In order to get a Nash equilbrium in region D2, however, ultimate unified best response lines for firm 1 and firm 2 should intersect inside region D2 as in example shown in Figure 5.6-c. We have stated before that the equilibrium's status (whether it exists and if exists where) changes according to parameter values shaped by patients, physician, government, pharmacy and manufacturers. Therefore, we have to define the relations between parameters required for Nash equilibrium in region D2.

First of all, in order to have Nash equilibrium at (Pow_{12}^*, Pow_{22}^*) in region D2, Pow_{12}^* and Pow_{22}^* values should definitely lie in $\left[Pow_{12}^{\min}, Pow_{12}^{\max}\right]$ and $\left[Pow_{22}^{\min}, Pow_{22}^{\max}\right]$ respectively. Next, equilibrium point (Pow_{12}^*, Pow_{22}^*) should satisfy $A_{12} \le Pow_{22}^* - Pow_{12}^* \le A_{12} + B_{12}$ since the intersection of best response lines are required to intersect inside region D2. Finally, the intersection of $BRC_{12}^{D2}(Pow_{22})$ and $BRC_{22}^{D2}(Pow_{12})$ must be an element of ultimate unified best rest response correspondence of both firm. In other words; when *Pow22* is Pow_{22}^*, Pow_{12}^* should be the best possible action for firm 1 and Pow_{22}^* must result in the highest profit when *Pow12* is Pow_{12}^*. The details of conditions to derive Nash equilibrium in region D2 are given in Appendix B with equations B.1 – B.9.

For cash segment drugs, Nash equilibriums might also take place inside region D6 where a specific portion of the prescribed drugs of firm 2 is replaced with drug 1 by pharmacy substitution. An example for this kind of equilibrium is given in Figure 5.6-d. We will first find the best response correspondence of both firms in region D6. We have already defined the best response correspondence of firm 1 in (5.16) which is:

$$BRC_{12}^{D6}(Pow_{22}) = \frac{Pow_{22}}{2} + \frac{pfill_{12} * (1+R_{12}) * \Pr ice_1}{2} + \frac{A_{22}}{2} - \frac{B_{22}}{2} * \frac{p_{vis} * p_{12} + p_{adv} + p_{req} * pr_1}{p_{vis} * p_{22}}$$

After taking the first derivative of firm 2's profit in region D6 with respect to *Pow22*, we find the best response for firm 2:

$$BRC_{22}^{D6}(Pow_{12}) = \frac{Pow_{12}}{2} + \frac{pfill_{22} * (1+R_{22}) * \Pr ice_2}{2} - \frac{A_{22}}{2} - \frac{B_{22}}{2} * \frac{p_{vis} * p_{22} + p_{req} * pr_2}{p_{vis} * p_{22}}$$

By solving this equation system with two unknowns (Pow_{12}^*, Pow_{22}^*), we can compute the intersection of the best response correspondences. When we assume that this intersection takes place inside region D6, the Nash equilibrium will be:

$$(Pow_{12}^*, Pow_{22}^*) =$$

$$\left(\begin{array}{l} \frac{2 * pfill_{12} * (1+R_{12}) * \Pr ice_1}{3} + \frac{pfill_{22} * (1+R_{22}) * \Pr ice_2}{3} + \frac{A_{22}}{3} - \frac{B_{22}}{3} * \frac{1 + p_{vis} * p_{12} + p_{adv} + p_{req} * pr_1}{p_{vis} * p_{22}} \\ \frac{pfill_{12} * (1+R_{12}) * \Pr ice_1}{3} + \frac{2 * pfill_{22} * (1+R_{22}) * \Pr ice_2}{3} - \frac{A_{22}}{3} - \frac{B_{22}}{3} * \frac{1 + p_{vis} * p_{22} + p_{req} * pr_2}{p_{vis} * p_{22}}, \end{array} \right)$$

(5.22)

Like the equilibrium we have found in region D2, this equilibrium given by (5.22) needs to be verified that no firm has an incentive to unilaterally deviate and take another action. The required equilibrium conditions in region D6 are also summarized in Appendix B.

5.3.3 Reimbursed Segment Drugs

For reimbursed segment drugs, we can identify the steady state equilibrium in a similar manner as performed for cash segment before. However, one should note that the cost of manufacturer involves the discount given to government ($Govdisc_i$) if the drug is sold in reimbursed segment. Further, all the patients are coming with prescription when the drug is reimbursed by the government. Finally, the pharmacy makes only one decision that is whether to replace the original drug with its cheaper generic alternative. There is no advising decision and no substitution form generic to original drug.

The ultimate unified best response correspondence of each firm is again found by deriving the best responses in all regions as we have done for cash segment. In Figure 5.2, we have indicated the optimal pharmacy decision drugs for reimbursed segment within the framework of feasible power levels of each manufacturer.

<u>Pharmacy Decision Region D1:</u>

When the pharmacy makes a decision in region D1, whole drug 2's are dispensed as written in the prescription and whole prescribed drugs of firm 1 are replaced by drug 2 in reimbursed segment (i.e. $psubs_{121}$ =1). Thus, firm 1 cannot sell any of his drugs to pharmacy and the profit (MP_{11}) turns out to be only the cost of detailing promotions:

$$MP_{11} \left| \left(Pow_{21} - Pow_{11} \geq A_{11} + B_{11} \right) = -Det_1 \right. \quad \textbf{(5.23)}$$

As it can be observed in 5.23; whatever firm 2 gives as a pharmacy discount firm 1 shouldn't give any discount to maximize the profit. Hence, firm 1's best response for power level is equal to $Pow_{11}^{\min}$.

$$BRC_{11}^{D1}(Pow_{21}) = Pow_{11}^{\min} \quad \textbf{(5.24)}$$

<u>Pharmacy Decision Region D2:</u>

If a specific portion of generic manufacturer's drugs (drug 2) are substituted for generic drugs (drug 1), this means the pharmacy gives a decision inside region D2. Firm 1's profit in decision region D2 is designated by 5.25:

$$MP_{11} \Big| \left(A_{11} \le Pow_{21} - Pow_{11} \le A_{11} + B_{11}\right) = N_1 * p_{11} * \left(1 - \frac{Pow_{21} - Pow_{11} - A_{11}}{B_{11}}\right)$$

$$*pfill_{11} * (1 + R_{11}) * \left[\frac{\Pr ice_1}{(1 + pm_1)} * (1 - disc_{11}) - \Pr ice_1 * Govdisc_1\right] - Det_1 \quad \textbf{(5.25)}$$

After taking the first derivative of firm 2's profit in region D2 with respect to *Pow21*, we find the best response for firm 2 for reimbursed segment as follows:

$$BRC_{11}^{D2}(Pow_{21}) = \begin{cases} Pow_{21} - A_{11} & \text{if } Pow_{21} < \Pr ice_1 * pfill_{11} * (1 + R_{11}) * (1 - Govdisc_1) + A_{11} - B_{11} * \left(1 + \frac{p_{req} * pr_1}{p_{vis} * p_{11}}\right) \\ Pow_{21} - A_{11} - B_{11} & \text{if } Pow_{21} > \Pr ice_1 * pfill_{11} * (1 + R_{11}) * (1 - Govdisc_1) + A_{11} + B_{11} * \left(1 - \frac{p_{req} * pr_1}{p_{vis} * p_{11}}\right) \\ \frac{Pow_{21}}{2} - \frac{A_{11}}{2} + \frac{pfill_{11} * (1 + R_{11}) * \Pr ice_1 * (1 - Govdisc_1)}{2} - \frac{B_{11}}{2} * \frac{p_{vis} * p_{11} + p_{req} * pr_1}{p_{vis} * p_{11}} & o/w \end{cases}$$

(5.26)

<u>Pharmacy Decision Region D3:</u>

If the pharmacy gives a decision in region D3 for reimbursed segment drugs, substitution does not occur. The profit function is as stated in 5.27:

$$MP_{11} \Big| \left(Pow_{21} - Pow_{11} \le A_{11}\right) = N_1 * p_{11} * pfill_{11} * (1 + R_{11}) * \left[\frac{\Pr ice_1}{(1 + pm_1)} * (1 - disc_{11}) - \Pr ice_1 * Govdisc_1\right] - Det_1 \quad \textbf{(5.27)}$$

According to 5.27 there is no point in giving discount from the aspect of firm 1. Therefore the best response correspondence in reimbursed segment is given by:

$$BRC_{11}^{D3}(Pow_{21}) = Pow_{11}^{\min} \quad \textbf{(5.28)}$$

Best response correspondence lines for each decision region in reimbursed segment (ranging from D1 to D3) are given in 5.24, 26 and 28. If we also find generic firm's best response correspondence for each region and plot all of them on a single graph, the resulting figure will be the one as demonstrated in Figure 5.7.

