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RELATIONSHIP MARKETING IN THE PHARMACEUTICAL INDUSTRY

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The last three years have been very important for me for a variety of reasons: I have started my path at Católica Lisbon School of Business and Economics in 2018, in the Executive Masters in Management with a specialization in Strategic Marketing. After that I've transitioned to the Master in Applied Management, in which I've been enrolled

for the past two years. I married in late 2019 and my wife and I are now expecting a child, that can arrive at any minute as I'm finishing this thesis.

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Abstract

Background: Patients trust the treatment choices that can make a difference to their health to physicians, giving room for an agency relationship to be established between both stakeholders. Additionally, pharmaceutical companies, which belong to one the most profitable sectors, invest a lot of money to get recognition of their brands by physicians, which may include, many times, a transfer of value from the manufacturers to medical doctors. These ways of working can be viewed with caution by the general

public, as it can give room for a potential conflict of interest towards the ultimate endpoint, that is improving patients' health. Despite this potential misperception, pharmaceutical companies keep their ways of working.

The objective of this work is to study the relationship between pharmaceutical industry and physicians on prescription behaviour, and the exact role it may play.

Methods: To study this problem statement, in an attempt to answer it, a combination of methods will be used. Literary review will be conducted to assess updated information on the problem being studied. This also includes checking information in Plataforma da Transparência of INFARMED, I.P. Nonetheless, the subject of this dissertation work will be mainly assessed through primary data collected via a market research study targeted to HIV physicians.

Results: Forty two HIV specialists participated in this market research. Efficacy was by far the most important attribute they value when selecting a treatment regimen. The combined three attributes that matter the most when choosing a treatment were efficacy, safety and convenience. The effectiveness on how companies communicated these attributes was found to have a positive impact on their prescription choices. Additionally, it was found that promotional sessions positively impact the prescription behaviour of physicians.

Conclusion: No major effects on prescription behaviour were found for most of the marketing activities performed by pharmaceutical companies, with exception for promotional sessions, that were found to have a positive impact on the prescription behaviour for naïve patients.

Keywords

Communication, conferences, continuous medical education, customer, engagement, marketing activities, marketing mix, meals, pharmaceutical, physician, prescription behaviour, promotional sessions, samples, speaker.

Introduction

Medical doctors, for their knowledge and ability to prescribe medicines, play a key role in choosing treatment options to cure or prevent diseases. In fact, medical doctors have a knowledge about disease and its treatment, that the common patient does not have, creating room for an agency relationship between physician and patient. The patient is the final user of a medicine, despite not having enough knowledge to make a scientific decision about it. Ultimately, patient trusts the physician, relying in his knowledge and experience, giving physician a privileged power over the patient's health. Because of this agency relationship between patient and physician, physicians' actions, decisions and conduct are heavily scrutinized, despite physicians making an oath when they graduate. The relationship between physicians and pharmaceutical companies has been under the eye of the public, often carrying a negative sentiment, as pharmaceutical companies are seen as a source of corruption for physicians, as the industry sells the products that physicians decide to use on a patient. On one hand, there is the pharmaceutical industry with their medicines and privileged information about it, and on the other hand we have the physicians that have a privileged decision power over a patient's health. At the end of the chain, there is the patient, that receives the treatment, but has very limited power over the choice. Furthermore, the pharmaceutical industry profits from treating illness and is one of the most profitable industries worldwide (Brax et al, 2017), which contributes to the suspicion of the general public.

Pharma companies invest a lot of money in marketing and sales to achieve strong brand name recognition among physicians (Brax et al, 2017). The marketing effort of pharmaceutical manufacturers often includes: i) product detailing to physicians; ii) supporting physicians to attend conferences; iii) managing and organizing promotional meetings for physicians, that can include providing hospitality, as meals and accommodation; and iv) paying physicians to speak at industry sponsored events (Fickweiler, Fickweiler and Urbach, 2017; Morse, Hannah and Mehra, 2019).

Some of the efforts described above include a transfer of value from a pharmaceutical company to a physician, the individual that is responsible to choose a patient's treatment option. Pharmaceutical manufacturers justify these efforts with the physicians' need for constant knowledge update and access to the most up-to-date information about diseases and medicines. Additionally, physicians, in general, state that these practices do not influence their actions regarding their prescription habits.

This relationship, of course, is seen as a potential conflict of interest by any player outside of this relationship, worrying that this relationship may have an influence on a physician's prescription behaviour.

Although the risk of misperception from the general public about this potentially conflicted relationship, pharmaceutical companies, in general, keep these practices and incentives until the present day, and physicians continue to engage in hospitality activities given by the companies.

The health sector is one of the most regulated sectors. In fact, pharmaceutical companies must follow very stringent laws and regulations to successfully operate and avoid penalties and bad reputation. For any new drug to be approved it must successfully meet a lot of requirements, going from laboratory tests, tests in animal models and then tests in humans. Extensive data dossiers from this process is then submitted to health authorities which, through designated committees and expert panels, may approve or reject it (U.S. Food and Drug Administration, 2018).

Additionally, there are very stringent transparency regulations that rule the interactions between pharmaceutical companies and physicians. The regulations include but are not limited to reporting to local and regional authorities of any transfer of value between a pharma company and a physician, that needs to be validated by both stakeholders. A transfer of value may range from an industry sponsored coffee-break during a conference, to a payment for speaking purposes. In the Portuguese case these reports are publicly available and can be checked in Plataforma da Transparência of INFARMED, I.P. (INFARMED).

Stringent rules apply also to the manufacturing and distribution of medicines, with regular inspections and audits by authorities and third-party auditing companies. However, the audit universe of a pharmaceutical company is not limited to the manufacturing and distribution activities. In fact, pharmaceutical companies are regularly audited, primarily by third-party auditing companies, but can also be audited by health authorities. Consequently, the companies are growing their compliance departments to ensure that the company follows all the applicable laws and regulations. As mentioned above, pharmaceutical companies keep the marketing practices described, although with increasing transparency and regulation, and despite the negative perception the general public may have about it.

Problem statement

The objective of this dissertation is to study the effect of the relationship between pharmaceutical industry and physicians on prescription behaviour, and the exact role it may play. Additionally, this work will aim to understand what factors or variables may impact the prescription behaviour of physicians.

Key Research Questions

To solve the problem statement, five key research questions should be answered:

1. What product features are important in the prescription decision-making process?
2. Does the relationship between pharmaceutical companies and physicians influence the prescription behaviour, and to what extent?
3. Does this relationship have an independent impact on the prescription behaviour?
4. What is the exact role on the prescription behaviour of the relationship between these companies and physicians?
5. What forms of company-customer engagement add value?

Methodology

A literature review will be conducted to explore the available published data on the subject of this dissertation.

To address the problem statement and answer the key research questions primary data will be used, through a survey directed to infectious diseases and internal medicine specialists that treat patients with HIV infection. Statistical analysis will be used to treat the results of the survey and the correlations previously mentioned.

The survey includes questions on past prescription behaviour, future prescription intention, company-customer interactions and the importance of those interactions for the physician. The author of this dissertation works at ViiV Healthcare, a company

specialized in marketing HIV medicines. For convenience and access purposes, the survey is focused around HIV treatment and is directed to infectious diseases and internal medicine specialists that treat patients with HIV infection.

The survey was created using Qualtrics and the aggregated responses were analyzed using SPSS.

Marketing in the pharmaceutical industry: state of the art and current trends

Pharmaceutical industry is one of the most profitable sectors in the economy. To achieve that pharmaceutical drug manufacturers invest a lot in sales and marketing activities, in an attempt to provide healthcare professionals with scientific and education information (Brax et al, 2017). The industry spent \$89.5 billion on interactions between physicians and sales representatives, in 2012, that accounted for 60% of the total spent of the industry in marketing and sales, globally (Fickweiler, Fickweiler and Urbach, 2017). Despite being one of the industry sectors that reinvest a significant proportion of its profit into research and development (R&D), the expenditure in sales and marketing is much higher than in R&D (Brax et al, 2017). In fact, the big pharmaceutical firms invest heavily in marketing to develop strong recognition of the brand name and a brand name among physicians (Murshid and Mohaidin, 2017). Across many industry sectors, companies implement marketing mix strategies to leverage the customer perceived value about a product and customer satisfaction, hence enhancing the competitiveness of companies. In fact, the 4P model created by Kotler, that comprises the product, promotional, place and price variables of marketing, in order to fulfil the needs of the target customers, has become a widespread standard marketing model in all industries. The pharmaceutical industry is no exception, and, in fact, pharmaceutical companies implement marketing mix strategies to persuade physicians of the efficacy of the drug product in order to retain customer satisfaction, produce value and influence their prescription behaviour (Murshid et al, 2016).

Prescription behaviour

The effect of marketing mix of drugs on physicians' perceptions and satisfaction

As mentioned before, pharmaceutical companies implement marketing mix strategies to enhance physicians' perceived value and satisfaction about the product. The most important element of drug manufacturers' marketing mix strategies is the product, that is the drug, along with its attributes such as efficacy, quality and safety (Murshid et al, 2016). Dickov and Kuzman (2011) further define the quality of a pharmaceutical product as being a mix of the drug's efficacy and safety. Physicians perceived value of a drug may be represented by the difference between the perceived quality and the perceived sacrifices related to a therapeutic option. Additionally, the perceived value of a drug mediates customer satisfaction regarding the same drug, with the latter being an overall evaluation of all aspects of the drug (Murshid et al, 2016).

The research conducted by Murshid et al (2016) aimed to study the influence of marketing mix strategies on physicians' satisfaction and physicians' perceived value. According to the authors, all four elements of the marketing mix strategy contributed to a higher physician satisfaction, with price being the most important element. The authors further state that physicians prioritize the price of drug when choosing a treatment to ensure the patient can afford it. Of the marketing mix elements, promotion was the one that was less important for physician satisfaction, although having a positive impact on physician satisfaction. When investigating the influence of marketing mix elements on the physicians perceived value, the authors found out that promotion was the element that retained the strongest positive correlation with it. The investigators further add that, if promotional strategies are increased and improved, physicians perceived value will likely increase, as promotion increases physicians' product knowledge and their perception of the benefits and attributes of a drug. In a research conducted by Gönül et al (2001), the authors concluded that the main effects of personal selling increased the prescription of a given drug. Price was the second most impactful element on the perceived value of physicians, because physicians perceive high-quality drugs as being expensive. The product element did not have an impact on the perceived value physicians have of a drug. The authors state that this finding indicates that product has an indirect effect on physician perceived value of the drug (Murshid et al, 2016).

The prescription decision-making process

The physician decision making process towards prescription appears to be a hybrid one, with a mixture of different decision rules. The predominant drug choice criteria are the drug effectiveness (therapeutic effect) and the risk carried by the drug, or the side effects (Cook et al, 2020; Campo et al, 2006; Toroski et al, 2019). This non-compensatory process helps reducing the choice set. The research that has been done on this field points to the fact that physicians only consider a limited set of therapeutic options and choose between an even narrower set of drugs (Denig & Haaijer-Ruskamp, 1992; Campo et al, 2006). Physicians often prescribe the same set of drugs for chronic diseases, showing a high degree of inertia, hence keeping their prescription habits. This scenario changes when the physician is confronted with a non-responder patient or an entirely new patient (Campo et al, 2006).

Although the decision process of choosing a drug is an individual decision, it can also be influenced by peers and other group norms prevailing among their networks (Hollands, 2020).

This behaviour constitutes a challenge for pharmaceutical industries, their marketing strategies and their sales reps (Campo et al, 2006).

