How does pharmaceutical marketing influence doctors' prescribing behaviour?

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Preface

This CPB Special Publication is concerned with marketing for prescription pharmaceuticals and its effects on doctors' prescribing behaviour. It was jointly written by Eric de Laat, from CPB's Competition and Regulation unit, Frank Windmeijer, whose input was contracted from the Institute for Fiscal Studies in London, and Rudy Douven, from CPB's Health Care unit. Other people from CPB who have contributed to the research are Ton Brouwer, Marcel Canoy, Cindy Hermans, Esther Mot and Ed Westerhout.

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Henk Don
Director of CPB

Samenvatting (summary in Dutch)

1 Doel en hoofdlijnen

Het doel van deze studie is het beantwoorden van twee centrale vragen. Deze vragen en de antwoorden hierop geven we hieronder.

1. *Wat zijn de effecten in Nederland van de marketing van farmaceutische bedrijven voor recept-geneesmiddelen op het voorschrijfgedrag van artsen en wat betekent dit voor de welvaart?*
   Voorschrijvers zijn over het algemeen weinig prijsgevoelig en farmaceutische marketing maakt artsen nog minder prijsgevoelig in hun voorschrijfgedrag. Dit aspect van farmaceutische marketing werkt welvaartsverlagend, omdat het leidt tot hogere geneesmiddelenkosten door extra marktmacht bij geneesmiddelenproducenten. Farmaceutische marketing leidt ook tot een grotere vraag. Dit tweede effect bestaat uit zowel welvaartsverhogende als welvaartsverlagende deeleffecten in een onbekende verhouding; hierover kunnen daarom geen welvaartsuitspraken worden gedaan.

2. *Als er negatieve welvaartseffecten zijn, welke beleidsopties kunnen deze dan helpen verminderen?*
   Wij zien twee groepen van beleidsopties: (i) specifiek, gericht op het wegnemen van een bepaald ongewenst mechanisme binnen een bepaald marketinginstrument; (ii) algemeen, gericht op het verhogen van de prijsgevoeligheid van artsen (of patiënten) en het verminderen van hun informatie-achterstand. Onderzoek naar de optimale vormgeving en de maatschappelijke kosten van beleidsopties is noodzakelijk.

Waarom stellen we deze vragen over marketing voor receptgeneesmiddelen? Ten eerste omdat farmaceutische bedrijven veel geld uitgeven aan marketing: meer dan 20% van de omzet. Ten tweede worden deze marketingkosten indirect gefinancierd met publiek geld (via de prijzen van geneesmiddelen), omdat veel kosten voor receptgeneesmiddelen gedekt worden door de publieke zorgverzekering.

2 Achtergronden

2.1 Waarom zoveel marketing?

Drie eigenschappen van geneesmiddelen(markten) kunnen de omvang van de marketing-inspanningen verklaren: a) innovatie en imitatie, b) asymmetrische informatie en c) de prijselasticiteit.

Definities

Markt:	Farmaceutische markten corresponderen met aandoeningen (bijvoorbeeld depressie) of condities (verhoogde bloeddruk) die medicamenteus te behandelen zijn. Er worden ongeveer honderd van deze markten onderscheiden.
Geneesmiddel:	Bepaalde werkzame stof tegen een bepaalde aandoening of conditie. Voorbeeld: het geneesmiddel fluoxetine tegen depressie.
Receptgeneesmiddel:	Geneesmiddel dat uitsluitend op voorschrift van een arts afgeleverd mag worden.
(Farmaceutisch) product:	Geneesmiddel van een bepaalde producent. Voorbeeld: het product Prozac (= fluoxetine tegen depressie) van Eli Lilly.
Marketinginstrument:	Activiteit van een bedrijf met (onder andere) marketingdoeleinden. Voorbeelden: artsenbezoek, advertenties, sponsoring, onderzoek.
Marketingmechanisme:	Wijze waarop de effecten van marketing tot stand komen. Voorbeeld: bedrijven kunnen door middel van objectieve en relevante informatie artsen overtuigen op hun producten over te stappen. Het achterliggende marketingmechanisme is dan te benoemen als "het verschaffen van objectieve en relevante informatie".

Het verschil tussen marketinginstrumenten en -mechanismen wordt duidelijk door op te merken dat hetzelfde mechanisme binnen meerdere instrumenten werkzaam kan zijn (informatie wordt overgebracht door artsenbezoekers maar ook tijdens gesponsorde congressen) en dat binnen een instrument meerdere mechanismen hun werk kunnen doen (artsenbezoekers doen meer dan alleen informatie verschaffen).

Innovatie en imitatie

Er komen geregeld nieuwe geneesmiddelen op de markt, die oudere geneesmiddelen vaak verdringen. Producenten van merkgeneesmiddelen zijn afhankelijk van patenten om hun R&D-investeringen terug te verdienen. Wanneer het patent op een merkgeneesmiddel afloopt, wordt dit merkgeneesmiddel vaak verdrongen door generieke (merkloze) imitaties. Empirische studies laten zien dat hoge R&D-intensiteiten in bedrijfstakken vaak samengaan met een relatief hoge marketingintensiteit.

Een implicatie van het proces van innovatie en imitatie is, dat de terugverdientijd beperkt is. Het is dus belangrijk om een nieuw product snel tot een succes te maken, onder andere door middel vaneen marketingcampagne. Dit verklaart (ook) de sterke concentratie van de marketing-inspanningen rondom de eerste levensjaren van een product.

Asymmetrische informatie

De kennis van artsen op het gebied van geneesmiddelentherapieën is niet volledig. De producent van een bepaald geneesmiddel bezit meer kennis over het middel, omdat deze kan beschikken over alle onderzoeksresultaten. Deze informatie-asymmetrie tussen arts en producent heeft twee consequenties:

1. een grote informatiebehoefte bij artsen waarin geneesmiddelenproducenten kunnen voorzien;
2. de mogelijkheid dat geneesmiddelenproducenten de informatie-uitwisseling met artsen kunnen gebruiken voor andere marketingmechanismen dan pure informatievoorziening, bijvoorbeeld het veranderen van de prikkels van artsen (zie paragraaf 5).

Prijselasticiteit

Uit buitenlandse studies blijkt dat de prijselasticiteit van de vraag (van artsen en/of patiënten) naar receptgeneesmiddelen, net als voor andere medische producten en diensten, vaak laag is. Gegeven onder andere de hoge verzekeringsgraad valt te verwachten dat ook in Nederland de prijsgevoeligheid van artsen zeer laag is. Dit vermoeden wordt bevestigd in onze empirische analyse. Uit de literatuur is bekend dat een lage prijselasticiteit in een sector de oorzaak kan zijn van een hoge marketingintensiteit.

De focus van dit rapport ligt bij de invloed van marketing. Daarom betrekken we andere determinanten van het voorschrijfgedrag van artsen niet expliciet in onze beschouwing. Voorbeelden van deze determinanten zijn regulering (en informatievoorziening) door de overheid, invloed van individuele zorgverzekeraars en informatievoorziening door apothekers[1]. Onze conclusies over het voorschrijfgedrag van artsen en de invloed van marketing hierop moeten dus gezien worden binnen de gegeven randvoorwaarden.

2.2 Marketinginstrumenten

Opmerkelijk is de grote verscheidenheid aan marketinginstrumenten. Hieronder zijn gangbare instrumenten, zoals artsenbezoek (vertegenwoordigers), advertenties en direct mail, maar ook instrumenten meer specifiek voor de geneesmiddelensector, zoals het uitvoeren van post-marketing onderzoek, het organiseren van nascholing voor artsen en het sponsoren van onderzoek. Een verklaring voor deze verscheidenheid is waarschijnlijk dat de verschillende instrumenten complementair zijn. Een goed voorbeeld hiervan is de combinatie van symptoom-

[1] De margeconcurrentie binnen het apothekerskanaal blijft ook buiten beschouwing, omdat die het voorschrijfgedrag niet direct beïnvloedt.

reclame gericht op consumenten (“Hebt u last van …, ga dan naar uw huisarts.”) en gelijktijdig een mailing aan artsen over een geneesmiddel voor de betreffende kwaal[2].

3 Effecten van marketing

Wat beïnvloedt de vraag naar een bepaald geneesmiddel? En wat is de invloed van marketing hierop? We ontwikkelen een model aan de hand van het imaginaire product Exampil tegen WZ (Willekeurige Ziekte). Op basis van dit model kunnen we voor de empirische analyse, waarin we het model schatten met Nederlandse data, vier vragen formuleren.

3.1 Model zonder marketing, beschrijft het vraaggedrag na marketing

In eerste instantie bekijken we een model waarin marketing niet expliciet is opgenomen. Dit model beschrijft daarom het gedrag van artsen nadat marketing heeft plaatsgevonden. Welke factoren, buiten marketing, beïnvloeden de vraag naar Exampil?

- **Patiënten.** Het aantal mensen dat met WZ-achtige symptomen naar de dokter gaat en hun karakteristieken: hoe oud zijn ze? welke geneesmiddelen gebruiken ze al? enzovoort.
- **Prijzen.** De prijs van Exampil en de prijzen van concurrenten.
- **Subjectieve kwaliteit.** Het beeld dat artsen hebben van de kwaliteit van Exampil (en van het kwaliteitsverschil met de concurrenten.
- **Prijselasticiteit.** Een arts kiest voor Exampil als dit de beste verhouding biedt tussen prijs en subjectieve kwaliteit, gegeven patiëntenaantallen en -karakteristieken. De prijselasticiteit is de gevoeligheid van artsen voor prijsveranderingen gegeven de subjectieve kwaliteit.

Vraag 1: Hoe hoog is de prijselasticiteit van de vraag naar een bepaald geneesmiddel?

3.2 Model met marketing

In het tweede model nemen we marketing wel expliciet mee. Hierdoor kunnen we het vraaggedrag na marketing splitsen in het gedrag voor marketing en de mogelijke effecten daarop. Dit zijn er twee.

Hoeveelheidseffect

Het hoeveelheidseffect is het directe effect van marketing op de vraag, hetzij door een verandering in patiëntenaantallen en -karakteristieken, hetzij door een verandering van de subjectieve kwaliteit.

[2] Publieksreclame voor receptgeneesmiddelen is onder de huidige regelgeving in Europa nauwelijks toegestaan. Inmiddels is in een aantal rechtszaken in Nederland bepaald dat het verbod op publieksreclame ook van toepassing is op symptoomreclame.

Vraag 2: Richting van het hoeveelheidseffect: leidt meer marketing voor een product tot een hogere of tot een lagere vraag naar dat product?

We verwachten dat het hoeveelheidseffect positief is: meer marketing leidt tot een hogere vraag. Evenzo zal marketing voor Exampil ook kunnen leiden tot een lagere vraag naar producten van concurrenten. Een vraag voor de empirische analyse is dan welk deel van de gestegen afzet is "afgepakt" van concurrenten en welk deel (de rest) voortkomt uit een vergroting van de markt?

Vraag 3: Welk deel van het hoeveelheidseffect van marketing gaat ten koste van de vraag naar concurrerende producten en welk deel is marktvergroting?

Wat kunnen we zeggen over de welvaartseigenschappen van het hoeveelheidseffect? Niet veel. Indien een marketing-campagne ertoe leidt dat patiënten onnodig Exampil krijgen voorgeschreven, dan is dit slecht voor de welvaart. Maar de welvaart kan ook stijgen, bijvoorbeeld als de campagne ertoe leidt dat door adequate geneesmiddelentherapie leed voorkomen wordt. Het onderscheid tussen deze gevallen is binnen deze studie niet te maken. Aan de richting of de omvang van het hoeveelheidseffect verbinden wij daarom geen welvaartsconclusies.

Elasticiteitseffect

Door marketing kunnen artsen meer of minder prijsgevoelig worden. Dit is het elasticiteitseffect. Als we de vraag naar Exampil in een grafiek afzetten tegen de prijs, dan komt het hoeveelheidseffect overeen met een verschuiving van de vraagcurve en het elasticiteitseffect met een draaiing: de vraagcurve wordt steiler of vlakker.

Vraag 4: Richting van het elasticiteitseffect: leidt farmaceutische marketing tot een hogere of tot een lagere prijselasticiteit?

In tegenstelling tot het hoeveelheidseffect is aan de richting van het elasticiteitseffect wel een welvaartsconclusie te verbinden. Bij een hoge prijselasticiteit zetten bedrijven scherpe prijzen, omdat kleine prijsverschillen al een grote invloed op het marktaandeel kunnen hebben. Bij een lage prijselasticiteit zullen bedrijven geneigd zijn hoge marges te rekenen (marktmacht). Bij gegeven (subjectieve) kwaliteiten van producten leidt een hoge prijselasticiteit daarom tot een betere marktuitkomst dan een lage. (Merk op dat we de subjectieve kwaliteit in ons model hebben opgenomen, waardoor we de prijselasticiteit kunnen beschouwen als de elasticiteit bij gegeven kwaliteiten.) Als marketing de prijselasticiteit verlaagt, dan is dit dus welvaartsverlagend.

We merken op dat de welvaartseffecten van het hoeveelheidseffect betrekking hebben op patiëntenwelvaart (therapiekeuze) en die van het elasticiteitseffect op consumentenwelvaart (premiehoogte). Alleen aan de richting van het elasticiteitseffect kunnen we welvaartsconclusies verbinden. Het welvaartsoordeel verbonden aan de richting van het elasticiteitseffect staat daarom centraal in de empirische analyse.

Bij de hierboven beschreven welvaartseffecten past nog de volgende kanttekening. Met de analyse van effecten op voorschrijfgedrag blijven twee elementen buiten beschouwing:

- De *neveneffecten* buiten geneesmiddelenmarkten. Geneesmiddelen-advertenties in medische tijdschriften dragen bijvoorbeeld bij aan een goedkope verspreiding van de kennis in deze bladen. Deze neveneffecten kunnen welvaartsverhogend zijn.
- De *marketingkosten*. Deze kosten zijn per definitie welvaartsverlagend, net als alle andere kosten in iedere andere bedrijfstak, wanneer ze geïsoleerd van hun effecten worden beschouwd.

Per saldo is het niet waarschijnlijk dat de neveneffecten opwegen tegen de marketingkosten. Hierdoor zijn de totale welvaartseffecten van farmaceutische marketing ongunstiger dan alleen de effecten op het voorschrijfgedrag.

4 Empirische analyse: resultaten

Voor de empirische analyse hebben we het model geschat met Nederlandse voorschrijf- en marketingdata op productniveau voor 11 markten, waaronder hypertensie, maagzweer, astma, cholesterol en depressie. De marketingdata omvat artsenbezoek aan huisartsen en psychiaters, advertenties en mailings. De data bestreken alle 72 maanden in de periode 1994-1999.

4.1 Het elasticiteitseffect

Farmaceutische marketing verlaagt de prijselasticiteit in het voorschrijfgedrag van artsen. De prijselasticiteit *na* marketing verschilt niet significant van nul (vraag 1). Deze lage prijselasticiteit wordt mogelijk veroorzaakt door de hoge verzekeringsgraad en andere randvoorwaarden voor artsen, maar ook door marketing. De elasticiteit na marketing is namelijk te splitsen in een elasticiteit *voor* marketing, die wel significant van nul verschilt, en een significant elasticiteits-effect van marketing. Het elasticiteitseffect zorgt er dus voor dat artsen een lagere prijs-gevoeligheid tonen in hun voorschrijfgedrag, dan ze zouden doen bij afwezigheid van marketing. Dit effect verlaagt de maatschappelijke welvaart[3].

[3] Dit resultaat bleek niet gevoelig voor wijzigingen in de modelspecificatie, zoals andere functionele vormen, en evenmin voor beperkingen opgelegd aan de data, zoals het al dan niet toevoegen van middelen met generieke concurrenten. In econometrische termen: het resultaat is robuust.

We benadrukken wel dat het hier gaat om een gemiddeld resultaat. Het is zeker niet uitgesloten dat een deel van de marketing de prijselasticiteit verhoogt. Hierdoor kan het zijn dat op het niveau van een product of zelfs een hele markt het effect van marketing per saldo een hogere prijselasticiteit is. Ons resultaat zegt dat hiertegenover zoveel marketinginspanningen, producten en markten staan die de prijselasticiteit verlagen, dat de prijselasticiteit gemiddeld daalt door marketing.

4.2 Andere resultaten

Hoeveelheidseffect is positief

Een toename in marketing voor een product leidt gemiddeld tot een significant hogere vraag naar dat product. Dit effect wordt kleiner naarmate het niveau van marketing hoger is. Van dit hoeveelheidseffect is niet op voorhand vast te stellen of het de welvaart van patiënten verhoogt of verlaagt.

Welk deel van het hoeveelheidseffect gaat ten koste van concurrenten?

Marketing leidt ook tot een daling van de vraag naar concurrerende producten. Onze schattingen laten zien dat gemiddeld ongeveer 40% van het hoeveelheidseffect van marketing ten koste gaat van de vraag naar concurrerende producten. De andere 60% van de vraagstijging komt dus voort uit vergroting van de markt.

4.3 Interpretatie

Wat zijn de consequenties van het elasticiteitseffect voor de praktijk? Een vereenvoudigde weergave is dat een arts die moet kiezen tussen twee middelen van gegeven (subjectieve) kwaliteit waarvoor evenveel marketing heeft plaatsgevonden, eerder zal kiezen voor het duurdere middel naarmate het marketingniveau van de beide middelen hoger is. In werkelijkheid zullen marketingniveaus tussen middelen echter verschillen en zal marketing er bovendien toe leiden dat een middel in de ogen van de arts "beter wordt" (kwaliteit is niet gegeven). Ons resultaat laat zien dat ook binnen deze complexe beslissing marketing leidt tot meer marktmacht bij geneesmiddelenproducenten. Hierdoor ontstaat een opwaartse druk op de geneesmiddelen-kosten.

Resumerend, gemiddeld vinden we een significant welvaartsverlagend effect van farmaceutische marketing op de prijselasticiteit van artsen. Marketing verschaft geneesmiddelenproducenten additionele marktmacht. Hierdoor ontstaat een opwaartse druk op de kosten van geneesmiddelen. Aan het tweede, vraagverhogende, effect van marketing kunnen we geen welvaartsconclusies verbinden.

5 Implicaties voor beleid

De vaststelling dat farmaceutische marketing een welvaartsverlagend (deel)effect heeft, impliceert dat beleid op dit gebied zinvol kan zijn. De vraag is dan, wat voor beleid? Beleidsopties vallen uiteen in twee groepen: (i) specifiek beleid, gericht op een bepaald – welvaartsverlagend – marketinginstrument; (ii) algemeen beleid, gericht op het vergroten van de prijsgevoeligheid van artsen (en patiënten) en het verbeteren van hun productinformatie.

De hieronder te bespreken beleidsopties zijn in twee opzichten tentatief. Ten eerste is onduidelijk hoe hoog de maatschappelijke kosten zijn die aan de opties kleven. Aanvullend onderzoek naar deze maatschappelijke kosten is noodzakelijk, voordat opties geïmplementeerd kunnen worden. Ten tweede geven wij niet aan op welk niveau beleidsopties geïmplementeerd kunnen worden. Mogelijke niveaus zijn onder andere overheid/regelgeving, contracten tussen artsen en zorgverzekeraars en zelfregulering.

5.1 Specifieke mechanismen van marketing

In deze studie identificeren we vijf verschillende mechanismen van farmaceutische marketing. Twee hiervan zijn bij uitstek relevant voor beleid omtrent farmaceutische marketing.

Het wijzigen van de prikkels van artsen

Een arts treedt op als agent van zijn patiënten. Hij wordt geacht te handelen in het belang van zijn patiënten. Onderzoek laat zien dat dit in veel gevallen ook gebeurt. Financiële/materiële relaties met farmaceutische bedrijven verstoren echter de prikkel om het patiëntenbelang voorop te stellen. Soms behelst dit een directe prikkel om een bepaald product voor te schrijven, maar beïnvloeding gebeurt vooral via het reciprociteitsprincipe: de arts krijgt iets en voelt zich moreel verplicht iets "terug te doen" voor het bedrijf.

Het creëren van differentiatie

Marketing kan ertoe leiden dat artsen een beeld krijgen van (eigenschappen van) een geneesmiddel dat niet strookt met de beschikbare wetenschappelijke kennis over het middel. Dit kan door het verschaffen van onvolledige, niet-relevante of niet-objectieve informatie, maar ook via psychologische effecten, bijvoorbeeld het appelleren aan gevoelens van artsen om mee te gaan met de nieuwste technologie.

Hieronder geven we aan hoe marketinginstrumenten deze mechanismen in praktijk brengen en schetsen we beleidsopties die de negatieve invloed van de mechanismen kunnen beperken.

5.2 Marketinginstrumenten die artsenprikkels veranderen: beleidsopties

Hieronder bespreken we belangrijke concrete gevallen (instrumenten) waarbij prikkels van artsen veranderd kunnen worden. De bijbehorende beleidsopties zijn gericht op het zoveel mogelijk wegnemen van de financiële/materiële relatie tussen arts en bedrijf of het indirect maken van de relatie, bijvoorbeeld door een partij tussen de arts en het bedrijf te plaatsen.

Post-marketing-onderzoek

Bedrijven betalen artsen die deelnemen aan post-marketing-onderzoek per voorschrift, per ingestelde patiënt of een totaalbedrag (of cadeau) voor deelname. Een deel van deze onderzoeken dient geen wetenschappelijk doel en is uitsluitend gericht op het verwerven van marktaandeel door artsen te belonen voor het uitschrijven van de gewenste recepten. De discussie in de medische wereld over post-marketing-onderzoek richt zich vooral op deze niet-wetenschappelijke onderzoeken.

Opties voor beleid:

- *Verbieden van betalingen (in geld of natura) aan artsen voor deelname aan niet-wetenschappelijk post-marketing-onderzoek; een onafhankelijke (bestaande of nieuwe) organisatie kan vaststellen of onderzoek al dan niet wetenschappelijk is.*
- *Vaststellen van een redelijke maximum-vergoeding aan artsen voor deelname aan wetenschappelijk post-marketing-onderzoek.*

Gastvrijheid en cadeaus

Er is sprake van gastvrijheid indien bedrijven kosten van artsen financieren, zoals reis- en verblijfskosten rondom congressen en promotiebijeenkomsten. Het komt ook voor dat (de partner van) een arts goedkoop kan deelnemen aan nevenactiviteiten bij cursus, congres of promotiebijeenkomst. Daarnaast ontvangen artsen cadeaus, doorgaans van artsenbezoekers, via mailings of tijdens promotiebijeenkomsten. De meest in het oog springende activiteiten van de Sector Toezicht Geneesmiddelenreclame van de Inspectie voor de Gezondheidszorg in de laatste jaren hadden betrekking op het toezicht op en de handhaving van de regels rondom gastvrijheid.

Opties voor beleid:

- *Zoveel mogelijk verbieden van gastvrijheid en cadeaus.*
- *Omvang van gastvrijheid en cadeaus binden aan maxima, bijvoorbeeld analoog aan de regels hierover voor ambtenaren; deze optie wordt momenteel geïmplementeerd in de regelgeving rondom geneesmiddelenreclame.*

5.3 Marketinginstrumenten die differentiatie creëren: beleidsopties

Dit welvaartsverlagende mechanisme is in de praktijk vaak vervlochten met welvaartsverhogende relevante en objectieve informatie: welk deel van wat artsenbezoekers aan artsen vertellen is bijvoorbeeld informatie en welk deel is differentiatie? Deze situaties bieden daarom geen handvat voor beleid. Voor de concrete situaties hieronder is beleid wel mogelijk.

Nascholing voor huisartsen

Alle artsen zijn verplicht nascholing te volgen. Ongeveer de helft van de nascholing voor huisartsen wordt georganiseerd door of in opdracht van geneesmiddelenproducenten. Daarbij wordt de invloed op onderwerpen (aanbodsturing) en inhoud wel eens gebruikt voor het bedrijven van marketing. Dit is in strijd met de regels voor accreditatie gehanteerd door de Landelijke Huisartsen Vereniging. Daarnaast kunnen bedrijven hun cursussen combineren met aantrekkelijke locaties en nevenprogramma's, en de kosten hiervan afwentelen op verzekerden via de geneesmiddelenprijzen. Door deze kruissubsidiëring is de markt voor nascholing aan huisartsen onaantrekkelijk voor onafhankelijke commerciële aanbieders van nascholing.

Opties voor beleid:

- *Accreditatie (verlening, controle en intrekken in geval van overtredingen) bij voorkeur in handen van een onafhankelijk orgaan (onafhankelijk van zowel de industrie als de artsen).*
- *Farmaceutische bedrijven uitsluiten van het (laten) organiseren van nascholing.*
- *Organisaties die de regels voor accreditatie overtreden (tijdelijk) uitsluiten van het (laten) organiseren van nascholing.*
- *Alle gemaakte kosten door laten berekenen aan deelnemende artsen, bijvoorbeeld door accreditatie hiervan afhankelijk te maken*[4].

Opinion leaders

Artsen staan meer open voor de boodschap van een collega-arts, dan voor die van een marketing-medewerker. Daarom laten bedrijven tijdens symposia, promotiebijeenkomsten en nascholings-cursussen artsen met een gunstige mening over hun product (tegen betaling) als spreker optreden. Toehoorders zijn vaak niet op de hoogte dat deze *opinion leaders* (bewust of onbewust) optreden als verlengstuk van een marketingafdeling.

Opties voor beleid:

- *Betaling van farmaceutisch bedrijf aan arts voor optreden als spreker binden aan redelijk maximum.*
- *Sprekers (en auteurs) en de industrie verplichten financiële/materiële relaties te openbaren.*

[4] Artsen krijgen via hun tarief al een vergoeding voor nascholingskosten. Daarnaast is 140-180% van de inschrijvingskosten voor nascholing fiscaal aftrekbaar.

5.4 Determinanten van marketing: algemene beleidsopties

Naast bovenstaande specifieke beleidsopties zijn er ook algemene beleidsopties voor farmaceutische marketing. Deze sluiten aan bij twee van de determinanten van de geconstateerde omvang van de marketinginspanningen in deze sector (zie paragraaf 2):

- lage prijselasticiteit van de vraag naar geneesmiddelen;
- asymmetrische informatie tussen arts en geneesmiddelenproducent.

We bespreken hier alleen (beleidsopties rondom) de eerste determinant.

Lage prijselasticiteit

De lage prijselasticiteit in uit het voorschrijfgedrag van artsen is onder andere het gevolg van de hoge verzekeringsgraad voor receptgeneesmiddelen. Hierdoor hechten patiënten en artsen (hun agenten) weinig belang aan prijzen van en prijsverschillen tussen receptgeneesmiddelen.

Beleidsopties:

- *In het nieuwe zorgstelsel krijgen de zorgverzekeraars een regisseursrol. Zij kunnen in onderhandelingen met zorgaanbieders kostenbesparingen en kwaliteitsverbeteringen afdwingen. Indien het nieuwe stelsel zorgverzekeraars in staat stelt en een prikkel geeft deze rol op zich te nemen, kan dit ook leiden tot meer kostenbewustzijn bij voorschrijvers.*
- *Een grotere rol voor kosten-baten-analyses (farmaco-economisch onderzoek) bij de toelating van geneesmiddelen in het verzekerde pakket (wordt ingevoerd per 1 februari 2002) en het vaststellen van een vergoedingslimiet.*
- *Eigen betalingen voor receptgeneesmiddelen proportioneel met de prijs: patiënten betalen een percentage van de kosten uit eigen zak, met een voldoende hoog plafond.*

1 Introduction

1.1 Motivation, goal and questions

Pharmaceutical companies spend large sums of money on the marketing of prescription pharmaceuticals. In an absolute sense this is not surprising, since the pharmaceutical sector is large: in 1996, 1.2% of income in industrialised countries was spent on pharmaceuticals. Total expenditure on pharmaceutical goods in the Netherlands amounted to 0.9% of GDP or 2.8 billion euro. For the larger part this expenditure concerned prescription pharmaceuticals: 2.4 billion euro. But pharmaceutical marketing outlays are large in a relative sense as well. On average, pharmaceutical companies spend 20% or more of their revenues on marketing. This places prescription pharmaceuticals among the most heavily promoted products.