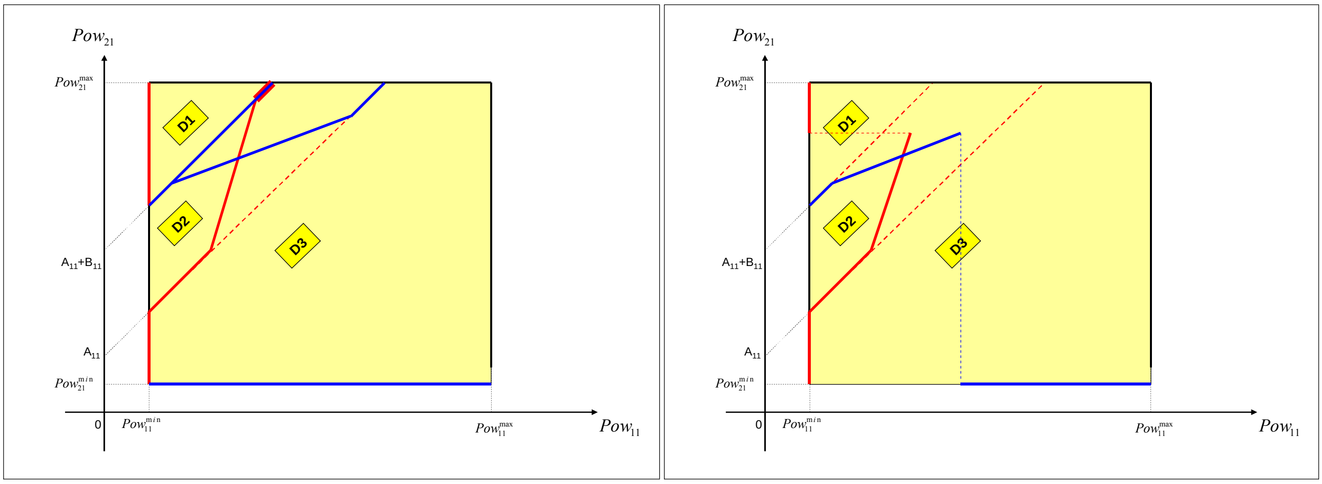


Figure 5.7 and 5.8: "Best response correspondence of firm 1 in reimbursed segment for each decision region" in one graph; Possible best response correspondence graph in reimbursed segment

Yet, we have not compared best response in each region to construct a unified optimal best response for each firm. The next step is to eliminate the best response lines (or portions of best response lines) that are inferior. The final unified best response correspondence varies due to different values of parameters, but the instance that we especially interested in is the one plotted in Figure 5.8. Due to the example in Figure 5.8 equilibrium occurs where a specific fraction of prescribed original drugs are replaced with generic drugs. We have already defined the best response correspondence of firm 1 in this region with 5.26 which is:

$$BRC_{11}^{D2}(Pow_{21}) = \frac{Pow_{21}}{2} - \frac{A_{11}}{2} + \frac{pfill_{11}*(1+R_{11})*\Pr ice_1*(1-Govdisc_1)}{2} - \frac{B_{11}}{2}*\frac{p_{vis}*p_{11}+p_{req}*pr_1}{p_{vis}*p_{11}}$$

After taking the first derivative of firm 2's profit in region D2 with respect to Pow_{21}, we find the best response for firm 2:

$$BRC_{21}^{D2}(Pow_{11}) = \frac{Pow_{11}}{2} + \frac{pfill_{21}*(1+R_{21})*\Pr ice_2*(1-Govdisc_2)}{2} + \frac{A_{11}}{2} - \frac{B_{11}}{2}*\frac{p_{vis}*p_{21}+p_{adv}+p_{req}*pr_2}{p_{vis}*p_{11}}$$

By solving this equation system with two unknowns (Pow_{11}^*, Pow_{21}^*), we can compute the intersection of the best response correspondences. When we assume that this intersection takes place inside region D6, the Nash equilibrium will be:

$$(Pow_{11}^*, Pow_{21}^*) = \left(\begin{array}{l} \frac{2*pfill_{11}*(1+R_{11})*(1-Govdisc_1)*\Pr ice_1}{3} + \frac{pfill_{21}*(1+R_{21})*(1-Govdisc_2)*\Pr ice_2}{3} - \frac{A_{11}}{3} - \frac{B_{11}}{3}*\frac{1+p_{vis}*p_{11}+p_{req}*pr_1}{p_{vis}*p_{11}}, \\ \frac{pfill_{11}*(1+R_{11})*(1-Govdisc_1)*\Pr ice_1}{3} + \frac{2*pfill_{21}*(1+R_{21})*(1-Govdisc_2)*\Pr ice_2}{3} + \frac{A_{11}}{3} - \frac{B_{11}}{3}*\frac{1+p_{vis}*p_{21}+p_{adv}+p_{req}*pr_2}{p_{vis}*p_{11}} \end{array} \right)$$

(5.29)

The equilibrium given by 5.29 needs to be verified that no firm has an incentive to unilaterally deviate and take another action. The required equilibrium conditions for reimbursed segment drugs are summarized in Appendix B.

5.4 Sensitivity Analysis

Before proceeding with sensitivity analysis, it will be beneficial to document all equilibrium discounting levels of cash segment and reimbursed segment drugs.

$$\left(Pow_{12}^*, Pow_{22}^*\right)^{D2} =$$
$$\left(\begin{array}{l}\frac{2*pfill_{12}*(1+R_{12})*\Pr ice_1}{3}+\frac{pfill_{22}*(1+R_{22})*\Pr ice_2}{3}-\frac{A_{12}}{3}-\frac{B_{12}}{3}*\frac{1+p_{vis}*p_{12}+p_{req}*pr_1}{p_{vis}*p_{12}},\\ \frac{pfill_{12}*(1+R_{12})*\Pr ice_1}{3}+\frac{2*pfill_{22}*(1+R_{22})*\Pr ice_2}{3}+\frac{A_{12}}{3}-\frac{B_{12}}{3}*\frac{1+p_{vis}*p_{22}+p_{adv}+p_{req}*pr_2}{p_{vis}*p_{12}}\end{array}\right)$$

(5.30)

$$\left(Pow_{12}^*, Pow_{22}^*\right)^{D6} =$$
$$\left(\begin{array}{l}\frac{2*pfill_{12}*(1+R_{12})*\Pr ice_1}{3}+\frac{pfill_{22}*(1+R_{22})*\Pr ice_2}{3}+\frac{A_{22}}{3}-\frac{B_{22}}{3}*\frac{1+p_{vis}*p_{12}+p_{adv}+p_{req}*pr_1}{p_{vis}*p_{22}}\\ \frac{pfill_{12}*(1+R_{12})*\Pr ice_1}{3}+\frac{2*pfill_{22}*(1+R_{22})*\Pr ice_2}{3}-\frac{A_{22}}{3}-\frac{B_{22}}{3}*\frac{1+p_{vis}*p_{22}+p_{req}*pr_2}{p_{vis}*p_{22}}\end{array}\right)$$

(5.31)

$$(Pow_{11}^*, Pow_{21}^*) =$$
$$\left(\begin{array}{l}\frac{2*pfill_{11}*(1+R_{11})*(1-Govdisc_1)*\Pr ice_1}{3}+\frac{pfill_{21}*(1+R_{21})*(1-Govdisc_2)*\Pr ice_2}{3}-\frac{A_{11}}{3}-\frac{B_{11}}{3}*\frac{1+p_{vis}*p_{11}+p_{req}*pr_1}{p_{vis}*p_{11}},\\ \frac{pfill_{11}*(1+R_{11})*(1-Govdisc_1)*\Pr ice_1}{3}+\frac{2*pfill_{21}*(1+R_{21})*(1-Govdisc_2)*\Pr ice_2}{3}+\frac{A_{11}}{3}-\frac{B_{11}}{3}*\frac{1+p_{vis}*p_{21}+p_{adv}+p_{req}*pr_2}{p_{vis}*p_{11}}\end{array}\right)$$

(5.32)

In these expressions, we preferred to use the explicit forms of each parameter instead of specifying as Pow_{ik}, A_{ik}, B_{ik}, or p_{ik}.

