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Ethical Challenges Related to Marketing Drugs

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Abstract

Drugs have unquestionably become a key factor in the progress of human health and the considerable prolongation of life extent. There are numerous signs showing that the advertising of medicines can actually affect understanding, attitudes, and expectations of patients in relation to the specific drug. It is therefore crucial that the pharmaceutical industry implements the highest ethical standards of good laboratory, clinical, and manufacturing practice. The health-care and well-being of patients should be the first priority. The promotion of drugs must be done in an ethical, accurate, and balanced way, while not being misleading. The proper assessment of the risks and benefits of the product use must be ensured. Medical doctors should always consider evidence-based medical facts and medical scientific knowledge in order to avoid prescribing specific drugs uncritically and under the influence of the pharmaceutical industry.

Keywords

Drugs; prescribing; ethics; patients; marketing.

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Abstract
Drugs have unquestionably become a key factor in the progress of human health and the considerable prolongation of life extent. There are numerous signs showing that the advertising of medicines can actually affect understanding, attitudes, and expectations of patients in relation to the specific drug. It is therefore crucial that the pharmaceutical industry implements the highest ethical standards of good laboratory, clinical, and manufacturing practice. The health-care and well-being of patients should be the first priority. The promotion of drugs must be done in an ethical, accurate, and balanced way, while not being misleading. The proper assessment of the risks and benefits of the product use must be ensured. Medical doctors should always consider evidence-based medical facts and medical scientific knowledge in order to avoid prescribing specific drugs uncritically and under the influence of the pharmaceutical industry.

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I. Introduction

Drugs have unquestionably become a key factor to the progress of human health and the considerable prolongation of life extent. Nowadays, the pharmaceutical industry uses the highest standards of good laboratory; clinical, and manufacturing practice, thus providing

users with adequate data on their products. This way, significant steps have been taken to ensure a compliant and ethical interaction between physicians and patients on one side and the representatives of the pharmaceutical industry, on the other [1].

The most profitable pharmaceutical products require notable annual financial expenditure solely for marketing. Moreover, at the end of the process, marketing expenses can notably increase the initial development costs of the drug. This implies that the manufacturer must be continuously involved in scientific research, medical education, health policy, the media, professional associations, patients' associations, etc.

It is now clear that advertising medicines can greatly influence the understanding, attitudes, and expectations of drug users in relation to the specific drug. Therefore, in some circumstances, drug advertising can be considered inappropriate and unnecessary, considering that the focus of this type of promotion is usually based on the emotional experience of the consumer in relation to an existing illness. Thus it is necessary to prevent the inappropriate increase of patient expectations associated with the potential therapeutic efficacy of the prescribed drugs.

Providing scientifically valid, accurate, and balanced information on medical products should be paramount for any pharmaceutical company. Promotion must therefore be ethical, balanced, accurate, and not deceptive. The information in promotional materials must support an adequate estimation of the risks and benefits of the drug use and must also inform on its proper and timely use [1].

An intense promotion of the drug immediately after its registration (including promotional, but not always scientific information) was associated with inappropriate drug–prescribing activities amongst physicians. Therefore, doctors should always take into account accepted medical facts and related scientific knowledge in order to avoid prescribing specific drugs uncritically, and under the pressure of the pharmaceutical industry. Thus, it is essential to have an adequate control (done by relevant professional associations) of possible fees, substantially-expensive gifts, or other privileges provided by pharmaceutical companies to doctors.

There is no doubt that pharmaceutical companies must always maintain the highest ethical standards and, when promoting drugs,

professional advertisers should adhere to the highest ethical standards and maintain objectivity based on medical facts [2]. It is essential that the drug information is up-to-date, which means that any information on therapeutic efficacy, adverse drug reactions and contraindications must mirror up-to-date scientific views [2]. The selection and further interpretation of scientific evidence regarding an individual medical product should receive the highest level of expertise. It is therefore necessary to ensure that any material used in the promotion does not conflict with the existing advertising regulations of a particular country. In addition, it is necessary to have a balance between motivating and appealing drug promotion in relation to the medically-supported accuracy of the information and messages provided. Finally, it should be underlined that non-critical drug prescription always carries the risk of denying drugs intended for patients in need of urgent health care.

II. Patients and drug marketing

There are increasing methods that the drug advertising industry uses to significantly influence the attitudes and expectations of patients. In most cases, the public is responsive to rapidly increasing health information resources (conventional news media, internet advertising, or social networking); however, it often has no reliable way of assessing the accuracy of health information presented in the media or in direct-to-consumer advertising (DTCA) [3]. The problem is not the availability of information, but rather in reliable information. Consequently, although the public has more access to health information than ever, patients are increasingly vulnerable to potentially-deceptive information [3].