The promotional element of pharmaceutical companies' marketing mix strategies relies mainly on the sales rep, that communicate sales promotions, act as public relations stakeholders, and are responsible for directly marketing the drugs to physicians (Murshid et al, 2016). A typical sales representative performs between 5-10 calls a day, corresponding to 5-10 doctors being impacted (Datta and Dave, 2017). Pharmaceutical companies rely heavily on detailing physicians about their drug, with the sales reps assuming an information function regarding the products they are responsible to sell. Physicians appreciate sales reps' visits and admit that they are an instant and important source of information. As reiterated before, physicians, due to time constraints and to the complexity of the therapeutic decisions they need to make, usually look for reliable and efficient information (Campo et al, 2006). Physicians seem to increase drug prescription rates after a sales call with a sales rep, with detailing having a positive impact on the prescription of a drug (Campo et al, 2006; Gönül et al, 2001). This behaviour gets more importance if we are talking about new or less known products,

because physicians get an increase in their product knowledge. In addition to contributing for a specific drug to be included in the considered set of drugs in a physician's mind, the sales reps calls also persuade physicians to request for drugs to be included in the hospital formulary, hence, becoming available for prescription (Campo et al, 2006). Datta and Dave (2017) concluded that detailing has a positive and significant effect on the number of new prescriptions for a drug.

It was mentioned above that the most important prescription criteria for physicians are the efficacy and effectiveness of a drug, and the risks associated with the drug (undesirable effects). Campo et al (2006) stated that this non-compensatory process of choosing drugs is the dominant process in a given therapeutic choice. Moreover, the author states that price is not an attribute of the utmost importance for physicians when selecting a treatment for a patient. The price variable, as an element of the pharmaceutical companies marketing mix strategies (as mentioned by Murshid et al, 2016) has to be investigated within the relevant context, as this variable may be impacted by health policies and the reimbursement context of the drug, hence impacting its relative importance for physicians. The investigators also pointed that, after the non-compensatory decision process, other elements, such as incentives to physicians may also affect their prescription behaviour. In fact, there is the idea among the public that pharmaceutical companies provide physicians with incentives and that those incentives impact their prescribing behaviour. In fact, there is a generalized practice of drug manufacturers to provide transfers of value to physicians, worldwide. Many authors have focused their research on this topic, both for the pharmaceutical industry as a whole and for specific therapeutic areas (Hollands, 2020; Morse, Fujiwara and Mehra, 2018; Morse, Hannah and Mehra, 2019; Bandari et al, 2017). These incentives include, but are not limited to, gifts, industry sponsored meals, conference attendance, continuous medical education, speaker services for industry sponsored events, samples, among others.

Sponsor physicians to attend conferences

It is a common practice for physicians to be sponsored to attend conferences and other medical education activities. According to Campo et al (2006), this is one the most

valued incentives by physicians, as they have the opportunity to look at the most up-to-date scientific information as well as connect with their peers. Research performed by Fickweiler, Fickweiler and Urbach (2017) evidenced that this type of financial interaction has a positive impact on the prescribing behaviour of physicians. Although not looking specifically to the effect of sponsoring physicians to attend conferences, Morse, Hannah and Mehra (2019) found that travel and lodging grants alone were not associated with increased branded drug prescription, in the case of otolaryngologists.

Continuous medical education

Sponsoring physicians to attend continuous medical education events or creating those events is an important marketing tool that is widely used by the pharmaceutical industry, in a way that these activities constitute an important touchpoint between physicians and branded drugs.

According to Brax et al (2017) and Fickweiler, Fickweiler and Urbach (2017) there is an important correlation between the facilitation to physicians to attend these events and their prescribing behaviour. According to these papers, physicians who attended continuous medical education events have increased rates of prescription of the drugs related to events they attended.

Industry-paid meals

Lunches and/or dinners sponsored by drug manufacturers are very common. In the research performed by Fickweiler, Fickweiler and Urbach (2017), the authors mentioned that most physicians are very often invited to attend free lunch and/or dinner sessions with staff of the drug manufacturers. In the research, the authors concluded that there is not a significant association between attending pharmaceutical industry provided free meal sessions and an increase of requests to include a given drug in the hospital formulary. However, in the research conducted by Brax et al (2017), a correlation is found between pharmaceutical companies provided meal sessions and increased prescription of anti-hypertensive drugs. The authors found that physicians who received drug samples were less likely to prescribe thiazide diuretics, that is the preferred

treatment for hypertension. The research conducted by Morse, Hannah and Mehra (2019) further supports this correlation between physicians being offered free meals and increase branded drug prescription, in the case of otolaryngologists.

Providing drug samples

Drug samples may play an important role in the performance of a given drug in a specific therapeutic area. Samples are usually given to physicians by the sales reps and contribute for the physician to get familiarized with the drug. They may also play an important role from a relationship marketing point of view, because it may contribute to maintain and build physician commitment towards the drug manufacturer and the sales rep (Campo et al, 2006). Some authors indeed state that receiving drug samples, given by the sales reps, puts physicians under a commitment to prescribe the promoted brand drug (Murshid Mohaidin, 2017). Fickweiler, Fickweiler and Urbach (2017) concluded that physicians that accepted drug samples had a positive attitude towards the sales representatives. Additionally, the authors concluded that higher acceptance of drug samples lead to an increase in the prescription of the corresponding drugs. Brax et al (2017), reiterated this conclusion with the analysis of the relationship between receiving drug samples and physicians' prescribing behaviour regarding anti-hypertensives. The authors found that medical doctors who did not have samples in their offices were more likely to follow treatment guidelines when choosing a therapeutic option.

Contracting physicians to speak at industry sponsored events

Engaging medical doctors and other key external experts is a generalized practice within the world of pharmaceutical industry. Looking at the research that has been done there is evidence that, physicians who received speaker fees to provide a lecture about a given drug on behalf of drug manufacturers at their events, such as symposiums, were more likely to request for the drug to be included in the hospital formulary (Fickweiler, Fickweiler and Urbach, 2017). Engelberg, Parsons and Tefft (2013) further looked at the effect of speaker fee payments and changes in physicians' prescription behaviour and

found that physicians who were provided speaker fees showed a significant increase in the prescription of the drugs they spoke about, particularly when comparing the prescription rates of branded drugs versus generic drugs. Despite this evidence, some researchers have found that there is no correlation between physicians receiving speaker fees from a pharmaceutical company and them changing their prescription patterns (Morse, Hanna and Mehra, 2019).

Given these conflicting findings, more research is needed to establish the existence of a relationship between contracting physicians to speak on behalf of drug manufacturers and increased drug prescription of their drugs, and what factors may influence that relationship.

ViiV Healthcare: a disruption from the pharmaceutical industry marketing paradigm?

ViiV Healthcare is a global specialist HIV company that is committed to delivering innovative new options for people living with HIV/AIDS, at care and treatment levels. The company was created in 2009 as a result of a joint venture between GSK and Pfizer. It was launched with ten medicines and with a strong commitment in developing new medicines that would help address resistance and dosing issues, being the only company solely focused on HIV. In fact, at the time of launch, the company had a pipeline of seven drugs, with the integrase inhibitor development programme being the most important one, which included the drug dolutegravir, originally developed by Shionogi, that led Shionogi to acquire 10 percent of ViiV Healthcare in 2012. Dolutegravir was the first second-generation integrase inhibitor, exhibiting several advantages over the several antiretrovirals at that time (Dow & Bartlett, 2014).

The Blockbuster Dolutegravir

Dolutegravir became the focus of the company, in terms of promotion, since its approval in 2013, creating a portfolio of products based in the molecule: Tivicay (dolutegravir) and Triumeq (dolutegravir/abacavir/lamivudine), and later, the so-called two-drug regimens, Juluca (dolutegravir/rilpivirine) and Dovato (dolutegravir/lamivudine). Triumeq is a complete HIV single-tablet regimen that showed superior efficacy versus

the standard of care at the time, high barrier to resistance, a favorable tolerability profile and no food or time restrictions (Castagna et al, 2014; Molina et al, 2015). Before dolutegravir entered the therapeutic armamentarium, HIV physicians would have to choose between regimens with high barrier to resistance, but with a not so positive tolerability profile, versus regimens with an excellent tolerability profile, but with a low barrier to resistance. Very often, physicians would have to make a trade-off when choosing an HIV regimen, because they could not have all these features in only one regimen. So, the patient profile and behaviour were a key thing to watch when selecting a treatment. As dolutegravir combined all these features in only one molecule, physicians didn't need to make that trade-off. Because of its profile, dolutegravir was rapidly adopted by all major HIV guidelines becoming a blockbuster, with sales of \$3.4 billion in 2018 (Kujawa, 2019).

From 2018 to 2020 two more products were added to the dolutegravir franchise, in Europe: Juluca (dolutegravir/rilpivirine) (Juluca SmPC, 2020) and Dovato (dolutegravir/lamivudine) (Dovato SmPC, 2020). With these two new products the company aims to change the paradigm of HIV treatment from three-drug regimens (regimens containing three different molecules) to two-drug regimens.

The Chinese Scandal

In 2013, the Chinese government accused GSK of bribery and corruption in the country, based on the fact that the company allegedly used a network of travel agencies to pay around \$489 million in bribes to health officials, and fined the company with a \$489 million bill. This scandal led the company to reform its marketing practices. Following the scandal the company announced that it would be abandoning individual sales targets and stopping payments to healthcare professionals for speaking engagements and to attend medical conferences, in an attempt to increase the company's transparency for its stakeholders ViiV Healthcare, being primarily owned by GSK, adopted the same practices (Sullivan, 2014; BBC, 2013).

At the end of 2018, the company has decided to have a change of heart and reversed its policy of not paying HCPs to speak on behalf of the company about their products. The company stated that the previous measures taken had led to a reduced understanding

of the company's products by HCPs, and ultimately restricted patients' access to truly innovative medicines (GSK, 2018).

The case for Triumeq

Triumeq, the first fixed-dose combination of dolutegravir, abacavir and lamivudine, was launched during the turmoil that hit GSK and the adoption of the new, more transparent marketing practices. These new practices could have a negative impact on the product's performance, however it achieved great success, becoming a blockbuster medicine, widely supported by its therapeutic features and benefits. Additionally, the company further restructured the promotion variable of the marketing mix, by abandoning the industry model of purely disseminating scientific data and jumping into a patient-focused scientific selling. This new approach consisted in: (I) defining three key messages, (II) transforming the features of the drug into benefits for the patient, and (III) depicting patient profiles highlighting a problem to be solved. In summary, the company redefined the way it communicated the product's characteristics.

In strategic terms, the company focused primarily only in one patient segment, the naïve patient. The HIV patient population can be divided into two main segments: (I) the naïve patients, who have the condition but haven't started treatment; (II) the switch patients, who are already prescribed with an antiretroviral regimen. The rationale behind this strategic choice was that the naïve patient is the unknown, unpredictable newly diagnosed patient for the physician and the physician does not have enough patient knowledge to predict the patient behaviour, acceptance and adherence to treatment.

The clinical studies supporting Triumeq back up this strategy as they were primarily performed in the naïve patient segment and the company focused its promotional communication in this HIV patient segment, because, if physicians believe that this medicine is effective in a naïve patient, they would automatically believe the medicine would be effective in the switch patient segment, as this patient segment is more easily managed by physicians because there is already some degree of knowledge between both stakeholders.

The following case study will be focused on the Portuguese HIV market and all the examples, information and product performances will be based on the Portuguese data.

Triumeq in Portugal: an unprecedented success case?

In Portugal, for a medicinal product to be marketed, it needs to be previously approved by the European Medicines Agency (EMA) and then reimbursed by the Portuguese medicines authority, INFARMED I.P. (INFARMED). The role of EMA in approving a medicinal product consists of certifying and validating the therapeutic value and indication of the given medicine. On the other hand, INFARMED is responsible for negotiating and setting a price for the medicinal product, applying specific processes whether the medicines are intended for ambulatory use or hospital use only. It is not surprising, that in Portugal any medicinal product would be available to prescribe sometime after its approval by EMA. In the case of the hospital products, this gap may be longer, as they are 100% reimbursed, so the patient does not have to pay anything for it.