This observation raises the question what effects these marketing outlays have and, more particularly, to what extent society benefits. Answering this question is more urgent for prescription pharmaceuticals than for other industries. More urgent, not only because of the amounts of money involved, but also because a large part of the marketing outlays is financed indirectly by public funds (through prices of pharmaceutical products), since the costs of prescription pharmaceuticals are typically covered by public health insurance. Therefore, the goal of this study is to answer the question above and, if necessary, to formulate policy implications.

The central questions of this study are:

1. Welfare: What are the effects of marketing for prescription pharmaceuticals by pharmaceutical companies in the Netherlands? How is welfare affected?
2. Policy: If policy intervention is necessary, which policy options (may) improve the market outcome?

In the Netherlands, pharmaceutical marketing has received much attention in the past few years, particularly in the popular media. Examples are a series of articles in the newspaper Trouw (2000/2001) and pharmaceutical industry specials on radio (Argos/VPRO) and television (Zembla/VARA). The public view is mostly rather critical towards the activities of the

pharmaceutical companies.[1] The issue is also prominent in international medical circles.[2] Much of the material on this issue is anecdotal and often takes a moral / ethical perspective to assess marketing activities. It singles out specific activities or specific companies and casts a – typically negative – verdict on these cases.

The added value of this study is the economic approach we use to answer the central questions. The economic perspective forces us to take a broad view and to include as many marketing activities as possible by as many pharmaceutical firms as possible. This enables us to formulate conclusions that pertain to the market as a whole, instead of the specific cases discussed by other work.

Markets for prescription pharmaceuticals are different from other product markets in many respects. They are highly regulated and involve a large degree of asymmetric information and a complex set of players. Pharmaceutical firms, doctors, patients, the government, insurance companies and pharmacists are the most important players, but not all. Still, the potential effects of marketing by pharmaceutical firms on prescribing behaviour by doctors are comparable to effects of marketing on consumers in other markets in most respects.[3] Thus, *for our analysis* we can consider pharmaceutical markets as regular markets. However, the reader should keep in mind that pharmaceutical marketing is not the only determinant of doctors' prescribing behaviour. Many other factors play a role, such as regulation (and information provision) by the government, the influence of individual insurance companies and information from pharmacists. These other factors do not play an explicit role in our analysis.

Another unusual characteristic of pharmaceutical markets is the phenomenon of margin competition in the supply channel producer-wholesaler-pharmacist. This phenomenon has no direct influence on the effects of marketing on prescribing behaviour. Therefore, it is also not explicitly taken into account.

The viewpoint we take also implies that our findings should not be interpreted as a moral or ethical judgment. More precisely, if we conclude that the market outcome is significantly flawed, this would be a consequence of the fact that pharmaceutical firms (and other players, such as

[1] In the USA, the public debate has not been decided yet; see for example Calfee (2000) for a pro-industry view and Public Citizen (2001a) for an opposing view.

[2] See for instance Wazana (2000) and the Internet site of Healthy Skepticism (formerly the Medical Lobby for Appropriate Marketing): http://www.healthyskepticism.org. Noteworthy is also the recent simultaneous editorial in the leading medical journals on sponsorship of research (Davidoff et al., 2001).

[3] An important difference is that pharmaceutical marketing is aimed at an advisor/decision maker who is not the consumer. We can, however, assume that the interest of the patient plays a role in the doctor's decision making.

doctors) follow strategies that serve their interest. This also implies that – again, if the market outcome is flawed – it is the responsibility of the government to improve the market outcome, for example through policies that modify the incentives of players in the pharmaceutical market place. Private enterprises cannot be blamed for following their incentives.

Finally, it is important to stress that our analysis leads to conclusions *on average*. This means that the general findings do not carry over to each individual marketing activity, marketing campaign, product, firm or doctor.

Our analysis consists of a theoretical and an empirical part. On the theory side, we analyse the existing economic literature on marketing and welfare and apply this to the specifics of the pharmaceutical industry. Empirically, we analyse Dutch pharmaceutical sales and marketing data covering a large part of the prescription pharmaceutical marketplace.

To arrive at the answer to our central questions, we break them down into three sets of research questions. The first set consists of descriptive issues:

- What are the relevant product and market characteristics?
- Which are potential sources of market failure?
- Which marketing activities are used in the pharmaceutical industry?
- Which suppliers perform these activities? At which demand-side players are they aimed?

The second set of research questions pertains to the first central question, regarding the welfare effects of prescription pharmaceutical marketing:

- What are the relevant welfare criteria?
- What are the possible (welfare) effects of marketing and how do they apply to markets for prescription pharmaceuticals?
- Do marketing activities have effects outside the pharmaceutical markets?
- Can we draw quantitative conclusions about the size of effects from an empirical analysis?

The last set of research questions tackles the policy issue:

- Through which general mechanisms do the effects of marketing activities come about?
- Which targeted policy options can substantially improve the welfare effects of specific marketing activities by mitigating undesirable mechanisms?
- What could be the effects of general policy options, such as introducing a maximum marketing-to-sales ratio?

1.2 Definitions

Market / therapeutic market

It is important to note that there is not just one pharmaceutical market, but about a hundred different ones. Firms compete with each other within therapeutic markets, defined by afflictions (asthma, depression) or conditions (hypertension). Within these therapeutic markets substitutability of one product for another exists, but between such markets substitutability is very low.[4]

Therapy

For most afflictions pharmaceutical therapy is not the only therapy. Typically, pharmaceutical therapy can be substituted by or complemented with changes in life style, psychotherapy, physiotherapy, surgery and many others. No therapy at all can be an option as well.

Total pharmaceutical market

All (therapeutic) markets taken together.

Pharmaceutical

Our definition of a pharmaceutical closely resembles the legal concept of medicinal product for human use: "any substance or combination of substances presented for treating or preventing disease in human beings ..." (Directive 65/65/EEC). We identify a pharmaceutical at the level of its active ingredient(s) and the affliction or condition it treats. For instance, the pharmaceutical fluoxetine against depression. We will not use the word "drug", because of its narcotic connotation.

(Pharmaceutical) product

A (pharmaceutical) product is a specified pharmaceutical from a specified supplier. For example, the product fluoxetine from Eli Lilly, better known as Prozac. (The comparable legal counterpart is "proprietary medicinal product for human use" ;Directive 65/65/EEC.) It is possible to make further differentiations, for instance according to modes of application (tablet or injection), strengths (250mg or 500mg) and package sizes. Most of the analysis in this study occurs at the level of pharmaceuticals or products.

[4] However, a small but increasing number of pharmaceuticals is used against more than one affliction. For example, apart from its classic use as a pain killer, acetyl-salycic acid – best-known under the brand name Aspirin – is currently also used as an anti-thrombotic agent to prevent heart attacks. The impact of these substitutabilities across markets is low. This is due to their small number and other distinctions between the products aimed at the different markets, such as distinct dosages across markets.

Prescription pharmaceutical

A pharmaceutical that can be delivered to a patient only with a prescription of a doctor.[5]

Marketing activity

Activity by a firm, undertaken for (among others) marketing purposes. Examples are detailing, advertising, sponsoring and some research activities.

Marketing mechanism

A mechanism of marketing is a way in which marketing activities produce an effect (here: change a doctor's prescribing behaviour). These mechanisms are important for the policy implications in Chapter 4. Examples of such mechanisms are providing objective and relevant information, and changing doctors' incentives. The difference with a marketing activity may become clear by observing that the same mechanism can be active within different activities (provision of information can be performed by detailers and it can also occur during sponsored conferences) and that several mechanisms can be active within one activity (detailers do not only provide information).

1.3 Structure

The study is structured as follows. Chapter 2 provides a descriptive analysis of the objects of this study: the pharmaceutical industry, pharmaceutical markets and marketing for prescription pharmaceuticals. Chapter 3 analyses the welfare effects of pharmaceutical marketing from the theory and the empirical side, the latter using Dutch sales and marketing data. Next, Chapter 4 addresses the policy questions. Chapter 5 concludes.

[5] Dentists and midwives can also prescribe a limited set of pharmaceuticals. They will not be considered separately in this study.

2 Pharmaceutical marketing: observations and explanations

2.1 Introduction

The aim of this chapter is to give a descriptive analysis of the pharmaceutical industry, pharmaceutical markets and marketing for prescription pharmaceuticals. Much has been written about the pharmaceutical industry and pharmaceutical markets. Which of this material is relevant, given our focus on marketing? We solve this problem by working backwards: we first discuss marketing intensity, the marketing life-cycle and other characteristics of pharmaceutical marketing and then investigate the link between these observations and specific characteristics of the industry and therapeutic markets.

The questions addressed in this chapter are:

- How large are marketing outlays in the pharmaceutical industry?
- What is the typical path of marketing spending for a product through time?
- Which suppliers promote their products (the most)?
- How is spending divided over different marketing activities?
- What is known about the effects of individual marketing activities?
- How is pharmaceutical marketing currently regulated?

For the description of marketing activities in the Netherlands, we draw upon two recent studies – IGZ (2001) and VWS (2001a) – on this subject.

Answering these questions yields observations about pharmaceutical marketing. We discuss characteristics of the pharmaceutical industry and of pharmaceutical markets that can explain these observations. These (possible) explanations are useful, because they yield hypotheses that can be tested in the empirical analysis, and because they provide a basis for policy options.

Despite the international character of the industry, prescription pharmaceutical markets have a strong national character. This is due to social and cultural differences between countries that influence demand. In addition, public insurance coverage differs from country to country and there are international differences in the regulation of the industry and of health care in general. As a result, there can be large differences in products offered and prices charged from country to country. Since the empirical analysis in Chapter 3 (and the policy implications in Chapter 4) pertains to the Netherlands, we concentrate on the Dutch situation in this chapter as well.

The remainder of the chapter has the following structure. Section 2.1 provides statistics about marketing intensity and gives possible explanations for these findings by investigating three

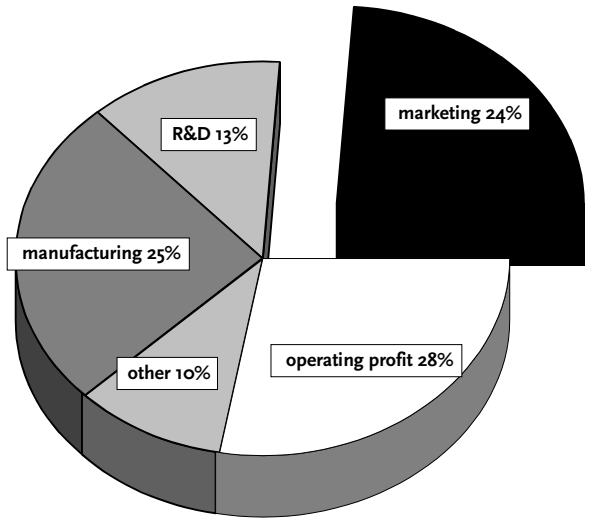
characteristics of supply and demand in this industry. Section 2.2 describes and explains marketing spending for a product through time. Section 2.3 gives an overview of the many different types of marketing activities (and their relative importance) and again provides tentative explanations. Section 2.4 concludes.

2.2 Explaining marketing intensity: R&D, information and price elasticities

OECD figures (Jacobzone, 2000) show that in 1989 the research-oriented pharmaceutical firms spent 24% of sales on marketing (see Figure 2.1). Separate figures for the Netherlands are not available. In Germany, the marketing to sales ratio in 1988 was 27% (Ballance et al., 1992).

How does this marketing intensity compare with other sectors? Scherer and Ross (1990) present the ten leading manufacturing industries in terms of the ratio between media advertising and sales in the U.S.A. in 1977. Over-the-counter (OTC) – i.e. non-prescription – pharmaceuticals are first with a ratio of 20%. Perfumes, cosmetics and other toilet preparations are second with 15%. Other sectors with high media advertising ratios include soft drinks (14%); razor blades; cereal breakfast foods; pet foods; distilled liquors; magazines; cigarettes; and soap products (8%). Arguably, media advertising is likely to constitute the bulk of marketing in these sectors, so that total marketing to sales ratios will not be much higher than the media advertising ratios.

Figure 2.1 Cost structure in the pharmaceutical industry, 1989



Note: Figures are based on data for research-oriented firms only. This means that these figures represent mainly the large pharmaceutical industries based in the main exporting countries.
Source: Jacobzone (2000).

For (prescription) pharmaceuticals this is different. In 1977, media advertising for prescription pharmaceuticals in the U.S.A. was still largely prohibited (as is still the case in most other countries). As a result, the ratio for prescription pharmaceuticals was (only) 4% (rank 28). However, the total marketing to sales ratio for prescription pharmaceuticals at that time was much higher: 19%. Non-media marketing was substantial for OTC pharmaceuticals as well: the total OTC marketing to sales ratio was 36% (Scherer 2000). According to these numbers pharmaceutical firms must be (among) the biggest spenders on marketing.

These numbers are not very recent, but we do not expect that marketing outlays for prescription pharmaceuticals have fallen substantially over the last decade. Scherer (2000) reports that "Total prescription drug advertising and promotion outlays in the U.S. market during 1997 were estimated to be $12 billion, or 18 percent of ethical pharmaceutical sales" (p. 1303). Public Citizen (2001a) provides an additional indication by reporting that in 2000, the eleven pharmaceutical companies appearing in the Fortune 500 rankings spent 30% of revenue on marketing and administrative cost.

How can we explain this marketing intensity? The economic literature provides three possible explanations:

1. Innovation and imitation: Scherer and Ross (1990) report that “Statistical investigations suggest that R&D/sales ratios are higher in industries with relatively intense advertising.” (p. 578).
2. Asymmetric information: “... empirical evidence shows that the advertising/sales ratio is three times greater for experience goods than it is for search goods.” (Cabral, 2000, p. 225).
3. Low price elasticity of demand: Dorfman and Steiner (1954) show that advertising intensity can be expected to be high, if the price elasticity of demand is low.

In the following three subsections we investigate to what extent each of these possible determinants of marketing intensity apply.

2.2.1 The process of innovation and imitation

The pharmaceutical industry is one of the most R&D-intensive industries. Scherer and Ross (1990) discuss a 1977 report in which the pharmaceutical industry has the highest R&D/sales -ratio: 10%. Figure 2.1 shows that the R&D/sales-ratio for the pharmaceutical industry in 1989 was 13%. Public Citizen (2001a) reports that in 2000, the eleven pharmaceutical companies appearing in the Fortune 500 rankings spent 12% of revenue on R&D. Table 2.1 gives an overview of the largest companies in the first six months of 2000.[1] Thus, the process of innovation and imitation is very important for this industry. We expand on it some more below.

[1] Changes in Big Pharma country are frequent. Many of the companies in the table are the results of recent mergers. In addition, in December 2000 Glaxo Wellcome merged with SmithKline Beecham to form a new top dog: GlaxoSmithKline. In the table they are mentioned separately.

Table 2.1 The top ten pharmaceutical companies worldwide

Ranking	Company	Pharmaceutical sales (in million USD)
1	Pfizer	9 640
2	Merck & Co	9 379
3	AstraZeneca	7 806
4	Glaxo Wellcome	7 214
5	Bristol-Myers Squibb	7 000
6	Aventis	6 540
7	SmithKline Beecham	6 508
8	Johnson & Johnson	6 263
9	Pharmacia	6 025
10	American Home Products	5 424

Source: Scrip (2001).

Therapeutic competition

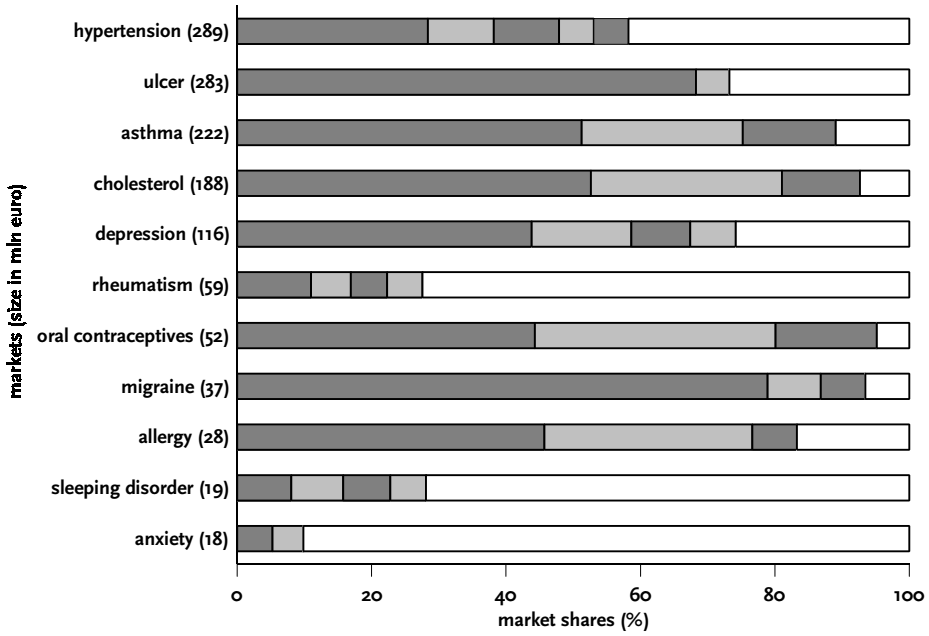
The pharmaceutical industry may be viewed as a product of the patent system. Almost every new pharmaceutical is patented. In the early stages of a pharmaceutical's product life, when it is protected by a patent, its only competitors are existing pharmaceuticals with different active ingredients, so-called therapeutic substitutes.[2] These therapeutic substitutes may differ in their efficacy, safety characteristics and side-effects. Therefore they are imperfect substitutes. Producers of new pharmaceuticals will try to acquire market share by pointing out the specific properties of the new product, such as improved efficacy (for certain patient groups) or less side-effects.

After a firm has patented a novel chemical substance for pharmaceutical use, competitors will often start research on similar chemical substances. *Me-too* products are the result: variations on a theme offered by the original innovator, entering the market not long after introduction of the "real" innovation. Me-too producers typically obtain patents as well. Successful innovations with important therapeutic gains over existing drugs often trigger a series of these me-too innovations, increasing the number of (close) therapeutic substitutes.

Therapeutic markets tend to be dominated by one or a very few firms. In 73 of the 102 Dutch therapeutic markets examined by Reekie (1981) the three-firm concentration ratio exceeded 75%. Figure 2.1 presents market shares of leading firms in 1999 for eleven Dutch therapeutic markets obtained from the data used for the empirical analysis of Chapter 3. The market sizes provided in the figure are the total cost for the patient/insurer (in million euro). The light and dark grey

[2] We do not consider so-called parallel imports – foreign, imported versions of the same product – as separate, competing products, since doctors cannot make a distinction between original and parallel-imported. In the empirical analysis, we have added sales of original and parallel-imported products and taken the average price.

Figure 2.2 Market shares in 11 Dutch markets, 1999



Note: Market sizes are the total cost for the patient/insurer. Light and dark grey areas represent firms with a market share of 5% or more. White areas are the combined smaller market shares.
Source: Geneesmiddelen Informatie Project /College voor Zorgverzekeringen, calculations by CPB.

areas represent firms with a market share of 5% or more. The white areas are the combined market shares of smaller firms. It is clear from the figure that also in 1999 a number of important markets was dominated by one or only a few companies.

Nevertheless, there are very few industries in which a market can be lost as quickly as in pharmaceuticals. One-third of all markets experienced a leadership change during the six years covered by the data of Reekie (1981). Analysis of Dutch data for the 1994-1999 period gives similar results: in 40% of the markets a leadership change occurred. This volatility in market share is a natural outcome of the process of innovation and imitation in the industry. Patents play an important role in this process. Firms depend on the emergence of new pharmaceuticals from their laboratories. Once a pharmaceutical is marketed and believed to be a major advance, it will gain acceptance, and other pharmaceuticals will lose position.

Generic Competition

After expiration of the patent other producers can and - in case the original pharmaceutical has some market share - will enter the market with generic copies of the pharmaceutical.[3] Generic producers are typically smaller companies that serve one or a few countries, although a multinational may decide to market a generic copy of its own branded pharmaceutical. Generic products are bio-equivalent to the original branded product: almost perfect substitutes with the same active ingredient, and in principle the same efficacy, safety characteristics and side-effects as the original (branded) pharmaceutical.[4] The only differences pertain to presentation: name, packaging, colour, size. This implies that price is an important marketing instrument at this stage.

The importance of generic products differs from country to country: in the United States, the United Kingdom, Germany and the Netherlands generics have a substantial market share (around 40-55% in number of prescriptions); France, Belgium and Switzerland have a small number of generic prescriptions (5-10%); Mediterranean countries and Ireland have almost no generic sales (GIP, 2000b; Jacobzone, 2000). It is not completely clear what is the cause of these differences; cultural differences (orientation toward branded products) and government policies to promote generics may play a role.

Generic pharmaceuticals have acquired a substantial market share in the Dutch pharmaceutical market. In number of prescriptions it has grown from 25% in 1990 to 44% in 1999 and in pharmaceutical costs from 9% in 1990 to 15% in 1999 (GIP 1997, 2000b).[5] The rise in the share of generics is due to the large number of patent expirations in this period (Jacobzone 2000) and probably also to an active policy to speed up market entry by generics and to stimulate physicians and pharmacists to prescribe and deliver generic pharmaceuticals.

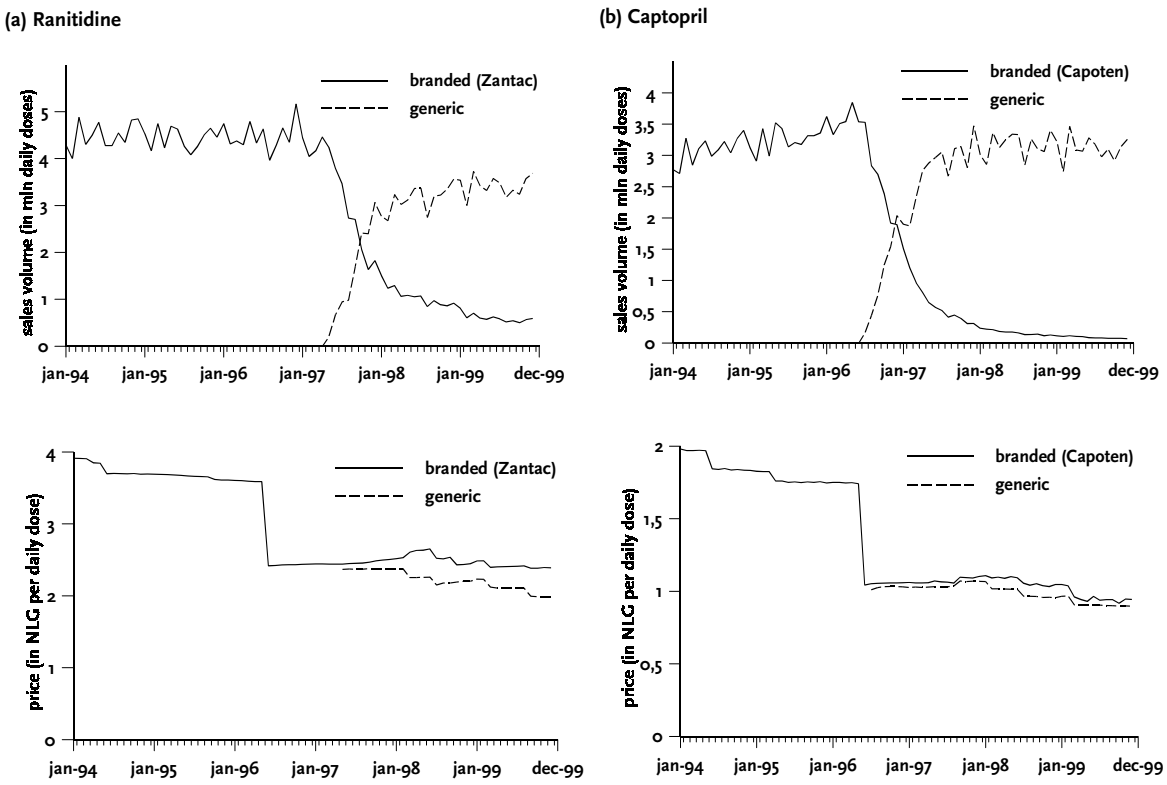
Nowadays, most doctors in the Netherlands are very much aware of the generic alternative. As a result, when a patent expires the market is taken over fairly quickly by generic producers. Figure 2.3 gives two examples of such a market takeover in the 1994-1999 period: ranitidine (an anti-

[3] In some cases, generic entry at the moment of patent expiry may not yet be possible due to the protection period on the clinical research file or due to an "orphan drug" status of the original product. In addition, generic entry may be hindered if the original pharmaceutical is protected by a second patent, for instance on a new indication of the pharmaceutical.

[4] Pronk (2001) discusses cases where some generic products may have substantially different effects than the branded originals. In these cases, switching from branded to generic may be hazardous for the patient. We interpret these cases as – socially undesirable – exceptions that confirm the rule.

[5] The difference between the shares in number of prescriptions and costs reflect two aspects: (i) the average price difference between pharmaceuticals with a valid patent (without generic alternatives) and those without patent protection; (ii) the price difference between generics and their branded counterparts.

Figure 2.3 Generics replacing branded products: two cases



Note: The sharp decline in prices in June 1996 is due to the introduction of price caps under the Pharmaceutical Prices Act (see the box *Regulation of prescription drug prices in the Netherlands*). Especially for the case of captopril – where generics were introduced in July 1996 – this decline should not be mistaken for a reaction to the introduction of generics.
Source: Geneesmiddelen Informatie Project / College voor Zorgverzekeringen, calculations by CPB.

ulcer pharmaceutical) and captopril (against high blood pressure). The figure gives both sales volumes (top) and prices (bottom).

The large role of generics in the Netherlands raises an important issue for our research. It is possible that there is a difference in marketing strategies between producers that face generic competition and those who do not. For instance, influencing the pharmacists choice between a branded product and a generic equivalent through *margin competition* becomes important at this stage. The effects of marketing may be different in the stage of generic competition as well. We take these potential differences into account in our empirical analysis.

2.2.2 Asymmetric information

Another possible explanation for the observed marketing intensity is the information asymmetry between prescribing doctors and suppliers of prescription pharmaceuticals. (There is also an

information asymmetry between patients and doctors; this is less relevant for this study.) Doctors cannot have complete information regarding all the product characteristics (and the prices) of all pharmaceutical products relevant for their practice. This implies that in their daily practice they have a great need for information regarding pharmaceuticals. We explore this point below.