Equilibrium discount levels for cash segment drugs:

We have found the power level equilibrium in region D2 for cash segment as shown in 5.30.

In 5.30, when we replace Pow_{i2}^* with $pfill_{i2}*(1+R_{i2})*\left[\Pr ice_i-\left(\frac{\Pr ice_i}{1+pm_i}\right)*\left(1-disc_{i2}^*\right)\right]$ and p_{i2}, A_{i2} and B_{i2} with values given in 4.3, 4.12 and 4.13 respectively, we come up with the following result:

$$\left(disc_{12}^{*}, disc_{22}^{*}\right)^{D2} =$$

$$\left(\begin{array}{l} 1-\dfrac{(1+pm_1)}{3}+\dfrac{pfill_{22}*(1+R_{22})*\Pr ice_2*(1+pm_1)}{3*pfill_{12}*(1+R_{12})*\Pr ice_1}-\dfrac{C_{comp}*\alpha_{lin}*\psi(Det_1)*(1+pm_1)}{3*(1+R_{12})*\Pr ice_1} \\ -\dfrac{2*C_{comp}*\alpha_{quad}*\psi(Det_1)*N_2*pfill_{12}*(1+pm_1)}{3*(1+R_{12})*\Pr ice_1}*\left(1+p_{vis}*\left(\dfrac{\xi(Det_1,Q_1,OOP_{12})}{\xi(Det_1,Q_1,OOP_{12})+\xi(Det_2,Q_2,OOP_{22})+1}\right)+p_{req}*pr_1\right), \\ \\ \dfrac{pfill_{12}*(1+R_{12})*\Pr ice_1*(1+pm_2)}{3*pfill_{22}*(1+R_{22})*\Pr ice_2}+1-\dfrac{(1+pm_2)}{3}+\dfrac{C_{comp}*\alpha_{lin}*\psi(Det_1)*pfill_{12}*(1+pm_2)}{3*pfill_{22}*(1+R_{22})*\Pr ice_2} \\ -\dfrac{2*C_{comp}*\alpha_{quad}*\psi(Det_1)*N_2*pfill_{12}^2*(1+pm_2)}{3*pfill_{22}*(1+R_{22})*\Pr ice_2}*\left(1+p_{vis}*\left(\dfrac{\xi(Det_2,Q_2,OOP_{22})}{\xi(Det_1,Q_1,OOP_{12})+\xi(Det_2,Q_2,OOP_{22})+1}\right)+p_{adv}+p_{req}*pr_2\right) \end{array}\right)$$

(5.33)

In 5.30, we can see the effect of various factors on discount equilibrium. When original manufacturer (firm 1) increases its own detailing spending (Det_1), increased detailing will provide an extra resistance for original manufacturer against substitution so that it will find the chance of decreasing its discount rate in order to sustain the substitution probability at a desired optimum level. Thus, equilibrium discount level maximizing firm 1's profit decreases with increasing own detailing. This situation explains why original manufacturers hold the discounts given to pharmacies in low levels while they do invest considerable amounts in detailing promotions.

On the other hand, the effect of original manufacturer's detailing on competitor generic manufacturer's (firm 2) discounting is ambiguous since we do not know the net effect of increasing and decreasing components in expression 5.30.

Generic detailing does not have an effect on complaint cost caused by pharmacy substitution in region D2 where substitution occurs from drug 1 to drug 2. Therefore, in equation 5.30, firm's detailing seems influential only on prescription probabilities. Increasing detailing of the competitor generic firm (Det_2) causes the probability of physician prescription of drug 1 to decrease and drug 2 to increase. Therefore; decreasing p_{12} and increasing p_{22}, which are result from raised Det_2, will raise the discount rate of original firm ($disc^*_{12}$) and decrement the discount rate of generic manufacturer ($disc^*_{22}$). This result is not surprising since aggressive investment of generic manufacturer in detailing will decrease the need for giving discount to pharmacy. On the other hand, firm 1 facing with a smaller prescription rate has an increased away substitution rate. Hence, firm 1 will try to balance the decrease in prescribed drugs by giving extra discount to pharmacy which will at least minimize the lost caused by substitution.

The effect of prices on optimum discount levels of both firms are more complicated than the detailing effect. Besides directly taking part in 5.30, price (*$Price_i$*) also influences the out of pocket expenditure (*OOP_{ik}*) and in turn the probability of filling the drug (*$pfill_{ik}$*) and the probability of drug prescriptions (*p_{ik}*). Therefore the net effect of a price change on equilibrium discounting levels is dependent on the price sensitivity of patients and physicians. One of the key parameters affecting the magnitude of resistance from patients and physicians against substitution is the future revenue loss from a single complaint (*C_{comp}*). As *C_{comp}* increases the equilibrium discount level of the original firm - which loses a specific proportion of its prescribed drugs to its generic alternative - decreases. The intuition is that a higher level of financial burden from a single complaint induces more resistance against generic substitution and this causes the substitution rate away from original drug to decrease. Thanks to an increased *C_{comp}* the original firm can decrease the discounts given to pharmacy, and still sustain substitution rate at the same level. On the other hand, the effect of an increase in *C_{comp}* on the equilibrium discount level of the generic manufacturer is not clear. When we take the first derivative of *$disc^*_{22}$* with respect to *C_{comp}*, we will have the following equation:

$$\frac{\partial\ disc^*_{22}}{\partial\ C_{comp}} = \left(\alpha_{lin} - 2*\alpha_{quad}*N_2*pfill_{12}*(1+p_{vis}*p_{22}+p_{adv}+p_{req}*pr_2)\right)*\frac{\psi(Det_1)*pfill_{12}*(1+pm_2)}{3*pfill_{22}*(1+R_{22})*\Pr ice_2} \quad \textbf{(5.34)}$$

If the linear term of the complaint cost (α_{lin}) is greater that the quadratic term ($2*\alpha_{quad}*N_2*pfill_{12}*(1+p_{vis}*p_{22}+p_{adv}+p_{req}*pr_2)$), an increase in *$C_{comp}$* will have a positive effect on equilibrium discount of generic firm. In the opposite case in which the quadratic term is greater, however, generic firm chooses to increase its equilibrium discount. The intuition behind these actions is that firm 2 will try to keep substitution rate in a high level unless quadratic term in the complaint cost dominate the linear term. But if the quadratic term is higher than a threshold, generic firm will cease to give high discounts.

The equilibrium of pharmacy discounts for cash segment drugs can also take place in region D6 where pharmacist favors original drug (drug 1) while advising the drug to the non-prescribed patients and substitutes drug 1 for a specific portion of prescribed drugs of generic manufacturer. In this case equilibrium discount levels will be like the ones given in 5.31. Replacing Pow^*_{12}, Pow^*_{22}, *p_{12}*, *A_{12}* and *B_{12}* with their corresponding explicit forms as we have done before, the equilibrium discount levels for firm 1 and 2 are as follows:

$$\left(disc_{12}^{*},disc_{22}^{*}\right)^{D6}=$$

$$\left(\begin{array}{l}\frac{pfill_{22}*(1+R_{22})*\Pr ice_2*(1+pm_1)}{3*pfill_{12}*(1+R_{12})*\Pr ice_1}+1-\frac{(1+pm_1)}{3}+\frac{C_{comp}*\alpha_{lin}*\psi(Det_2)*pfill_{22}*(1+pm_1)}{3*pfill_{12}*(1+R_{12})*\Pr ice_1}\\ -\frac{2*C_{comp}*\alpha_{quad}*\psi(Det_2)*N_2*pfill_{22}^2*(1+pm_1)}{3*pfill_{12}*(1+R_{12})*\Pr ice_1}*\left(1+p_{vis}*\left(\frac{\xi(Det_1,Q_1,OOP_{12})}{\xi(Det_1,Q_1,OOP_{12})+\xi(Det_2,Q_2,OOP_{22})+1}\right)+p_{adv}+p_{req}*pr_1\right),\\ \\ 1-\frac{(1+pm_2)}{3}+\frac{pfill_{12}*(1+R_{12})*\Pr ice_1*(1+pm_2)}{3*pfill_{22}*(1+R_{22})*\Pr ice_2}-\frac{C_{comp}*\alpha_{lin}*\psi(Det_2)*(1+pm_2)}{3*(1+R_{22})*\Pr ice_2}\\ -\frac{2*C_{comp}*\alpha_{quad}*\psi(Det_2)*N_2*pfill_{22}*(1+pm_2)}{3*(1+R_{22})*\Pr ice_2}*\left(1+p_{vis}*\left(\frac{\xi(Det_2,Q_2,OOP_{22})}{\xi(Det_1,Q_1,OOP_{12})+\xi(Det_2,Q_2,OOP_{22})+1}\right)+p_{req}*pr_2\right)\end{array}\right)$$