Triumeq was reimbursed by INFARMED in June 2016, though approved by EMA in 2015. The commercial strategy for Triumeq in Portugal was very aligned with its global strategy: promote the product for the naïve patient segment. For one and a half years, this was the only patient segment aimed by the promotional effort of the company. Eventually, when the naïve patient segment was conquered and the product established its leadership in this segment, the promotion of the product evolved to include communication in the switch segment, specifically by targeting specific patient profiles within this group. As there are a lot more patients on treatment versus naïve patients, focusing on sub-targets within the switch segment was deemed necessary to help physicians choose and prioritize which patients they should switch to Triumeq, to further position the product in this segment and gain market share.

Additionally, ViiV Healthcare adopted a pricing and discount strategy for Triumeq, that was unique at the time for the HIV market in Portugal, lowering the price of the medicine to become affordable by public hospitals in a widely fashion. Additionally, the Ministry of Health issued a directive where it was established that any HIV patient couldn't cost, to the public health budget, no more than 6000€ per annum, meaning that, per month, the total expense with any HIV patient should be inferior or equal to 500€. This amount included the following costs: test costs, appointment costs and treatment costs.

Since its launch, until today, Triumeq was established as the preferential regimen to be used, both in naïve and switch patients. The product achieved number 1 status in the Portuguese HIV market in 2018 and it kept growing after its promotion ended in June 2018, remaining the number one product in this therapy area at the end of 2020.

Triumeq was also considered the best launch in the HIV therapy area in Portugal in the decade, surpassing a performance of medicines launched previously to the 2010 crisis. Additionally, this performance, was achieved during the period that GSK and ViiV reformed their marketing practices and no direct payment to healthcare providers, for promotional purposes, took place. Furthermore, when GSK and ViiV Healthcare restarted payments to physicians for promotional purposes, promotion of Triumeq was already ended, but, nevertheless, the product kept growing during this period.

Below is the market share evolution for the HIV market from 2016 and 2018.

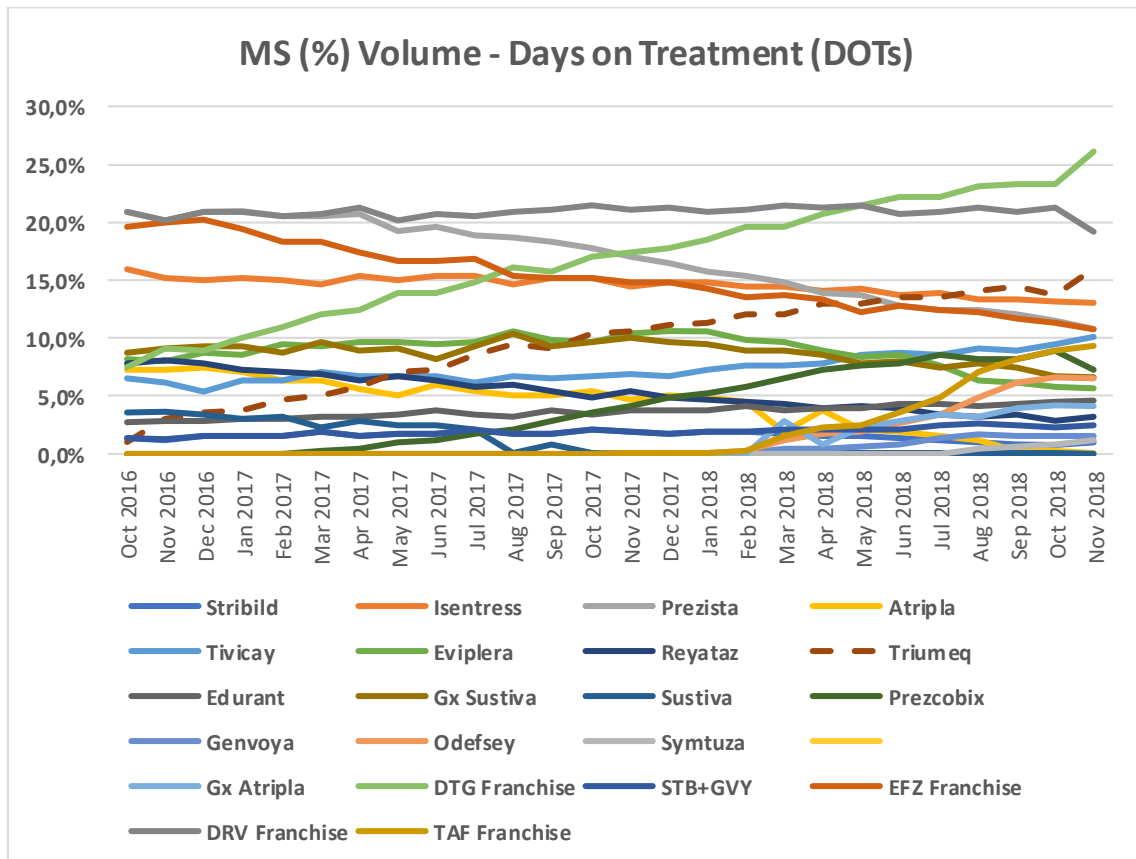


Figure 1 - Evolution of HIV products' market share (%) by volume of days on treatment

Below are the comparisons of HIV product performances since launch, in Portugal.

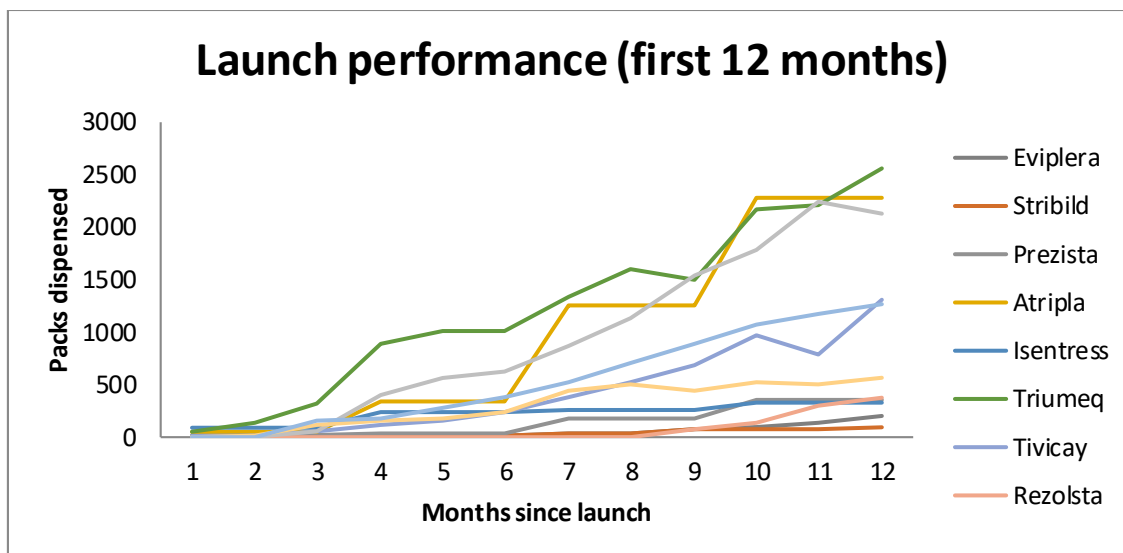


Figure 2 - Packs dispensed of HIV products reimbursed in Portugal after 2008, during the first twelve months after reimbursement

Atripla was considered the best launch in the HIV market, until Triumeq was launched. The figure above highlights the superior performance of Triumeq, versus the main competitors in this therapy area. Additionally, no brand launched after Triumeq has, until now, surpassed this product's performance (Stribild, Genvoya, Rezolsta, Symtuza, Juluca and Biktarvy).

From 2016 to 2019, ViiV Healthcare Portugal did not spend a single euro paying directly to physicians for promotional efforts. This information can be checked in INFARMED's "Plataforma da Transparência". The only payments made directly to physicians were made for advisory board purposes, where the objective is to seek advice from these stakeholders about the subject matter (clinical study data, pricing strategies, promotional tactics). Moreover, it was through advisory boards that ViiV Healthcare could hear out its customers and adapt its practices effectively, through unprecedented times.

A new trend or just a once in a lifetime phenomenon?

From the literature review, there seems to be a positive association between the relationship that pharma companies establish with physicians and their prescription behaviour, particularly at the levels of facilitating the registration of physicians to attend conferences and inviting physicians to attend continuous medical education events.

In the case depicted, leadership was achieved without any incentives paid to physicians for promotional purposes, except for proper hospitality, that included industry-paid meals, at promotional sessions (which are considered an indirect transfer of value). However, handing incentives to physicians, that includes facilitating the registration for them to attend conferences and providing accommodation for it, paying physicians to speak at industry sponsored meetings, and providing free meals (coupled with promotional sessions), is a common promotional practice within the pharmaceutical industry sector.

To study the impact of these incentives in the prescribing behaviour of physicians and to find out which types of incentives may have a significant influence in it, a market research needs to be conducted to shed a light on this topic.

Market Research

Methodology

In an attempt to answer the proposed research questions, in order to fulfil the objective of this dissertation, a market research study was conducted to measure the impact of each of the variables highlighted during the literature review on the prescription behaviour.

A questionnaire of 20 questions was built, using Qualtrics^{XM}, and the results were analysed through IBM SPSS Statistics 26.0.

This study was performed in the HIV therapy area and the target audience for this survey were physicians that are eligible to prescribe antiretroviral drugs in Portugal. The survey was distributed to the target audience, through an anonymous link, via ViiV Healthcare staff.

The questionnaire was divided into four sections. The first section was related to the audience demographics, including medical specialty, type of hospital, region, and graduation (specialist versus intern). The second section was related to the prescription behaviour of the audience. The questions included in this section were open to retrieve a spontaneous answer from the respondent. The third section focused on the future intention to prescribe some antiretroviral agents. The fourth section aimed to capture

which attributes were valued by the audience when selecting an antiretroviral treatment, and how they classify each company in this therapy area in terms of communicating those attributes. The fifth section asked specifically in which of the listed marketing activities the respondents participated in the past, and for each activity which for which company they participated in most of each activity. The sixth section was more focused on the role of conference sponsorship and promotional meeting attendance on the relationship between the respondent with the company, and in understanding the benefits of a company's product and the patients that could benefit with that product.

Results

Study demographics

A total of 42 respondents completed the survey. The respondents of the survey were all physicians in the HIV therapy area. The demographics of the study are shown in table 1.

Specialty, % (n)	Results
Infectious Diseases	71,4% (30)
Internal Medicine	28,6% (12)
Type of Hospital, % (n)	
University Hospital	52,4% (22)
District/central Hospital	47,6% (20)
Other	0
Region of the country, % (n)	
North	28,6% (12)
Centre	11,9% (5)
South	59,5% (25)
Madeira	0
Azores	0
Graduation status, % (n)	
Specialist	69,0% (29)
Intern	31,0% (13)

Table 1 - Study demographics

Through crosstab analysis, it was possible to find out that 29 out of 30 of the infectious diseases specialists work at a University Hospital, while 11 out of 12 internal medicine specialists practice at a District or Central Hospital. This distribution was statistically significant and can be observed in tables 2 and 3.