There are approximately 100 therapeutic markets. In 1998, there were more than one thousand different pharmaceuticals (active ingredients) on these markets, supplied by an estimated number of around two hundred different manufacturers (GIP 2000a, IMS HEALTH). In addition, the product characteristics of pharmaceuticals can be broken down into many different aspects:[6]

1. the probability that the pharmaceutical is effective;
2. the speed at which it becomes effective;
3. differences in effectiveness across patient categories;
4. what happens if a patient takes one tablet too many or too few (therapeutic window)?
5. how does the product interact with other pharmaceuticals?
6. how many side effects does the pharmaceutical have?
7. how serious are the side effects and how often do they occur?
8. differences in side-effects across patient categories;
9. the mode of application (tablet, injection, ...);
10. the size of – for instance – the tablet;
11. the number of applications (once per day or four times per day);
12. .....

All these aspects together determine the quality of a pharmaceutical and of pharmaceutical products. It is clear that quality differences between pharmaceuticals in a therapeutic market can occur in many dimensions. In some cases it may be possible to claim that one product is better than the other (in economic terms: vertical product differentiation), but in many cases product characteristics will be better in some dimensions and worse in others, or just different (horizontal differentiation).

It is clear that with such a complex supply side, doctors can typically have only a fraction of the available information about (properties of) pharmaceutical products. The manufacturers, on the other hand, will (make it a point to) have almost all available information about their own

[6] Note that many of these aspects are dependent on unobservable patient characteristics: a pharmaceutical works for some patients, but not for others.

products. The information gap between doctors and producers is largest at the introduction of a new pharmaceutical, when there is no information about its effects in practice.[7] The available information at that stage is from the controlled pre-marketing clinical studies necessary to prove efficacy and safety to market admission authorities and to apply for insurance coverage. Some of these studies are not publicly available and even if all were available, getting a complete overview would require considerable time and effort.

When the pharmaceutical has been on the market for several years and used on a significant scale, more information about its quality will become publicly available. Nevertheless, there will always remain a significant information gap between doctors and producers, simply because doctors do not have the time to absorb all this information. Since the scope of health problems in the practice of specialists is narrower than for general practitioners (GP's), the information gap with producers is probably broader for GP's than for specialists.

Therapeutic decision making: determinants

One implication of the information asymmetry between doctors and producers is, that doctors have a great need for information about pharmaceuticals and that the pharmaceutical industry can supply (parts of) this need. As a result of the complexity, physicians do not only need a large amount of information, but they also require that this information is presented in a certain way. It is in the interest of pharmaceutical companies to meet these requirements. In the words of VWS (2001a): "Although physicians report that information can be acquired without the industry as well, the format and way in which the industry usually attends to this is appreciated by a number of physicians." (p. 15).

It is therefore not surprising that the pharmaceutical industry features as an information source in models of therapeutic decision making by doctors. One model is by Haaijer-Ruskamp and Denig (2001).[8] In this model, doctors are influenced by many sources, on two different levels.

On the first level, a doctor uses his professional expertise to form a personal choice set (or, using marketing terminology, the evoked set) for a specific health problem. The second level of

[7] Experience with a pharmaceutical in the market often reveals new effects of interaction with other pharmaceuticals or new side-effects. Sometimes these newly discovered effects are serious, as was the case with the anti-allergy pharmaceutical terfenadine - its status was changed from over-the-counter to prescription only upon discovery of potentially lethal interaction effects - and more recently with the anti-cholesterol pharmaceutical cerivastatine - removed from the market after discovery of a side-effect causing many deaths. Thus, for new pharmaceuticals there is asymmetric information as well as substantial uncertainty concerning quality.

[8] Other work on decision making and prescribing behaviour by doctors includes Bradley (1991) – an international literature survey – and Denig and Haaijer-Ruskamp (1992).

decision making concerns the practical decision of applying the expertise to the personal choice set in order to arrive at a therapy choice for an individual patient.

Haaijer-Ruskamp and Denig (2001) report that little is known of how physicians form their personal choice sets. The first sets are probably formed when students copy the behaviour of their teachers. Estimates imply that these sets change infrequently. On average a GP does not change more than five pharmaceuticals in his set per year. GP's and specialists differ in their reasons for introducing new pharmaceuticals in their personal choice set. Specialists seem to rely more on scientific meetings and critical appraisal of the literature, while for the GP it seems a more diffuse process with clear influence of the pharmaceutical industry and the specialist (Jones et al. 2001).

Table 2.2 states the sources of influence in the two stages. A striking feature of these lists is that pharmaceutical price as a possible separate source of influence is absent on both levels.[9] Denig and Haaijer-Ruskamp (1995) provide an overview of the role of prices in therapeutic decision making. We will come back to the influence of price as a decision variable below in Section 2.1.3.

Some of the elements in the table may need some clarification. The influence of regulation by government and insurers indicates that the doctor is not completely free to prescribe any product.[10] Most prescription pharmaceuticals are covered by public (and private) health insurance, but some are not or not completely. Doctors will be reluctant to prescribe products that are not (completely) covered, especially if alternatives exist that are. Generic prescribing is also stimulated by the government. In addition, the government promotes standards and

Table 2.2 A model of doctors' prescribing behaviour

Level 1: Doctor's choice set	Level 2: Decision per patient
- education	- individual patient characteristics
- the pharmaceutical industry	- therapeutic goal
- regulation (by government and insurers)	- medication surveillance
- standards and other guidelines	- electronic prescription system
- meetings with pharmacist (FTO)	- advice (colleague, specialist, pharmacist)
- personal experience	- intuition
- colleagues	- doctor's emotions

Source: Haaijer-Ruskamp and Denig (2001).

[9] This may appear to contradict the claim in 2.1.1 that cheap generics often gain market share quickly from off-patent branded products. Remember, however, that deciding on a pharmaceutical means choosing a specific active ingredient, not choosing the producer, which occurs when choosing between branded and generic.

[10] Doctors are not legally restricted a priori. They can prescribe any pharmaceutical that has been admitted to the market. Of course, they can be held legally responsible for damages due to wrong prescription choices.

guidelines – for instance by promoting the use of a centralised electronic prescription system – and financially stimulates meetings with pharmacists (see below). Health insurers may also have agreements/contracts with doctors concerning their prescribing behaviour. With the planned introduction of a new health (insurance) system in the Netherlands in 2005 (VWS 2001c), we expect a shift from regulation by government to a more decentralised influence over prescribing behaviour by health insurers. Doctors make their therapeutic decisions given the limiting conditions laid out by government and insurers. This also means that the results of the empirical analysis concerning prescribing behaviour (Chapter 3) also reflect these limiting conditions.

Standards and guidelines refer to the Dutch NHG-standards and regional guidelines (for GP's) and to CBO-guidelines (for specialists). The NHG-standards follow the principle of evidence-based medicine and are quite authoritative, also internationally: they have been translated into many languages. GP's follow the NHG-standards in approximately 70% of their prescriptions (Spies and Mokkink 1999);[11] according to Kamps (1999) GP's follow regional guidelines in 30%–70% of the prescriptions (depending on the definition).

Another element are the pharmaco-therapeutic consultancy meetings between a pharmacist and GP's in his region, the so-called FTO (*farmaco-therapeutisch overleg*). During these regular peer review meetings, pharmacists give the GP's information about new pharmaceuticals, discuss therapy alternatives for specific diseases and conditions and answer questions from the GP's (see De Vries, 1998).

The influence of colleagues over doctor's choice sets to (in)formal direct contacts with colleagues. It may also be established by physician-speakers during courses, conferences and symposia (see also 2.3.6, under Opinion leaders). Colleagues may also influence therapeutic decision making on the second level, through advice. A special case of this is when a patient visits a GP for a repeat prescription of pharmaceutical therapy initiated by a specialist. One could view the specialist's choice in this case as implicit advice to the GP. Changing the medication may be harmful for the patient and, if not, is generally difficult to explain. Even a switch from a branded product to a generic pharmaceutical, which is therapeutically equivalent, may be obstructed by a patient's unwillingness to change from a blue tablet in a red box to a pink tablet in a white one.

Patient characteristics are also a determinant of therapy choice. One of these characteristics is the amount of direct influence a patient tries to have over the doctor's decision. Formally, a

[11] More precisely, Spies and Mokkink conclude that GP's follow the do's in 67% of the cases and the don'ts in 78%.

patient's influence over the therapy chosen has not changed over the past decades: it still follows the principle of informed consent. However, the informal influence of patients has changed considerably. Patients are better educated, better informed through mass media and the Internet, better organised in patients' associations, more often receive advertising messages and are generally less impressed by a physician's status. As a result, patient attitudes have changed from "OK doctor, if you say so" to a more assertive "But I've seen on television that ..." or "I really would prefer to have medication X."

Finally, doctors often have software that helps them when choosing pharmaceutical therapy by presenting the relevant options given the diagnosis (and patient characteristics). It is the aim of the Dutch government that in 2002 every GP uses the same centralised electronic prescription system (EVS, *electronisch voorschrijfsysteem*).

When taking a decision regarding individual patients, the physician chooses a product from the personal choice set. This, and the fact that physicians' personal choice sets rarely change, would make it crucially important for pharmaceutical producers that their product is an element of as many of the doctors' personal choice sets as possible. We will see in Section 2.3 that marketing activities of pharmaceutical firms are indeed aimed at all of the influence sources of level 1 and also at some of level 2.

2.2.3 Price elasticity of demand

In their 1954 article, Dorfman and Steiner show that marketing intensity can be expected to be higher in markets with a low sensitivity of consumer demand to prices. The reason for this is that the price increases necessary to finance these higher marketing expenses reduce demand by relatively small amounts. How sensitive are patients and doctors to pharmaceutical prices?

Both doctors and patients are fairly insensitive to prices of pharmaceuticals. There are several studies into the price elasticity of the demand for pharmaceuticals. These have different outcomes, depending on the institutional setting of the country or state (in the U.S.A.) where the research took place.

Studies performed using data from the United Kingdom (mentioned in Jacobzone 2000) find elasticities in the range of only -0.1 to -0.3. These imply that a 10% increase in the prescription charge will lead to a fall of no more than 1 to 3% in the number of prescriptions. Phelps (1997) discusses a natural experiment in the U.S.A. showing a pharmaceutical price elasticity of -0.4. Higher sensitivities in the U.S.A. may reflect the fact that only 58% of the pharmaceutical costs in the U.S.A. are covered by insurance (Rizzo, 1999). This is less than, for example, in the Netherlands and the U.K.

Another study for the U.S.A. mentioned by Jacobzone (2000) concludes that a fixed prescription charge of around $1.50 decreased the number of prescriptions by around 10%, and that an increase to $3 per prescription reduced it again by another 10%. It is difficult to derive an elasticity estimate from these numbers, since we have no data on the average costs per prescription. In addition, it is possible that the (higher) prescription charge also resulted in larger prescriptions being written, for instance prescriptions for three instead of two weeks.

Jacobzone considers the Rand Health Insurance Experiment to be the most important and relevant study into sensitivity to prices. This study shows that with co-payments of 25% demand would fall by 25% and that if patients bore 95% of the costs this would reduce demand by 43%. Although not provided by Jacobzone, these findings imply an average price elasticity of -0.1 in the range between 25% and 95% co-payments.

The low sensitivity of pharmaceutical demand with respect to prices may be due to several factors:

- **Large value.** People typically attribute a large value to health improvement. Especially in cases of severe afflictions, patients will be prepared to spend large sums of money.
- **Insurance.** Many people are (partially) insured against pharmaceutical costs. This lowers the weight of the price of a pharmaceutical when deciding on a therapy.
- **Intermediation.** Patients are not the key decision makers in pharmaceutical selection, physicians are. And since physicians do not bear the cost consequences of their medication choice, they may be less price sensitive than their patients.
- **Price regulation.** Price elasticities typically increase with higher prices. Price caps and other price regulation measures can restrict prices to low-elasticity levels.
- **Marketing.** An effect of marketing may be that it increases price sensitivity by providing information. Marketing may also increase brand loyalty, resulting in a lower sensitivity to prices. For instance, Rizzo (1999) finds that without marketing demand for anti-hypertensive pharmaceuticals in the U.S.A. would respond quite elastically to changes in price and that product marketing lowers the sensitivity to prices significantly. We investigate this effect in Chapter 3, where we will have to take into account that marketing efforts may be the cause as well as an effect of low price elasticity.

Almost every inhabitant of the Netherlands is insured for almost all costs for presciption pharmaceuticals. In addition, Dutch pharmaceutical prices are heavily regulated (see box *Regulation of pharmaceutical prices in the Netherlands*). Therefore, it is reasonable to expect that price-elasticities in pharmaceutical markets in the Netherlands are very low. However, there is little research into the price elasticity of Dutch demand for pharmaceuticals to verify this. Moreover, available work does not settle the issue raised above, whether low price elasticity is the

Regulation of prescription drug prices in the Netherlands

Pharmaceuticals Reimbursement System (Geneesmiddelenvergoedingensysteem, GVS). Within this system, products are clustered into small groups of close substitutes. The maximum reimbursement price (GVS-limit) within a group is a (complicated) weighted average of the prices of the products in the group at some baseline date (currently January 1998). Patients who receive prescriptions for products with a price exceeding its GVS-limit have to pay the difference out-of-pocket. Products without close substitutes (typically new products) are not clustered and have no maximum reimbursement price. Upon introduction of the system in 1991 most product prices in excess of the GVS-limit were lowered to this limit. The same happened in 1999 when GVS-limits were recalculated with new baseline prices.

Pharmaceutical Prices Act (Wet geneesmiddelenprijzen, WGP). Almost every pharmaceutical product has a price cap. It is not allowed to charge a higher price. The cap is the mean of the price for that pharmaceutical in Belgium, France, Germany and the United Kingdom.* Price caps are recalculated twice per year, to correct for price changes, market admissions and market withdrawals in the reference countries and for exchange rate fluctuations. The first price caps became effective in June 1996 and caused an average price decrease of approximately 15% (Figure 2.3 also shows the effects of the introduction of price caps). Since that date recalculations have led to higher price caps, mostly due to increases in the exchange rate between the Dutch Guilder and the British Pound.

*For this act, a pharmaceutical is defined by the active ingredient, the dosage and the application form. For example, all fluoxetine 250 mg tablets have the same price cap, which is an average of fluoxetine 250 mg tablet prices in the four reference countries.

result of intensive marketing efforts (Rizzo 1999) or the cause of these efforts (Dorfman and Steiner 1954). In our empirical analysis we will address both issues: what is the level of price sensitivity in the Netherlands and to what extent does the level of marketing determine this sensitivity?

2.2.4 Discussion

In this section, we have shown that the three possible explanations for the observed marketing effort – high R&D intensity, asymmetric information and low price elasticity – all apply to the pharmaceutical industry. As we will see in the following sections, the process of innovation and imitation and the information asymmetry can also explain several other observations concerning pharmaceutical marketing.

R&D, information and elasticities cannot only explain the marketing expenditure, but also the price-cost margins of pharmaceutical producers. According to Public Citizen (2001a), Fortune magazine's rankings show that the pharmaceutical industry has been the most profitable in the U.S.A. in every year since 1982. Scherer (2000) reports that "among 459 ... manufacturing industries covered by the U.S. Census in 1987, pharmaceuticals ... had the sixth-highest

price/cost margin at 61.4%; the average for all manufacturing industries was 30.5%." (p. 1302).[12] The explanation offered by Scherer is that demand-side characteristics such as intermediation by doctors, insurance coverage and low price elasticities interact with the presence of monopoly power on the supply side (patents, brand loyalty) to support prices that commonly exceed production costs by a substantial margin.

A justification for the high profitability of the pharmaceutical industry is generally believed to be the large risks associated with pharmaceutical R&D. An often cited number is the $500 million of R&D-outlays needed on the average before one successful new pharmaceutical can be marketed (this amount includes the many R&D-failures). In a recent report, however, Public Citizen (2001a) brings this estimate down to $110 million and provides several arguments against the belief that being in Big Pharma is a risky business.[13]

2.3 Marketing life-cycle

The previous section investigated the overall marketing effort level. This section looks at marketing expenses at the product level through time.

Marketing outlays on a specific product appear to follow a more or less fixed cycle, depicted in Figure 2.4. The data acquired for our empirical analysis show that marketing spending for a specific product reaches a sharp peak in the second year, evens out a little at around 50% of this value between years four and seven and gradually declines after this initial period. After fifteen years marketing spending is no more than 20% of the peak value. At this level it evens out and very slowly declines toward zero.

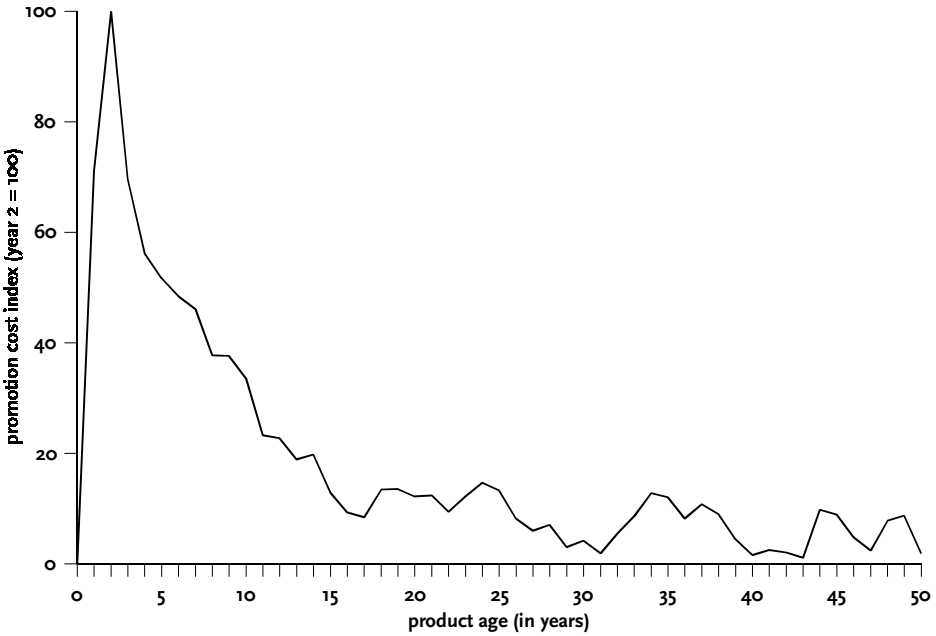
The fact that the bulk of marketing activity occurs in the first years of a pharmaceutical's life implies that research-oriented firms are the main investors in marketing. This is confirmed by the data for our empirical analysis: generic producers generated not more than 1.5% of the costs for detailing, advertising and direct mail in 1999.

Another interesting feature of the marketing cycle is that between years nine and fourteen, the period when patents expire and generics are introduced, marketing spending is still significant. This spending is still mostly done by the supplier of the branded product. This is in line with the result of Berndt et al. (1995) that in the anti-ulcer market even after generic entry, financial

[12] Price/cost margin = (price – costs)/price.

[13] They put forward (i) that pharmaceutical R&D is often substantially subsidised, (ii) that for almost 20 years, the pharmaceutical industry has been the most profitable in the U.S.A., and (iii) that only 22% of the new products in the last 20 years were innovative pharmaceuticals with important therapeutic gains over existing pharmaceuticals.

Figure 2.4 Marketing spending and product age



Note: This graph probably overestimates average marketing costs at larger product ages, since the data only pertain to products with non-zero efforts in the period 1994-1999. Products with zero marketing costs in that period (not in the data) are likely to be "old" products.
Source: IMS HEALTH, calculations by CPB.

resources devoted to marketing continue to play a key role in explaining the market share of the original branded product. This would imply that marketing is not only used as an instrument to obtain market share in the stage of therapeutic competition, but that it can be an instrument to defend market share against generic competitors as well.

Notwithstanding this last observation , figure 2.4 clearly shows that marketing efforts are concentrated in the first years of a product's life. Explanations for this observation can be found in the process of innovation and imitation.

First of all, because another company may introduce a better pharmaceutical and because – even if this does not happen – the effective patent period is limited to approximately 10 years,[14] the period to earn back the R&D (and other) investments is limited. Therefore, producers of pharmaceuticals are in a relatively big hurry. They do not have the time to sit and wait for their

[14] Approximately half of the official patent period of 20 years is taken up by development, (clinical) testing and the procedure to gain market access (Jacobzone, 2000; Nefarma, 2001). For this reason it is now possible to apply for a protection certificate that extends the intellectual property protection for up to another five years. It is not yet clear to what extent these licenses increase the average effective patent period.

products to become best-sellers. The best-seller status will have to be accomplished as soon as possible.

Secondly, for a product at the end of its patent period the producer has little incentive to defend its market share against new, patented pharmaceuticals entering the market, for instance by countering the entrant's marketing campaign with an own campaign. After all, upon patent expiry the market share will dwindle anyhow (Figure 2.3). In addition, after patent expiry individual generic producer's market shares are typically not large enough to justify extensive marketing efforts to defend the pharmaceutical's collective market share (free riding problem).

These two points together can be used to make a third. Since producers of older patented and off-patent products have little incentive to defend their market share against newcomers, the strategy of launching a new pharmaceutical with an extensive marketing campaign can be attractive for all new products, irrespective of their quality. Thus, it can be worth wile to market a new pharmaceutical with relatively low quality, where in other product markets the prospect of (marketing) competition with high quality competitors would make a potential entrant decide not to market the product.

2.4 Marketing activities

The previous sections discussed spending on pharmaceutical marketing (through time). In this section we describe the different activities financed by these outlays and – where available – literature about their effects on the medical profession. We start with an overview of the activities and their relative importance.

Little is known about how companies' marketing budgets are divided over the different activities. The Dutch Advertising Supervision unit of the Health Care Inspection has recently investigated 28 marketing plans. Their report (IGZ, 2001) shows the division of marketing costs presented in Table 2.3.

In addition, we were able to derive some quantitative information from the data acquired from IMS Health Nederland for our empirical analysis. These data provide a rough indication for a subdivision between the costs for detailers (i.e. the wage costs), advertising and direct mail: respectively 68%, 20% and 12% in 1999. Given this large share of detailers' wage costs, we expect that detailing (budgets plus wages) has the highest cost share of all marketing activities. For this reason detailing is at the top of the list in Table 2.3.

Table 2.3 Pharmaceutical marketing activities and their relative costs

Marketing activity	Cost share
Detailing budgets (excl. wage costs)	12 %
Direct mail / advertising / public relations	20 %
Post-marketing research	20 %
Courses / conferences	19 %
Promotion events	11 %
Sponsorships / other expenditures	5 %
Opinion leaders	3½%
Direct-to-consumer advertising	3 %
Prescribing systems	½%
Other activities	6 %
Total	100 %

Note: These numbers were derived from marketing plans for specific products. Costs of non-product-specific marketing are absent. Note also that the wage costs of detailers were not included in the marketing plans.
Source: IGZ (2001).

From these numbers, we conclude that types of marketing that are common in other sectors as well, such as detailing and advertising/direct mail/public relations, are also important groups of marketing activities for pharmaceuticals. But groups of activities that are much more specific for the pharmaceutical industry have substantial shares too. Examples of these are post marketing research and courses/conferences.

Why is there so much diversity in marketing activities? To explain this, we must know more of the activities themselves. Below we discuss the activities, drawn from two recent Dutch studies – IGZ (2001) and VWS (2001a) – and several interviews. We start with the five most important (groups of) activities in terms of costs (2.3.1 – 2.3.5). The remaining activities are briefly treated in 2.3.6. Where available we also present evidence on the effects of these activities.[15] Finally, we address the question of explaining the observed diversity (2.3.7).

2.4.1 Detailing

Company representatives (detailers) visit doctors, both general practitioners and specialists, typically to discuss one of the company's products. Examples of discussion topics during detailing visits are (new/scientific) information regarding the product or the doctor's own experiences with the product. In addition, detailers can present the doctor with written material, small gifts (typically with the product name) or small samples of the product. During the visit the detailer can also invite the doctor to promotion events or symposia or invite him to take part

[15] Some of this evidence is from the Netherlands. Most of the additional evidence comes from an article by Wazana (2000). This is a survey article, covering 29 scientific papers on (effects of) doctor-industry interaction. Most of these papers reported on research conducted in the U.S.A. or Canada.

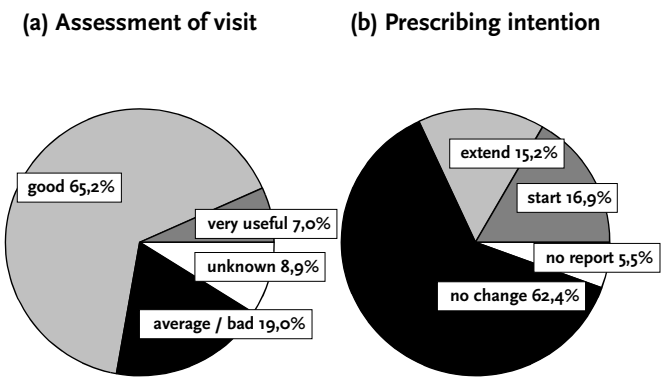
in post-marketing research (see below). Visits typically vary in length from 10 to 20 minutes. A small number of doctors choose not to be visited by detailers. Others restrict the number of detailing visits, for instance to one per week.

The IMS HEALTH-data we use for our empirical study shed light on the effects of detailing in the Netherlands. Figure 2.5a below shows that for the large majority (72%) of detailing talks the reporting doctor gives an assessment of "very useful" or "good"; only 19% receives an "average" or "bad" verdict. Moreover, 32% of the doctors reports to intend to start prescribing the product discussed or to extend their prescribing behaviour; 62% do not intend to change their behaviour (Figure 2.5b). Thus, in 1999 one-third of all detailing visits was immediately successful in terms of influencing doctors' prescribing intentions.

Wazana (2000) reports on many studies investigating the effects of detailing. There is evidence of an interaction between detailing visits and formulary addition requests, where "... most of the requested pharmaceuticals presented little or no therapeutic advantage over existing formulary pharmaceuticals ..." and where it could be argued to be "... unlikely that the interaction occurred because the physician was already convinced of that pharmaceutical's influence" (Wazana 2000, p. 375).

Regarding free samples Wazana presents evidence that accepting them is associated with more rapid prescription of a new pharmaceutical. For other gifts the effect on prescribing has not been investigated, but both samples and other gifts correlate with a positive attitude toward detailers. Moreover, doctors who receive gifts are significantly more likely to believe that detailers have no impact on prescribing behaviour.

Figure 2.5 Effects of detailing in the Netherlands, 1999



Source: IMS HEALTH, calculations by CPB.

2.4.2 Advertising, direct mail and public relations

Many of the advertisements in scientific medical journals and other magazines aimed at doctors are advertisements for pharmaceutical products. The amount of product information an advertisement can provide is very limited. Advertisements are therefore aimed at creating brand awareness or communicating one or two properties of the product. As far as we know there are no studies into the effects of pharmaceutical advertising on prescribing behaviour. An important side-effect of advertising is that it makes dissemination of the knowledge in medical journals less costly.

Doctors also receive mailings from pharmaceutical companies. Through these mailings companies can provide product information and/or invite doctors to a promotion event, course or symposium. There are also no studies into the effects of mailings on prescribing behaviour.

Since the pharmaceutical industry is heavily regulated, government decisions can be influential for pharmaceutical companies. Public relations expenses refer to people and organizations hired by pharmaceutical companies, to have regular contacts with the press, members of parliament, government officials and health insurers for lobbying purposes. This lobbying may be product specific, for instance aimed at gaining market access or public insurance coverage for a product. A well-known Dutch example of product lobbying are the efforts in 1996 by Frits Bolkestein, leader of the Dutch liberal party and member of the Advisory board of a large pharmaceutical firm, with Health Minister Els Borst. But lobbying may also be aimed at serving the interests of (a part of) the pharmaceutical industry, for instance by opposing a new act.[16] Lobbying may also occur indirectly, through patients' associations.