(5.35)

The equilibrium in pharmacy decision region D6 given by 5.35 is, indeed, perfectly symmetric with the equilibrium given in 5.31. Merely, firm 1 and firm 2 swap the equilibrium discount levels. All the results listed for equilibrium of cash segment drugs at region D2 will apply to the equilibrium at region D6 except that the results for $disc_{12}$ at region D6 will be the ones given for $disc_{22}$ at region D2 and visa versa. For instance, an increase in generic firm's own detailing (Det_2) will definitely decrease the equilibrium discount level of firm 2 ($disc_{22}$) offered to pharmacy.

Equilibrium discount levels for reimbursed segment drugs:

Now, let us to examine equilibrium discount levels of firms that are purely competing in the reimbursed segment. In the reimbursed segment case; the generic firm offers pharmacy discount to capture more expensive prescribed original drugs while the original firm only offers discounts to avoid loss of its own prescribed drugs to the generic competitor. Replacing Pow_{11}^{*}, Pow_{21}^{*}, p_{11}, A_{11} and B_{11} with their corresponding explicit forms, the equilibrium discount levels are as follows:

$$\left(disc_{11}^{*},disc_{21}^{*}\right)^{D2}=$$

$$\left(\begin{array}{l}1-\frac{(1+pm_1)*(1+2*Govdisc_1)}{3}+\frac{pfill_{22}*(1+R_{22})*\Pr ice_2*(1-Govdisc_2)*(1+pm_1)}{3*pfill_{12}*(1+R_{12})*\Pr ice_1}-\frac{C_{comp}*\alpha_{lin}*\psi(Det_1)*(1+pm_1)}{3*(1+R_{12})*\Pr ice_1}\\ -\frac{2*C_{comp}*\alpha_{quad}*\psi(Det_1)*N_2*pfill_{12}*(1+pm_1)}{3*(1+R_{12})*\Pr ice_1}*\left(1+p_{vis}*\left(\frac{\xi(Det_1,Q_1,OOP_{12})}{\xi(Det_1,Q_1,OOP_{12})+\xi(Det_2,Q_2,OOP_{22})+1}\right)+p_{req}*pr_1\right),\\ \\ \frac{pfill_{12}*(1+R_{12})*\Pr ice_1*(1-Govdisc_1)*(1+pm_2)}{3*pfill_{22}*(1+R_{22})*\Pr ice_2}+1-\frac{(1+pm_2)**(1+2*Govdisc_1)}{3}+\frac{C_{comp}*\alpha_{lin}*\psi(Det_1)*pfill_{12}*(1+pm_2)}{3*pfill_{22}*(1+R_{22})*\Pr ice_2}\\ -\frac{2*C_{comp}*\alpha_{quad}*\psi(Det_1)*N_2*pfill_{12}^2*(1+pm_2)}{3*pfill_{22}*(1+R_{22})*\Pr ice_2}*\left(1+p_{vis}*\left(\frac{\xi(Det_2,Q_2,OOP_{22})}{\xi(Det_1,Q_1,OOP_{12})+\xi(Det_2,Q_2,OOP_{22})+1}\right)+p_{adv}+p_{req}*pr_2\right)\end{array}\right)$$

(5.36)

All the results found for equilibrium of cash segment drugs in region D2 are also applicable to the equilibrium of reimbursed segment drugs given in 5.36. Additionally, we also analyze the sensitivity to the governmental discounts required from all manufacturers included in the reimbursement list. In section 3.2.3, we presented the current rates for the governmental discounts. As discussed before, this discount rate depends on the type of the drug - whether it is original or generic. Even though the generic and original drugs are subject to distinct discount rates, typically changes in these rates are proportional to their current governmental discount levels [4]. Higher level of governmental discounts decreases equilibrium discounting levels of both firms as can be easily deducted from equation 5.36. To understand this, recall that governmental discounts have no effect on the pharmacist's profit but diminish the manufacturer's revenue. Higher levels of governmental discounts mean lower marginal profit from a single drug sold, which in return provides weak incentives for the firms to offer discounts.

Chapter 6

CONCLUSION

In this thesis we have study the pharmacist's role and the impact of pharmacy discounts in the Turkish prescription drug market. First, we give a brief literature about pharmaceutical marketing, and conclude that although many studies focus on patient and physician directed marketing activities, there is a gap in understanding the motives of the pharmacist; and in particular the profit maximizing decision of the pharmacist as a function of pharmacy discounts. Next, we present a detailed overview of Turkish pharmaceutical market to be able to construct a relevant and accurate model of the market. As the result of our modeling, we derive the profit maximizing substitution and non-prescription product advice decisions by the pharmacist for a market with one original and one generic drug in the same reimbursement equivalence class; for the cash payment and reimbursed situations. We discuss the effect of both (original and generic) manufacturer's discounts and detailing activities on pharmacist's rational decisions; and illustrate the resulting impact on the drug sales in both reimbursed and cash segments.

The results show that the pharmacist's profit maximizing decision for substitution and non-prescription product advice depends on the difference of the discount rates from both manufacturers, weighted by other factors such as price, government regulated profit margin and the out-of-pocket expenditure for the patient. Therefore, there is an incentive for the manufacturers to get into a discount war. On the other hand, increased detailing is another defense strategy that increases the minimum discount needed for the pharmacist to start substituting away from the defender. Detailing also decreases the percentage substitution per increase in offensive discount. The original manufacturer - due to the asymmetry in allowed substitution in reimbursed segment - will only discount to defend its prescribed units and potentially capture the pharmacist's advised units for cash patients, while the generic can try - if profitable - to discount in order to switch the prescribed original units away.

We also included manufacturers in our analysis by utilizing a two-stage game in which original and generic manufacturers first decide up on their discounting levels and then pharmacy follows them by deciding substitution and non-prescription product advice. The best response correspondences for both original and generic manufacturers are identified to find out the subgame perfect Nash equilibrium of this two-stage game. In the final step equilibrium pharmacy discounts offered by manufacturers are analyzed to reveal the effect of exogenous parameters on them. The results found after conducting sensitivity analysis are listed in Table 6.1:

increase in \ Equilibrium discount of	cash segment drugs in region D2		cash segment drugs in region D6		reimbursed segment drugs	
	$disc^*_{12}$	$disc^*_{22}$	$disc^*_{12}$	$disc^*_{22}$	$disc^*_{11}$	$disc^*_{21}$
Det_1	↓	?	↓	↑	↓	?
Det_2	↑	↓	?	↓	↑	↓
C_{comp}	↓	?	?	↓	↓	?
$Govdisc_i$	-	-	-	-	↓	↓

Table 6.1: Sensitivity Analysis

As it is seen in Table 6.1, increase in either original or generic detailing results in own discounting level to decrease to optimize the profit. This situation suggests that *detailing and pharmacy discount are substitute of each other* when profitability is the main concern. Although we do not have market data on hand, the interviews we conducted with original and generic manufacturers' managers validates this result. The interview with an original firm's manager reveals that the positive impact of original firms' detailing expenditure on physician's prescribing choice is bigger than the impact of same amount of generic detailing expenditure. Therefore; original firms, willing to derive benefit from this competitive advantage, are likely to spend more aggressively on detailing than generic firms. On the other hand; the regulation, which does not allow cheaper drugs to be replaced by expensive alternatives in reimbursed segment, orients generic manufacturers to pharmacy discounts. Producing usually cheaper alternatives, generic manufacturers do not have to worry about possible losses caused by pharmacy substitution. Thus, they readily concentrate their marketing effort on pharmacy discounts to be able to capture prescribed drugs of their original competitors. As a result, most of original manufacturers in the market prefer not to invest in pharmacy discounts as much as generic firms do. This picture perfectly matches what we have found in the sensitivity analysis about substitutability.