Qual o tipo de hospital em que exerce a sua prática clínica? * Qual a sua especialidade? Crosstabulation

Count

		Qual a sua especialidade?		Total
		Doenças Infeciosas	Medicina Interna	
Qual o tipo de hospital em que exerce a sua prática clínica?	Hospital Universitário	21	1	22
	Hospital Central/Distrital	9	11	20
Total		30	12	42

Table 2 - Specialty by type of hospital

	Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided) Exact Sig. (1-sided)
Pearson Chi-Square	13,068 ^a	1	,000	
Continuity Correction ^b	10,712	1	,001	
Likelihood Ratio	14,593	1	,000	
Fisher's Exact Test				,000 ,000
Linear-by-Linear Association	12,757	1	,000	
N of Valid Cases	42			

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 5,71.

b. Computed only for a 2x2 table

Table 3 - Chi-square tests for specialty by hospital type

Prescribing behaviour

Regarding the prescription behaviour, when the top of mind regimen was analysed, Triumeq (DTG/ABC/3TC) surges with a 90,5% score (Figure 3). For the vast majority of respondents, this is the number 1 regimen prescribed. After recoding each top of mind regimen to the correspondent company, we can see that ViiV Healthcare is present in 90,5% of the responses (Figure 4). When analysing the 3 preferred regimens of physicians, Triumeq (DTG/ABC/3TC) continues to lead physicians' preference, although dropping to a share of 31,7%.

Market Share most prescribed regimen (%)

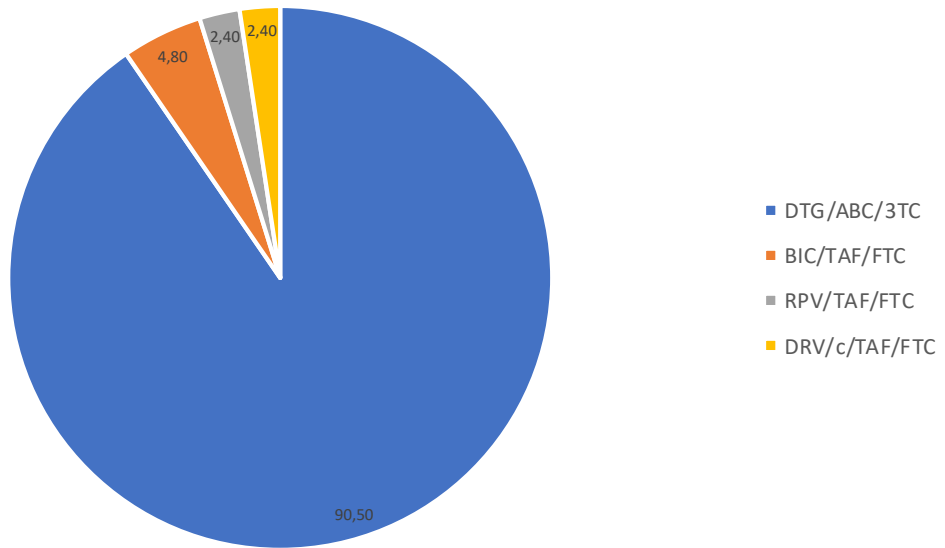


Figure 3 - Most prescribed regimen

Market share for most prescribed regimen - company (%)

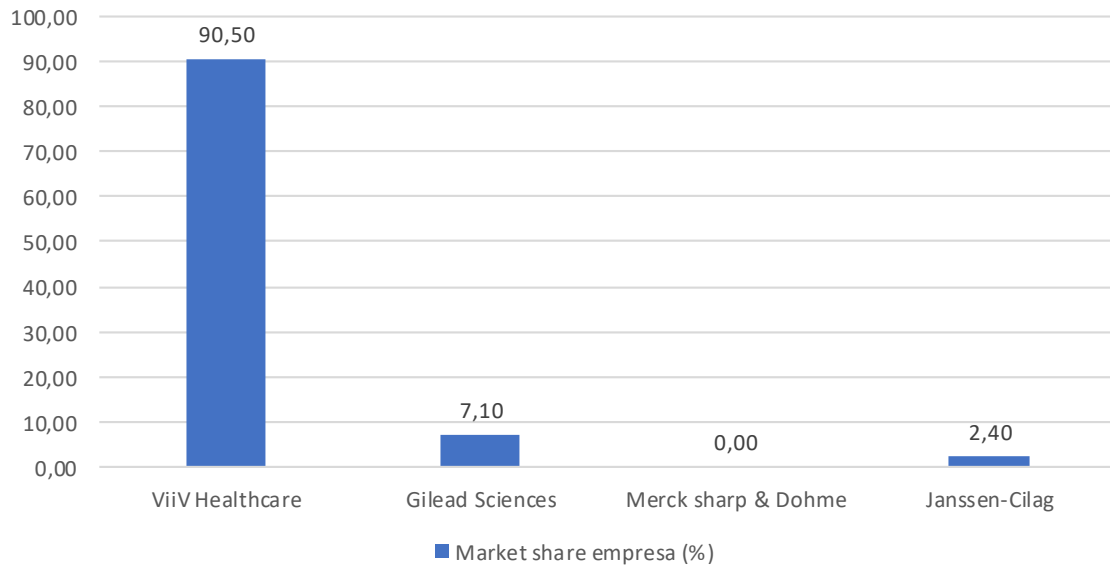


Figure 4 - Company with the most prescribed regimen

When correlating the demographic variables with the top of mind regimen, no statistically significance differences were found.

For the naïve patient segment, Triumeq (DTG/ABC/3TC) also retained the leadership, however a drop was observed from 90,5% in the overall use to 69,0% of use in the naïve patients (Figure 5). Grouping regimens by company, ViiV Healthcare has an overall top of mind market share in the naïve patient segment of 81,0%, as shown in the graph below (Figure 6).

Market share most prescribed regimen in naive patients (%)

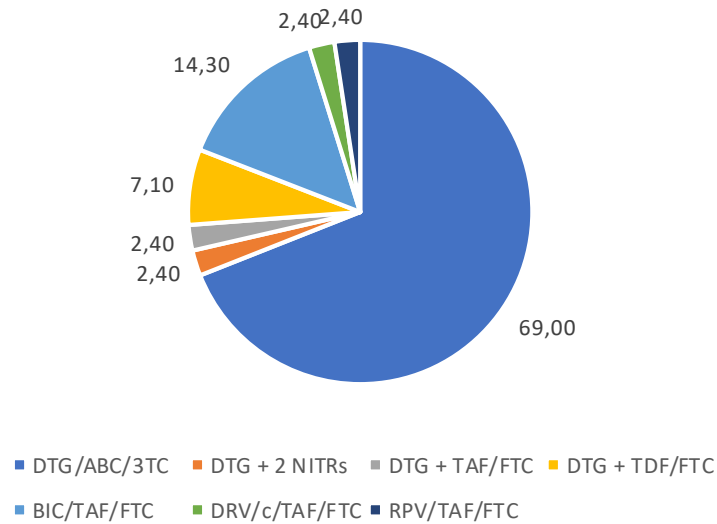


Figure 5 - Most prescribed regimen in naive patients

Market share for most prescribed regimen in naive patients - company (%)

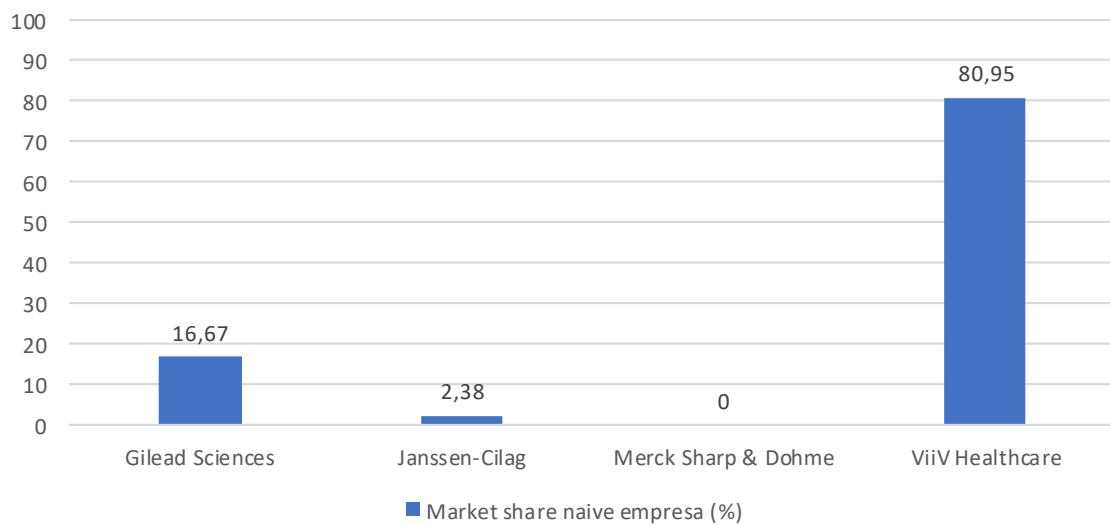


Figure 6 – Company with the most prescribed regimen in naive patients

After correlating the demographic variables with the top of mind regimen for naïve patients, statistically significant differences were found only for the region where the physician works, with a p-value of 0,041. The results are shown in table 4 and 5.

It is possible to observe that the share of Triumeq (DTG/ABC/3TC) is higher (75%) among physicians that work in the north of the country. On the opposite, Biktarvy (BIC/TAF/FTC), the main competitor of Triumeq (DTG/ABC/3TC) has its highest share (16%) among physicians who work in the south of the country.

Crosstab

Count

Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si, para os seus doentes naive: - Regime 1

			BIC/TAF/FTC	DRV/c/TAF/FTC	DTG + 2 NITRs	DTG TAF/FTC	DTG TDF/FTC	DTG/ABC/3TC	DTG/TAF/FTC	RPV/TAF/FTC	Total
Em que região do país se situa o seu hospital?	Norte		0	0	0	1	2	9	0	0	12
	Centro		0	0	1	0	0	3	0	1	5
	Sul		4	1	0	0	1	17	2	0	25
Total			4	1	1	1	3	29	2	1	42

Table 4 - Prescription behaviour in naive patients by region

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	24,411 ^a	14	,041
Likelihood Ratio	20,637	14	,111
N of Valid Cases	42		

a. 22 cells (91,7%) have expected count less than 5. The minimum expected count is ,12.

Table 5 - Chi-Square test for prescription behaviour in naive patients by region

What attributes do HIV specialists value when selecting an antiretroviral regimen?

When asked about the 3 most important attributes when selecting an antiretroviral regimen, efficacy was by far the most important attribute, with 71,4% of respondents pointing it as the number one attribute (Figure 7). When looking at the combined three attributes that physicians most appreciate when selecting a treatment, efficacy (32,5%), convenience (19,8%) and safety (19%) were the most important attributes that an antiretroviral regiment should combine.