2.4.3 Post-marketing research

Post-marketing research (PMR) refers to research into the (side-)effects of pharmaceutical products that have been admitted to the market (as opposed to the clinical pre-marketing research required to gain market access). The research consists of gathering information from doctors who prescribe the product and keep records of the effects on their patients. Depending on the product that is researched, PMR programs may involve general practitioners, specialists or both. Participating doctors are typically paid (in money or in kind) for their efforts. This may be a fee per prescription or per patient or a lump sum for participation.

PMR programs may have a purely scientific background. European regulations require pharmaceutical companies to provide safety update reports at regular intervals about (among others) the noted side-effects of their products. Pharmaceutical companies can conduct PMR to

[16] An example of lobbying (and an indication of the cost) from the USA is in Public Citizen (2001b).

gather this information. In addition, market access authorities can grant market access with requirements of additional PMR, for instance investigating the effects on children, who are typically not included in pre-marketing clinical trials.

Besides these scientific kinds of PMR there are also various sources that mention forms of PMR without scientific – i.e. with pure marketing – purposes. Non-scientific PMR programs are also referred to as seeding trials.[17] One of the sources mentioning seeding trials is the article by Roos (1999), who describes them as activities "that have no scientific value whatsoever, but only serve the financial interest of the participating doctor and the industry." (p. 1671). IGZ (2001) reports that 20% of planned marketing expenses are for PMR (see Table 2.3). It seems fair to assume that PMR programs in marketing plans are of the non-scientific kind, especially since IGZ (2001) also reports that 68% of the PMR plans state that the goal is to influence prescribing or to build a relationship with doctors. For the remaining 32% the marketing plans did not explicitly state a research goal.

As far as we could ascertain there is no research into the effects of PMR on doctors' prescribing behaviour.

2.4.4 Courses and conferences

Since 1996, physicians are obliged to participate in continuing medical education (CME). As a rule, general practitioners earn their CME-credits by following courses, while specialists also visit a number of conferences.

Approximately half of the CME-courses followed by GP's are organised by or on behalf of pharmaceutical firms. Van der Linde (2001) provides many examples of how companies use the influence this gives them over:

- Topics: Pharmaceutical firms prefer to organise and sponsor commercially interesting courses on topics like osteoporosis, hypercholesterolemia and hypertension.
- Content: An organising firm can influence content, for instance by selecting teachers with a favourable opinion of their products and preparing course material.

Visitation of 22 industry-sponsored courses resulted in withdrawal of accreditation for 15 courses due to product promotion during the courses, which violates the accreditation rules of the Dutch GP association (LHV, Landelijke Huisartsen Vereniging). In many of these cases some of the therapy advice given was not in accordance with NHG-standards.

[17] Names typically (but not exclusively) used for scientific PMR are post-marketing surveillance and phase-IV research (phases I-III are the pre-marketing clinical research phases).

Besides the work of Van der Linde, there are no Dutch data on the effects of industry-sponsored courses on prescribing behaviour. Wazana (2000) reports that "[d]rug company CME sponsorship affected presentation content in that the sponsor's pharmaceutical was always preferentially highlighted..." and that "[c]hanges in prescribing practice (self-reported) in favor of the sponsor's pharmaceutical were also found." (p. 377).

Medical conferences can be roughly divided into three separate categories:

- scientific conferences;
- post-graduate educational conferences;
- symposia.

The first two categories are organised by medical associations and typically cover a broad range of topics. They are sponsored by several pharmaceutical (and other) firms to lower the registration costs for participating physicians, comparable to sponsorships of conferences in other scientific areas. A pharmaceutical firm can also sponsor the travel and lodging expenses of a participating doctor (see 2.3.5). Compared to scientific and educational conferences, symposia are more often organised by or on behalf of a pharmaceutical company and typically focus on one or a few topics. Such a topic may be a specific pharmaceutical. At these events invited doctors may be exposed to company representative speakers. In all three categories, companies may sponsor travel and lodging costs for (some of) the attending physicians (2.3.5).

We have not found studies that investigate effects of visiting conferences and symposia on doctors' prescribing behaviour.

2.4.5 Hospitality and other gifts

Gifts are not mentioned as a separate marketing activity in Table 2.3. This is because gifts are an integral part of several other marketing activities, for example detailing. Another kind of gift from pharmaceutical companies to doctors is known under the term *hospitality*. This pertains to companies sponsoring physician's travel, lodging or registration costs for courses, conferences, symposia and promotion events. Firms may also offer side events not related to the main educational program (sometimes not only for the doctor, but for his entire family), such as meals, theatre visits, other forms of entertainment (golf, skiing), etcetera.

Much of this hospitality offered by companies appears to be aimed at creating a "sense of indebtedness" with the attending physicians. "The industry does not impose an obligation to write prescriptions but the doctors involved feel a moral obligation to return a favour." (VWS 2001a, p. 30). The evidence in Wazana (2000) suggests that accepting funding to attend an educational event increased the likelihood of a formulary addition request (see 2.3.6, under

clinical trials) for the sponsor's pharmaceutical. Wazana also found evidence that accepting all-expenses-paid trips to a pharmaceutical sponsored symposium had an impact on prescribing behaviour: "[A] 4.5- to 10-fold increase in pre-conference prescribing rate of [the] sponsor pharmaceutical (compared with [a] 2.5- to 3.5-fold national rate increase) …" (p. 378).

Current Dutch regulation requires that doctors themselves bear a substantial part of their travel, lodging and registration costs for courses and conferences (see box *Regulation of pharmaceutical marketing in the Netherlands*). These expenses are covered through a lump-sum (and non-ear marked) CME component in doctors' tariffs. In addition, 140-180% of GP's registration costs for CME courses are tax-deductible.

2.4.6 Other activities

Promotion event

Short presentation for invited doctors by a pharmaceutical representative about his company's product(s). Such events are often combined with some hospitality (2.3.5).

Research sponsorships

In the last two decades, commercial funding of scientific research has grown considerably in the Netherlands, due to falling government subsidies. Sponsorship gives pharmaceutical firms influence over research topics (the share of pharmaceutical research in medical research has increased), and also to some extent over research results and the publication decision (Stelfox et al. 1998, Davidoff et al. 2001). In addition, research sponsorships may also influence the researcher's behaviour in his role as a doctor: Wazana (2000) concludes that receiving research support was associated with a formulary addition request (see below, under clinical trials) for the sponsor's pharmaceutical. These sponsorships also have effects outside pharmaceutical markets: they stimulate the creation of scientific knowledge.

Opinion leaders

Pharmaceutical firms pay doctors to give presentations during seminars, symposia, promotion events and CME courses.

Direct-to-consumer advertising

Due to the trend that patients have become more assertive (2.1.2), consumers have become interesting targets for pharmaceutical marketing as well. Consumers can be reached by pharmaceutical firms through the mass media and through folder material available in public pharmacies and doctors' waiting rooms. In the Netherlands, the legal possibilities for suppliers

Regulation of pharmaceutical marketing in the Netherlands

On 31 March 1992 the European Community issued a directive on the marketing of medicinal products for human use (EC 1992). This directive has been implemented in Dutch legislation in 1994. The European directive was motivated by the need for harmonisation of the member states' legislation on this aspect, and also by the observation that prescribers should be able to carry out their mechanism objectively and without being influenced by direct or indirect financial inducements.

The directive and the Dutch implementation set general rules regarding public advertising (mostly prohibited), advertising aimed at prescribers, detailing, gifts and hospitality and free samples. One of the problems regarding enforcement of these rules is the lack of clarity in the legislation. For example, the legislation does not give a definition of advertising when prohibiting public advertising of prescription pharmaceuticals. Another example can be found in Article 10 of the EC directive: "... hospitality [at events for purely professional and scientific purposes] must always be reasonable in level and remain subordinate to the main scientific objective of the meeting" (EC 1992). But what is reasonable? And are a free dinner and theatre visit after a scientific workshop of one afternoon subordinate or not? Currently, the Dutch government is working on changes in legislation and additional guidelines to bring more clarity into these matters. These include maximum values per year and per event for hospitality and gifts; per year and per event, doctors should not accept more; per event, companies should not offer more (VWS 2001b).

More clarity can also come from rulings in court cases. Since April 1999 the Advertising Supervision unit of the Health Care Inspection is occupied with supervision and enforcement of pharmaceutical marketing rules. Their activities have resulted in three court cases against pharmaceutical companies and equally many convictions: two for illegal public advertising and one for offering unreasonable hospitality.* The ruling in one of the cases has given a legal definition of what is meant by the term advertising: any action that is aimed at stimulating sales (even if the company's product is not mentioned).

Fines for violating the advertising rules are relatively low (a maximum of 4,500 euro per infringement; totals per case of up to 160,000 euro). In some situations, (the possibility of) having to pay these fines may not be sufficient to deter pharmaceutical firms from penal offences. Therefore, the negative publicity that firms get when being prosecuted and (possibly) convicted for breaking the advertising law may be stronger disincentives than the fines (regulation by embarrassment).

* So far, doctors have not been prosecuted for accepting unreasonable hospitality. There are indications that this may change (Medisch Contact 2001, Zembla 2001).

of prescription pharmaceuticals to reach the public through mass media are very limited (see box *Regulation of pharmaceutical marketing in the Netherlands*).[18]

[18] In the USA, the (partial) liberalisation of direct-to-consumer (DTC) advertising in 1997 has led to an enormous increase in DTC marketing spending: from $ 0.8 billion in 1996 to $ 2.5 billion in 2000. For illustration, in 1998 one particular pharmaceutical was advertised even more than Coca-Cola (Public Citizen, 2001a).

Other information sources

In 2.1.2 we have seen that doctors make use of several independent information sources to arrive at a prescribing decision, like the electronic prescribing system (EVS), pharmacist-doctor consultation meetings (FTO) and (regional) formularies. The marketing plans of pharmaceutical firms reveal that they aim to influence EVS, FTO and formulary committees as well (IGZ 2001). Pharmaceutical firms can influence the information provided to GP's during FTO-meetings by supplying pharmacists with support material for the meetings, such as printed information, presentation material, quantitative data or samples.

Clinical trials

If a specific pharmaceutical therapy is often initiated within a hospital, it is important for the producer of this therapy that its product appears on many hospital shortlists – or *formularies*. Apart from the price charged to hospitals[19] clinical trials may be an instrument to achieve this goal: Denig et al. (1991) find a significant relation between the testing of semi-innovative pharmaceuticals in clinical trials in a Dutch university hospital and the introduction of these pharmaceuticals for general use within the same hospital. They do not find this relationship for innovative pharmaceuticals.[20]

2.4.7 Diversity of activities: possible explanations

Now that we have gained insight into the details and backgrounds of many pharmaceutical marketing activities and their effects, we can return to the question posed in the introduction to this section: Why are there so many different marketing activities? We see two possible explanations: complementarity of activities and synergy between activities.

Complementarity of activities can occur in different dimensions:

- **Sources of influence for doctors' prescription choice:** In 2.1.2 we have seen that there are many sources of influence on the (pharmaceutical) therapy decision. Several of the marketing activities pertain to these sources of influence: courses and conferences have their effects through education, opinion leaders give authoritative advice, lobbying influences regulation, etcetera.
- **Heterogeneity of doctors:** Some activities are specifically directed at general practitioners, others at specialists.

[19] Pharmaceutical prices for hospitals are typically significantly lower than outside of hospitals. Price reductions of more than 50% are not uncommon.

[20] In their paper, Denig et al. (1991) give definitions of innovative pharmaceuticals (new pharmaceuticals or combinations of existing pharmaceuticals, *for new applications or purposes*) and of semi-innovative pharmaceuticals (new or existing pharmaceuticals, *without clearly novel elements in their claims*).

- **Time:** Immediately after introduction of a new pharmaceutical the focus may be on activities that stimulate brand awareness (advertising, direct mail). At a later stage activities aimed at convincing doctors to prescribe the product may become more important (organising courses).

Synergy between marketing activities may exist as well. One is between consumer advertising and marketing aimed at GP's. An example of this may be the strong increase in sales of a pharmaceutical against a specific fungus infection of the nails after a series of television commercials about the symptoms. This caused a strong increase of patients with the infection visiting their GP (Trouw, 16 June 2001). A mailing had given GP's advance notice of these commercials and had reminded them of the product. Another indication of possible synergies is the trend reported in interviews toward relationship marketing: activities may be aimed just at establishing a good relation between doctor and detailer, with the objective of making other marketing activities more effective.

2.5 Conclusion

Innovation-oriented pharmaceutical companies spend 20% or more of their prescription pharmaceutical sales on marketing. This places pharmaceuticals among the most heavily promoted products. Another conspicuous property of pharmaceutical marketing is the large diversity in marketing activities.

2.5.1 Marketing intensity

In this section we have identified three properties of the pharmaceutical industry that can explain this high marketing intensity.

Innovation and imitation

New pharmaceuticals regularly appear on the market, often displacing older pharmaceuticals. The producers of these branded products depend on patents to recoup their R&D-investments. When the patent expires, generic (non-branded) imitations typically displace the branded original. This process of innovation and imitation has three implications for marketing:

1. R&D-intensive industries tend to be marketing-intensive as well. Pharmaceutical R&D and marketing intensities are in accordance with this empirical observation.
2. At the end of the patent period (or after expiry) a producer has little incentive to defend its market share against an entrant with a new pharmaceutical, for instance by countering the entrants marketing campaign with an own campaign. After all, the older product will lose its market share quickly anyhow.
3. The earn-back time is short. Therefore, it is important to make a product a market success quickly, through intensive marketing. Since older market players have limited incentives to

defend their market shares (implication 2), this strategy can be attractive as well if the new product has relatively low quality.

The last two implications do not necessarily explain the intensity of pharmaceutical marketing, since they work in opposite directions. But they do explain the observed strong concentration of marketing efforts in the first years of a product's life cycle.

Asymmetric information

The knowledge of doctors concerning pharmaceutical therapies is incomplete. The producer of a particular pharmaceutical has most of the knowledge about it, since he has at his disposal all the clinical and other research with the pharmaceutical. There are two implications to this information asymmetry between doctors and producers:

1. doctors have a large need for information, that can be satisfied by producers;
2. given the asymmetric information and the amount of information doctors require and (probably) receive, it is difficult for them to assess the quality of the information. Pharmaceutical producers can use the information exchange with doctors for other marketing mechanisms than pure provision of information, for instance by changing doctors' incentives.

As in many other medical markets, there is also an information asymmetry between doctors and patients. This second kind of asymmetric information is not so relevant for this study.

Price sensitivity

Studies for the U.S.A. and the U.K. show that the price elasticity of demand (by doctors and/or patients) for prescription pharmaceuticals can be quite low, as it can be for other medical products and services. Given that almost every Dutch inhabitant is insured against almost all costs for prescription pharmaceuticals, we expect price elasticities in the Netherlands to be low as well. From the economic literature we know that a low price elasticity can be the cause of a high marketing-intensity. The observed marketing efforts in the pharmaceutical industry are in accordance with this result as well.

2.5.2 Diversity in marketing activities

The large diversity of pharmaceutical marketing activities comprises activities that are common in other sectors as well, such as detailers (pharmaceutical company representatives), advertising and direct mail. But there are also activities that are more specific for the pharmaceutical sector, such as conducting post-marketing research, organising courses for doctors and research sponsorships. Consumer advertising of prescription pharmaceuticals is largely prohibited under current European regulation.

The diversity in activities can possibly be explained by complementarities and synergies between them. A good example of such a synergy is the combination of symptom advertising aimed at consumers ("Are you troubled by ..., go see your doctor.") and a simultaneous mailing to doctors reminding them of your product against this condition.

3 The effects of pharmaceutical marketing

3.1 Introduction

In Chapter 2 we have seen that three characteristics of markets for prescription pharmaceuticals can explain that marketing expenditure in these markets is high: the process of innovation and imitation through which market shares can erode quickly; asymmetric information (doctors know less about pharmaceuticals than the producers of these pharmaceuticals); low price elasticity of demand for prescription pharmaceuticals. This brings us to the first central questions of this study: What are the effects of these pharmaceutical marketing expenditures? And more particularly, how do they affect welfare?

The goal of this chapter is to answer these questions. We do this in four stages:

1. investigating the theory of (possible effects of) marketing;
2. developing a model based on this theory;
3. deriving empirical research questions regarding the effects of marketing;
4. answering the questions, using Dutch marketing and sales data covering 11 therapeutic markets.

In developing our model we draw on existing theoretical and empirical work from the economic literature. The theory on (welfare) effects of advertising is in Dorfman and Steiner (1954), Nelson (1974), Dixit and Norman (1978), Shapiro (1980), Milgrom and Roberts (1986) and Cabral (2000). Overviews of empirical results about the general effects of marketing are given by Comanor and Wilson (1979) and Schmalensee (1986). Models of effects of marketing in pharmaceutical markets can be found in Grabowski and Vernon (1992), Rizzo (1999), King (2000) and Gönül et al. (2001).

This chapter contributes in two ways to the empirical economic literature on the effects of (prescription pharmaceutical) marketing. Firstly, to our knowledge this is the first empirical work to use Dutch data: given the institutional differences with (for instance) the USA, marketing effects may well be different for the Netherlands. Secondly, our data cover more than half of the total prescription pharmaceuticals markets, as opposed to existing studies (Rizzo 1999, King 2000, Gönül et al. 2001), which all focus on a single market. As Gönül et al. (2001) put it: "... because our results are based on a single product category (pharmaceuticals for a specific therapeutic condition), a cross-category analysis will substantially strengthen or challenge the findings ..." (p. 89). This chapter provides such a cross-category analysis.

The rest of this chapter is structured as follows. Section 3.1 separates the effects of pharmaceutical marketing into main effects (prescribing behaviour), side effects and costs, and

explains why we focus on the main effects (but do not ignore the others). In Section 3.2 we explain what we mean by "welfare" and why it is possible to assess welfare consequences of the main effects to begin with. Section 3.3 presents a general model of how marketing may affect the pharmaceutical therapy choice of doctors and from this model derives hypotheses and questions to be tested and answered in the ensuing empirical analysis. This empirical analysis starts with a description of the data in Section 3.4. Next, Section 3.5 briefly discusses the model we estimate; this is a formalisation of the model developed in Section 3.3. Section 3.6 gives the estimation results. Finally, Section 3.7 discusses these results and concludes. For a more elaborate treatment of the empirical analysis – especially the technical details – we refer to Windmeijer et al. (forthcoming), a separate CPB Discussion Paper.

3.2 The effects of marketing: a separation into three parts

Before we address the questions posed at the beginning of this chapter, it is useful to differentiate between three separate classes of effects of marketing activities:

- **Main effects, within prescription pharmaceutical markets:** These are the changes in prescribing behaviour of doctors brought about by pharmaceutical marketing activities.
- **Side effects, outside pharmaceutical markets:** One example of these side effects is the fact that prescription pharmaceutical advertisements in medical journals help to keep these journals affordable for more doctors than they would be without the advertising income.
- **The costs of marketing.**

The analysis in this chapter is mainly concerned with the effects of marketing on prescribing behaviour, i.e. the main effects. This is because the available literature and data on side effects and costs of marketing does not allow an extensive analysis. A complete welfare analysis of marketing, however, answers the question whether the social benefits from the (main and side) effects of marketing justify its costs. Therefore, side effects and costs should not be ignored. We discuss them here, before moving on to the analysis of the main effects.

3.2.1 Side effects of marketing

The side effects of the marketing activities of pharmaceutical firms can be found in several places. We already mentioned lower subscription fees for medical journals due to advertising. Other examples are the (beneficial) effect on the quality of GP care when a pharmaceutical firm chooses to sponsor a general practice assistant, and the creation and dissemination of knowledge due to research sponsorships by companies. The variety of instances where these

side effects may occur is too large to give a complete overview. The general impression is, however, that these side effects are predominantly good for social welfare.[1]

3.2.2 Costs of marketing

For any investment in any market, if one looks at the costs of the investment in isolation, i.e. separate from the effects, the costs constitute a welfare loss. Incurring costs if they have no effects is simply a waste. Of course, this is also true for pharmaceutical marketing costs. Thus, the costs of pharmaceutical marketing have an unambiguously negative welfare effect.

3.2.3 Conclusion

The side effects of pharmaceutical marketing probably improve social welfare, the costs decrease social welfare. Although a complete and precise analysis is impossible, it seems plausible that the costs of marketing outweigh the benefits from the side effects. For a complete welfare assessment, these findings should be added to the analysis in the remaining sections of the main effects of marketing on prescribing. Thus, we should keep in mind that the overall welfare effects of pharmaceutical marketing are less favourable (or more unfavourable) than only its effects on prescribing.

The side effects of pharmaceutical marketing are unlikely to outweigh the costs. Therefore, the overall welfare effect is probably less favourable than the welfare effects on prescribing behaviour only.

3.3 Welfare

In the remainder of this chapter we focus on the main effects of marketing, that is the effects on prescribing decisions by doctors. Are these effects on prescribing good for social welfare? Before we can address this question two more fundamental issues have to be settled:

- What do we mean by welfare:
  - what type of welfare?
  - whose welfare?
- Is it possible to give a welfare assessment of the effects?

We discuss these issues below.

[1] Another side effect are the employment opportunities for marketeers created by pharmaceutical firms' investments. This side effect is welfare-neutral, since the value added for society by these marketeers is completely captured by the main effects on prescribing and the other side effects. In other words, the value for society of job opportunities for pharmaceutical marketeers is equal to the value of what these marketeers accomplish, the topic of this study.

3.3.1 What type of welfare?

So far, we have not specified what we mean when we speak of welfare. In economics, we can use (combinations of) three welfare concepts:

- **productive efficiency:** are the pharmaceuticals produced efficiently?
- **allocative efficiency:** does supply meet demand? do patients receive the "optimal" pharmaceuticals (amount, type, quality)?
- **dynamic efficiency:** do market characteristics provide sufficient incentives for innovation?

In this study, we concentrate on allocative efficiency as the criterion for a welfare assessment. This is because (i) marketing is not likely to have a substantial effect on productive efficiency, and (ii) by concentrating on allocative efficiency, we do not ignore dynamic efficiency. We explain the second reason below.

It is not difficult to motivate that allocative efficiency is a relevant welfare criterion to assess marketing activities. After all, marketing affects the therapy choices made by doctors and thus the allocation in the pharmaceutical market. To assess the desirability of marketing we need to know whether the therapy chosen after marketing is better, worse or equal to the therapy before marketing.

It may come as a surprise that there is no need to look at dynamic efficiency as well. After all, many debates regarding the pharmaceutical industry centre around the question whether firms have sufficient incentives to invest in R&D to discover and develop new substances and products, i.e. dynamic efficiency. In fact, this is an issue here as well: firms advertise to increase their profits by stimulating sales. If marketing were somehow to be restricted, firms might gain less profits, thus reducing the incentives to innovate.

Why then do we not include dynamic efficiency in the picture? As a matter of fact, we do. This is because whatever is good for allocative efficiency, is good for dynamic efficiency as well, and vice versa. In other words, if a specific marketing activity is welfare-positive in the allocative sense it will be dynamically welfare-positive as well.

An example will illustrate this point. Consider the case of so-called me-too pharmaceuticals (see 2.1.1). Suppose that the performance of me-too products is only marginally different from the original innovation, implying that real innovations are socially more valuable than me-too pharmaceuticals. Suppose also that it would take large marketing outlays for me-too producers to gain market share and make profits. Then, restricting marketing for me-too products - if such a thing were possible - would increase the incentives for real innovations by decreasing the incentives for me-too innovations.

The crucial element here is that marketing that increases profits irrespective of whether the allocation improves or not, increases the incentives for "good" innovations, which will improve the allocation in the long run, but also for "bad" innovations, which will worsen the allocation. Or, to put it simply, if "bad" marketing - in the sense that it reduces allocative efficiency - increases profits, this will give an incentive to perform innovations that are made profitable through "bad" marketing. And since dynamic efficiency will improve only in the case of (incentives to perform) "good" innovations, marketing that worsens the allocation will also decrease dynamic efficiency.

3.3.2 Whose welfare?

A second question to be answered is, the welfare of which players do we investigate? When we study allocative efficiency, we are actually searching for possible cases of allocative inefficiency. These cases can be divided into two categories, affecting different sets of people:

1. **patients** may receive sub-optimal treatment;
2. **consumers** may pay insurance premiums that are too high, due to overpriced pharmaceuticals.

This means that – from a welfare point of view – doctors should not only act on behalf of their patients, but also on behalf of all consumers.

In Section 3.3 we will see that pharmaceutical marketing can have an effect on two measures that have a one-to-one relationship with these categories:

- the quantity effect: more or less patients using a certain pharmaceutical, which may be a better or worse treatment than before marketing;
- the elasticity effect: doctors becoming more or less sensitive to prices, resulting in lower or higher pharmaceutical prices than before marketing.

At this stage, we include both patient and consumer welfare in our analysis and do not restrict ourselves to only one of these categories. However, we will also explain in Section 3.3 that in an empirical analysis it is not possible to draw welfare conclusions from a quantity effect. Only if we find an elasticity effect, we can draw a welfare conclusion. Thus, although we do not exclude changes in patient welfare through better/worse treatment a priori, our analysis only allows conclusions concerning consumer welfare.

3.3.3 How to assess welfare: evidence-based medicine

Picture a doctor who must choose between therapies A and B for a specific patient. How can we assess whether he should choose one or the other?

Let us move away from pharmaceuticals and consider the case of soft drinks. Suppose that a consumer watches a commercial for Pepsi and decides to switch from Coca-Cola to Pepsi, how can we tell whether this is good for welfare or bad? We can not. Or, more precisely, we cannot do better than assume that the switch was good for welfare, because only the consumer knows his preferences. The consumer knows best.

Copying this argument to prescription pharmaceuticals would imply that we cannot do better than assume that any change in prescribing behaviour brought about by pharmaceutical marketing is good for welfare. But this is not the case. Why not?

The relevant difference between pharmaceuticals and soft drinks is twofold. First, there is asymmetric information: when choosing between pharmaceuticals, the consumer does not know best. Even if a patient insists on product A, product B may still be a better choice. Second, for each specific case (patient, diagnosis, other circumstances) it is possible in principle to rank pharmaceuticals according to suitability for the case at hand based on current scientific medical knowledge about the disease and its possible cures. This principle is known as *evidence-based medicine* (EBM). A patient's personal preferences (or "taste") are not so important.[2] In other words, for prescription pharmaceuticals quality is a much more objective measure than in many other markets.

It may be the case that pharmaceuticals cannot be ranked based on available scientific knowledge. This would lead to clinical uncertainty: doctors do not know which pharmaceutical is the best choice.[3] This does not weaken our case for science as the leading welfare principle: if science cannot decide, patients should be indifferent and - from the viewpoint of welfare - doctors should choose the cheapest alternative.

Now that we have identified allocative efficiency as the relevant welfare criterion and observed that due to the principle of EBM unobservable preferences are relatively unimportant for optimal product choices in pharmaceuticals markets, we can return to the welfare consequences of the effects of marketing. How does marketing affect doctors' therapy decisions?

[2] Another way of putting this, is that EBM incorporates average patient preferences. For instance, suppose that for chronic disease X pharmaceuticals A and B are available. Product A is effective against X, but it has infertility as a side-effect. Product B is somewhat less effective, but does not have the side-effect. In this case many patients would prefer B as the product of first choice. EBM will then also reflect this preference for less efficacy in the trade-off against infertility. Only strong well-founded preferences that differ substantially from the average – example: someone with a preference for A due to strong fears of disease X – may lead to situations where diverting from EBM is good for welfare.