In our analysis, we assumed that the drugs at issue are purely consumed by either reimbursed segment patients or cash segment patients. In reality, however, most of the drugs are purchased both by reimbursed segment patients and patients who pay the whole price out of pocket. Although this fact seems to decrease the applicability of our results, one should keep in mind that for most drug categories the demand structure is bimodal - either predominantly reimbursed, or predominantly - or all cash, as is the case with the drug categories that are being taken out of reimbursement lists - the target market for these drugs becomes merely the cash segment buyers. Although a clearly defined OTC policy is not announced, prospective OTC drugs might also be the concern of our cash segment analysis. On the other hand, drugs heavily consumed by reimbursed segment patients might cause producers to focus their attention strictly on reimbursed segment revenues which gives meaning to our reimbursed segment analysis. Therefore, this study does not fail to provide deeper insights to manufacturers whose demands are predominantly coming from a single segment (reimbursed or cash segment).

Though the analysis is conducted for pharmacy and pharmaceutical manufacturers in this study, the results can also be utilized by regulators of pharmaceutical industry to maximize social welfare of the society. Investigating the strategies and decisions of pharmacists and manufacturers in depth, government can become more prone to take accurate cost containment measures regarding prescription drug market. There is an ongoing debate about direct to consumer (DTC) advertising of pharmaceuticals in Turkey. The possible consequences of the regulations allowing DTC advertising might be captured by adding DTC in the model. A model including DTC and its effects on physician and patient is discussed by Gur Ali et al. (2006) [20].

A crucial assumption that we used in our analysis is the homogeneity of the patients and physicians. In reality, however, response to drug prices undoubtedly varies across patients. Alternatively, the value each physician attributes to quality or detailing may vary across physicians. For instance, Brekke et al. (2006) [19] constructed a model in which patients vary with respect to their susceptibility to treatment with the chemically differentiated drugs. It might have also been possible, in our analysis, to allow heterogeneity by assuming heterogeneous physician response to detailing which would probably be a more realistic assumption. However, our model already has a complex prescribing choice function, though we have assumed homogenous physician response to detailing. Hence, this practice would turn our model to a more complicated one.

As a further research, the model constructed and results found in this study can be supported by researchers interested in governmental implications in prescription drug market. A possible extension is the interface of pharmaceutical marketing with governmental welfare implications. Especially, papers by Brekke et al. (2006) [19], Jelovac et al. (2005) [33], Kong et al. (2004) [34], Ellickson et al. (1999) [35] and Cabrales (2003) [36] are striking works about welfare computation and analysis of pharmaceuticals. However, one should keep in mind that inclusion of welfare analysis would promote the model one step further and possibly cause the model to be much more complicated. The backward induction method, which we have utilized in this study, would first start solving the game with manufacturers' rational discounting behavior, then continue with pharmacy profit maximization, and in the final step finalize with government's social welfare problem. Even, in our case involving only pharmacy and manufacturers, we have derived quite complicated equilibrium discount levels. Hence, if current model is utilized for welfare analysis, we might come up with much more complicated outcomes that are uneasy to interpret. In order to overcome this problem, one possible solution can be to simplify the model. To give a case in point: non-prescribed patients directly requesting a specific drug without asking pharmacy advice (p_{req}) do not have any influence on our sensitivity analysis in the last step. For the sake of simplicity, sales of manufacturers by this mean can be omitted in our model. (i.e. p_{req} can be dropped from equation 4.2. which gives the number of patients from cash segment, who are treated with a specific drug)

Another promising future direction is to conduct the same analysis in this paper with numerical valuations. In order to perform that; parameters, such as price sensitivity of patients, detailing sensitivity of physicians and complaint costs of patients subject to substitution, need to be estimated. Further, statistics related with the fraction of cash paying patients visiting physician, asking for pharmacist's advice or directly requesting a drug should be collected to execute an empirical application of our study.

Although Turkish governments try to regulate few markets as much as they do the pharmaceutical market, the prescription drug market still needs innovative reforms. Though paid on a regulated fixed margin basis, pharmacies find different ways of increasing their unit profits. They are known to receive unknown but thought to be generous pharmacy discounts from manufacturers in the form of free goods. Since the governmental authorities do not regulate the extent of such discounts, an evaluation of pharmacy and manufacturer incomes has never taken place. In this thesis, we conducted a research to assess the pharmacy discounts and its effects on profit maximizing behavior of both pharmacies ad manufacturers. The result of this study can be utilized by regulators of the pharmaceutical market to protect public health, guarantee patient access to safe and effective medicines, and ensure that pharmaceutical expenditure does not become excessive.

Appendix A

SUFFICIENT OPTIMALITY CONDITIONS

The profit maximization problem of pharmacy in cash segment can be modeled as follows:

$$\text{Max } PP_2 = \sum_{i=1}^{2} n_{i2} * (1+R_{i2}) * \Pr ice_i - \sum_{i=1}^{2}\left[n_{i2} * (1+R_{i2}) * \frac{\Pr ice_i}{1+pm_i} * \left(1 - disc_{i2}\right)\right] - \sum_{i=1}^{2} CC_{i2}$$

Subject to

$$1 - psubs_{112} - psubs_{122} = 0$$

$$1 - psubs_{212} - psubs_{222} = 0$$

$$1 - pa_1 - pa_2 = 0$$

$$psubs_{112}, psubs_{122}, psubs_{212}, psubs_{222}, pa_1, pa_2 \geq 0$$

All possible decisions of pharmacy in cash segment are listed below:

	$psubs_{112}$	$psubs_{122}$	$psubs_{212}$	$psubs_{222}$	pa_1	pa_2
Case 1	0	1	0	1	1	0
Case 2	0	1	0	1	0	1
Case 3	0	1	0	1	Y	1-Y
Case 4	1	0	0	1	0	1
Case 5	0	1	1	0	1	0
Case 6	X_{12}	$1-X_{12}$	0	1	0	1
Case 7	0	1	X_{22}	$1-X_{22}$	1	0

Table A.1: All possible pharmacy decisions

Karush Kuhn Tucker Sufficient Optimality Theorem

Assume $x = \{psubs_{112}, psubs_{122}, psubs_{212}, psubs_{222}, pa_1, pa_2\}$ be a feasible solution. Now, let's label the objective function and constraints of the above problem as follows:

$$f(x) = PP_2$$

$$h_1(x) = 1 - psubs_{112} - psubs_{122} = 0 \quad h_2(x) = 1 - psubs_{212} - psubs_{222} = 0 \quad h_3(x) = 1 - pa_1 - pa_2 = 0$$

$$g_{11}(x) = -psubs_{112} \leq 0 \quad g_{21}(x) = -psubs_{212} \leq 0 \quad g_{31}(x) = -pa_1 \leq 0$$

$$g_{12}(x) = -psubs_{122} \leq 0 \quad g_{22}(x) = -psubs_{222} \leq 0 \quad g_{31}(x) = -pa_2 \leq 0$$

Now we can write the pharmacy problem as follows:

Max $f(x)$

Subject to $g_{ij}(x) \leq 0$; $h_i(x) = 0$ for $i =$ 1,2,3 and j = 1,2

Let $\bar{x}$ be an optimum solution to the problem and let I = {{i,j}: g_{ij} $(\bar{x})$ = 0}. Then KKT conditions should hold at $\bar{x}$, that is, there should exist scalars $\bar{u}_{ij} \geq 0$ for {i,j} Є I and $\bar{v}_i$ for i = 1, 2 such that $\nabla f(\bar{x}) - \sum_{i \in I} \bar{u}_{ij} \nabla g_{ij}(\bar{x}) - \sum_{i=1}^{2} \bar{v}_i \nabla h_i(\bar{x}) = 0$ **(A.1)**

Below, we have found the sufficient optimality condition for Case 1 (in which there is no substitution but drug 1 is favored by pharmacist in non-prescription product advice). Optimality conditions for all cases listed in Table A.1 can be found by the same method that we have used for Case 1 below.