Attribute top of mind (%)

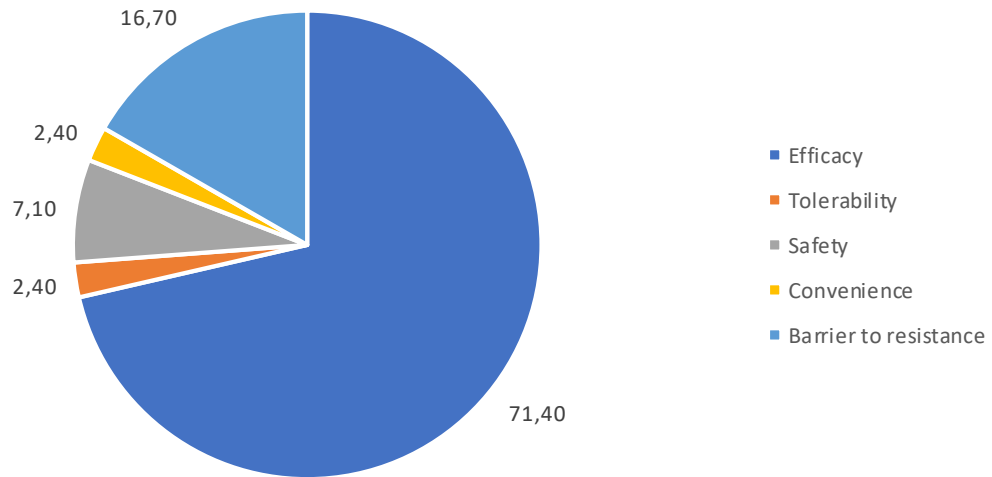


Figure 7 - Number 1 attribute when selecting an antiretroviral regimen

When cross-analysing the top of mind attribute with the most prescribed regimen for all patients, a statistically significant correlation was found ($p=0,005$). These results are shown in tables 4 and 5. Additionally, when cross-analysing the top of mind attribute with the most prescribed regimen in naïve patients, 52,4% of respondents simultaneously valued efficacy and prescribed Triumeq (DTG/ABC/3TC) as the most prescribed treatment regimen. Triumeq (DTG/ABC/3TC) is an antiretroviral regimen, based on the integrase inhibitor dolutegravir (DTG), which is associated with high and rapid efficacy. Regarding the attribute barrier to resistance, this was the reason to prescribe Triumeq (DTG/ABC/3TC) (7,1%), Biktarvy (BIC/TAF/FTC) (7,1%) and Symtuza (DRV/c/TAF/FTC) (2,4%). In fact, these regimens are mentioned in the literature as having a high barrier to resistance. All the safety and tolerability attribute seekers selected DTG/ABC/3TC as most prescribed regimen for these patients. Physicians who value convenience as the most important attribute, selected Odefsey (RPV/TAF/FTC) as the most prescribed regimen for treatment-naïve patients. The differences observed were statistically significant ($p=0,000$).

These results are available in tables 6 and 7.

Quando institui um regime antirretrovírico quais os 3 atributos que mais valoriza? - Atributo 1 * Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si, para os seus doentes naive: - Regime 1 Crosstabulation

Count

		Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si, para os seus doentes naive: - Regime 1								Total
		BIC/TAF/FTC	DRV/c/TAF/FTC	NITRs	DTG + 2 TAF/FTC	DTG + TDF/FTC	DTG + DTG/ABC/3TC	DTG/TAF/FTC	RPV/TAF/FTC	
Quando institui um regime antirretrovírico	Barreira à resistência	3	1	0	0	0	3	0	0	7
os 3 atributos que mais valoriza? - Atributo 1	Comodidade	0	0	0	0	0	0	0	1	1
	Eficácia	1	0	1	1	3	22	2	0	30
	Segurança	0	0	0	0	0	3	0	0	3
	Tolerabilidade	0	0	0	0	0	1	0	0	1
Total		4	1	1	1	3	29	2	1	42

Table 6 - Prescription behaviour in naive patients by valued attribute

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	60,671 ^a	28	,000
Likelihood Ratio	25,445	28	,604
N of Valid Cases	42		

a. 39 cells (97,5%) have expected count less than 5. The minimum expected count is ,02.

Table 7 - Chi-square tests for prescription behaviour in naive patients by valued attribute

Prescription intention

Prescription intention for the next twelve months showed that the respondents intent to increase prescription of recently reimbursed regimens, such as Dovato (DTG/3TC), Biktarvy (BIC/TAF/FTC) and, in some extent, Delstrigo (DOR/TDF/FTC). All the inquired physicians stated that they will increase the prescription of Dovato (DTG/3TC). Additionally, the respondents mentioned the intent of decreasing the rate of prescription of established regimens, such as Tivicay + Truvada (DTG + TDF/FTC), Symtuza (DRV/c/TAF/FTC) and Isentress + 2 nucleoside inhibitors (RAL + 2 NITRs), and to a lesser extent Triumeq (DTG/ABC/3TC). As for which regimens will remain unchanged

in terms of prescription share, there is a lot more consensus around Triumeq (DTG/ABC/3TC) and Odefsey (RPV/TAF/FTC).

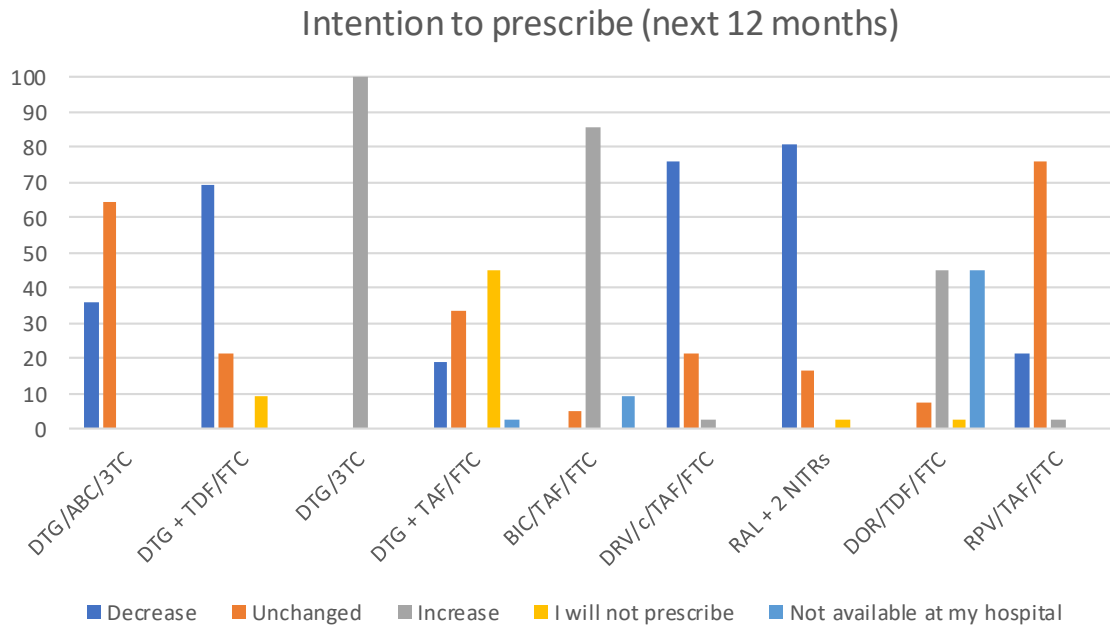


Figure 8 - Intention to prescribe (next 12 months)

How effectively do companies communicate?

In this study, the effectiveness of communicating the most important attributes for physicians was evaluated. The results are shown in figure 9. Of the study sample, 66,7% of respondents selected ViiV Healthcare as the company that better communicated the attributes that were important for them when choosing a treatment regimen. Additionally, ViiV Healthcare was selected as the company that simultaneously had the most regimens prescribed and better communicated the attributes that are important for choosing those regimens (table 8). This relationship was statistically significant, as observed using the chi-square test, retrieving an asymptotic significance for the Pearson chi-square of 0,005 (table 9).

Comunicação_assertividade_top * Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si para a globalidade dos seus doentes com infeção por VIH: - Regime 1

Crosstabulation

Count

		Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si para a globalidade dos seus doentes com infeção por VIH: - Regime 1				Total
		BIC/TAF/FTC	DRV/c/TAF/FTC	DTG/ABC/3TC	RPV/TAF/FTC	
Comunicação_assertividade_top	Gilead	2	0	7	1	10
	Jansse	0	1	2	0	3
	MSD	0	0	1	0	1
	ViiV	0	0	28	0	28
Total		2	1	38	1	42

Table 8 - Prescribing behaviour versus communicating valued attributes

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	23,542 ^a	9	,005
Likelihood Ratio	14,880	9	,094
N of Valid Cases	42		

a. 14 cells (87,5%) have expected count less than 5. The minimum expected count is ,02.

Table 9 - Chi-square tests for prescribing behaviour versus communicating valued attributes

Company that better communicates important attributes (%)

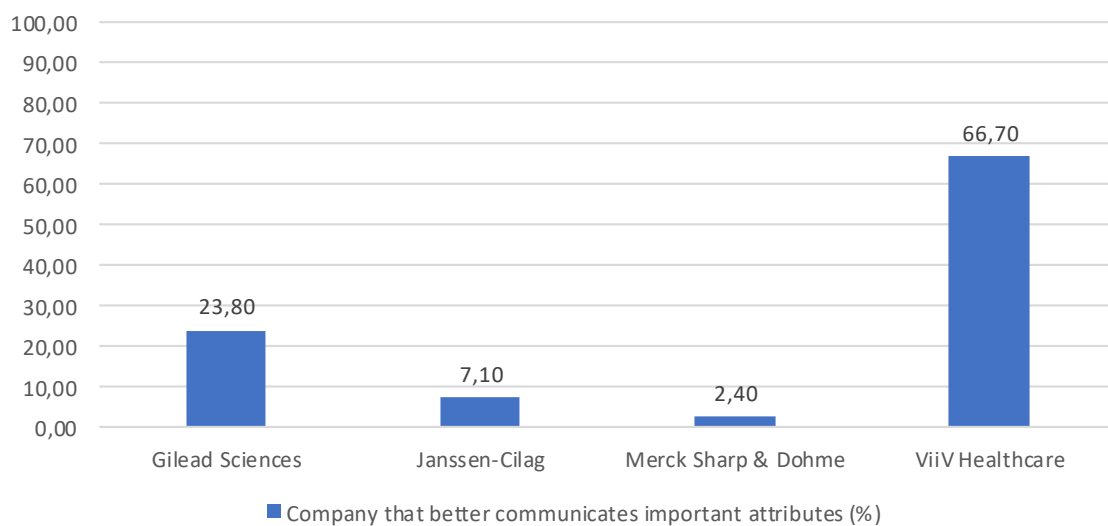


Figure 9 - Share of attribute top communicator

The distribution of each company by rank was also assessed. ViiV Healthcare was the company most ranked in number one regarding attribute communication, with Gilead Sciences being the company that was most ranked in the second place. Merck Sharp & Dohme appears to be the company that worst communicate the attributes that are important for physicians when building a treatment regimen, being mainly ranked in the fourth place (figure 10).

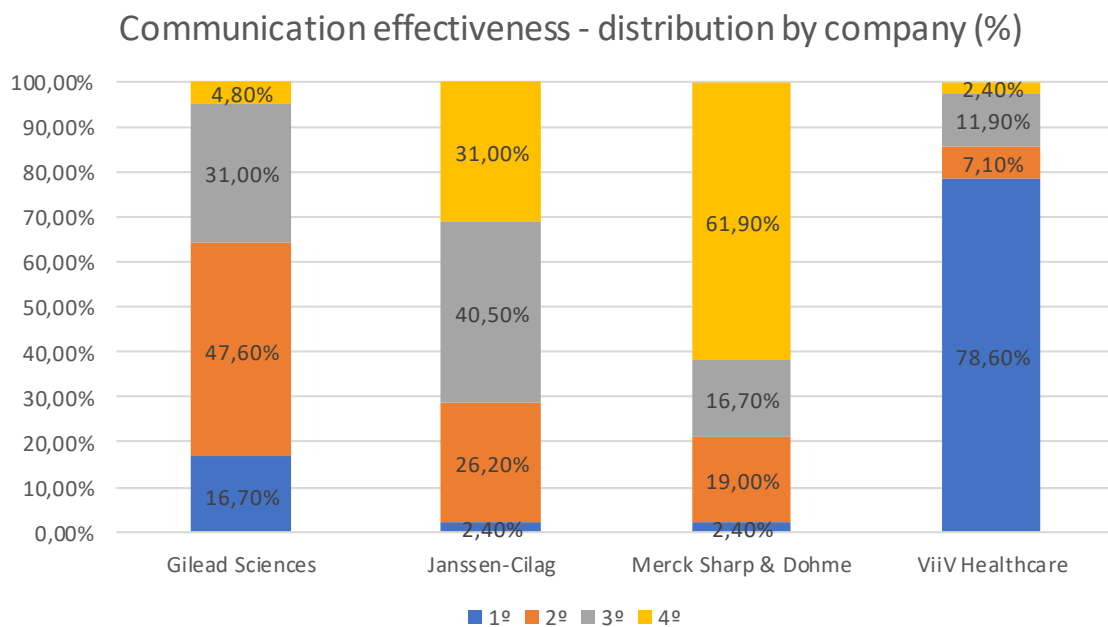


Figure 10 - Communication effectiveness distributed by company

Marketing activities

In this study it was evaluated how the companies performed in terms of marketing activities, used within the pharma industry sector. These included: promotional sessions, such as clinical sessions or symposiums; sponsorship physicians to attend international conferences; sponsorship physicians to attend national conferences; sponsorship physicians to attend continuous medical education events; and engaging physicians as speakers in pharma sponsored events. These results are displayed in figure 11.