[3] Clinical uncertainty arises in every situation where a doctor is unsure, i.e. also if EBM points clearly toward a specific choice.

3.4 Therapeutic choices and marketing

The questions we seek to answer in this section are:

- Which factors are of influence for (changes in) doctors' therapy choices? Or, in economic terms, what is an appropriate way to model demand for prescription pharmaceuticals? Since we are interested in changes, this will have to be a model of demand through time.
- What are the effects of marketing on these influences? In economic words, how do marketing efforts enter this model?
- How do the effects of marketing affect allocative efficiency?

In addition, recurring in each of these questions is, which empirical research issues arise?

3.4.1 What determines the demand for a therapy?

Picture a doctor who has been confronted with a particular patient, has made a diagnosis and now has to choose a therapy. This may be a pharmaceutical therapy, but also some other therapy (see Section 2.1) or no therapy at all. Which factors are of influence for this doctors' therapy choices? We first answer this question without taking into account the effects of marketing.

Suppose the doctor was fully informed about all relevant aspects of possible therapies. Then the factors of influence would be:

- patient characteristics: one of these is the patient's medication history (if a patient has been taking a specific pharmaceutical for some time, it may be harmful to switch to another product; or there may be harmful interactions with another pharmaceutical the patient is using);
- the prices of the alternatives and possible differences in out-of-pocket costs for the patient;
- all relevant properties of the pharmaceutical product alternatives and other therapies, bundled in the term *quality*. In Section 4.2.2 we explained why for prescription pharmaceuticals such an objective quality measure exists (EBM).

It is important to note that these factors may change as time goes by: patient characteristics change, prices may change, new therapies (pharmaceuticals) may be introduced on the market. At any point in time the doctor would then choose the therapy alternative with at that moment the best quality-to-price ratio, given the patient characteristics. The weight that doctors attach to price in this ratio (relative to quality) can differ from doctor to doctor.

However, doctors are not fully informed about all properties of all alternatives. Their choice will be based on what they think or expect the properties to be. We will call this the *perceived quality* of therapy alternatives. The doctor chooses the therapy alternative with the best ratio of perceived quality to price, given the patient characteristics. If the perceived quality of the

alternatives coincides with the real quality, then the doctor will make the correct choices. If perceived quality differs from real quality, there is a probability of an inappropriate therapy choice (allocative efficiency). This probability grows as the difference between perceived and real quality grows.

Thus, in his therapy choice for a specific patient with a specific diagnosis a doctor is influenced by the perceived qualities of the possible therapies and their prices. Aggregating this model over all patients with that diagnosis and over all doctors, we arrive at a model of the demand for the possible therapies with that diagnosis. The demand for some therapy A at some point in time is influenced by:

- the number of patients with a diagnosis for which therapy A is indicated and the distribution of their characteristics;[4]
- the prices of therapy A and the alternatives ("competitors") at that moment;
- the distribution over all doctors of the perceived quality of therapy A and the alternatives.[5]

In 2.1.2 we explained that the doctor is not completely free to prescribe any product, due to the influence of regulation by government and insurers. Doctors make their therapeutic decisions given the limiting conditions laid out by government and insurers, guidelines, and information provision by (among others) pharmacists. We cannot take (the effect of) these limiting conditions and other factors explicitly into account in our model, only the effect of changes in policy. (Our data pertain to products covered by public insurance.) This means that the results of the empirical analysis concerning prescribing behaviour also reflect the effect of these limiting conditions and other factors.

Having derived this model, the next question is how strongly a change in each of these factors influences the demand. In fact, we only have data on price changes, not on changes in patient numbers and characteristics or perceived qualities. Thus, we will only investigate the effect on demand of a price change. In economic terms this effect of a price change is known as the *price elasticity of demand* and it can be interpreted as the weight doctors attach to price (relative to perceived quality) in their therapy choice, given the patient characteristics. The size of this

[4] Some pharmaceuticals are also prescribed for diagnoses for which they are not indicated (doctors are free to do so). Actually, convincing doctors that a product is effective against non-indicated health problems can be an important goal of marketing. We will not pursue this effect, since our data do not allow us to differentiate between marketing (or prescriptions) for indicated and non-indicated health problems.

[5] Characteristics of the doctor may also affect the therapy choice. For instance, high work pressure may bring doctors to write more prescriptions (a relatively time-saving therapy choice for doctors). Our empirical analysis investigates doctors' medication choice, *given that the doctor has already decided to write a prescription*. Therefore and because we have no data on doctor characteristics, we do not include these characteristics in the model.

elasticity is a matter that we can investigate in the empirical analysis. In Chapter 2 we found evidence that the price elasticity of demand for prescription pharmaceuticals in other countries is not very high. Moreover, since almost everybody in the Netherlands is insured against almost all prescription pharmaceutical costs, we expect that price elasticity will be even lower in the Netherlands. This brings us to the first question for our empirical analysis:

Question 1: How large is the price elasticity of demand for prescription pharmaceuticals in the Netherlands?

So far, in our model the demand for a therapy depends on the number and characteristics of patients, prices, perceived qualities and the weight doctors attach to prices (relative to perceived quality). We have not yet explicitly incorporated (the effects of) marketing, which is the next step. This will allow us to make a distinction between the situation before marketing takes place and the changes brought about by marketing. The model that does not explicitly incorporate marketing implicitly assumes that marketing has already taken place and the effects have materialised.

Which of the elements in the previous model does marketing affect and how can we include this in the model? We see two effects of marketing on prescribing behaviour: a quantity effect and an elasticity effect.

3.4.2 Marketing in the model: the quantity effect

The quantity effect of marketing pertains to the possibility that as marketing expenditure for a specific pharmaceutical product grows, the quantity sold of this product (and of competing products) is affected. This may have several reasons. Marketing efforts for a specific product may:

1. Increase the number of patients for which the product is a possible therapy: For instance, direct-to-consumer advertising may prompt consumers with certain symptoms to visit a doctor where they would not have done so without marketing (Trouw, 16/6/2001). Or patients may become aware of the existence of a new product.[6] Marketing may also convince doctors that the product can be used more broadly than for the indications for which it has been admitted to the market. An example is the pharmaceutical rofecoxib against arthrosis. Jabaaij et al. (2001) report that more than 80% of rofecoxib prescriptions in 2000 were for other diagnoses than arthrosis. In addition, the distribution of patient characteristics may change. For instance, marketing may convince doctors that a product is effective and safe for children as well.

[6] For example, publicity about a new oral contraceptive with a claim that the product does not have weight increase as a side-effect may lead to more women visiting their doctors.

2. Increase the price of that product: Marketing expenses result in higher costs. These may be translated into higher prices.
3. Change perceived qualities: The objective of detailers visiting doctors is, that after the visit doctors will have a more favourable opinion of the product discussed than before the visit (see Section 2.3).

To capture the effect of marketing on the number and characteristics of patients through time and on perceived qualities we include a direct effect of marketing on demand in the model. In addition, a constant (or *intercept*) in the model and time itself can capture the initial number and characteristics of patients and changes in these unrelated to marketing. The value of the intercept can differ between markets, since patient numbers differ between markets. For initial perceived qualities we use product-specific constants to capture differences between perceived qualities of products.[7] Changes in perceived quality are part of the direct effect of marketing on demand.

It is possible to capture the effect of marketing on prices in a similar way. However, we want to estimate price elasticities and determine the effect of marketing on these elasticities. (We have data on prices, not on patient numbers or perceived qualities.) Therefore, we do not explicitly model the influence of marketing efforts on prices.

Thus, the quantity effect of marketing in the model captures the effect of marketing on patient numbers and on perceived qualities, but not on prices. Since more marketing efforts for a specific product can be expected to lead to higher patient numbers and a higher perceived quality for that product, we expect that the quantity effect of marketing is positive. Our second empirical research question is:

Question 2: *What is the sign of the quantity effect of marketing for a product on demand for that product: does more marketing lead to higher or lower demand?*

As we pointed out in 3.2.2, this effect has consequences for the welfare level of patients who receive different treatment due to marketing. What can we say about the welfare properties of the quantity effect? Not much. Allocative efficiency may be enhanced by larger patient numbers, for instance if this leads to earlier detection of health problems and therefore to prevention of severe illness or prevention of the need for surgery. Likewise, a higher perceived quality may be justified, for example if a doctor learns from a detailer that the marketed product has less side

[7] In fact, by including product-specific intercepts the market-specific intercepts become redundant, since the product-specific intercepts will capture structural demand differences across markets as well. In the empirical model (Section 3.5) we therefore only use product-specific intercepts.

effects than competing products. With this information, the doctor can make better choices (increase allocative efficiency).

On the other hand, allocative efficiency may also deteriorate, for instance if some of the additional patients receive unnecessary treatment. Or if the information a doctor receives from a detailer is inaccurate. Since we cannot make a distinction in the model between the welfare-positive and the welfare-negative side of the quantity effect, a welfare assessment of the quantity effect cannot be given. This is also the case if the quantity effect – unexpectedly – turns out to be negative.

Market making versus market stealing

The quantity effect in the model pertains to the effect of, for instance, an advertising campaign for a product on the demand for that product. An interesting question then is, how does this campaign affect the demand for other, competing products? There are two extreme situations:

- The demand increase for the promoted product goes entirely at the expense of competing products. We call this *market stealing*.
- The total market grows; competing products do not suffer any demand reduction. We call this *market making*.

Typically, the total quantity effect will be a combination of these two situations. Thus, an interesting issue for our empirical research is:

Question 3: How much of the quantity effect of marketing is market stealing and how much is market making?

3.4.3 Marketing in the model: the elasticity effect

In the model of 3.3.1, the demand for a therapy depends on the number and characteristics of patients, prices, perceived qualities and the weight doctors attach to prices relative to perceived quality. The quantity effect (3.3.2) can capture the effect of marketing on patient numbers, prices and perceived qualities. (Remember, however, that we did not model the effect on prices explicitly.) The elasticity effect captures the effect of marketing on the weight of prices relative to perceived quality; in other words, on the price elasticity of demand.

The easiest way to think of this, is the following. If products are perfect substitutes (for a specific patient) in the minds of doctors, the price is an important factor for choosing one or the other. Thus, between perfect substitutes price elasticities are high. If products are very different in the minds of doctors (for instance, the doctor believes that product A is clearly best for younger patients and product B is by far the optimal choice for older patients), the price will not be

important, and price elasticities between A and B will be low. An effect of marketing may be that it changes the amount of differentiation between products in the minds of doctors.

The question then is, does marketing influence the price elasticity of demand and, if so, does marketing increase it or decrease it? This question is particularly interesting, since the welfare assessment of the effect changes with the direction: if marketing increases the elasticity, doctors respond more intensely to price changes, implying fiercer price competition (less brand loyalty), which is good for allocative efficiency: consumers will gain through lower health insurance premiums. The reverse is also true: if marketing reduces price elasticities, then there will be more brand loyalty, and therefore higher markups. As a result, allocative efficiency will be lower.

We must add here that we can only draw these welfare conclusions if elasticities are estimated as if doctors choose between alternatives of equal perceived quality (perfect substitutes). To achieve this we have to explicitly model the influence of perceived quality on demand in the empirical model. We do this by including fixed effects: product-specific intercepts that capture (among others) the influence of perceived quality on demand (see Section 3.5).

Thus, we have arrived at another research question for the empirical analysis:

Question 4: *Does marketing change the price elasticity of demand? If so, does marketing increase this elasticity (good for welfare) or decrease it (bad for welfare)?*

The elasticity effect raises an important issue. In 2.1.3 we pointed out the role of price sensitivity as a possible determinant of marketing intensity: a low price elasticity may lead to high marketing expenditure (Dorfman and Steiner 1954). The elasticity effect works the other way around: marketing efforts leading to a higher or lower price elasticity. We have to ensure that we measure the right effect in the empirical analysis.

The following box summarises the empirical research questions derived in this section:

Empirical research questions

Question 1:	How large is the price-elasticity of demand for prescription pharmaceuticals in the Netherlands?
Question 2:	Direction of the quantity effect: does more marketing for a product lead to more or to less demand for that product?
Question 3:	How much of the quantity effect of marketing is market stealing and how much is market making?
Question 4:	Does marketing change the price-elasticity of demand? If so, does marketing increase this elasticity (good for welfare) or decrease it (bad for welfare)?

3.5 The data

To estimate this model, we acquired two separate sets of data and linked these sets. Both sets contained product-level data covering all 72 months in the period 1994-1999.

3.5.1 Marketing data

The first set consisted of data on the marketing of pharmaceuticals and was purchased at IMS Health Nederland (IMS HEALTH). The IMS HEALTH-database contained figures pertaining to:

- detailing, obtained from a panel of GP's and (since February 1995) psychiatrists;
- advertising, derived from inspection of medical journals;
- direct mail, obtained from a panel of physicians (GP's and specialists).

In addition, the product specifications of IMS HEALTH contained data on product age.

3.5.2 Sales data

The second set contained data on the sales of pharmaceutical products and was provided by the Geneesmiddelen Informatie Project of the College voor Zorgverzekeringen (GIP/CvZ). Based on their records covering the pharmaceutical declarations to nine of the Dutch sickness funds, the GIP/CvZ-files gave an estimate for the Netherlands of:

- the total amount of money spent on a specific pharmaceutical product in a specific month, split into (publicly) insured costs and out-of-pocket payment;
- the quantities sold of a specific product in a specific month, expressed in defined daily doses (DDD), a standard measure to compare pharmaceutical use across different pharmaceuticals.

Both the costs and volume were subdivided further according to the prescriber: GP or other (typically specialists, but also containing dentists, midwives, and unknown). Prices were obtained by taking the ratio of costs and volume. We received these figures for all products in the fifty largest ATC3-groups, measured by total costs in 1999.

3.5.3 Refinements on data for estimations

The data that we linked and used for our regressions cover 11 therapeutic markets: pharmaceuticals against allergy, anxiety, asthma, cholesterol, depression, hypertension, migraine, pregnancy (oral contraceptives), rheumatism, sleeping disorders and ulcers.[8] These markets together cover 58% of the total Dutch market for reimbursed prescription pharmaceuticals measured in pharmaceutical costs (GIP, 2000b) and 55% measured in the costs for the types of marketing in the IMS HEALTH data.

[8] Appendix B to this chapter contains the specific ATC3-groups included in the analysis.

In addition, we restricted the data-set to quantities sold due to prescriptions written by general practitioners (GP's) and did not take prescriptions by specialists into account, except for the markets for pharmaceuticals against anxiety and depression. The main reason to do this was that the detailing data - which accounts for 70% of the marketing costs - were obtained from a panel consisting of only GP's and psychiatrists. Thus, we had little data concerning marketing directed at specialists other than psychiatrists. In our choice of the markets included in the analysis we also took this limitation of the marketing data into account by selecting markets where GP's or psychiatrists are responsible for a substantial fraction of the prescriptions.

3.6 The empirical model

The empirical model we use resembles the model used by Rizzo (1999). Rizzo investigated the effects of detailing on sales made by producers of anti-hypertension pharmaceuticals in the United States. Like us, he focussed on the effect on the estimated price elasticity of demand. Our model is a dynamic version of Rizzo's.

Since our sales data reflect medication choices by doctors, the model in this section describes demand for pharmaceutical therapies covered by public insurance, *given the decision to write a prescription for a product covered by insurance*. In other words, given diagnosis and patient characteristics doctors choose between pharmaceutical products A, B and C. Non-reimbursed pharmaceutical therapy as well as surgery, physiotherapy, psychotherapy and no therapy at all are not options in the context of this model.

In the model, the quantity sold of a particular pharmaceutical product in a particular month (the *dependent variable*) is explained by nine (groups of) *explanatory variables*. Below, we discuss each of these variables. A more technical representation of our model is contained in the box *The econometric model*.

Dependent variable: quantity sold in the current month

The variable to be explained is the quantity sold of a specific product in a specific month, expressed in daily doses. Remember from 3.4.3 that – for data-related reasons – we restricted quantities sold to prescriptions from GP's (and, for two markets, psychiatrists). For non-data reasons, we applied three further refinements.

Firstly, generic products are not included in the sample, since it is likely that generic marketing strategies and their effects are different from marketing for branded products. Thus, we only look at the effects of marketing on the sales of branded products.

The second refinement is that we only used the quantities sold of branded products without a generic equivalent as dependent variables.[9] The reason to exclude branded products with a generic equivalent is that these producers are in a different situation than producers of branded products without generic equivalent (see Section 2.1.1). Therefore, they are also likely to employ different strategies that have different effects. To obtain clear results, it is prudent to isolate one set of effects. We chose the group of brands without generic alternative, since it is the largest by far.

Finally, we excluded the products for which no marketing takes place during the entire sample period, because we did not have product ages for these *no-marketing products*. After the previous two refinements, the number of these products was very small.

Now we turn to the nine (groups of) explanatory variables.

Quantity sold in previous periods

This is the dynamic component that is absent in Rizzo's model. We added this component to account for the possibility of habit persistence in prescribing behaviour. An additional reason is, that it may not be easy to change (repeat) prescriptions immediately after a price change or a marketing increase for an alternative pharmaceutical. In fact, we also estimated a version without this dynamic component and found that the component adds considerably to the explanatory power of the model. An implication of this dynamic component is, that we have to differentiate between short-term and long-term effects of (changes in) marketing efforts.

Product-specific intercepts (perceived quality)

A different constant (technically: intercept) for each product captures fixed product-specific and market-specific aspects. One of the product-specific aspects is the initial perceived quality of the product relative to its competitors. (The change in perceived quality due to marketing is part of the marketing effect on demand.) The coefficients for (among others) prices and marketing will then reflect the influence of prices and marketing given perceived quality levels and other product and market characteristics.

[9] In the cases of products for which a generic equivalent appeared on the market during the sample period, we only included the period before introduction of the generic equivalent in the sample.

The price of the product in the current month

The average price of competing pharmaceuticals in the current month

The question to be answered here is, which pharmaceuticals are competitors and which are not? In our estimations we have taken products in the same ATC3-group to be competitors.[10] These include generic and no-marketing products (these products are only excluded as dependent variables).

The amount of marketing for the pharmaceutical in the current and previous months

It is likely that the effect of marketing lingers for several periods. A detailing visit, for instance, may still influence a doctor's prescribing behaviour four months later. Like Rizzo, we capture this effect by constructing a stock of marketing (in addition to the marketing flow: marketing in the current period). This stock is depreciated every period to reflect the petering-out effect and increased with the amount of marketing in the current period. The depreciation rate is chosen in such a way that the explanatory power of the model is maximised.[11]

Marketing by competitors in the current and previous months

As in the case of prices we took ATC3-groups as the set of competing products, again including generic and no-marketing products.

Product age

On average the sales of pharmaceuticals appear to follow a specific life cycle (see for example Berndt et al. 1999). To take this into account, we included product age (as well as its square) as an explanatory variable in the model.

Time effects

For some pharmaceutical markets, it is likely that seasonal effects play a role in explaining sales. The market for allergy pharmaceuticals is an obvious example (hay fever). To account for this, we have included month dummies, with a separate interaction with the allergy pharmaceuticals market. Year dummies were taken up as well, to allow for structural, industry-wide growth.

[10] The ATC classification system is explained in Appendix A to this chapter.

[11] In our estimations, this depreciation rate turns out to be 55% per year.

The econometric model

The econometric model we used is defined in terms of logartihms: *ln*. The model is similar to that of Rizzo (1999) and can be specified as follows:

$$\begin{aligned}\ln q_{it} = {} & \rho_1 \ln q_{i,t-1} + \rho_2 \ln q_{i,t-2} + \gamma_i + \\ & + (\alpha_1 + \alpha_2 \ln mes_{it}) \ln p_{it} + (\alpha_3 + \alpha_4 \ln mes_{it}) \ln pc_{it} + \\ & + \alpha_5 \ln mef_{it} + \alpha_6 \ln mes_{it} + \alpha_7 \ln mefc_{it} + \alpha_8 \ln mesc_{it} + \\ & + \beta x_{it} + \varepsilon_{it}\end{aligned}$$

where:

- q_{it} represents the quantity sold of product *i* in month *t* in daily doses (the estimations showed that including two lagged months was sufficient, additional lags had insignificant coefficients);
- the γ_i are product-specific intercepts that, among other things, control for unobservable differences in perceived quality between pharmaceuticals that are constant over time;
- p_{it} is the nominal price of a daily dose of product *i* in month *t*;
- pc_{it} is the average price in month *t* of competing products for product *i*, where sets of competing products (markets) are defined by ATC3-groups;
- mef_{it} is the marketing expenditure flow for product *i* in month *t* (the marketing expenditure in that month);
- mes_{it} is the marketing expenditure stock for product *i* in month *t* (reflecting the lingering effect of marketing expenditure in previous months);
- $mefc_{it}$ and $mesc_{it}$ are the marketing expenditure flow and stock in month *t* of competing products for product *i*, where again markets are defined by ATC3-groups;
- x_{it} represents (logarithms of) several additional variables, including product-age, year and month dummies, and dummies for policy changes;
- finally, ε_{it} is the error term.

Since the model is defined in terms of logarithms, the coefficients can be interpreted as elasticities. Thus, if we impose the restrictions $\alpha_2 = 0$ and $\alpha_4 = 0$ (this means that there is no elasticity effect, as in model 1 of Section 3.6), then α_1 is the average own price elasticity of demand for an individual pharmaceutical product and α_3 is the average cross price elasticity. (If $\alpha_2 \neq 0$, the own price elasticity is given by $\alpha_1 + \alpha_2 \ln mes_{it}$.) For example, if the estimation results gave a value of -0.5 for α_1 this would mean that an increase of 10% in the price of a particular product would result on average in a sales decrease of 5%.

The interaction between the product's own price and competitors' prices on the one hand and marketing expenditures on the other, enables one to test for the effect of marketing expenditure on the price elasticity of demand. If $\alpha_2 > 0$ and/or $\alpha_4 < 0$, then marketing adversely affects the own and/or cross price elasticity of a product. If, on the other hand, $\alpha_2 < 0$ and/or $\alpha_4 > 0$, this indicates a socially beneficial effect of marketing on price elasticities.

Policy changes

In the period covered by our data (1994-1999), several policy changes occurred that may have affected pharmaceutical sales. Policy changes that exactly coincide with calendar years, such as the co-payment scheme of 1997-1998, are accounted for by year dummies (see above under Time effects). Other policy changes included in our model were:

- the industry-wide 5% price reduction of June 1994;
- the Pharmaceutical Prices Act that came into effect in June 1996;
- the recalculation of GVS reimbursement prices of February 1999.

These policy changes were accounted for by including dummies in the model.

3.7 Results

3.7.1 The baseline estimation

Table 3.1 contains the results for our baseline estimation: a dummy variable least squares (DVLS) estimation of the model of Section 3.5, with 140 product-specific dummies, estimated with marketing and sales data for the period 1994-1999. In the box *Robustness* (and in the main text, below) we discuss other estimations. Further details can be found in Windmeijer et al. (forthcoming).

The first striking feature of the results is that they indicate a strong persistence in prescribing behaviour: the coefficients on previous months' quantities sold sum up to 0.82. This means that there is a strong habit persistence/brand loyalty: if – for some reason, for instance due to marketing – quantity sold in this month rises with 10%, then quantity sold in the next month will increase with 6.8%, the month after that with 6.0% (= $[0.14 + 0.68^2] \times 10\%$) and so on. Thus, it takes a long time before the effects of price changes and changes in marketing efforts on quantities sold are fully established: 2-3 years. This also explains why the coefficients on other variables are rather small: these are the short-run effects. The long-run effects, that we will present below, are larger.

Price elasticity of demand and the elasticity effect

Table 3.1 presents the results for two versions of the model. In Model 1 the elasticity effect of marketing on price sensitivity is set to be zero. Model 2 includes this elasticity effect. As explained in Section 3.3, Model 1 gives the price elasticity of demand after the effects of marketing have occurred (Question 1 of Section 3.3). Model 2 allows this after-marketing elasticity to be separated into a before-marketing elasticity and the effect of marketing on this elasticity (Question 4).

Table 3.1 Baseline estimation results

Variable	Model 1	Model 2
Quantity sold, one month back	** 0.68	** 0.68
Quantity sold, two months back	** 0.14	** 0.14
Elasticity effect		
Own price	0.01	* -0.18
Elasticity effect, own price		** 0.02
Competitors' prices	0.00	0.10
Elasticity effect, competitors' prices		* -0.01
Quantity effect		
Own marketing expenditure flow	** 0.02	** 0.01
Own marketing expenditure stock	** 0.04	** 0.04
Comp. marketing expenditure flow	** 0.01	** 0.01
Comp. marketing expenditure stock	** -0.03	** -0.03
Explanatory power (R-squared)	0.8701	0.8705
Number of observations: 7040		
Number of products: 140		

Notes: Estimation method: dummy variable least squares, with 140 product-specific dummies. Most variables have been omitted from the table (the total number of variables in the model is very large). Only the coefficients of variables directly related to our research questions are shown. * indicates significant coefficient on a 90% probability level, ** indicates significant coefficient on a 95% probability level. Significance established using standard errors that are robust for heteroscedasticity.

From the table we see that if the elasticity effects are not taken into account (model 1), the sensitivity of quantity sold to its own price equals 0.01, but is not significant. (The statistical probability that in reality the coefficient is zero – the *p-value*, not in the table – is p = 0.70.) This indicates that the average after-marketing own price elasticity is practically zero.

In the version with elasticity effects (model 2), the coefficient on (the log of) own price is negative (-0.18) and significant (p = 0.05). It is not appropriate to interpret this value as being the price elasticity when there is no marketing. There are only a few observations in the data where the marketing stock is equal to zero, which occurs only in cases of newly introduced products, just before marketing starts. For the observations with a positive marketing stock, the value of the log of the stock is between 7 and 15. Interpreting this coefficient as being the price elasticity when there is no marketing would rely too heavily on extrapolation outside the support of the data.

From model 2 we also see that the effect of marketing on own price elasticity is positive (0.02) and significant (p = 0.01). The positive coefficient for the elasticity effect on own price means that marketing reduces this own price elasticity.

With regard to competitors' prices, the results are similar but less distinct. Without elasticity effect (model 1) the competitors' price elasticity is clearly zero (p = 0.99). With the cross-effect the coefficient is positive (0.10) and much less insignificant (p = 0.15), with a negative elasticity effect (-0.01; p = 0.07) that – again – reduces this sensitivity.

Robustness

The results in Table 3.1 suggest that pharmaceutical marketing decreases the price-elasticity of doctors significantly. Before we can draw strong conclusions, we must find out how robust this result is: how sensitive are the estimations for changes in the model, the data-set (sample choices) or the estimation method? We find that the significant elasticity-effect is robust: it appeared in all estimations we ran. Below, we report on the robustness checks we executed. Windmeijer et al. (forthcoming) provides more details on (the outcomes of) these robustness checks.

Model versions

Section 3.5 describes the baseline model, yielding the results presented in Table 3.1. In the main text we mention other model versions needed to derive additional results. In addition to those versions we ran the following checks:

- *Shares instead of levels:* The dependent variable in the baseline model is the level of product quantities sold. We also ran regressions with the product's share in total quantity sold as the dependent variable (and marketing shares instead of levels as explanatory variables).
- *ATC4-groups instead of ATC3-groups:* To determine competitors' (average) prices and marketing levels, we used ATC3-groups in the baseline model. Using ATC4-groups instead did not yield qualitatively different results.
- *Non-dynamic model:* The main difference between our model and that of Rizzo (1999) is the dynamic component. This dynamic component ads considerably to the explanatory power. Without it the elasticity effect is still significant and positive.