KKT Optimality Conditions for Case 1:

Assume $\bar{x}$ = {0,1,0,1,1,0}. Since A.1 should hold, we come up with the following equation set:

$$\frac{\partial f(\bar{x})}{\partial psubs_{112}} - \bar{u}_{11} \frac{\partial(-psubs_{112})}{\partial psubs_{112}} - \bar{v}_1 \frac{\partial(1 - psubs_{112} - psubs_{122})}{\partial psubs_{112}} = 0 \quad \textbf{(A.2)}$$

$$\frac{\partial f(\bar{x})}{\partial psubs_{122}} - \bar{u}_{12} \frac{\partial(-psubs_{122})}{\partial psubs_{122}} - \bar{v}_1 \frac{\partial(1 - psubs_{112} - psubs_{122})}{\partial psubs_{122}} = 0 \quad \textbf{(A.3)}$$

$$\frac{\partial f(\bar{x})}{\partial psubs_{212}} - \bar{u}_{21} \frac{\partial(-psubs_{212})}{\partial psubs_{212}} - \bar{v}_2 \frac{\partial(1 - psubs_{212} - psubs_{222})}{\partial psubs_{212}} = 0 \quad \textbf{(A.4)}$$

$$\frac{\partial f(\bar{x})}{\partial psubs_{222}} - \bar{u}_{21} \frac{\partial(-psubs_{222})}{\partial psubs_{222}} - \bar{v}_2 \frac{\partial(1 - psubs_{212} - psubs_{222})}{\partial psubs_{222}} = 0 \quad \textbf{(A.5)}$$

$$\frac{\partial f(\bar{x})}{\partial pa_1} - \bar{u}_{31} \frac{\partial(-pa_1)}{\partial pa_1} - \bar{v}_3 \frac{\partial(1 - pa_1 - pa_2)}{\partial pa_1} = 0 \quad \textbf{(A.6)}$$

$$\frac{\partial f(\bar{x})}{\partial pa_2} - \bar{u}_{32} \frac{\partial(-pa_2)}{\partial pa_2} - \bar{v}_3 \frac{\partial(1 - pa_1 - pa_2)}{\partial pa_2} = 0 \quad \textbf{(A.7)}$$

If we express the equations A.2 – A.7, we find the equations listed from A.2' to A.7':

$$N_2 * p_{vis} * p_{12} * pfill_{12} * (1 + R_{12}) * \left[\Pr ice_1 - \frac{\Pr ice_1}{(1 + pm_1)} * (1 - disc_{12}) \right] + \bar{v}_1 = 0 \quad \textbf{(A.2')}$$

$$N_2 * p_{vis} * p_{12} * pfill_{22} * (1 + R_{22}) * \left[\Pr ice_2 - \frac{\Pr ice_2}{(1 + pm_2)} * (1 - disc_{22}) \right]$$
$$-C_{comp} * \psi(Det_1) * \begin{pmatrix} \alpha_{lin} * \left[N_2 * p_{vis} * p_{12} * pfill_{12} \right] + \\ 2 * \alpha_{quad} * N_2^2 * p_{vis}^2 * p_{12}^2 * psubs_{122} * pfill_{12}^2 \end{pmatrix} + \bar{u}_{12} + \bar{v}_1 = 0 \quad \textbf{(A.3')}$$

$$N_2 * p_{vis} * p_{22} * pfill_{12} * (1+R_{12}) * \left[\Pr ice_1 - \frac{\Pr ice_1}{(1+pm_1)} * (1-disc_{12}) \right]$$
$$-C_{comp} * \psi(Det_2) * \begin{pmatrix} \alpha_{lin} * \left[N_2 * p_{vis} * p_{22} * pfill_{22} \right] + \\ 2 * \alpha_{quad} * N_2^2 * p_{vis}^2 * p_{22}^2 * psubs_{212} * pfill_{22}^2 \end{pmatrix} + \bar{u}_{21} + \bar{v}_2 = 0 \quad \textbf{(A.4')}$$

$$N_2 * p_{vis} * p_{22} * pfill_{22} * (1+R_{22}) * \left[\Pr ice_2 - \frac{\Pr ice_2}{(1+pm_2)} * (1-disc_{22}) \right] + \bar{v}_2 = 0 \quad \textbf{(A.5')}$$

$$N_2 * p_{adv} * pfill_{12} * (1+R_{12}) * \left[\Pr ice_1 - \frac{\Pr ice_1}{(1+pm_1)} * (1-disc_{12}) \right] + \bar{v}_3 = 0 \quad \textbf{(A.6')}$$

$$N_2 * p_{adv} * pfill_{22} * (1+R_{22}) * \left[\Pr ice_2 - \frac{\Pr ice_2}{(1+pm_2)} * (1-disc_{22}) \right] + \bar{u}_{32} + \bar{v}_3 = 0 \quad \textbf{(A.7')}$$

By solving equations A.2' and A.3' together, we have found $\bar{u}_{12}$, $\bar{u}_{21}$ and $\bar{u}_{32}$ as follows:

$$\bar{u}_{12} = N_2 * p_{vis} * p_{12} * \left\{ \begin{array}{l} pfill_{12} * (1+R_{12}) * \left[\Pr ice_1 - \frac{\Pr ice_1}{(1+pm_1)} * (1-disc_{12}) \right] \\ -pfill_{22} * (1+R_{22}) * \left[\Pr ice_2 - \frac{\Pr ice_2}{(1+pm_2)} * (1-disc_{22}) \right] \\ +C_{comp} * \psi(Det_1) * \left(\alpha_{lin} * \left[N_2 * p_{vis} * p_{12} * pfill_{12}^2 \right] \right) \end{array} \right\} \quad \textbf{(A.8)}$$

$$\bar{u}_{21} = N_2 * p_{vis} * p_{22} * \left\{ \begin{array}{l} pfill_{22} * (1+R_{22}) * \left[\Pr ice_2 - \frac{\Pr ice_2}{(1+pm_2)} * (1-disc_{22}) \right] \\ -pfill_{12} * (1+R_{12}) * \left[\Pr ice_1 - \frac{\Pr ice_1}{(1+pm_1)} * (1-disc_{12}) \right] \\ +C_{comp} * \psi(Det_2) * \left(\alpha_{lin} * \left[N_2 * p_{vis} * p_{22} * pfill_{22}^2 \right] \right) \end{array} \right\} \quad \textbf{(A.9)}$$

$$\bar{u}_{32} = N_2 * p_{adv} * \left\{ \begin{array}{l} pfill_{12} * (1+R_{12}) * \left[\Pr ice_1 - \frac{\Pr ice_1}{(1+pm_1)} * (1-disc_{12}) \right] \\ -pfill_{22} * (1+R_{22}) * \left[\Pr ice_2 - \frac{\Pr ice_2}{(1+pm_2)} * (1-disc_{22}) \right] \end{array} \right\} \quad \textbf{(A.10)}$$

By KKT sufficient conditions, $\bar{u}_{12}$, $\bar{u}_{21}$ and $\bar{u}_{32}$ are required to be equal to or greater than zero. Thus; in order to have an optimum solution $\bar{x} = \{0,1,0,1,1,0\}$like the one given in Case 1 of Table A.1, following conditions should satisfy:

$$\left\{\begin{array}{l} pfill_{22}*(1+R_{22})*\left[\Pr ice_2-\dfrac{\Pr ice_2}{(1+pm_2)}*(1-disc_{22})\right] \\ -pfill_{12}*(1+R_{12})*\left[\Pr ice_1-\dfrac{\Pr ice_1}{(1+pm_1)}*(1-disc_{12})\right] \end{array}\right\} \le C_{comp}*\psi(Det_1)*\alpha_{lin}*N_2*p_{vis}*p_{12}*pfill_{12}^2 \quad \textbf{(A.11)}$$

$$\left\{\begin{array}{l} pfill_{12}*(1+R_{12})*\left[\Pr ice_1-\dfrac{\Pr ice_1}{(1+pm_1)}*(1-disc_{12})\right] \\ -pfill_{22}*(1+R_{22})*\left[\Pr ice_2-\dfrac{\Pr ice_2}{(1+pm_2)}*(1-disc_{22})\right] \end{array}\right\} \le C_{comp}*\psi(Det_2)*\alpha_{lin}*N_2*p_{vis}*p_{22}*pfill_{22}^2 \quad \textbf{(A.12)}$$

$$pfill_{12}*(1+R_{12})*\left[\Pr ice_1-\frac{\Pr ice_1}{(1+pm_1)}*(1-disc_{12})\right] \ge pfill_{22}*(1+R_{22})*\left[\Pr ice_2-\frac{\Pr ice_2}{(1+pm_2)}*(1-disc_{22})\right] \quad \textbf{(A.13)}$$