Clinical sessions are defined as small meetings, typically with less than 10 physicians attending and predominantly aggregates physicians from the same hospital or, in some cases, two hospitals. Symposiums are defined as larger promotional meetings, normally taking place at conferences, and usually aggregate a minimum of 50 physicians in the same session

ViiV Healthcare outperformed the remaining companies regarding the number of promotional sessions (clinical sessions and/or symposiums) that the respondents recalled attending. However, in the remaining activities, ViiV Healthcare was associated to negligible or null activity, which would be expected given the restrictions the company faced previously to 2019 and the transition period it entered thereafter.

Regarding sponsoring physicians to attend conferences, Gilead Sciences leads the way, with a gap for the other companies for international conferences. All the companies are relatively tied in terms of sponsoring physicians to attend national conferences. When assessing which companies are most active in granting continuous medical education sponsorships, Gilead Sciences stays ahead of the other companies, however, the difference is smaller than for international conferences sponsorships. Gilead Sciences was also number one regarding speaker engagement for pharmaceutical events, followed by Merck Sharp & Dohme.

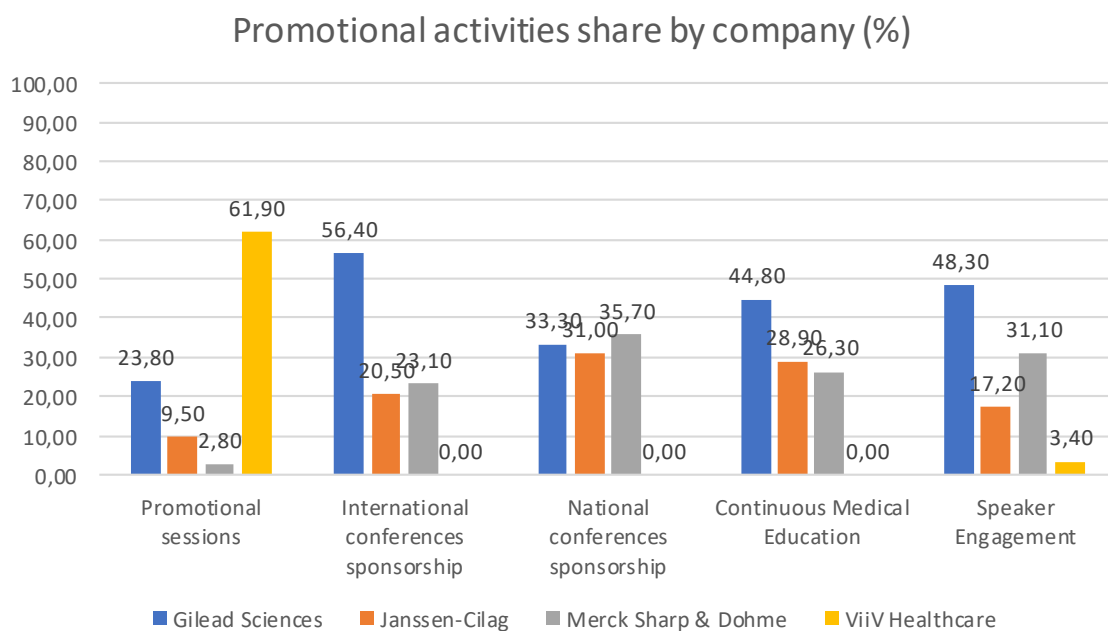


Figure 11 - Promotional activities by company

When correlating these marketing activities with the overall prescribing behaviour, no statistically significant association was found for the company physicians recalled attending most of the promotional sessions. However, a statistically significant association was found between attending ViiV Healthcare promotional sessions and the prescription behaviour in naïve patients ($p=0,037$). In this case, 57,1% of respondents simultaneously selected ViiV Healthcare as the company for which they have mostly attended and have chosen a ViiV Healthcare regimen as the most prescribed regimen in naïve patients (table 10 and 11).

Crosstab

Count

		Regime preferencial nos doentes naive			Total
		ViiV Healthcare	Gilead Sciences	Janssen-Cilag	
Relativamente ao ano de 2019, por	1	24	2	0	26
favor ordene os laboratórios	2	6	4	0	10
farmacêuticos de acordo com o	3	1	0	0	1
número de sessões clínicas em que participou (em primeiro lugar deverá selecionar o laboratório para o qual participou num maior número de sessões clínicas): - ViiV Healthcare	4	3	1	1	5
Total		34	7	1	42

Table 10 - Preferred regimen in naive patients by participation in ViiV Healthcare promotional sessions

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	13,395 ^a	6	,037
Likelihood Ratio	9,864	6	,130
Linear-by-Linear Association	6,623	1	,010
N of Valid Cases	42		

a. 10 cells (83,3%) have expected count less than 5. The minimum expected count is ,02

Table 11 - Chi-square tests for preferred regimen in naive patients by participation in ViiV Healthcare promotional sessions

It is worthy to note that, apparently, sponsoring physicians to conferences or engaging them as speakers, alone, are not predictive of leadership in terms of regimen market share, although this relationship was not statistically significant in this research. The same rationale may apply to providing continuous medical education events. Although not predictive of market share leadership, the effects of these activities alone should be

studied to understand if they have the potential to increase, maintain or decrease prescription of the sponsoring company drugs.

It was also researched the impact of promotional sessions (clinical sessions and symposiums) and sponsoring physicians to attend conferences (national and international) on: building/strengthening the relationship between physicians and pharma companies; allowing physicians to understand the attributes of the treatment regimen; and allowing physicians to understand which patients might benefit from a company’s regimen. Results are available in figure 12 and figure 13, respectively.

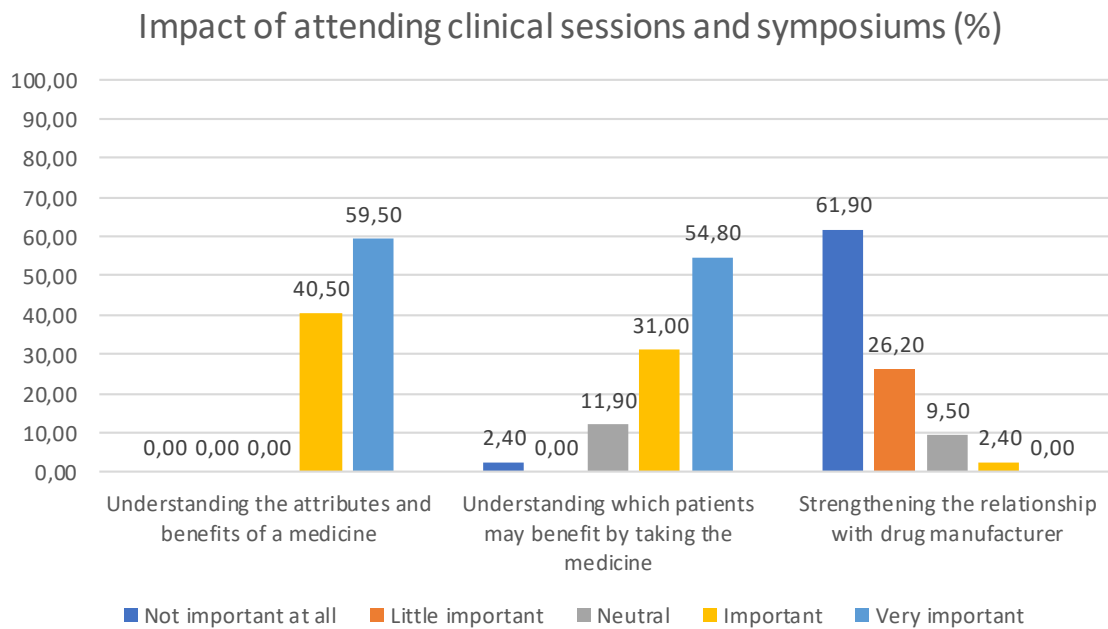


Figure 12 - Impact of attending promotional events

Regarding the impact of attending promotional meetings, all respondents answered the question (n=42), and it is possible to see in figure 12 that its main impact resides in understanding the attributes and benefits of a medicine. Overall, physicians rated that attending these meetings is important (40,5%) or very important (59,5%) to understand the attributes and benefits of the drug the company is promoting. Regarding the impact of these activities in understanding the patient profiles that may benefit from being treated with the drug, there was more diversity in the responses. However, overall, the majority of respondents (85,8%) mentioned that these meetings are important (31,0%) or very important (54,8%) to highlight which patients should be put on a particular company regimen.

In general, physicians rated the importance of attending promotional meetings in strengthening the relationship they have with pharma companies as being not important at all (61,9%) and being of little importance (26,2%).

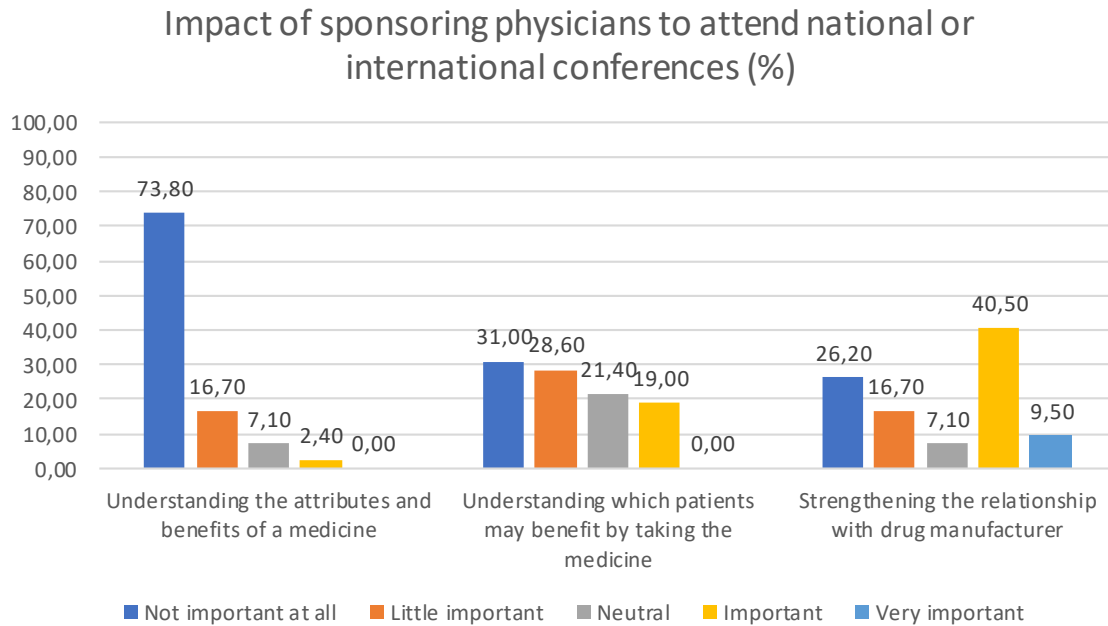


Figure 13 - Impact of sponsoring physicians to attend conferences

When analysing the results for the impact of attending national or international conferences in the three outcomes listed, the responses were more balanced and diverse, compared to the impact of attending promotional events. All the respondents answered the question (n=42) and the results are available in figure 13. In general, the respondents, stated that attending conferences is not important, at all, in understanding the attributes or benefits of a medicine (73,8%). However, there seems to be more balance in the rating of understanding which patients could benefit from using the medicine, with 31,0% of respondents stating that attending conferences doesn't have any importance at all in this outcome, 28,6% say it has little importance, 21,4% attributing a score of neutral, and 19,0% of participants highlighting that attending conferences is important to understand the patient profiles that will benefit from the medicine of the sponsor company.