Data-subsets

The data for our baseline results pertain to the entire 1994-1999 period – with the refinements described in 3.4.3 and Section 3.5 – and encompassed all products without a generic alternative. The robustness checks we ran with different sample choices include:

- regressions with data covering all products, those with and those without generic alternatives;
- regressions with only new products, i.e. with first sales occurring after January 1994;
- regressions with only old products, i.e. with sales in January 1994.

Estimation method

The baseline results are those of a so-called dummy variable least squares (DVLS) estimation. We also ran regressions with the instrumental variables (IV) method (with product-specific dummies), using lagged prices and marketing levels as instruments. This method also yielded a significant and positive elasticity effect. According to the standard statistical test to compare DVLS and IV outcomes, the difference between the two was not significant.

Besides the baseline estimation presented in Table 3.1, the significant elasticity effect was an outcome of all other estimations we executed, with different versions of the model, with other sample choices and with another estimation method. In econometric terms: the result proved to be *robust*. Some of these additional estimations we discuss below, the box *Robustness* mentions all other estimation runs.

Another issue to resolve before we can draw a conclusion, is causality: does more marketing cause a lower price elasticity (Rizzo 1999), or does an inherently lower price elasticity lead to more marketing (Dorfman and Steiner 1954)? To resolve this issue, we took the same approach as Rizzo. This approach is based on the observation that, if our result only reflects the Dorfman-Steiner relation, then allowing for differences in price elasticities between products should remove the elasticity effect. We checked whether this is the case by estimating a model version that allowed for different price elasticities for different markets and product-ages. This estimation still yielded a significant interaction effect, which implies that causality runs from marketing efforts to lower elasticities.[12]

It is important to note here that the estimations represent an average effect in the eleven markets included in our analysis. We did not always observe the elasticity effect in separate estimations for each of the markets, nor is it equally strong in all markets where the effect occurs. Moreover, some of the markets are too small to derive reliable results for these markets alone.

Based on the results and considerations above, we can draw the following conclusion:

On average, pharmaceutical marketing significantly reduces doctors' price elasticity of demand.

The quantity effect

Table 3.1 also gives estimates for the direct effect of marketing on quantity sold. We see that all marketing variables (own/competitors' and flow/stock) have significant coefficients. Both the flow and the stock of own marketing expenditure have a positive coefficient, indicating that marketing for a product leads to an increase in demand for that product. Thus, as one might expect, the quantity effect of pharmaceutical marketing is positive (Question 2 of Section 3.3).

[12] Another reason to expect this direction of causality, is that since the introduction of the Pharmaceuticals Prices Act (see the box *Regulation of pharmaceutical prices in the Netherlands* in Chapter 2), price setting for the Netherlands no longer reflects the price elasticity/marketing expenditure tradeoff of producers. (The Dorfman-Steiner relation between price elasticity and marketing was derived from a situation where a monopolist sets price and marketing expenditure simultaneously.)

To check whether the quantity effect increases or decreases as marketing expenditure grows, we also performed estimations with the squares of marketing expenditure flow and stock as additional explanatory variables. This estimation yielded a significant and negative coefficient for the square of own marketing stock, indicating that the quantity effect becomes weaker as marketing expenditures increase. The coefficients on the squares of own marketing flow and of competitors' marketing stock and flow were not significant.[13]

This leads us to the following conclusion:

Pharmaceutical marketing for a product increases demand for that product. This effect becomes weaker at higher levels of marketing expenditure.

The effect of competitors' marketing expenditure on quantity sold is unclear, since we find opposite signs for the coefficients for competitors' marketing flow (positive) and stock (negative). This may indicate that a marketing increase by competitors increases quantity sold in the short run (positive flow coefficient) but decreases it in the longer run (negative stock coefficient). The overall effect of a change in competitors' marketing cannot be deduced from the results in Table 3.1. This overall effect will have to be derived from the steady-state elasticities.

3.7.2 Steady-state elasticities

As explained above, it takes a long time before the effects of changes in marketing or prices on demand have been completely established. Therefore, it is interesting to look at the long-run effects of changes. Table 3.2 presents these long-run effects in terms of the steady-state elasticities. A steady-state elasticity gives the effect of a permanent change in prices or marketing on demand, everything else equal. After 2-3 years these changes have taken their effect and the model is in a new 'steady state'. Thus, the steady-state own marketing elasticity value of 0.30 in model 1 implies, that on average a permanent 10% increase in marketing expenditure for a product (and everything else equal) would lead to a 3% increase in demand, where the demand increase takes 2-3 years to become fully established.

[13] With this estimation we performed the same check on the elasticity effect, using squared marketing interacted with price as additional explanatory variables. The coefficients for these variables were all insignificant, implying that the size of the elasticity effect – significant in this estimation as well – did not change significantly with marketing expenditure.

Table 3.2 Steady-state elasticities

Variable	Model 1	Model 2
Own price	0.06	
Own price at 5 percentile marketing		-0.26
Own price at 95 percentile marketing		0.29
Competitors' prices	0.00	
Comp. prices at 5 percentile marketing		0.11
Comp. prices at 95 percentile marketing		-0.24
Own marketing	** 0.30	** 0.32†
Competitors' marketing	** -0.12	** -0.10

Notes:
†The steady-state own marketing elasticity in model 2 varies with the price level (in the same way as the steady-state price elasticities vary with the marketing level), due to the interaction between price and marketing. The presented elasticity is the elasticity at the median price level.
* indicates significant coefficients on a 90% probability level; ** indicates significant coefficients on a 95% probability level.

The long-run elasticity effect

The long-run effect of marketing on price elasticities cannot be read directly from Table 3.2, but it can be inferred from the change in steady-state price elasticities across different levels of marketing (model 2). Due to the interaction between prices and marketing in model 2, steady-state price elasticities vary with the marketing level (and steady-state own marketing elasticities vary with the price level). Table 3.2 presents two steady-state own price elasticities, one at a low marketing level (at the 5th percentile of the marketing level distribution) and the other at a high marketing level (95th percentile). Although the elasticities themselves are estimated quite imprecisely, the difference in the own-price elasticity at different marketing levels is apparent: it is -0.26 at the 5th percentile and 0.29 at the 95th percentile. We can also calculate the steady-state elasticity effects. (These are not steady-state elasticities and therefore not included in the table.) Estimates for these steady-state elasticity effects are given by 0.09 (own price) and -0.06 (competitors' prices) respectively, indicating that a permanent 1% increase in marketing expenditures increases the own-price elasticity by 0.0009.

The long-run quantity effect

When looking at steady-state marketing elasticities, there is no difference between marketing expenditure flow and marketing expenditure stock. After all, a permanent 10% increase in marketing flow means that in the long run, marketing stock increases permanently with 10% as well. This allows us to investigate the overall effect of an increase in competitors' marketing expenditure. From Table 3.2 it is clear that this overall effect is negative: demand for a product falls if competitors increase their marketing efforts.

Market making versus market stealing

Thus, we find that demand for a product increases with own marketing expenditure and falls with marketing expenditure for competing products. Now we can turn to Question 4 of Section 3.3: how much of the quantity effect of marketing is compensated by a reduction in demand for competing products (market stealing) and how much is due to market growth (market making)?

From Table 3.2 we can derive market stealing and market making estimates by looking at both the effects of own marketing and competitors' marketing on sales. Suppose all players in a market increase their marketing levels with 1%. According to the coefficients of model 1, the net effect of this market-wide marketing increase is that all sales increase with 0.18% (0.30 0.12). Since the market stealing effects will cancel out if all players increase their marketing equally, 0.18 out of 0.30 is the market making effect. The market stealing effect then equals 0.12. Thus, market making accounts for 60% of the total quantity effect, market stealing for 40%.[14]

3.8 Conclusions and discussion

From the empirical results presented in the previous section we draw the following conclusions:

Conclusions from the empirical analysis

1. The average after-marketing price elasticity in the prescribing behaviour of doctors is zero.
2. The average pre-marketing price elasticity is negative and statistically significant. On average, marketing significantly reduces the price elasticity.
3. There is also a significant direct effect of marketing on the quantity sold. Approximately 60% of this quantity effect is due to market growth, the other 40% is compensated by lower demand for competing products.

Below, we discuss these conclusions and their implications.

3.8.1 The price-elasticity of demand and the elasticity effect

The empirical results show that after marketing the sales volume is insensitive to price changes on average, i.e. changes in individual product prices as well as industry-wide price changes. This insensitivity to prices in the prescribing behaviour of doctors is probably partly due to the high level of insurance in the Netherlands: almost all prescription pharmaceuticals are covered by

[14] Taking the coefficients of model 2 instead of those of model 1 changes these estimates slightly. Then market making accounts for 69% and market stealing for 31%.

public (and private) health insurance. Dutch regulation of pharmaceutical prices and other factors may also partly explain the observed price elasticities.

The estimations also show that this insensitivity to prices is partly due to marketing activities. The estimated pre-marketing own price elasticity is significant and negative, but for median levels of marketing this sensitivity of doctors disappears. The equivalent opposite statements can be made for the effects of marketing on the elasticity for competitors' prices, although these results are less distinct.

In absolute terms the elasticity effect we find is not large. The elasticity effect found by Rizzo (1999) is larger. However, Rizzo estimated his model with data for the U.S.A., where insurance coverage is lower and where price regulation is largely absent. In other words, there is more room for an elasticity effect to materialise in the U.S.A. than in the Netherlands. In that sense, there was no reason to expect a large elasticity effect for Dutch pharmaceutical marketing. It is therefore quite remarkable that we find such a clear and robust elasticity effect.

How can we interpret this result? It is not easy to put the practical consequences of the elasticity effect into words. A simplified description is that of the case in which a doctor faces a choice between two products with given (perceived) quality levels and prices. The doctor has received the same amount of marketing for both products. The implication of our result in this situation is, that the probability that the doctor chooses the more expensive product increases as the amount of marketing for both products increases. The difference in perceived qualities has not changed, but the doctor now attaches less weight to the price difference relative to the difference in perceived quality.

Of course, in reality marketing levels are not equal across products. Moreover, marketing will result in increases in perceived quality (quality is not given). Our result shows that also in these situations of more complex decision making, marketing provides pharmaceutical producers with additional market power, on average. As a result, pharmaceutical costs will tend to increase.

This result does not contradict the notion that doctors' choices are based on quality. In the model we have separated the influence of perceived quality (and other product-specific aspects) from the influence of prices. This means that marketing can change the perceived quality such that doctors are convinced to prescribe the more expensive product, but at the same time lower

the price elasticity to accommodate this change in prescribing behaviour.[15] The perceived quality reason to switch is captured by the quantity effect, which may be either welfare-positive or welfare-negative.

We find that the elasticity effect also plays a statistically significant role. This average effect of marketing on price elasticities is unambiguously welfare-negative. This is because the effect we see is an effect after correcting for quality differences and this allows us to interpret the lower sensitivity to prices as brand loyalty not supported by product characteristics. This is socially undesirable.

Two observations strengthen this result. Firstly, remember that our empirical welfare analysis only pertains to the direct effects of marketing on prescribing behaviour, and does not include the side-effects of marketing or the cost. In Section 3.1 we argued that the side-effects are predominantly welfare positive, but probably not sufficient to justify the costs of marketing. Thus, the total welfare-effect of marketing is likely to be lower than the results from the empirical analysis suggest.

The other observation pertains to the data. The marketing data used to derive the result above are limited to statistics on detailing, advertising and direct mail. These types of marketing are relatively common and perform mechanisms with - on theoretical grounds - both positive and negative welfare effects (see Section 4.1). Data about other important types of marketing more specific for the pharmaceutical industry, such as post-marketing research, gifts and hospitality, were not available. These types of marketing mainly perform mechanisms that - again on theoretical grounds - decrease welfare. If it had been possible to use data on these types, we expect that our welfare-negative result would probably have emerged even more clearly than at present.

3.8.2 The direct effect of marketing on sales, market stealing, market making

The results show that - as could be expected - marketing expenditures have a significant, positive effect on sales: on average a permanent 1% marketing increase results in 0.30% more sales in the long run. This quantity effect is stronger for low levels of marketing effort and becomes weaker for higher levels. Of this sales rise, approximately 35% is compensated by sales decreases of competing products (market stealing), the remaining 65% is due to market growth.

[15] The choice between two classes of anti-depressants - TCA's and SSRI's - appears to be a fitting example. SSRI's are approximately three times as expensive as TCA's, but also more heavily promoted and more often prescribed than TCA's. However, guidelines and standards do not support this strong preference for SSRI's, at least not for general practitioners (RIVM 1999, Van der Linde 2001).

It is not possible to give a welfare assessment of the quantity effect: on average, patients may benefit from the changes in prescribing behaviour brought about by marketing or they may not.

3.8.3 Policy implications

In the analysis of this chapter, we find a robust and significant welfare-negative effect of pharmaceutical marketing. This may be a reason for policy intervention. However, marketing is likely to have welfare-positive partial effects as well. Thus, policy should ideally be aimed at removing the welfare-negative effects of marketing while keeping the welfare-positive ones. For this we need more insight in what brings about the welfare-negative and welfare-positive effects: the mechanisms of marketing. In the next chapter, we develop these insights and formulate policy options.

Appendix A: The ATC classification system

Every pharmaceutical (active ingredient) has a unique ATC-code, assigned by the World Health Organization. ATC stands for Anatomical-Therapeutical-Chemical. The complete ATC-code has 5 levels: letter-number-letter-letter-number. For example, the antidepressant fluoxetine = N06AB03. This can be dissected as follows:

ATC1 (anatomical):	N = brains and nervous system ('N' for 'neuro')
ATC2 (therapeutical):	N06 = psycho-analeptics
ATC3 (therapeutical):	N06A = antidepressants
ATC4 (therapeutical / chemical):	N06AB = selective serotonine re-uptake inhibitors
ATC5 (chemical):	N06AB03 = fluoxetine

Relevant markets within the pharmaceuticals sector are comprised of patients with the same affliction, for example people that suffer from depression. The product on this market are the pharmaceuticals aimed at alleviating or curing this affliction, in the example this are the antidepressants. Often such a product market corresponds fairly well with one or more ATC-codes on the ATC3-level. For example, the antidepressants are gathered in group N06A.

An example of a product market consisting of several ATC3-groups is the market for pharmaceuticals that treat high blood pressure (hypertension). Examples of important ATC3-groups of anti-hypertensives are C02A, C03A, C07A and -B, C08C and -D and C09A through -D ('C' for 'cardiovascular': heart- and artery afflictions). These pharmaceuticals are in separate groups, because of the different physiological mechanisms on which they are based. However, they are (to some extent) substitutes: therefore they constitute one single market.

Appendix B: Markets (ATC3-groups) covered by the empirical analysis

Table 3.3 specifies the eleven markets and the respective ATC3-groups. The table also presents some core statistics for each of the markets. The statistics are for the year 1999.

Table 3.3 The markets (ATC3-groups) and selected statistics, The Netherlands, 1999

Therapeutic market	ATC3-group(s)[a]	Pharma-ceuticals (nr)	Brands (nr)	Generics (nr)	Generics (mkt share)	Costs (mln euro)	Sales volume (mln ddd)	Marketing[b] (mln euro)
Ulcers	A02B	15	16	4	16.2%	282.8	204.3	1.57
Hypertension[c]	C03A, C07A, C08C, C08D, C09A - C09C	57	70	16	21.4%	296.7	797.9	6.94
Cholesterol	C10A	12	12	3	0.7%	187.8	228.4	2.80
Pregnancy (oral contraceptives)	G03A	13	19	0	-	51.6	587.8	0.46
Rheumatism	M01A	18	32	8	61.2%	58.7	160.3	1.37
Migraine	N02C	10	10	2	2.0%	37.3	10.3	2.41
Sleeping disorder	N05B	14	13	9	68.4%	19.1	133.4	0.14
Anxiety	N05C	15	15	11	74.1%	18.0	115.3	0.07
Depression	N06A	23	24	7	11.2%	115.8	141.6	4.25
Asthma	R03A, R03B	14	21	4	4.9%	222.3	413.8	1.92
Allergy	R06A	21	20	7	5.8%	27.6	68.4	1.60
Total (these markets)		212	252	71	15.1%	1 317.7	2 861.5	23.53
Total (all markets)		± 1 080	± 900	± 300	14.8%	2 258.7	± 4 700	50.10[d]

a ATC-groups and markets do not completely coincide; our analysis is based on ATC-groups.

b Marketing statistics pertain to detailing, advertising and direct mail; moreover, the statistics given should be interpreted as indications.

c The hypertension market consists of three additional, small ATC3-groups for which we did not have the data: C02A, C07B, C09D.

d Total (all markets) marketing statistic pertains to more pharmaceuticals (non-prescription and/or non-reimbursed) than other statistics in this row.

Sources: IMS HEALTH, calculations CPB (marketing); GIP (2000b), GIP/CvZ-data, calculations CPB (total all markets, excl. marketing); GIP/CvZ-data, calculations CPB (all others).

4 Implications for policy

4.1 Introduction

In the previous chapter we identified a statistically significant welfare-negative effect of marketing on the price elasticity of demand: marketing makes doctors less sensitive to price changes. Thus, there may be a reason for policy intervention. It is the aim of this chapter to identify policy options that can exploit this potential.

A natural distinction to be made when looking for policy options is between policy aimed at specific marketing activities and general policy.

Concerning activity-specific policy options, it is important to note that the welfare-negative elasticity effect we found is the result of welfare-negative and welfare-positive partial effects. For instance, marketing conveys useful information to doctors. The quantity effect – for which a welfare assessment can not be given – is probably a combination of positive and negative partial effects as well. Therefore, activity-specific policy options should be aimed at removing the welfare-negative effects while keeping the welfare-positive ones. To do this, we need to know how the welfare-positive and welfare-negative effects come about. How does marketing work, what are the mechanisms of pharmaceutical marketing?

For the general policy options we return to Chapter 2, where we identified three determinants of the marketing intensity in the pharmaceutical industry. Two of these – asymmetric information and low price sensitivity – give rise to policy options.

The policy options presented in this chapter are tentative, in two respects:

- The options are probably to some extent effective, but it is unclear how large the associated social costs are. Further investigations into these social costs are necessary before these options can be implemented.
- For many policy options the design is not completely specified. Two examples:
  - We may not specify the level of implementation for an option. Possible levels are government/legislation, contracts between doctors and health insurers, and self-regulation.
  - Several of the policy options discussed involve a central agency performing certain tasks. We do not specify whether one organisation should perform all these tasks, nor whether this should be a new agency or whether (an) existing organisation(s) is/are suited for these tasks. For instance, in the case of accreditation of post-marketing research programs, there may be a role for the current Medical and Ethical Testing Committees (*Medisch-ethische toetsingscommissies,* METC's) that review (clinical) research in hospitals. For other policy options,

there may be a role for the Pharmaceuticals Evaluation Board (*College ter beoordeling van geneesmiddelen*, CBG) or the Health Insurance Board (*College voor Zorgverzekeringen*, CvZ).

Effectiveness and social costs are likely to differ between design specifications. Here also, additional investigations are necessary.

The structure of this chapter is as follows. Section 4.1 identifies five mechanisms through which the effects of pharmaceutical marketing come about. Next, Sections 4.2 and 4.3 specify policy options to mitigate two of the welfare-negative mechanisms: changing doctors' incentives and creating differentiation. Section 4.4 treats general policy options. Section 4.5 concludes.

4.2 Mechanisms of marketing

In this section we identify and define five mechanisms, two welfare-positive and three welfare-negative ones. Typically, marketing activities have several mechanisms, both welfare-positive and welfare-negative ones. For instance, detailers can provide useful information, but they may also stress the efficacy of a product and forget to mention the side-effects.[1] For each of the mechanisms we indicate for which marketing activity they are relevant. This provides insight into what constitutes the negative welfare effects for each marketing activity, so that we can formulate policy options to remove these welfare-negative effects in subsequent sections.

4.2.1 Providing relevant and objective information

The first mechanism of marketing is to convey relevant and objective information: about existence, about product characteristics, about price, etcetera. In our case of pharmaceuticals markets, detailers can inform physicians about newly marketed pharmaceuticals and about side-effects and counter-indications for certain pharmaceuticals. Marketing aimed at consumers can prompt consumers to visit their doctor by informing them about the early symptoms of certain serious afflictions - for which they offer a cure, of course.

This mechanism allows physicians to make better prescribing decisions, simply because they know more about the available pharmaceuticals. In the terminology of the previous chapter, relevant and objective information ensures that perceived quality is more in line with real quality. Therefore, the welfare effect of this mechanism is positive.

Almost every marketing activity performs this mechanism to some extent. Examples are:

- detailers and direct mail can provide product information;
- post-marketing research may generate relevant and objective information;

[1] In the literature these mechanisms of (pharmaceutical) marketing are often called "information" and "persuasion" (Leffler 1980, Hurwitz and Caves 1988).

- courses and conferences can help to educate doctors;
- advertising informs about product existence;
- sponsorships of pharmaceutical research helps to create new information.

4.2.2 Signalling product quality

A second welfare-positive mechanism of pharmaceutical marketing – signalling the quality of a product – is only relevant for the situation of new product introductions. Moreover, the product must be an experience good – i.e. quality can only be observed by consuming the product – and repeat purchases must be important. All these conditions are satisfied for the case of new pharmaceuticals.

The intuition behind advertising as a signal was developed by Nelson (1974) and formalised by Milgrom and Roberts (1986). The point is that a firm with a high-quality pharmaceutical has more to gain from getting doctors to try the product than a firm selling a low-quality product. This is because at a given price, high-quality will attract more repeat purchases. For this reason, there exists a level of marketing expenditure that a high-quality firm is willing to incur to get doctors to try its pharmaceutical, but that a low-quality firm is not. This implies that, in an equilibrium of Milgrom and Roberts' model, a specific (minimum) amount of marketing expenditure is a sure sign that the product is of high quality.

Thus, Milgrom and Roberts find that signalling the quality of the new good is always possible. In addition, they find that the amount of advertising needed to establish such a signalling outcome is highest, if the production costs of the high and low quality products are equal. This fits very well with the case of pharmaceuticals, since the production costs for a new pharmaceutical are fixed for the developing company before it learns the quality of the pharmaceutical.

Milgrom and Roberts consider the case of monopolistic entry: the producer is the first to enter a new market and therefore the only informed player who can give a signal. To investigate the effects of competitive signalling on the existence of signalling outcomes, De Laat and Hermans (2001) analysed a model in which the firm is an entrant into an existing market, with a single incumbent producer. Their analysis shows that realising the signalling effect of marketing may not be so straightforward. Thus, the relevance of the signalling mechanism of marketing in this case is uncertain and we need an empirical analysis to test whether it occurs. Unfortunately, the data acquired for the empirical analysis in Chapter 3 cannot be used to settle this issue.

4.2.3 Changing doctors' incentives

The previous mechanisms treat the doctor – who is the main pharmaceutical marketing target – as if he is the end user of the pharmaceuticals she prescribes. But of course this is not the case: the patient is the end user. The physician merely advises patients whether therapy is needed and which therapy to choose, since the patient typically does not have sufficient knowledge to make a diagnosis or choose a therapy.

From an economic viewpoint, a doctor acts as an intermediary of the patient on the market for (pharmaceutical) therapy.[2] As is the case with any advice, the advice of doctors is based upon the perceived interest of the patient *and* upon their own interest, where the weight a doctor attaches to his own interest may differ from doctor to doctor. The advisor-client interaction – here the doctor-patient interaction – leads to the best possible result (the best advice for the patient), if the interests of the doctor coincide as much as possible with those of the patient. If this is the case, the patient can expect to receive the best advice possible, given the physician's knowledge and capabilities. If their interests differ substantially, the advice will deviate from the optimal advice. The size of the deviation depends on the gap between patient's and doctor's interest and the weight this doctor attaches to his own interest.

To achieve coinciding interests, it is important that there are no (financial) ties between the doctor and the pharmaceutical industry. If such an interest exists, this will typically conflict with the patient's interest.[3] As a matter of fact, there are many ties between physicians and pharmaceutical companies. An obvious example are the seeding trials, where sometimes doctors are paid (in kind) to prescribe a (new) pharmaceutical to patients. Such a direct financial tie gives a physician an incentive to deviate from acting in the interest of her patients.

But there are also indirect financial ties. Indirect, because they require no immediate favour in return, such as a prescription. Instead they create in doctors a "sense of indebtedness" based on the economic principle of *reciprocity*. "The industry does not impose an obligation to write prescriptions but the doctors involved feel a moral obligation to return a favour." (VWS 2001a, p. 30). These indirect ties include the companies' hospitality and gifts toward doctors, medical opinion leaders acting as advisors to companies, and companies sponsoring doctors' (pharmaceutical) research. In general, an incentive to do something in return for a pharmaceutical company will interfere with the incentive to act in the patient's best interest.

[2] In fact, the advice of a doctor is much more commanding than the advice of intermediaries on other markets, such as insurance intermediaries or real estate brokers.

[3] An example of such ties in another sector are the commission payments by insurance firms to insurance intermediaries.

But can doctors not be expected to be relatively insensitive to these incentives, for instance compared to commercial advisors? This claim is supported by the observation in Section 2.1.2, that GP's follow NHG-standards in approximately 70% of their prescriptions. However, there is also evidence that doctors are certainly not immune to the influence exerted by financial incentives. For instance, Wazana (2000) mentions several studies that support this claim.[4] And in VWS (2001a) industry representatives claim that some doctors actively request specific favours in return for prescriptions. This leads to the conclusion that physicians do not always have only Hippocrates on their minds.

The theory of intermediation points out that the influence of the financial ties might be mitigated if reputation effects are strong. Reputation effects are strong if patients can recognize a bad advice after they followed it. The question then is, if the prescribed pharmaceutical does not have the desired effect, can a patient be fairly certain that the doctor who prescribed it did a bad job? The answer is no, he cannot, since the effects of pharmaceuticals depend on patient characteristics that are unobservable (even to the patient). The pharmaceutical may have been an excellent choice, and the disappointing result just a matter of bad luck. Thus, reputation effects are weak, implying that they cannot mitigate the influence of financial ties.

Thus, the mechanism of changing the incentives of doctors has a negative effect on allocative efficiency. The ties with the industry may make doctors deviate from the optimal therapy choice from the patient's viewpoint. Incidentally, doctors may not be aware that they deviate, excluding perhaps the case of direct payments for prescriptions in seeding trials. But even in this case, since most products are to some extent horizontally differentiated, many prescribing decisions can be rationalised. This makes it possible for doctors who have financial ties with the industry to believe that their behaviour is not affected by the industry's attentions. As we saw earlier, however, it is unlikely that pharmaceutical companies would spend large sums on ineffective activities.

4.2.4 Creating differentiation

The second welfare-negative mechanism of pharmaceutical marketing is to create differentiation in other ways than by conveying relevant and objective information. This brings us in the realm of psychological effects of advertising, such as the lifestyle and image-based types of advertising in soft drinks markets. A type of marketing in this category that is more relevant for pharmaceuticals, however, is the exaggeration of small advantages of pharmaceuticals over competing products. As a result, doctors may perceive very similar pharmaceuticals to be quite

[4] Other examples, not related to pharmaceuticals, are in Delnoij (1995), Greenberg (1998) and Croxson et al. (1998).