Combining A.11, A.12 and A.13, we have the following condition for the optimal solution in Case 1:

$$0 \le \left\{\begin{array}{l} pfill_{12}*(1+R_{12})*\left[\Pr ice_1-\dfrac{\Pr ice_1}{(1+pm_1)}*(1-disc_{12})\right] \\ -pfill_{22}*(1+R_{22})*\left[\Pr ice_2-\dfrac{\Pr ice_2}{(1+pm_2)}*(1-disc_{22})\right] \end{array}\right\} \le C_{comp}*\psi(Det_2)*\left(\alpha_{lin}*\left[N_2*p_{vis}*p_{22}*pfill_{22}\right]\right) \quad \textbf{(A.14)}$$

When we utilize the conversions listed in 4.11 and 4.13, we come up with the ultimate condition for pharmacy decision in region D5 given by 4.10:

$0 \le Pow_{22} - Pow_{12} \le A_{22}$ **(A.15)**

Consequently; when the power difference between drug 1 and drug 2 in cash segment (Pow_{22}-Pow_{12}) is between 0 and A_{22}, the pharmacy will choose not to substitute any brand and will dispense drug 1 for non-prescribed patients asking for his/her advice as the optimal decision.

Appendix B

THE NECESSARY CONDITIONS FOR EQUILIBRIUM

Equilibrium of Cash Segment Drugs in Region D2

The equilibrium we construct for cash segment drugs in pharmacy decision region D2 assumes following conditions[1]:

1) The power difference between two drugs (Pow_{22} - Pow_{12}) is between A_{12} and $A_{12} + B_{12}$ since the equilibrium takes place in region D2:

$A_{12} \leq Pow_{22}^{*} - Pow_{12}^{*} \leq A_{12} + B_{12}$ **(B.1)**

2) The equilibrium power levels are feasible. In other words, they are between minimum and maximum power levels that are product of no discount and %100 discount respectively.

$Pow_{12}^{\min} \leq Pow_{12}^{*} \leq Pow_{12}^{\max}$ **(B.2)**

$Pow_{22}^{\min} \leq Pow_{22}^{*} \leq Pow_{22}^{\max}$ **(B.3)**

3) The equilibrium power levels are found by assuming that everywhere the profit function equals the one which is valid in region D2. However, the profit function differs for every region of the graph. Hence, we should check whether other power levels result in a worse profit than the equilibrium level. When $Pow_{22} = Pow_{22}^{*}$, Pow_{12} should be the profit maximizing power level for firm 1. Likewise; if $Pow_{12} = Pow_{12}^{*}$, firm 2's profit should be maximized with Pow_{22}. We can also demonstrate this situation with the example given in Figure B.1. When we assume that equilibrium takes place at the intersection of best response lines in region D2, the point X having coordinates ($Pow_{12}^{*}, Pow_{22}^{*}$) should guarantee for firm 1 at least as high profit as the ones acquired at points K, L and M. Further declaring X as the Nash equilibrium requires better profits for firm 2 at point X than the ones acquired at point N and P.

[1] Expressions given here like Pow_{ik}, Pow_{ik}^{*}, $Pow_{ik}^{\min}$, $Pow_{ik}^{\max}$, A_{ik}, B_{ik} are same as the ones of which explicit forms are provided in the main text.

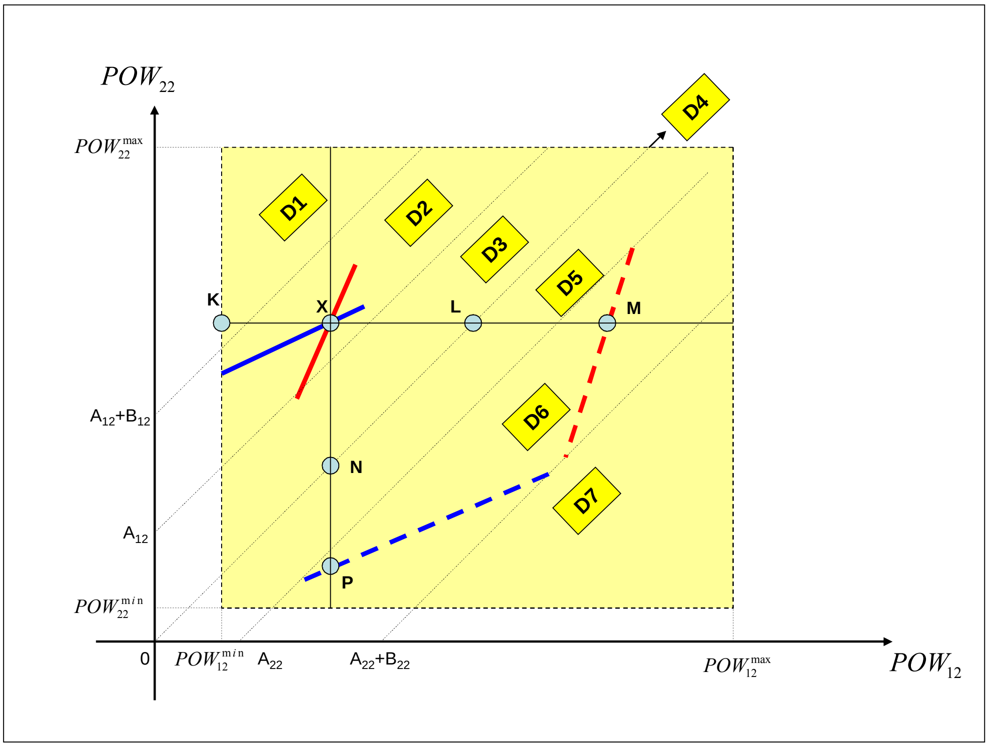


Figure B.1: Necessary Conditions for equilibrium in cash segment

Now, let us summarize remaining necessary conditions required for equilibrium of cash segment drugs in pharmacy decision region D2:

The profit of firm 1 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at the point $(Pow_{12}^{\min}, Pow_{22}^*)$ if this point takes place in region D1:

$$MP_1\left(Pow_{12}^*, Pow_{22}^*\right) \geq MP_1\left(Pow_{12}^{\min}, Pow_{22}^*\right)\Big| \left[Pow_{22} - Pow_{12} \geq A_{12} + B_{12}\right]^2 \quad \textbf{(B.4)}$$

The profit of firm 1 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at the point $(Pow_{22}^* + \varepsilon, Pow_{22}^*)$ if this point takes place in region D5:

$$MP_1\left(Pow_{12}^*, Pow_{22}^*\right) > MP_1\left(Pow_{22}^* + \varepsilon, Pow_{22}^*\right)\Big| \left[0 < Pow_{12} - Pow_{22} \leq A_{12}\right] \quad \textbf{(B.5)}$$

The profit of firm 1 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at the point $\left(\frac{Pow_{22}^*}{2} + \frac{pfill_{12} * (1 + R_{12}) * \Pr ice_1}{2} + \frac{A_{22}}{2} - \frac{B_{22}}{2} * \frac{p_{vis} * p_{12} + p_{adv} + p_{req} * pr_1}{p_{vis} * p_{22}}, Pow_{22}^*\right)$ if this point takes place in region D6:

---

[2] Here the inequality needs to be satisfied only if the condition $\left[Pow_{22} - Pow_{12} \geq A_{12} + B_{12}\right]$ exists.

$$MP_1\left(Pow_{12}^*, Pow_{22}^*\right)$$
$$\geq MP_1\left(\frac{Pow_{22}^*}{2}+\frac{A_{22}}{2}+\frac{pfill_{12}*(1+R_{12})*\Pr ice_1}{2}-\frac{B_{22}}{2}*\frac{p_{vis}*p_{12}+p_{adv}+p_{req}*pr_1}{p_{vis}*p_{22}}, Pow_{22}^*\right) \Big| \left[A_{22} \leq Pow_{12}-Pow_{22} \leq A_{22}+B_{22}\right]$$
(B.6)