When looking at the impact of sponsoring physicians to attend conferences in strengthening the relationship with the sponsor pharma company, 50,0% of respondents stated that being sponsored by pharma companies to attend conferences

is important to reinforce the relationship with them, with 40,5% giving it an important score, and 9,5% giving it a score of very important.

When correlating the perceived impact of these activities in the outcomes described and the most prescribed regimens, both overall and in the naïve patient segment, there were no statistically significant differences.

Conclusions

At the start of this work, five key research questions were set:

1. What product features are important in the prescription decision-making process?
2. Does the relationship between pharmaceutical companies and physicians influence the prescription behaviour, and to what extent?
3. Does this relationship have an independent impact on the prescription behaviour?
4. What is the exact role on the prescription behaviour of the relationship between these companies and physicians?
5. What forms of company-customer engagement add value?

These questions will be answered, where applicable, throughout this section.

The results of this research showed that Triumeq (DTG/ABC/3TC) is without any doubt the most prescribed regimen, and still the preferred regimen for new patients, although new brands have landed at the market since Triumeq (DTG/ABC/3TC) was launched, These findings are in line with market data, but the market share per se does not represent the real market shares observed in the market. The reason for this difference is that this study only included newer or the most prescribed brands observed in the market. There are some older drugs, that are not actively prescribed anymore, however its prescription can be maintained in follow-up patients (patients that do not change any part of their treatment regimen). This fact doesn't represent a new prescription, but rather a renewal of previous prescriptions.

The prescription pattern observed in this study is consistent between infectious diseases specialists and internal medicine specialists. However, statistically significant differences were observed in prescription habits by region, where south hospitals account for 59,5%

of the study sample. It is possible to conclude that despite Triumeq (DTG/ABC/3TC) has a strong adoption across all subgroups, nonetheless, Biktarvy (BIC/TAF/FTC) has a significant penetration among physicians who work at south hospitals.

Additionally, when looking at the intention to prescribe analysis, it is possible to observe that physicians are likely to maintain the prescription of Triumeq (DTG/ABC/3TC), despite its already high market share.

Nevertheless, some action is observed regarding the newly available brands, particularly Biktarvy (BIC/TAF/FTC), marketed by Gilead Sciences, and Dovato (DTG/3TC), marketed by ViiV Healthcare.

Looking at a drug manufacturer marketing mix, price and promotion are the variables that, although obeying to a global matrix and guideline, can be fine-tuned locally. Price was out of scope of this research study, because additionally to being negotiated with the country regulator, its introduction in hospitals is a binary option: If it is above the threshold defined by the Ministry of Health, it may not get access in hospitals, or it may have access with restrictions.

Although pharmaceutical companies are, in general, global companies, with standardized practices and approaches towards marketing and promoting medicines, differences can occur at a country or regional level, due to the social, cultural and economic context of each region or country. This work focused on the promotion variable, as this is the one that is more linked with prescription behaviour and may reflect physicians' free choices.

In what regards to research question number one, related to the important attributes that physicians value when selecting a treatment, efficacy was the most important, with barrier to resistance following, as a top of mind attribute. However, when combining the three attributes are important to physicians when selecting a treatment option, efficacy, safety and convenience were the ones that mattered the most. In this sense, brands (and the companies that market them) should take these three attributes into account in their value proposition. These findings provide the answer (or, at least, a starting point) to the first research question.

Regarding research question number two, it was found that pharmaceutical companies differ regarding how effectively they communicate the attributes and benefits that matter to physicians, when positioning a brand. Moreover, the effectiveness of

communicating the important regimen attributes for physicians was found to have a positive impact on the prescription behaviour, retaining statistical significance.

From the literature review, mixed results were found regarding the existence of a possible correlation between marketing activities. The only marketing activities, that were unanimously positively correlated with increasing, or changing, prescription behaviour was related to sponsoring physicians to attend continuous medical education events and offering industry-paid meals. In this study, no correlation could be verified between attending continuous medical education events and the prescription behaviour of physicians, because of the absence of statistical significance. However, the results may lead to a conclusion that sponsoring or attending continuous medical education events, alone, is not a factor that impacts the prescription behaviour of HIV specialists, but rather a catalyst when combined with other activities. On the other hand, there was a positive correlation, that yields statistical significance, between attending promotional meetings, that include clinical sessions and symposiums and the brands prescribed for naïve patients. Although this activity may sound different than simply inviting physicians to lunch or dinner, the majority of the industry-paid meals happen coupled to a clinical session or a symposium, particularly in the Portuguese hospital market. Studying the isolated influence of meals on the prescription behaviour may be difficult, particularly in Portugal, because of the misperception it may cause, or the sensitivity associated with it, however these results may demonstrate that organizing promotional sessions, such as clinical sessions and symposiums are positive factors that lead to brand adoption and usage. Nonetheless, and in what relates to research question number three, no definitive conclusions can be taken regarding any potential independent impact of this variable on the prescription behaviour. Additionally, the physicians that took this survey mentioned that these sessions were important to 1) understand the attributes and benefits of the brand being promoted, and 2) understand which patients might be suitable to be prescribed the regimen, thus answering research question number five. Regarding the other marketing activities highlighted in the literature review, namely sponsoring physicians to attend conferences (national and international) or engaging them to be speakers at industry events, these did not yield a positive relationship with prescription pattern, although these findings were not statistically significant. Given these findings, it was not possible to answer research question number four, and more

research is needed to understand the exact role of the relationship between pharma companies and physicians on the prescription behaviour of the latter.

In summary, no major effects on prescription behaviour were found for most of the marketing actions performed by pharmaceutical companies, with exception for promotional sessions and communication of valued attributes, that were found to have a positive impact on the prescription behaviour.

Limitations and future research

The author of this study is full-time employee of ViiV Healthcare, a company that markets HIV drugs and this study was distributed to HIV physicians by the author of the study and company's sales representatives. In this research there is room for social desirability bias for two reasons that are connected: 1) the main topics of this research can be unpleasant to answer by the participants, as a negative view on their attitudes and motivations can be drawn, depending on the answers provided, and a potential conflict of interests may be observed; 2) As the participants of this study are acquaintances of the individuals who distributed the survey, an innate need to please the distributors of this study may also be observed, along with the potential need to depict a positive perspective on their attitudes and motivations.

Another limitation of this research is the lack of statistical significance of the potential correlations between the major topics of this study. This lack of statistical significance may be due to the dominant share of one sole company (ViiV Healthcare) combined with the fact that the same company was restricted from performing some of the marketing activities studied.

As a consequence, more research is needed in this field to study the isolated impact of the marketing activities highlighted in this study. Research should be conducted in a more competitive market or therapy area, where no differences in restrictions are observed between companies or players.

Teaching notes

Pharmaceutical companies invest significant sums of money in marketing in sales, to capitalize their assets.

The marketing practices and activities within the pharmaceutical industry space often include a transfer of value to healthcare professionals, whether it is through supporting physicians to attend conferences, organizing meetings where paid meals and accommodation may be included, or engaging healthcare professionals to be speakers at industry promoted events.

The literature review provides a guidance on the marketing practices that are used by pharmaceutical companies to leverage and capitalize their assets, to meet their growth and sales targets. As mentioned before, these practices often include a transfer of value to healthcare professionals and are common across the industry. This may lead to an overestimation on the effects of these practices and an underestimation on the impact of the marketing basics and mix.

The case study depicted highlights a real case where some of the marketing activities were not adopted, namely the ones that included any transfer of value to healthcare professionals, but still brand recognition and adoption was achieved, with a strong bet on understanding the attributes that physicians valued when adopting a brand in the HIV therapy area, thus aligning the brand's value proposition with those attributes.

The main objective of the case study was to highlight that marketing basics, concepts and mix are applicable to this industry, and should be on the basis of any marketing strategy. The practices widely used by the pharmaceutical manufacturers should build on that, and add on the brand adoption and recognition, instead of being a catalyst per se. Additionally, betting on marketing practices that include transfers of value to healthcare professionals, without understanding or complying to the marketing mix of the brand, may lead to an overinvestment, without the proper return on the investment. The case study is intended for individuals studying marketing and management, that simultaneously hold a marketing position within the pharmaceutical sector or want to hold such position.

There is no predefined teaching plan, however, students are strongly encouraged to read the literature review and the case study presented in this work, and try to transport the findings of those particular pieces to their daily work, to try to understand if the premises highlighted in those sections are observed in their daily work environment.

Nonetheless, basic knowledge in marketing is needed to study the scalability of the findings depicted in this study to their work reality, namely understanding the marketing mix and how it can be adapted, as well as its impact on a brand's performance.

References

Bandari J, Turner RM, Jacobs BL, Canes D, Moinzadeh A, Davies BJ. 2017. The relationship of industry payments to prescribing behavior: a study of degarelix and denosumab. *Urol Pract*; 4(1):14-20.

BBC. 2013. GSK to stop paying doctors to make speeches. *BBC*. Updated in 17th December 2013. Accessed in 10th February 2021. Available at: <https://www.bbc.com/news/business-25415485>.

Brax H, Fadlallah R, Al-Khaled L, Kahale L, Nas H, El-Jardali F, Akl EA. 2017. Association between physicians' interaction with pharmaceutical companies and their clinical practices: a systematic review and meta-analysis. *PLoS ONE*; 12(4): e0175493. <https://doi.org/10.1371/journal.pone.0175493>.

Campo K, De Staebel O, Gijsbrechts E, van Waterschoot W. 2006. Physicians' decision process for drug prescription and the impact of pharmaceutical marketing mix instruments. *Health Marketing Quarterly*; 22(4):73-107.

Castagna A, Maggiolo F, Penco G, Wright D, Mills A, Grossberg R, Molina J-M, Chas J, Durant J, Moreno S, Doroana M, Ait-Khaled M, Huang J, Min S, Song I, Vavro C, Nichols G, Yeo JM. 2014. Dolutegravir in antiretroviral-experienced patients with raltegravir- and/or elvitegravir-resistant HIV-1: 24-week results of the phase III VIKING-3 study. *J Infect Dis*; 210(3):354-362.

Cook N, Geier A, Schmid A, Hirschfield G, Kautz A, Schattenberg JM, Balp M-M. 2020. Assessing physician preferences on future therapeutic options and diagnostic practices in non-alcoholic steatohepatitis. *JHEP Reports*; 2(2):e100081. <https://doi.org/10.1016/j.jhepr.2020.100081>.

Datta A, Dave D. 2017. Effects of physician-directed pharmaceutical promotion on prescription behaviours: longitudinal evidence. *Health Econ*; 26(4):450-468.

Denig P, Haaijer-Ruskamp FM. 1992. Therapeutic decision making of physicians. *Pharm Weekbl*; 14(1):9-15.

Dickov V, Kuzman B. 2011. Specific features of pharmaceuticals marketing mix. *Journal of Management & Marketing in Healthcare*; 4(3):160-167.