Information or differentiation?

Consider the case of Kotler's Disease (KD). This is an obscure affliction with rather nasty symptoms that will not be discussed here. The market for pharmaceuticals against KD is monopolised by Breand Inc. with a pharmaceutical called Perfectopil. This pharmaceutical has an average success rate of 60%: 80% for men and 40% for women.

Clearly, there is something to be gained where KD-pharmaceuticals for women are concerned. After many years of expensive R&D, another company, Stolkebein GmbH enters the market with Bettestil. And indeed, this new pharmaceutical has a much improved success rate for women: 82%. The success rate for men is worse, however: 42%. The table below summarises the efficacy percentages.

Efficacy percentages for Perfectopil and Bettestil

	Average	Men	Women
Perfectopil	60%	80%	40%
Bettestil	62%	42%	82%

Obviously, it would be best if physicians prescribed Perfectopil for male KD-patients and Bettestil for females. marketing by Stolkebein for Bettestil of the information type would stress the improved success rate for women (and be honest about the inferior success rate for men), thus enabling doctors to make the correct choice.

However, gaining only a 50% share of the KD-market may not be enough for Stolkebein to recoup their R&D-investments, which may prompt them to aim for something more. To achieve this, they could instruct their detailing force to assess first whether the doctor they visit is aware that success rates for KD-drugs differ strongly between men and women. If yes, the detailer should stress the success rate for women. But if the doctor is unaware of this difference, the detailer should stress the average success rates. This would be marketing of the differentiating kind. Because of the higher average success rate uninformed doctors might be prompted to switch to Bettestil for male KD-patients as well.

This example may seem a little silly at first: in the simple case described here, doctors will most probably not be fooled. And even if they are, Stolkebein will suffer a loss of reputation when doctors who were fooled at first become aware of the male-female difference. The probability that this will happen is large, since Breand has an incentive to put doctors right. Hence, Stolkebein will probably not venture into such clearly unethical differentiating marketing strategies in a clear-cut case like this.

But comparing drugs is almost never simple. Remember that drug quality has many dimensions (see Section 2.1). Two drugs will typically differ in many (if not all) of these dimensions. Therefore, it is difficult to tell the whole story in an advertisement or during a ten minute detailing visit. And if the whole story cannot be told, the distinction between information and differentiation may not be so straightforward.

different and make a choice based on perceived product characteristics where a price-based choice would have been better. This allows producers to charge and earn a mark-up.

In general, it is not possible to assess the welfare effect of this mechanism, since one cannot exclude the possibility that the taste change should be taken account of. For instance in the cola market, one could argue that an initially indifferent adolescent who develops a strict preference for Pepsi after being exposed to advertising, may actually derive utility from belonging to the group of Pepsi-consumers. As argued in Section 3.2.2, however, the principle of evidence-based medicine renders these taste-effects largely irrelevant for pharmaceuticals. Therefore, for the pharmaceutical sector we can conclude that creating differentiation has a negative welfare effect.

It is often difficult to ascertain when information is relevant and objective. Therefore it is difficult to separate the mechanism of providing information from the mechanism of creating differentiation. The box *Information or differentiation?* illustrates the distinction with an example.

Many marketing activities can perform the mechanism of creating differentiation:

- Detailers can stress the positive characteristics of a pharmaceutical, for instance by presenting only/mainly favourable scientific results/publications. At promotion events and in direct mail, firms also have these possibilities.
- Post-marketing research may give a firm information about the experience of individual doctors with their product. A detailer can refer to the personal experiences as a benchmark – instead of the more informative general post-marketing research results – when visiting doctors with good experiences (see the box *Post-marketing research as market research* for an imaginary example).
- Advertising may influence doctors in the same way as it influences consumers in other sectors.
- Organising courses and conferences gives firms the opportunity to influence the content of the event, for instance by selecting speakers (opinion leaders) with a known favourable opinion of the company's product (Van der Linde 2001).
- Sponsorship of pharmaceutical research may allow the sponsoring firm to influence the outcomes, for example by withholding publication of unfavourable research results (Stelfox et al. 1998, Davidoff et al. 2001).

4.2.5 Deterring entry

The idea that marketing investment can act as a barrier to entry goes back to the 1950s. Entry deterrence through marketing can occur in three ways (Sutton 1991; Church and Ware 2000):

- Marketing as an exogenous sunk cost, for example the marketing needed to create brand awareness. In this case, entry deterrence is an effect, not a mechanism. The mechanism is to provide information about the existence of a product (Section 4.1.1).
- Marketing as an endogenous sunk cost, for example to create a quality image. In this case as well, the effect is that entry is deterred, but it is not the mechanism. The mechanism is to create an image; in other words creating differentiation (Section 4.1.4).

Post-marketing research as market research

One way to create differentiation is to use the outcomes of post-marketing research in the same way as market research results in other sectors. To illustrate this mechanism of marketing we start with an imaginary example.

Consider the pharmaceutical market for a stomach affliction with the acronym BAD. Until recently, the dominant product on this market was a pharmaceutical called Notnimor. It has proven to be reasonably effective: the current estimate is that it is effective for 70% of BAD patients. But now there is a new product: Tummicure. It is not yet clear how effective this new pharmaceutical is, but Tummicure's producer, Makerov-Stommek Drugs (a Russian-Polish merger), has launched a massive marketing campaign, claiming that Tummicure is significantly more effective than Notnimor.

Part of the marketing campaign is a post-marketing research program among all GPs. For this program, GPs receive a palm-top computer and are asked to start ten BAD patients on Tummicure. Their experience with these ten patients should be entered into the computer and the floppy with these results sent to Makerov-Stommek Pharmaceuticals. (GPs who do not choose to take part in this program are kindly requested to return the palm-top computer, those who do take part can keep it.)

In addition to gathering the information on product performance, the post-marketing research program allows people at Makerov-Stommek to identify GPs who had relatively good experiences with Tummicure. Knowing that doctors who have had bad experiences with Tummicure will be very reluctant to switch from Notnimor to Tummicure, they can focus their (marketing) attention, such as detailing visits, on the doctors who seem more promising targets. This will increase the expected gain per marketing euro.

In the written material about marketing in the pharmaceutical industry that we have reviewed, this opportunistic use of information does not feature anywhere. Is it possible that pharmaceutical companies have not yet discovered this mechanism? This seems unlikely. Looking closely, there is not much difference between using post-marketing research for this purpose and the general notion of market research. Both are instruments to discover the personal "tastes" of potential customers. This information can then be used to divide the potential market into segments and formulate a targeting strategy for each of these segments. Thus, although this mechanism has not received much attention to date, it is unlikely that it is not relevant for the analysis here.

- Marketing as an instrument for strategic entry deterrence. This is a new mechanism. We will explore it somewhat further below.

  An incumbent producer can use marketing as a strategic weapon to deter entry. By investing in the goodwill of doctors the firm can commit to tough competition with the entrant, either through prices (if the potential entrant is a generic producer) or through marketing (if it is a firm working on a so-called *me-too* product), should the potential entrant choose to enter. Since successful entry deterrence restricts competition, it will have a negative welfare effect in general.

The relevance of this mechanism depends on the characteristics of marketing in this market. If marketing prior to entry creates "goodwill", which lowers the sales that an entrant can make for any given euro of its own marketing, marketing prior to entry can deter entry. However, the opposite result is also possible: if marketing "locks in" doctors by creating brand loyalty, it may make an incumbent firm less willing to lower its price in case of entry, because he will lose profits on all the locked-in doctors. Thus, the lock-in effect of marketing facilitates entry. The goodwill-effect seems more likely if the products are close substitutes, for example in the case of potential generic entry. The lock-in-effect is more plausible if the products differ considerably.

The previous paragraph suggests that entry deterrance is more likely to be relevant in the case of close substitutes, such as generic competitors. Scott Morton (1995) has examined the role of brand advertising just before patent expiration to see if it affects the entry decisions of generic pharmaceutical manufacturers in the U.S.A. The results of her empirical research bring her to the conclusion that brand advertising is not a barrier to entry by generic firms. This result casts doubts on the relevancy of entry deterrence as a mechanism of pharmaceutical marketing.

4.2.6 Conclusion and discussion

To summarise the previous four sections, Table 4.1 gives an overview of the possible mechanisms performed by pharmaceutical marketing, their welfare-effects and whether the mechanisms are (likely to be) relevant for the pharmaceutical sector.

One remarkable feature of pharmaceutical markets is, that creating differentiation in other ways than by providing relevant and objective information is unambiguously bad for welfare. The reason for this is, that the principle of evidence-based medicine largely determines what is the optimal therapy for a patient. Tastes, image or peer-group associations play a relatively insignificant role. The utility that a Pepsi-consumer derives from belonging to the group of Pepsi-consumers, for instance, has no parallel in pharmaceutical markets.

In the following sections we will discuss policy options aimed at removing welfare-negative mechanisms from specific marketing activities. Table 4.1 shows that relevant welfare-negative

Table 4.1 Mechanisms of pharmaceutical marketing and their welfare-effects

Mechanism	Welfare-effect	Relevant?
Providing information	positive	yes
Signalling product quality	positive	uncertain
Changing doctors' incentives	negative	yes
Creating differentiation	negative	yes
Deterring entry	negative	uncertain

mechanisms are changing doctors' incentives – for which we present policy options in Section 4.2 – and creating differentiation – Section 4.3. Before we turn to the policy options, we discuss an important implication from the table.

Table 4.1 illustrates once more that in general the welfare effect of marketing is a combination of welfare-positive and welfare-negative partial effects. This implies that it is difficult to point out specific cases of marketing in specific markets that decrease(d) welfare. However, we will show here that for the case of generic competition – between a branded pharmaceutical and its generic equivalents – a direct welfare conclusion is possible.

Generic competitors are perfect substitutes. In the case of perfect substitutes, there is no relevant and objective information about product characteristics that can create a competitive advantage. The only relevant information pertains to the existence of generics and to the prices of the alternatives (generics and branded products). This implies that, from a welfare point of view, competition should be based on prices. But it is exactly to prevent such price-based competition, that companies resort to differentiating marketing strategies. These strategies lead to higher prices, in two ways:

- supply side: marketing => higher costs => higher prices;
- demand side: marketing => brand loyalty => higher margins => higher prices.

Another mechanism of marketing in the case of generic competition can be to deter entry, since brand loyalty in a market with close substitutes is primarily a matter of goodwill (see 4.1.5). As one physician quoted in VWS (2001a) puts it: "When you have a choice between pharmaceuticals of similar quality, you prescribe the product of a company with which you have a pleasant relation." (p. 14).

Both mechanisms, creating differentiation and deterring entry, have a negative welfare effect. From a social viewpoint, the marketing outlays in the case of generic competition can therefore be qualified as wasted money with negative effects on allocative efficiency. Note that the results in the previous chapter were derived with data covering products that have no generic alternative. Thus, the conclusion in this paragraph strengthens the conclusion of the previous chapter, that pharmaceutical marketing leads to a lower sensitivity to prices.

4.3 Policy options on changing doctors' incentives

In this section we discuss policy options to remove the mechanism of changing doctors' incentives from specific marketing activities. In 1.1.3 we gave examples of activities for which this mechanism (may) be relevant. Below, we discuss these activities and policy options.

Post-marketing research

In some cases, post-marketing research (PMR) programs have no scientific goals (IGZ 2001) and/or involve substantial payments or gifts to participating doctors – for participating, per prescription or per new patient (VWS 2001a). Regarding these practices a policy option could be to prohibit any payment (in nature) for participation in PMR programs. This would remove the incentive for doctors to write unnecessary prescriptions. Instead, companies would have to convince doctors to participate by pointing out the scientific value of the PMR program. To make it easier for doctors to recognize scientifically valuable programs, an agency could be given the task of accreditation of PMR programs.[5] If doctor participation in scientifically valuable programs is (expected to be) too low, a second task of the agency could be to reward doctors for participation.

Hospitality and gifts

Several types of marketing appear to be aimed primarily at changing the incentives of doctors – either by direct financial ties or through the mechanism of reciprocity. Particularly hospitality and gifts – including covering doctors' travel and lodging expenses for conference attendance – perform only this mechanism, which has an unambiguously negative welfare effect. This seems to be a good reason to prohibit these types of marketing (as much as possible). One of the possibilities to do this is to design rules concerning accepting gifts analogous to existing rules for civil servants in the Netherlands: maximum values for hospitality and other gifts per event, per doctor and per period. This option is currently being implemented in pharmaceutical marketing regulation (VWS 2001b).

Furthermore, there may be a role for the government to regulate the financing of course and conference attendance. Possibilities include the current practice of fiscal deductibility of expenses for course and conference attendance and giving doctors budgets or vouchers for these purposes. A part of doctors' tariffs is already meant to cover costs for course and conference attendance.

Sponsorships of non-pharmaceutical research

Sponsorship of (scientific) non-pharmaceutical research can have a positive welfare effect outside the pharmaceutical industry. However it can also influence the doctors conducting the research by creating with them a sense of indebtedness towards the promoting company. A solution for this problem may be to create a research fund. Companies that wish to sponsor research can donate to this fund, with a possibility to specify a destination for the money

[5] As explained in the introduction to this chapter (Section 4.1) we do not specify whether this should be a new agency or whether existing agencies – such as, in this case, the Medical and Ethical Testing Committees that assess clinical research in hospitals – could perform the task.

(research field or topic). In this way the direct financial link between researchers and donor firm is severed, adding to the independence of the researching physicians. An effect of introducing a research fund may be that companies will donate much less to the fund than they did to direct sponsorships. This is not necessarily a disadvantage of the option, since this may indicate that currently research sponsorships are aimed primarily at influencing doctors.

4.4 Policy options to prevent differentiation

Courses

There is evidence that pharmaceutical companies organise and sponsor courses for GP's in order to influence the program of and the message conveyed during these courses. Van der Linde (2001) gives several examples of health problems appearing frequently in course programs after introduction of a new product against this health problem. He also provides examples of instructors diverging from current evidence-based standards of GP medical science to perform product marketing during such courses. Especially the influence over content leads to artificial differentiation in the minds of doctors.[6] This is welfare-negative.

What can be done about this influence over content? First of all, prohibiting excessive hospitality surrounding these courses and letting doctors pay the full cost gives independent organisers of courses an equal opportunity to attract GP's. After all, independent organisers cannot offer these levels of hospitality, since they cannot transfer the costs to patients through pharmaceutical prices.

In addition, the current accreditation and visitation system of the Dutch GP Association (LHV) can be extended to provide companies with stronger incentives to refrain from product marketing. Such extensions include (temporarily) blacklisting sponsors, organisers and instructors who (repeatedly) fail to follow regulations.

Finally, it is clear that accreditation of courses, control (visitation) and withdrawal of accreditation should be performed by an organisation that is independent of the pharmaceutical industry. However, the LHV may not be the right organisation to perform the functions of controlling courses and withdrawing accreditation. After all, withdrawal of accreditation for a course means that participating doctors loose the accreditation points and they may react to this by resigning their LHV membership. This threat weakens the incentives for extensive control and strict application of accreditation rules. An organisation that is more independent of the

[6] In fact, the hospitality surrounding these courses may be aimed at attracting doctors to attend these courses – giving the companies an opportunity to convey their message – more than creating a sense of indebtedness.

participating doctors may therefore be a better choice to perform the tasks of controlling courses and withdrawing accreditation.

Opinion leaders

Several companies have medical advisory boards consisting of (among others) practising physicians. In addition, the same and/or other physicians receive payments from companies for teaching at courses and speaking at conferences and promotion events. These are the so-called opinion leaders. It is likely and there is evidence that the information provided by opinion leaders at these events is favourable for the company paying them. Given this bias, it is important that the doctors receiving the information know about it. A policy option in this respect is therefore to establish transparency about (financial) relations between doctors and pharmaceutical firms, by requiring speakers and authors and the industry to reveal such relations through self-regulation.

Post-marketing research

We observe that the aggregated information about (side-)effects of pharmaceuticals generated by post-marketing research (PMR) programs is in itself valuable. However, the company conducting the PMR program can also use the information about individual participating doctors in an opportunistic – welfare-negative – way. A possible solution for this is that not the company, but an independent party such as a central agency gathers the information. This agency then has the task of aggregating results or making the results anonymous before passing them on to the company.[7] This does not exclude the possibility that a company instructs detailers to inquire after participating doctors' personal experiences and proceed from there. To discourage companies from this type of behaviour the central agency could also use the information gathering mechanism to inform doctors about the overall results.

Detailing

Pharmaceutical companies consider detailing to be the most important marketing activity (VWS 2001a). This is also reflected in the large amounts of money companies spend on detailers. The policy options in the previous section may already restrict welfare-negative behaviour by detailers (opportunistic use of PMR results and gifts). There appear to be no additional policy options – on top of existing regulation[8] – that reduce the welfare-negative effects of detailing without also damaging the provision of information mechanism. Thus, we do not propose additional policy options specifically aimed at detailing.

[7] An alternative is to issue regulations stipulating that collected data regarding PMR should be anonymous. This is less costly, but also more difficult to enforce and therefore probably less effective.

[8] Existing regulation concerning detailing pertains to the education of the detailer, a minimum standard for information provision during a detailing visit and rules concerning free samples and gifts.

Advertising / direct mail

Like detailing, advertisements and mailings are relatively common types of marketing. The amount of relevant and objective information they can provide is not so large, although larger for direct mail than for advertising. However, the same goes for their potential for creating differentiation. Thus, intensifying policy for these types is not necessary. It is sufficient to screen advertising and mailing campaigns ex-post for illegal claims, statements and omissions. Random ex-ante screening is a possibility as well. (Complete ex-ante screening is most probably not cost-efficient.)

Promotion events

Pharmaceutical companies organise events specifically aimed at promoting (one of) their products. The relevant and objective information provided relative to the differentiation created during these events is substantially lower than at other events such as courses and conferences. This observation would call for policies specifically aimed at promotion events. However, implementing the policy option of prohibiting hospitality and gifts (see 6.2.1) can be expected to substantially reduce the attractiveness of these promotion events for doctors. This is probably sufficient so that no other policies aimed at promotion events are necessary.

Sponsorship of pharmaceutical research

Research into the (side) effects of pharmaceuticals – both clinical and non-clinical – and its results are used to gain market access and to obtain public insurance coverage, but also to promote pharmaceuticals. There are indications that pharmaceutical companies sometimes have too much influence at different stages of the research process (set-up, implementation, results, publication). Examples would be instances where companies terminate research projects with unwanted (intermediary) results or withhold publication of the results.[9] This is damaging for social welfare. These undesired influences can be mitigated by requiring companies and research institutions to give prior notice of pharmaceutical research projects. Announcing proposed research with a central agency allows the agency to assess the set-up of the projects with respect to certain minimum requirements regarding quality and independence, including unconditional publication of the results. Results of unannounced research are not included in the central pharmaceutical information system (see 6.3.1) and are not taken into consideration in procedures to gain market access and public insurance coverage. Moreover, (absence of) the central agency's hallmark is then an indicator for doctors of the quality of the research when it is used for marketing purposes.

[9] Another example can be found in Stelfox et al. (1998), who examined the medical literature on the safety of calcium-channel antagonists (CCA's; against hypertension). They found that authors who arrived at conclusions supporting CCA's were significantly more likely to have financial relationships with manufacturers of CCA's.

4.5 General policy options

Many of the policy options in the previous section treat the symptoms but not the causes of the problem. We identified these causes of marketing intensity in Chapter 2: the process of innovation and imitation, asymmetric information and a low price elasticity of demand. In this section we discuss options that can help to mitigate two of the causes:[10] the low price elasticity in 4.4.1 and the asymmetric information in 4.4.2.

4.5.1 Low price elasticity of demand

The low price elasticity of demand is not only a result of marketing, it is primarily also one of the fundamental determinants of the marketing intensity in this sector. It is therefore sensible to strive for increased sensitivity to prices for (patients and) doctors.[11]

Larger role for health insurers

Policy makers currently plan to renew the Dutch health care system. One of the aims of these plans is to increase cost-consciousness among consumers and health care providers by giving health insurance firms more financial risk and a greater influence on health providers (VWS, 2001c). Insurance firms are expected to pass on some of their new incentives for cost efficiency to doctors, making them more cost sensitive. Insurance firms are in a good position to do this, since they have detailed information concerning individual doctors' prescribing behaviour.

It is not yet clear whether these plans to renew the health care system will indeed result in the desired countervailing power, since many different and complex health care related issues play a role. For instance, it is not certain that health insurance firms will indeed start to compete more intensely upon the change in their incentives or whether they will resort to other changes in their behaviour. This issue is outside the scope of this research.

We can say, however, that if the current policy proposals lead to an increased price sensitivity of doctors, it is reasonable to expect a reduction in the marketing outlays of pharmaceutical companies. This is due to the general economic notion that advertising levels can be expected to be lower in sectors where consumers are more price sensitive (Dorfman and Steiner 1954). For

[10] It is not clear which changes in the process of innovation and imitation would lead to less marketing. Moreover, changes in this process may not be desirable. Therefore, we do not propose any policy options aimed at influencing this process.

[11] There is evidence that increasing the price sensitivity of patients (for instance through out-of-pocket payments) leads to more price sensitivity of doctors as well. See e.g. Kasje et al. (2000) for evidence from the Netherlands and Lundin (2000) for a study with Swedish data. Companies expect this as well: both at the introduction of out-of-pocket payments in the Netherlands in 1991 and at the recalculation in 1999, companies reduced the prices for almost all products that had out-of-pocket payments.

instance, insurance firms may implement some of the activity-specific policy options of Sections 4.2-4.3 and other general options below by making them part of their contracts with (preferred) health care providers.

Incentives for doctors

In addition or as an alternative, other options can also increase price sensitivity. One of these is to create direct incentives for cost-conscious prescribing behaviour by doctors. A regional experiment between a public health insurance firm and general practitioners has already started in 2001: savings due to rational prescribing are used to finance higher tariffs for evening and weekend services. In 2002 there will be a national experiment concerning rational prescribing of three specific groups of pharmaceuticals.

Pharmaco-economics

Another alternative is to give cost-benefit analyses a larger role in deciding which pharmaceuticals are covered by public health insurance. Starting in 2002, such *pharmaco-economic* considerations will play a part in the decision process in the Netherlands (Spoorendonk 2001). As a next step, pharmaco-economics can also be used to establish maximum reimbursement levels in the current reference price system (*geneesmiddelenvergoedingensysteem*, GVS), so that differences between maximum reimbursement levels can reflect the quality difference between pharmaceuticals. This would require that these pharmaco-economic considerations are not only applied within GVS-clusters (close substitutes), but also across clusters (imperfect substitutes). The latter point is especially relevant for new pharmaceuticals that cannot be clustered with other pharmaceuticals.

Out-of-pocket payments

Another alternative is to introduce – or better, reintroduce – substantial out-of-pocket payments for patients proportional to the price, for instance own payments of 25%. To maintain desired levels of income solidarity and risk solidarity, special arrangements would probably be needed for low-income and for high-cost patients. Van den Brink en Meijer (2001) discuss conditions for an effective system of out-of-pocket payments for health care in general.

4.5.2 Asymmetric information

A crucial element in the analysis is that there is an information asymmetry between doctors and pharmaceutical companies. Narrowing this gap would reduce doctors' dependence on information from pharmaceutical companies. Still, it is not likely that the gap can be closed, implying that policies that tackle other aspects of the issue remain relevant.

Central information agency

Relevant and objective information about the medical effects of pharmaceuticals is scarce and/or not easily accessible, especially for GP's. In addition, doctors do not make optimal use of available independent information sources and turn to the pharmaceutical industry for a considerable part of their information needs, or base their decisions on their own experiences and medical opinion leaders.

To mend this bias in doctors' preferences regarding information gathering, an option could be to create an independent central agency occupied with gathering and providing relevant and objective information about the (side) effects of pharmaceuticals. This central information agency can give doctors information and advice – solicited as well as unsolicited – for instance about first choice products or to give additional information in response to a company's advertising campaign. Since doctors have expressed appreciation for the industry's modes of presenting their information (VWS 2001a), this agency should give much attention to the way in which the information they give is presented. Therefore, so-called *academic detailing* may be a promising way to implement this option.

Independent information sources

From 2.1.2 we know that besides the pharmaceutical industry doctors have several other, more independent, sources of influence over their therapeutic decision making: education, standards and guidelines, pharmacist-doctor consultation meetings (FTO), the centralised electronic prescription system (EVS). The discussion of marketing activities in 2.3 showed that pharmaceutical firms – in addition to their direct interactions with doctors – also make an effort to influence these independent sources. However, as a countervailing power to the possibly coloured information doctors receive during their direct interactions with industry representatives, doctors depend on independent information sources being truly independent. De Vries (1998) concludes that these peer review meetings can be used "as a critical counterbalance for marketing by the pharmaceutical industry" (p. 106). We have already discussed policy options concerning education (CME-courses) in Section 4.2. Additional policy options could inhibit the influence of pharmaceutical companies over formulary committees, FTO and EVS.

Pharmacists

In the current situation, pharmacists do not play a large role in the therapy choice for a patient. Still, the pharmacist is an expert in the field of pharmaceuticals and pharmaceutical therapy. Therefore, a larger role for the pharmacist – as an advisor or even a (co-)decision maker – would seem logical. However, at present the pharmacist has a direct financial interest in the therapy choice. This makes it unwise to make the pharmacist a prominent player. If at any point in the

future (a subset of) pharmacists become financially independent of the therapy choice, their role concerning the therapy choice can be upgraded. Given the current trend of wholesalers taking over pharmacies, we are moving away from this situation rather than moving towards it.

4.6 Concluding remarks

In this chapter we have presented several – tentative[12] – policy options that may help to mitigate welfare-negative effects of pharmaceutical marketing. To conclude this policy chapter we make three remarks, concerning (i) the interaction between activity-specific and general policy options, (ii) direct-to-consumer marketing, and (iii) possibilities for self-regulation.

Specific and general policy: interaction

If successful, one of the effects of the general policy options of Section 4.4 will be less marketing expenditure.[13] However, it is not certain that less marketing also means less welfare-negative marketing. After all, companies will have to decide which marketing activities will be terminated and which continued, where the contribution of the different activities to the company's profitability will play a leading role. It is possible that precisely the marketing activities with a strong negative effect on welfare are also the ones that contribute most to the company's profits. Activity-specific policy can help to ensure that less marketing also results in less welfare-negative marketing.

Direct-to-consumer marketing

Although direct-to-consumer (DTC) marketing is not part of the focus of this study, a number of observations can be made.

Several investigations of the Advertising Supervision unit of the Health Care Inspection are concerned with instances of DTC advertising. We observe that the maximum fines for breaking the rules are – given the profitability of pharmaceuticals – relatively low and are not a strong deterrent from illegal advertising practices. Investigation, prosecution and conviction now mainly constitute a form of regulation by embarrassment, because of the negative publicity. Increasing the maximum fines will give pharmaceutical companies a stronger incentive to abide by the rules.

[12] See our remarks concerning social costs and the design of policy options in the introduction to this chapter.

[13] Lower marketing expenditures can also be established directly by setting a maximum to marketing expenditures, for instance a maximum ratio of marketing to sales. However, such a policy would be much more invasive than the other general policy options. For that reason we have not mentioned it in Section 4.4. Only if the other options fail or cannot be implemented, a general ceiling on marketing expenditure can be contemplated.