The profit of firm 2 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $(Pow_{12}^*, Pow_{22}^{\min})$ if this point takes place in region D7:

$$MP_2\left(Pow_{12}^*, Pow_{22}^*\right) \geq MP_2\left(Pow_{12}^*, Pow_{22}^{\min}\right) \Big| \left[Pow_{12}-Pow_{22} \geq A_{22}+B_{22}\right]$$ **(B.7)**

The profit of firm 2 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $(Pow_{12}^*, Pow_{12}^*+\varepsilon)$ if this point takes place in region D3:

$$MP_2\left(Pow_{12}^*, Pow_{22}^*\right) \geq MP_2\left(Pow_{12}^*, Pow_{12}^*+\varepsilon\right) \Big| \left[0 < Pow_{22}-Pow_{12} \leq A_{22}\right]$$ **(B.8)**

The profit of firm 2 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $\left(Pow_{12}^*, \frac{Pow_{12}^*}{2}+\frac{pfill_{22}*(1+R_{22})*\Pr ice_2}{2}-\frac{A_{22}}{2}-\frac{B_{22}}{2}*\frac{p_{vis}*p_{22}+p_{req}*pr_2}{p_{vis}*p_{22}}\right)$ if this point takes place in region D6:

$$MP_1\left(Pow_{12}^*, Pow_{22}^*\right)$$
$$\geq MP_1\left(Pow_{12}^*, \frac{Pow_{12}^*}{2}+\frac{pfill_{22}*(1+R_{22})*\Pr ice_2}{2}-\frac{A_{22}}{2}-\frac{B_{22}}{2}*\frac{p_{vis}*p_{22}+p_{req}*pr_2}{p_{vis}*p_{22}}\right) \Big| \left[A_{22} \leq Pow_{12}-Pow_{22} \leq A_{22}+B_{22}\right]$$
(B.9)

Equilibrium of Cash Segment Drugs in Region D6

The equilibrium we construct for cash segment drugs in pharmacy decision region D6 assumes following conditions:

1) The power difference between two drugs ($Pow_{12} - Pow_{22}$) is between A_{22} and $A_{22} + B_{22}$ since the equilibrium takes place in region D6:

$$A_{22} \leq Pow_{12}^* - Pow_{22}^* \leq A_{22} + B_{22}$$ **(B.10)**

2) The equilibrium power levels are feasible. In other words, they are between minimum and maximum power levels that are product of no discount and %100 discount respectively.

$$Pow_{12}^{\min} \leq Pow_{12}^* \leq Pow_{12}^{\max}$$ **(B.11)**

$$Pow_{22}^{\min} \leq Pow_{22}^* \leq Pow_{22}^{\max}$$ **(B.12)**

3) The profit of firm 1 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $(Pow_{12}^{\min}, Pow_{22}^*)$ if this point takes place in region D1:

$$MP_1\left(Pow_{12}^*, Pow_{22}^*\right) \geq MP_1\left(Pow_{12}^{\min}, Pow_{22}^*\right)\Big| \left[Pow_{22} - Pow_{12} \geq A_{12} + B_{12}\right] \textbf{ (B.13)}$$

The profit of firm 1 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $(Pow_{22}^* + \varepsilon, Pow_{22}^*)$ if this point takes place in region D5:

$$MP_1\left(Pow_{12}^*, Pow_{22}^*\right) \geq MP_1\left(Pow_{22}^* + \varepsilon, Pow_{22}^*\right)\Big| \left[0 < Pow_{12} - Pow_{22} \leq A_{12}\right] \textbf{ (B.14)}$$

The profit of firm 1 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $\left(\frac{Pow_{22}^*}{2} + \frac{pfill_{12} * (1+R_{12}) * \Pr ice_1}{2} - \frac{A_{12}}{2} - \frac{B_{12}}{2} * \frac{p_{vis} * p_{12} + p_{req} * pr_1}{p_{vis} * p_{12}}, Pow_{22}^*\right)$ if this point takes place in region D2:

$$MP_1\left(Pow_{12}^*, Pow_{22}^*\right)$$
$$\geq MP_1\left(\frac{Pow_{22}^*}{2} + \frac{pfill_{12} * (1+R_{12}) * \Pr ice_1}{2} - \frac{A_{12}}{2} - \frac{B_{12}}{2} * \frac{p_{vis} * p_{12} + p_{req} * pr_1}{p_{vis} * p_{12}}, Pow_{22}^*\right)\Bigg| \left[A_{22} \leq Pow_{12} - Pow_{22} \leq A_{22} + B_{22}\right]$$

(B.15)

The profit of firm 2 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $(Pow_{12}^*, Pow_{22}^{\min})$ if this point takes place in region D7:

$$MP_2\left(Pow_{12}^*, Pow_{22}^*\right) \geq MP_2\left(Pow_{12}^*, Pow_{22}^{\min}\right)\Big| \left[Pow_{12} - Pow_{22} \geq A_{22} + B_{22}\right] \textbf{ (B.16)}$$

The profit of firm 2 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $(Pow_{12}^*, Pow_{12}^* + \varepsilon)$ if this point takes place in region D3:

$$MP_2\left(Pow_{12}^*, Pow_{22}^*\right) \geq MP_2\left(Pow_{12}^*, Pow_{12}^* + \varepsilon\right)\Big| \left[0 < Pow_{22} - Pow_{12} \leq A_{22}\right] \textbf{ (B.17)}$$

The profit of firm 2 at (Pow_{12}^*, Pow_{22}^*) should be greater than the profit at $\left(Pow_{12}^*, \frac{Pow_{12}^*}{2} + \frac{pfill_{22} * (1+R_{22}) * \Pr ice_2}{2} + \frac{A_{12}}{2} - \frac{B_{12}}{2} * \frac{p_{vis} * p_{22} + p_{adv} + p_{req} * pr_2}{p_{vis} * p_{12}}\right)$ if this point takes place in region D2:

$$MP_1\left(Pow_{12}^*, Pow_{22}^*\right)$$
$$\geq MP_1\left(Pow_{12}^*, \frac{Pow_{12}^*}{2} + \frac{pfill_{22} * (1+R_{22}) * \Pr ice_2}{2} + \frac{A_{12}}{2} - \frac{B_{12}}{2} * \frac{p_{vis} * p_{22} + p_{adv} + p_{req} * pr_2}{p_{vis} * p_{12}}\right)\Bigg| \left[A_{22} \leq Pow_{12} - Pow_{22} \leq A_{22} + B_{22}\right]$$

(B.18)

Equilibrium of Reimbursed Segment Drugs

Since substitution is only allowed from original drug to its cheaper generic alternative for drugs in reimbursed list, we will have three decision regions (D1-D3) and only 5 necessary conditions for equilibrium. Now, let us summarize these conditions:

1) The power difference between two drugs (Pow_{21} - Pow_{11}) is between A_{11} and A_{11} + B_{11} since the equilibrium takes place in region D2:

$A_{11} \leq Pow_{21}^{*} - Pow_{11}^{*} \leq A_{11} + B_{11}$ **(B.19)**

2) The equilibrium power levels are feasible. In other words, they are between minimum and maximum power levels that are product of no discount and %100 discount respectively.

$Pow_{11}^{\min} \leq Pow_{11}^{*} \leq Pow_{11}^{\max}$ **(B.20)**

$Pow_{21}^{\min} \leq Pow_{21}^{*} \leq Pow_{21}^{\max}$ **(B.21)**

3) The profit of firm 1 at $(Pow_{11}^{*}, Pow_{21}^{*})$ should be greater than the profit at the point $(Pow_{11}^{\min}, Pow_{21}^{*})$ if this point takes place in region D1:

$MP_1\left(Pow_{11}^{*}, Pow_{21}^{*}\right) \geq MP_1\left(Pow_{11}^{\min}, Pow_{21}^{*}\right)\Big| \left[Pow_{21} - Pow_{11} \geq A_{11} + B_{11}\right]$ **(B.22)**

The profit of firm 2 at $(Pow_{11}^{*}, Pow_{21}^{*})$ should be greater than the profit at $(Pow_{11}^{*}, Pow_{21}^{\min})$ if this point takes place in region D3:

$MP_2\left(Pow_{11}^{*}, Pow_{21}^{*}\right) \geq MP_2\left(Pow_{11}^{*}, Pow_{21}^{\min}\right)\Big| \left[Pow_{21} - Pow_{11} \leq A_{11}\right]$ **(B.23)**

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