ViiV Healthcare. 2021. Dovato EU SmPC. *EMA*:1-37

Dow DE, Bartlett JA. 2014. Dolutegravir, the Second-Generation of Integrase Strand Transfer Inhibitors (INSTIs) for the Treatment of HIV. *Infect Dis Ther*;3(2):83-102. doi: 10.1007/s40121-014-0029-7. Epub 2014 Jun 24.

Engelberg J, Parsons C, Tefft N. 2013. First, do no harm: financial conflicts in medicine. *Working Paper*, http://papers.ssrn.com/sol3/papers.cfn?abstract_id=2297094.

Fickweiler F, Fickweiler W, Urbach E. 2017. Interactions between physicians and the pharmaceutical industry generally and sales representatives specifically and their association with physicians' attitudes and prescribing habits: a systematic review. *BMJ Open*; 7:e016408. doi:10.1136/bmjopen-2017-016408.

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

GlaxoSmithKline. 2018. GSK updates policy for working with healthcare professionals. *GSK*. Updated in 2nd of October 2018. Accessed in 10th February 2021. Available at: <https://www.gsk.com/en-gb/media/press-releases/gsk-updates-policy-for-working-with-healthcare-professionals/>.

Hollands S. 2020. Receipt of promotional payments at the individual and physician network level associated with higher branded antipsychotic prescribing rates. *Administration and Policy in Mental Health and Mental Health Services Research*; 47:73-85.

ViiV Healthcare. 2021. Juluca EU SmPC. *EMA*:1-31.

Karolina Kujawa. 2019. Datamonitor Healthcare;DMKC0057936:1-16. Available at: <https://pharmastore.informa.com/product/triumeq/>.

Molina J-M, Clotet B, van Lunzen J, Lazzarin A, Cavassini M, Henry K, Kulagin V, Givens N, de Oliveira CF, Brennan C. 2015. Once-daily dolutegravir versus darunavir plus ritonavir for treatment-naïve adults with HIV-1 infection (FLAMINGO): 96 week results from a randomised, open-label, phase 3b study. *Lancet HIV*;2(4):e127-e136.

Morse E, Fujiwara RJT, Mehra S. 2018. The association of industry payments to physicians with prescription of brand-name intranasal corticosteroids. *Otolaryngology – Head and Neck Surgery*; 159(3):442-448.

Morse E, Hanna J, Mehra S. 2019. The association between industry payments and brand-name prescriptions in otolaryngologists. *Otolaryngology – Head and Neck Surgery*; 161(4):605-612.

Murshid MA, Mohaidin Z, Yen Nee G, Fernando Y. 2016. Physician perceived value as a mediating variable between marketing mix strategy and physician satisfaction. *Asia Pacific Journal of Marketing and Logistics*; 28(5):780-806.

Murshid MA, Mohaidin Z. 2017. Physicians' perceptions towards brand medicine and its effect on prescribing: a narrative review. *Journal of Generic Medicines*; 0(0):1-27.

Sullivan T. 2014 GSK Chinese Bribery Scandal Ends in \$489 Million Fine, Executive Sentenced. *Policy & Medicine*. Updated in 26th of May 2018. Accessed in 10th of February 2021. Available at: <https://www.policymed.com/2014/09/gsk-chinese-bribery-scandal-ends-in-489-million-fine-executive-sentenced.html>.

Toroski M, Kebriaeezadeh A, Esteghamati A, Karyani AK, Abbasian H, Nikfar S. 2019. Patient and physician preferences for type 2 diabetes medications: a systematic review. *Journal of Diabetes & Metabolic Disorders*; 18:643-656.

U.S. Food and Drug Administration. 2018. Step 4: FDA Drug Review. *FDA*. Updated in 1st of April 2018. Accessed in 10th of February 2021. Available at: <https://www.fda.gov/patients/drug-development-process/step-4-fda-drug-review>.

Annexes

Questionnaire

Q1	Qual das seguintes opções melhor descreve a sua especialidade?	[Escolher opção]
Q1	Medicina interna (com valência em infecciologia)	1
Q1	Doenças Infecciosas	2
Q2	Qual o tipo de hospital em que exerce a sua prática clínica?	[Escolher opção]
Q2	Hospital Universitário	1
Q2	Hospital Central/Distrital	2
Q3	Em que etapa da sua formação se encontra?	[Escolher opção]
Q3	Médico especialista	1
Q3	Médico interno da especialidade	2
Q4	É responsável pela decisão terapêutica e prescrição da mesma em doentes com infeção por VIH?	[Escolher opção]
Q4	Sim	1
Q4	Não	2 [Agradecer e terminar]
Q5	Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si, para os seus doentes naïve?	[Resposta aberta]
Q6	Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si, para os seus doentes naïve, durante a pandemia de COVID-19.	[Resposta aberta]
Q7	Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si, para os seus em que mudou a terapêutica, antes da pandemia de COVID-19	[Resposta aberta]
Q8	Indique por ordem de preferência os 3 regimes antirretrovíricos preferenciais/mais utilizados por si, para os seus em que mudou a terapêutica, durante a pandemia de COVID-19.	[Resposta aberta]

INTENÇÃO DE PRESCRIÇÃO

Q9	Nos próximos 12 meses, qual é a sua intenção ou percepção de futura utilização dos regimes antirretrovíricos para o tratamento de doentes com infeção por VIH diretamente tratados por si:	[Escolher opção em linha]				
Q9	Regimes antirretrovíricos					
		Diminuir	Manter Inalterado	Aumentar	Não irei prescrever	Não aplicável /Disponível
Q9	BIC/TAF/FTC	1	2	3	4	5
Q9	DRV/c/TAF/FTC	1	2	3	4	5
Q9	DTG/3TC/ABC	1	2	3	4	5
Q9	DTG + 2NITRs	1	2	3	4	5
Q9	DTG/3TC	1	2	3	4	5
Q9	RAL + 2NITRs	1	2	3	4	5
Q9	DOR/TDF/3TC	1	2	3	4	5
Q9	DOR + 2NITRs	1	2	3	4	5
Q9	RPV/TAF/FTC	1	2	3	4	5
Q10	Quando institui um regime antirretrovírico quais os atributos que valoriza?	[Resposta aberta]				
Q11	Por favor classifique os seguintes atributos de regimes antirretrovíricos relativamente à sua importância na decisão terapêutica	[Escolher opção em linha]				
Q11	Eficácia	Nada importante	Pouco importante	Neutro	Importante	Muito importante
Q11	Barreira à resistência	1	2	3	4	5
Q11	Segurança	1	2	3	4	5
Q11	Comodidade para o doente	1	2	3	4	5
Q11	Preço	1	2	3	4	5
Q11	Origem (empresa produtora)	1	2	3	4	5

Q1 2	Por favor ordene os seguintes laboratórios de acordo com a clareza e assertividade na comunicação dos atributos anteriormente descritos (ver atributos)	[Ordenar opções]
Q1 2	Abbvie	1
Q1 2	Gilead Sciences	2
Q1 2	Janssen-Cilag	3
Q1 2	MSD	4
Q1 2	ViiV Healthcare	5
Q1 3	No ano de 2019, participou em sessões clínicas de algum dos laboratórios listados? (ver lista)	[Escolher opção]
Q1 3	Sim	1
Q1 3	Não	2 [Passar para Q14]
Q1 3.1	Relativamente ao ano de 2019, ordene os seguintes laboratórios, do qual participou num maior número de sessões clínicas para o laboratório em que participou num menor número de sessões clínicas	[Ordenar opções]
Q1 3.1	Abbvie	1
Q1 3.1	Gilead Sciences	2
Q1 3.1	Janssen-Cilag	3
Q1 3.1	MSD	4
Q1 3.1	ViiV Healthcare	5
Q1 4	No ano de 2019, algum dos laboratórios listados lhe possibilitou a participação em congressos nacionais? (ver lista)	[Escolher opção]
Q1 4	Sim	1
Q1 4	Não	2 [Passar para Q15]
Q1 4.1	Relativamente ao ano de 2019, ordene os seguintes laboratórios, do laboratório que lhe possibilitou a participação num maior número de congressos nacionais para o laboratório que lhe possibilitou a participação num menor número de congressos nacionais	[Ordenar opções]
Q1 4.1	Abbvie	1
Q1 4.1	Gilead Sciences	2
Q1 4.1	Janssen-Cilag	3
Q1 4.1	MSD	4
Q1 4.1	ViiV Healthcare	5
Q1 5	No ano de 2019, algum dos laboratórios listados lhe possibilitou a participação em congressos internacionais? (ver lista)	[Escolher opção]
Q1 5	Sim	1
Q1 5	Não	2 [Passar para Q16]
Q1 5.1	Relativamente ao ano de 2019, ordene os seguintes laboratórios, do laboratório que lhe possibilitou a participação num maior número de congressos internacionais para o laboratório que lhe possibilitou a participação num menor número de congressos internacionais	[Ordenar opções]
Q1 5.1	Abbvie	1
Q1 5.1	Gilead Sciences	2
Q1 5.1	Janssen-Cilag	3
Q1 5.1	MSD	4
Q1 5.1	ViiV Healthcare	5
Q1 6	No ano de 2019, participou em algum evento de educação médica contínua patrocinado por algum dos laboratórios listados? (ver lista)	[Escolher opção]
Q1 6	Sim	1
Q1 6	Não	2 [Passar para Q17]
Q1 6.1	Relativamente ao ano de 2019, ordene os seguintes laboratórios, do laboratório que mais promove eventos de educação médica contínua para o laboratório que menos promove eventos de educação médica contínua	[Ordenar opções]
Q1 6.1	Abbvie	1
Q1 6.1	Gilead Sciences	2
Q1 6.1	Janssen-Cilag	3
Q1 6.1	MSD	4
Q1 6.1	ViiV Healthcare	5
Q1 7	Durante o ano de 2019, para qual (quais) das seguintes empresas foi mais vezes palestrante em reuniões/eventos promocionais? Poderá escolher mais do que uma opção	[Escolher opção]
Q1 7	Abbvie	1

Q1 7	Gilead Sciences								2
Q1 7	Janssen-Cilag								3
Q1 7	MSD								4
Q1 7	ViiV Healthcare								5
Q1 7	Não fui palestrante em reuniões/eventos promocionais de nenhuma das empresas listadas								6
Q1 8	Por favor indique a importância da sua presença em sessões/reuniões clínicas para os seguintes atributos	Nada importante	Pouco importante	Neutro	Importante	Muito importante		[Escolher opção em linha]	
Q1 8	Melhor entendimento dos atributos e benefícios do medicamento promovido pela empresa farmacêutica patrocinadora	1	2	3	4	5			
Q1 8	Melhor entendimento dos doentes que mais poderão beneficiar do medicamento promovido pela empresa farmacêutica patrocinadora	1	2	3	4	5			
Q1 8	Fortalecimento da relação com a empresa farmacêutica promotora	1	2	3	4	5			
Q1 9	Por favor indique a importância da sua presença em congressos nacionais e internacionais para os seguintes atributos	Nada importante	Pouco importante	Neutro	Importante	Muito importante		[Escolher opção em linha]	
Q1 9	Melhor entendimento dos atributos e benefícios do medicamento promovido pela empresa farmacêutica patrocinadora	1	2	3	4	5			
Q1 9	Melhor entendimento dos doentes que mais poderão beneficiar do medicamento promovido pela empresa farmacêutica patrocinadora	1	2	3	4	5			
Q1 9	Fortalecimento da relação com a empresa farmacêutica promotora	1	2	3	4	5			
Q2 0	Nas reuniões/eventos promocionais em que foi palestrante, qual o seu grau de experiência clínica com o medicamento promovido?							[Escolher opção]	
Q2 0	Baixa								1
Q2 0	Média								2
Q2 0	Elevada								3