Although DTC advertising is still largely prohibited in Europe, it is not unthinkable that in the long run more forms of DTC marketing will have to be permitted in these countries. For instance, the EC is currently planning an experiment to allow controlled DTC advertising aimed at patients with AIDS, asthma/COPD and diabetes. It would be prudent to consider this possibility in time and to develop modes of regulation for DTC advertising such that the welfare-positive aspects dominate and welfare-negative aspects are prevented as much as possible. To achieve this, the experiences with DTC advertising in the USA can be used as a reference point (NIHCM 2000, Wilkes et al. 2000, Crommentuyn 2001).

Finally, the Internet already offers consumers and patients an important possibility to obtain information directly from the supplier of pharmaceuticals. As this possibility is discovered by more and more people, it becomes important to investigate these web sites and their links for information, claims and statements that violate advertising regulation.

Self regulation

Currently, the pharmaceutical industry, doctors and other interested parties are in the process of developing a code of conduct regarding specific issues like hospitality, gifts, research sponsorships and transparency about opinion leaders. Some of the policy options in this chapter can be made part of such a code. This willingness for self regulation reflects the awareness of these parties that their behaviour and culture should be modified according to the social views on this point (and the economic issues pointed out in this study). The advantage of self-regulation is that it is a stronger basis for changes in behaviour than government-imposed policy measures. However, this does not mean that the interests of companies and doctors now coincide with the general interest. Therefore, it remains a government task to supervise whether (the effects of) the self regulation are sufficiently close to this general interest.

5 Summary and conclusions

5.1 Outline

The innovative pharmaceutical companies spend large amounts on marketing for prescription pharmaceuticals. This money is spent on many different activities: common activities such as detailing, advertising and direct mail; and also activities more specific for the pharmaceutical industry, such as conferences, travel, research sponsorships and others. In this study we have investigated the backgrounds of these outlays, their (welfare) effects on prescribing behaviour by doctors as well as policy options to improve the outcome, if necessary. Results on the effects of marketing were obtained by estimating a model of product demand with Dutch sales and promotion data.

In a nutshell, and in answer to the central questions stated in Chapter 1, our findings are the following:

Conclusions

1. *What are the effects of marketing for prescription pharmaceuticals by pharmaceutical companies in the Netherlands? How is welfare affected?*
   Pharmaceutical marketing in the Netherlands gives producers additional market power by decreasing doctors' sensitivity to prices in prescribing behaviour. This effect lowers social welfare. Pharmaceutical marketing also leads to a demand increase. We cannot assess the welfare properties of this second effect.

2. *If policy intervention is necessary, which policy options (may) improve the market outcome?*
   We suggest several specific policy options – aimed at reducing specific undesirable effects of specific marketing activities – as well as general policy options. Further investigations into the social costs of implementing these options is necessary.

5.2 Explaining marketing intensity

What can explain the marketing intensity in the pharmaceutical industry? We have identified three possible explanations:

- The process of innovation and imitation: High R&D outlays are associated with high marketing efforts in other industries as well. This process also provides an explanation for the strong concentration of marketing efforts in the first few years of the product life-cycle.
- The asymmetric information between doctors and producers: This implies a high need for information on the part of doctors.

- The insensitivity of patients (and therefore doctors) to prices: Industries with a low price elasticity tend to have a high marketing intensity.

5.3 Possible effects of marketing

Classes of effects

First of all, we have made a distinction between three separate classes of effects of marketing.

- Main effects, within pharmaceutical markets: these are the changes in prescribing behaviour due to marketing.
- Side effects, outside pharmaceutical markets: An example is that pharmaceutical advertisements in medical journals reduce subscription rates and therefore make the dissemination of the knowledge in these journals less expensive.
- Marketing costs.

In our study, we focus on the main effects, on prescribing behaviour. Regarding the other two classes: although the side-effects appear to be predominantly good for welfare, it seems implausible that these side-effects alone are sufficient to justify the costs. This implies that the welfare properties of the total effect of marketing are less favourable than the welfare analysis of the main effects indicates.

Our focus on the effects of marketing on prescribing behaviour implies that we do not explicitly analyse the impact of other determinants of prescribing behaviour, like government regulation, influences from insurance firms, and information provision by pharmacists.

Model

Which factors *apart from marketing* influence the demand for a specific product?

- patient numbers and their characteristics;
- price of the product and prices of competitors;
- perceived quality relative to competing products;
- price elasticity: the average weight doctors attach to prices relative to perceived quality; we expect that this price elasticity in the Netherlands is very low, on average.

Question 1: How large is the price elasticity of demand in the Netherlands?

Now we include marketing. How does marketing for a product affect the factors above and – as a result of this – how does it affect demand? There are two effects.

Quantity effect

Marketing has a direct effect on demand, either through changes in patient numbers and characteristics or through changes in (relative) perceived qualities. This is the quantity effect. We expect that this direct effect is positive: more marketing, higher demand. A more open question is, how much of the quantity effect is at the expense of demand for competitors' products and how much (the rest) is due to market growth?

Question 2: *Direction of the quantity effect: does more marketing for a product lead to higher or to lower demand for that product?*

Question 3: *Which part of the quantity effect of marketing is at the expense of demand for competing products and which part is due to market growth?*

Through the quantity effect, marketing affects the welfare of patients. The direction of the welfare change is ambiguous. More demand due to marketing may be good for welfare or bad, depending on whether the "new" patients benefit from taking the product or not, on average. In this general analysis, we cannot make this distinction. Therefore, we can draw no welfare conclusions from the sign or size of the quantity effect.

Elasticity effect

Marketing changes the price elasticity of doctors. Marketing can make them more sensitive to prices (given perceived qualities) or less. The elasticity effect corresponds to a turn in the demand curve of doctors, where the quantity effect can be represented by a shift of the demand curve.

The welfare properties of the elasticity effect are not ambiguous. Given perceived qualities, a high price elasticity is better for welfare than a low price elasticity. High price elasticities provide more incentives for price competition: consumers benefit through lower health insurance premiums. Therefore, if marketing increases the average price elasticity of doctors, welfare increases, and if marketing lowers this average elasticity, welfare falls.

Question 4: *Does pharmaceutical marketing result in a higher or in a lower price elasticity of demand?*

The answer to this empirical research question is the main result of this report.

5.4 Empirical analysis

For the empirical analysis we used data sets for the marketing (detailing, advertising and direct mail) and sales of prescription pharmaceuticals in the Netherlands, both on a product level, for every month in the 1994-1999 period. The data covered eleven therapeutic markets; together these markets covered 58% of all markets for prescription pharmaceuticals when measured by total sales and 55% when measured by marketing expenditure.

The empirical analysis leads us to the following conclusions. These are average results; they do not necessarily apply to individual marketing efforts, products, doctors or markets.

1. To start with the main result (Question 4): Pharmaceutical marketing reduces the price elasticity in the prescribing behaviour of doctors. This effect is statistically significant. After marketing this elasticity does not differ significantly from zero (Question 1). This low price elasticity may be partly due to price regulation, the high level of insurance and other limiting conditions for doctors in the Netherlands, but it is also caused by marketing. The insignificant post-marketing elasticity is a combination of a significant pre-marketing elasticity and a significant elasticity effect. Thus the elasticity effect makes doctors less sensitive to prices when deciding which pharmaceutical he should prescribe. This is unambiguously bad for welfare. The result proved to be robust.

2. The results show that marketing expenditures have a statistically significant, positive effect on sales (Question 2): a 1% marketing increase results in 0.30% more sales ($p = 0.00$). Of this sales rise, approximately 35% is compensated by sales decreases of competing products, the remaining 65% is due to market growth (Question 3).

5.5 Marketing mechanisms and policy implications

The results above imply that in principle there is potential for welfare improvement through regulating marketing activities. To design policy options, we have to know how marketing achieves its welfare-negative effects. What are the mechanisms behind marketing? Which – tentative[1] – specific policy options may help to remove specific welfare-negative mechanisms for specific marketing activities? Which tentative general policy options exist?

[1] The policy options are tentative in two respects: (1) They are probably effective, but it is unclear how large the associated social costs are. Further investigations into these costs are necessary before the options can be implemented. (2) For many policy options the design – for instance, the level of implementation – is not completely specified. Here also, additional investigations are necessary.

Marketing mechanisms

In Chapter 4 we identify five possible mechanisms of pharmaceutical marketing. Two of these are particularly relevant for policy:

- *Changing the incentives of doctors*: Direct financial / material relations between doctors and pharmaceutical companies distort doctors' incentives to act on behalf of patients. In practice, incentives are changed mainly according to the principle of reciprocity: a doctor receives something (a gift, sponsorship) from a firm and feels a moral obligation to return the favour.
- *Creating differentiation*: Marketing may result in misperceptions by doctors of the properties of pharmaceuticals (compared to the available scientific knowledge), for instance if information is withheld or if firms appeal to doctors' feelings to follow technological progress.

Changing doctors' incentives: policy options

Specific marketing activities that may be aimed at changing the incentives of doctors are:

- *Post-marketing research (PMR)*: Companies pay doctors who take part in PMR per prescription of a particular product, per patient or a fixed fee (in money or in kind). There is no current policy regarding PMR. Suggestions for policy options to prevent PMR from changing doctors' incentives are:
  - (i) no payments (in nature) to participating doctors for non-scientific PMR; independent agencies can decide on scientific or non-scientific nature;
  - (ii) a reasonable maximum fee for participation in scientific PMR.

- *Hospitality and gifts*: Companies pay (parts of) doctors' travel, lodging and registration costs for continuing medical education, conferences and promotion events. In addition, doctors receive gifts from detailers, through direct mail or at promotion events. Policy options concerning hospitality and gifts are:
  - (i) prohibit hospitality and gifts;
  - (ii) maximum levels of hospitality and gifts per event, per doctor and per period, for instance analogous to existing rules for civil servants; this option is currently being implemented in pharmaceutical marketing regulation.

Creating differentiation: policy options

Firms can create differentiation through many marketing activities. However, it is often not possible to separate relevant and objective information from misinformation and psychological appeals that create differentiation (which parts of a detailer's message constitute information and which are differentiation?). Therefore, in many cases effective policy options are not available. For the following situations effective policy options do exist:

- *Continuing medical education (CME)*: Half of the CME courses for general practitioners (GP's) is organised by or on behalf of pharmaceutical companies. In a number of cases this results in courses being used for product marketing, in violation of accreditation regulations by LHV (Dutch GP Association). In addition, pharmaceutical firms cross-subsidize these courses with their revenues in pharmaceuticals, thus making the CME market unattractive for independent commercial suppliers. Suggestions for policy options:
  (i) accreditation, control and withdrawal of accreditation preferably by an independent organisation;
  (ii) no accreditation for CME courses organised by or on behalf of pharmaceutical firms;
  (iii) (temporarily) blacklisting organisations that violate accreditation regulations;
  (iv) prohibit cross-subsidisation: all costs must be charged to participating doctors.

- *Opinion leaders*: Pharmaceutical firms pay doctors with a favourable opinion of their products to give presentations during seminars, symposia, promotion events and CME courses. Doctors in the audience may not be aware of this relation. And even if they are, they may still be more receptive to a colleague acting as a marketing officer than to a detailer. Policy options:
  (i) reasonable maximum fee for medical speakers payed by pharmaceutical firm;
  (ii) transparency: clearly state speakers' (and authors') relations with industry to audience.

General policy options: determinants of marketing

In Chapter 2 (and Section 5.1) we identified determining factors for the amount of marketing for prescription pharmaceuticals. In addition to the specific policy options mentioned above, general policy options directed at two of these determinants of marketing – the low sensitivity to prices and asymmetric information between producers and doctors – may help to mitigate welfare-negative effects. Here we only discuss policy concerning price sensitivity.

Regarding the low price elasticity, plans for policies already exist: a larger role for health insurance firms to create more countervailing power. If these planned policies are successful, in the sense that health insurers are able and willing to bring about more cost sensitive (prescribing) behaviour by doctors, they are also likely to reduce marketing expenditure. If these policies are unsuccessful, direct incentives for doctors (experiments are running), a larger role for "pharmaco-economic" cost-benefit analyses (first step implemented in 2002), and reintroducing out-of-pocket payments for patients proportional to product prices may be alternatives.

References

Ballance, R., J. Pogány and H. Forstner, 1992, *The world's pharmaceutical industries: An international perspective on innovation, competition and policy*. Edward Elger, Aldershot.

Berndt, E., L. Bui, D. Reiley and G. Urban, 1995, "Information, marketing and pricing in the U.S. anti-ulcer drug market." *American Economic Review*, 85: 100-105.

Berndt, E.R., R.S. Pindyck and P. Azoulay, 1999, "Network effects and diffusion in pharmaceutical markets: antiulcer drugs." NBER Working Paper 7024, National Bureau of Economic Research, Cambridge MA.

Bradley, C.P., 1991, "Decision making and prescribing patterns: A literature review." *Family Practice*, 8: 276-287.

Brink, R.J. van den, and A.G. Meijer, 2001, "Zorg voor eigen betalingen" [in Dutch: Care for own payments]. *ESB*, 86: 779-781.

Cabral, L.R.M., 2000, *Introduction to Industrial Organization*. MIT Press, Cambridge MA.

Calfee, J.E., 2000, *Prices, Markets, and the Pharmaceutical Revolution*. American Enterprise Institute. AEI Press, Washington DC.

Church, and Ware, 2000, *Industrial Organization: A Strategic Approach*. McGraw-Hill, Boston.

Comanor, W.S., and T.A. Wilson, 1979, "The effect of advertising on competition: A survey." *Journal of Economic Literature*, 17: 453-476.

Crommentuyn, R., 2001, "Vraag het uw arts" [in Dutch: Ask your physician]. *Medisch Contact*, 56(4): 122-124.

Croxson, B., C. Propper and A. Perkins, 1998, "Do doctors respond to financial incentives? UK family doctors and the GP fundholder scheme". CMPO Working Paper No. 98/001, Centre for Market and Public Organisation, Bristol.

Davidoff, F., C.D. DeAngelis, J.M. Drazen, J. Hoey, L. Højgaard, R. Horton, S. Kotzin, M.G. Nicholls, M. Nylenna, A.J.P.M. Overbeke, H.C. Sox, M.B. Van Der Weyden and M.S. Wilkes, 2001, "Sponsorship, authorship, and accountability." *New England Journal of Medicine*, 345: 825-827.

Delnoij, D.J.M., 1995, "Het honoreringssysteem van artsen en kostenbeheersing in de gezondheidszorg" [in Dutch: The system of compensation for doctors and cost control in health care]. Paper presented at symposium "Medische sociologie: Empirisch-theoretisch onderzoek", Utrecht.

Denig, P., and F.M. Haaijer-Ruskamp, 1992, "Therapeutic decision making of physicians." *Farmaceutisch Weekblad*, 14: 9-15.

Denig, P., and F.M. Haaijer-Ruskamp, 1995, "Do physicians take cost into account when making prescribing decisions?" *Pharmaco Economics*, 8: 282-290.

Denig, P., F.M. Haaijer-Ruskamp, H. Wesseling and A. Versluis, 1991, "Impact of clinical trials on the adoption of new drugs within a university hospital." *European Journal of Clinical Pharmacology*, 41: 325-328.

Dixit, A., and V. Norman, 1978, "Advertising and welfare." *Bell Journal of Economics*, 9: 1-17.

Dorfman, R., and P.O. Steiner, 1954, "Optimal advertising and optimal quality." *American Economic Review*, 44: 826-836.

EC, 1992, "Council Directive 92/28/EEC of 31 March 1992 on the advertising of medicinal products for human use." European Community, Brussels.
Internet (14 March 2001): http://europa.eu.int/eur-lex/en/lif/dat/1992/en_392L0028.html

GIP, 1997, "GIPeilingen 89-96: Kengetallen farmaceutische hulp (9)" [in Dutch: Core statistics on pharmaceutical care 89-96]. Geneesmiddelen Informatie Project / Ziekenfondsraad, Amstelveen.

GIP, 2000a, "GIPeilingen 1998: Kengetallen farmaceutische hulp (14)" [in Dutch: Core statistics on pharmaceutical care 1998]. Geneesmiddelen Informatie Project / College voor Zorgverzekeringen, Amstelveen.

GIP, 2000b, "GIPeilingen 1991-1999: Kengetallen farmaceutische hulp (15)" [in Dutch: Core statistics on pharmaceutical care 1991-1999]. Geneesmiddelen Informatie Project / College voor Zorgverzekeringen, Amstelveen.

Gönül, F.F., F. Carter, E. Petrova and K. Srinivasan, 2001, "Promotion of prescription drugs and its impact on physicians' choice behavior." *Journal of Marketing*, 65: 79-90.

Grabowski, H.G., and J.M. Vernon, 1992, "Brand loyalty, entry, and price competition in pharmaceuticals after the 1984 drug act." *Journal of Law and Economics*, 35: 331-350.

Greenberg, W., 1998, *The Health Care Marketplace*. Springer-Verlag, New York.

Haaijer-Ruskamp, F.M., and P. Denig, 2001, "Invloeden bij het kiezen van geneesmiddelen" [in Dutch: Influences on the choice of pharmaceuticals]. *Geneesmiddelenbulletin*, 35: 37-42.

Hurwitz, M.A., and R.E. Caves, 1988, "Persuasion or information? Marketing and the shares of brand name and generic pharmaceuticals." *Journal of Law and Economics*, 31: 299-

IGZ, 2001. "Marketingplannen voor UR-geneesmiddelen: De feitelijke stand van zaken" [in Dutch: Marketing plans for prescription pharmaceuticals: The actual situation]. Inspectie voor de Gezondheidszorg, sector Reclametoezicht.
Internet (31/07/2001): http://www.minvws.nl/documents/gmv/Rapport/2191036C.pdf

IMS HEALTH, Medische Promotie Index.

Jabaaij,L., L.J. Stokx and D.H. de Bakker, 2001, "Artrosemiddel in de lift: Huisartsen schrijven rofecoxib breder voor dan geïndiceerd is" [in Dutch: Arthrosis drug on the rise: General practitioners prescribe rofecoxib more broadly than indicated]. *Medisch Contact*, 56: 1493-1496.

Jacobzone, S., 2000, "Pharmaceutical policies in OECD countries: Reconciling social and industrial goals." Labour Market and Social Policy - Occasional Papers No. 40, Organisation for Economic Cooperation and Development, Paris.

Jones, M.I., S.M. Greenfield and C.P. Bradley, 2001, "Prescribing new drugs: Qualitative study of influences on consultants and general practitioners." *British Medical Journal*, 323: 378.

Kamps, G.B., 1999, *Formularia en het Voorschrijven door Huisartsen* [in Dutch: Formulariums and Prescribing by General Practitioners]. PhD-thesis, Groningen University. MediTekst, Amsterdam.

Kasje, W.N., J.W. Timmer, P.M. Boendermaker and F.M. Haaijer-Ruskamp, 2000, "Dutch GP's perceptions: The influence of cost on prescribing". Mimeo, University of Groningen.

King, C. III, 2000, "Marketing, product differentiation, and competition in the market for antiulcer drugs." Working Paper 01-014, Harvard Business School, Cambridge MA.

Laat, E. de, and C. Hermans, 2001, "Pharmaceutical marketing as a signal of product quality." CPB Report 2001/2: 56-63.
Internet: http://www.cpb.nl/nl/cpbreport/2001_2/s2_7.pdf

Leffler, K.B., 1980, "Persuasion or information? The economics of prescription drug advertising." *Journal of Law and Economics*, 24: 45-74.

Linde, H. van der, 2001, "Nascholing als marketinginstrument" [in Dutch: Continuing medical education as a marketing activity]. *Medisch Contact*, 56: 97-99.

Lundin, D., 2000, "Moral hazard in physician prescription behavior." *Journal of Health Economics*, 19: 639-662.

Medisch Contact, 2001, "Artsen verhoord over gratis slipcursus" [in Dutch: Doctors interrogated about free skid courses]. *Medisch Contact*, 56: 1308.

Milgrom, P., and J. Roberts, 1986, "Price and advertising signals of product quality." *Journal of Political Economy*, 94: 796-821.

Nefarma, 2001, "De ontwikkelingsgang van een geneesmiddel: van molecuul tot medicijn" [in Dutch: The development of a pharmaceutical: from molecule to medicine]. Farmafeiten, Nefarma.

Nelson, P., 1974, "Advertising as information." *Journal of Political Economy*, 81: 729-754.

NIHCM, 2000, "Prescription drugs and mass media advertising." NIHCM Research Brief, National Institute for Health Care Management, Washington DC.

Phelps, C., 1997, *Health Economics*. Addison-Wesley, Boston MA.

Pronk, E., 2001, "Generiek is niet identiek" [in Dutch: Generics are not identical]. *Medisch Contact*, 56: 1228-1230.

Public Citizen, 2001a, "Rx R&D myths: The case against the drug industry's R&D 'scare card'." Public Citizen Congress Watch, Washington DC.
Internet: http://www.citizen.org/congress/drugs/R&Dscarecard.html

Public Citizen, 2001b, "The other drug war: Big Pharma's 625 Washington lobbyists." Public Citizen Congress Watch, Washington DC.
Internet: http://www.citizen.org/congress/drugs/pharmadrugwar.html

Reekie, W.D., 1981, "Price and quality competition in drug markets: Evidence from the United States and the Netherlands". In R.B. Helms (ed.), *Drugs and health: Issues and policy objectives*. American Enterprise Institute, Washington DC,.

RIVM, 1999, "Stijgende geneesmiddelenkosten: theoretische en praktische inzichten" [in Dutch: Rising pharmaceutical costs: theoretical and practical insights]. RIVM rapport 278620 001, National Institute of Public Health and the Environment, Bilthoven.

Rizzo, J.A., 1999, "Advertising and competition in the ethical pharmaceutical industry: The case of antihypertensive drugs." *Journal of Law and Economics*, 42: 89-116.

Roos, J.C., 1999, "Klinisch onderzoekers en farmaceutische industrie: Liaisons dangereuses" [in Dutch: Clinical researchers and the pharmaceutical industry: Dangerous liaisons]. *Nederlands Tijdschrift voor Geneeskunde*, 143: 1668-1671.

Scherer, F.M., 2000, "The pharmaceutical industry." In: Culyer, A.J., and J.P. Newhouse (eds), *Handbook of Health Economics, Volume I*, Elsevier, Amsterdam.

Scherer, F.M., and D. Ross, 1990, *Industrial Market Structure and Economic Performance*. Houghton Mifflin Company, Boston.

Schmalensee, R., 1986, "Advertising and market structure." In: Stiglitz, J., and F. Mathewson (eds), *New Developments in the Analysis of Market Structure*, MIT Press, Cambridge MA.

Scott Morton, F.M., 1995, "Barriers to entry, brand advertising, and generic entry in the US pharmaceuticals industry." Research paper no. 1389, Stanford Graduate School of Business.

Scrip, 2001, "GlaxoSmithKline takes its place at the top of the league." *Scrip Magazine*, Feb. 2001, 46-47.

Shapiro, C., 1980, "Advertising and welfare: Comment." *Bell Journal of Economics*, 11: 749-752.

Spies, T.H., and H.G.A. Mokkink, 1999, "Toetsen aan standaarden: Het medisch handelen van huisartsen in de praktijk getoetst" [in Dutch: Testing against standards: Medical actions by general practitioners tested in practice]. Final report. WOK/NHG, Nijmegen/Utrecht.

Spoorendonk, P.A.R., 2001, "Farmaco-economische toetsing in Nederland: Panacee of nieuwe horde?" [in Dutch: Pharmaco-economic assessments in the Netherlands: Panacea or new hurdle?]. *Pharmaceutisch Weekblad*,136: 674-679.

Stelfox, H.T., G. Chua, K. O'Rourke and A.S. Detsky, 1998, "Conflict of interest in the debate over calcium-channel antagonists." *New England Journal of Medicine*, 338: 101-106.

Sutton, J., 1991, *Sunk Costs and Market Structure: Price Competition, Advertising, and the Evolution of Concentration*. MIT Press, Cambridge MA.

Trouw, 2000/2001, "De verdieping: Farmaceutische industrie" [in Dutch: Specials: Pharmaceutical industry]. *Trouw*, 25 articles, 31 March 2000 – 20 July 2001.
Internet: http://www.trouw.nl/980322272063.html

Vries, C.S. de, 1998, "Collaboration in Health Care: The Tango to Drug Safetyz". PhD-thesis, Groningen University.

VWS, 2001a, "Interacties zonder ongewenste bijwerkingen" [in Dutch: Interactions without undesirable side-effects]. Ministry of Health, Welfare and Sports, The Hague.
Internet (31/07/2001): http://www.minvws.nl/documents/gmv/Rapport/2191036B.pdf

VWS, 2001b, "Reclame voor geneesmiddelen" [in Dutch: Advertising pharmaceuticals]. Letter GMV-2191036 of 15 June 2001 from Minister to Parliament, Ministry of Health, Welfare and Sports, The Hague.
Internet (31/07/2001): http://www.minvws.nl/documents/gmv/Kamerstuk/2191036.pdf

VWS, 2001c, "Vraag aan bod: Hoofdlijnen van vernieuwing van het zorgstelsel" [in Dutch: A chance for demand: Outlines for renewing the health care system]. Government paper. Ministry of Health, Welfare and Sports, The Hague.

Wazana, A., 2000, "Physicians and the pharmaceutical industry: Is a gift ever just a gift?" *Journal of the American Medical Association*, 283: 373-380.

Wilkes, M.S., R.A. Bell and R.L. Kravitz, 2000, "Direct-to-consumer prescription drug advertising: Trends, impact, and implications." *Health Affairs*, 19(2): 110-128.

Windmeijer, F., A.R. Brouwer, R.C.M.H. Douven, E.A.A. de Laat and E.S. Mot, forthcoming, "Pharmaceutical promotion and GP's prescription behaviour." CPB Discussion Paper, CPB Netherlands Bureau for Economic Policy Analysis, The Hague.

Zembla, 2001, "Gouden pillen" [in Dutch: Gold pills]. Zembla television special broadcast on 21 June 2001, VARA.

Abbreviations

ATC	Anatomical-Therapeutical-Chemical (a classification system for pharmaceuticals)
CME	continuing medical education
CvZ	College voor Zorgverzekeringen
DDD	defined daily dose
DTC	direct-to-consumer (advertising)
DVLS	dummy variable least squares (an empirical estimation method)
EBM	evidence-based medicine
EVS	elektronisch voorschrijfsysteem (electronic prescription system)
FTO	farmaco-therapeutisch overleg (pharmacist-GP consultation meeting)
GIP	Geneesmiddelen Informatie Project (data supplier, part of CvZ)
GP	general practitioner
GVS	geneesmiddelenvergoedingensysteem (pharmaceuticals reimbursement system)
IGZ	Inspectie voor de Gezondheidszorg (Health Care Inspection)
IMS	IMS Health Nederland (data supplier)
IV	instrumental variables (an empirical estimation method)
LHV	Landelijke Huisartsen Vereniging (Dutch GP Association)
METC	Medisch-ethische toetsingscommissie (Medical and ethical testing committee)
NHG	Nederlands Huisartsen Genootschap (Dutch GP Society)
OECD	Organisation for Economic Cooperation and Development
OTC	over-the-counter (pharmaceuticals)
PMR	post-marketing research
RIVM	Rijksinstituut voor Volksgezondheid en Milieu
SSRI	selective serotonine re-uptake inhibitor
TCA	tri-cyclical antidepressant
VWS	Volksgezondheid, Welzijn en Sport (Ministry of Health, Welfare and Sports)
WGP	Wet geneesmiddelenprijzen (Pharmaceutical Prices Act)