The term "personalized medicine" implies that the right drug should be prescribed to the right patient at the right time [4]. Therefore, assertive drug marketing (which usually leads to uncritical prescription of drugs) should be restricted, while inappropriate stimulation of patient expectations should be prevented. Still, autonomy is a fundamental ethical foundation of current medicine and highlights the necessity of each individual to be in charge of their own well-being [5]. As a result, drug consumers have more privileges and opportunities considering preferential treatment choices. Accordingly, many patients have certain expectations regarding the care they want to receive [3]. This choice depends on personal or family wishes, beliefs, past

experiences of the self and others although the patient often makes no genuine effort to understand evidence-based medical facts. Moreover, in today's electronic environment, an increasing number of patients use the Internet in anticipation of more comprehensive and accurate drug-related information [6].

Direct-to-consumer advertising (DTCA) mirrors the patient's growing role in making decisions about the prescribed drug, the need for more detailed information, and ultimately the distrust in providers. It is therefore not surprising that the audience of DTCA sees it as a fitting extension of patient empowerment, whereas opponents discard it as unsuitable and misleading [7]. Specifically, supporters claim that DTCA: (a) provides educational information, (b) improves doctor-patient relationships, (c) enhances adherence to prescription drug protocols, (d) stimulates competition, and (e) leads to lower drug prices. Opponents argue that: (a) consumers lack the expertise to evaluate the quality of ad content, (b) the promotional feature of advertising will not efficiently transfer all risk information, (c) it will impair the doctor-patient relationship, (d) it will lead to increased drug selling prices, (e) it will lead to increased liability and litigation; and (f) it will promote increased use of drugs [7]. It seems that DTCA risks creating unrealistic expectations for patients and conflicts of interest for physicians [8].

Three DTCA categories are usually recognized and overall accepted: (a) advertisements where a specific product must be presented through a brief summary with a fair balance of benefits and risks; (b) help-seeking advertisements where information on diseases or conditions is provided to encourage consumers to consult their doctors on treatment options; however specific prescription drugs or treatments cannot be mentioned, nor can the advertisement contain links to materials identified with a specific product; and (c) reminder advertisements where materials provided cannot contain or suggest the clinical role of the product [7].

DTCA-related ads are often persuasive, as ads connect to their target audiences by means of emotions [9, 10] and by emphasizing pharmacological efficacy, simple use, adequate symptom control, and innovative features – although not the costs [11]. Because of the strong subjective influence of drug marketing in choosing a specific pharmacological treatment, problems in the doctor-patient relation in the drug selection process seem inevitable; however, physicians who

listen carefully, communicate effectively, and show compassion and concern are nevertheless important for the decision of each and every patient [12].

III. Medical doctors and the drug marketing

As treatment options are constantly increasing, medical doctors need to be up to date with scientific innovations, including new pharmaceuticals. Thus the interaction of physicians with pharmaceutical companies can commonly take several forms, such as detailing (providing information on new drugs through direct visits by pharmaceutical representatives to physicians), industry gift-giving, dispersing free drug samples, or attending industry-sponsored meals and events. In addition, medical doctors are involved in industry-funded research, they obtain royalties to recommend or use medical devices, give consultancy services, play an active role in advisory boards, prepare industry-sponsored presentations, or attend industry-supported medical educations [13]. Communication between pharmaceutical companies (key players in the development and manufacture of medicines) and the doctors who prescribe their drugs is essential for the appropriate, effective, and rational use of prescription pharmaceuticals [1].

It is essential that the information provided by pharmaceutical companies is scientifically accurate and fair; moreover, all interactions between pharmaceutical companies and doctors should be transparent at all times and be in the benefit of the patient care [1]. Unfortunately, inappropriate drug prescribing is largely the result of the aggressive drug promotion immediately after registration, such as organizing various forms of educational meetings with a promotional, but not always a scientific character. However, aggressive marketing could be diminished by stimulating the off-label use of drugs [14]. This would ensure that a doctor's practice is not influenced in any way, such as by financial support from pharmaceutical or other commercial companies [15].

It is therefore obvious that the relationship between the pharmaceutical industry and the medical profession enhances the potential of doctors to be involved in conflicts of interest [14].Gifts from the pharmaceutical industry most probably generate potential conflicts of interest that can affect the doctors' decision making,

jeopardizing professional objectivity and potentially compromising patient welfare [16]. Doctors who do not primarily take into consideration the acknowledged medical facts and scientific achievements of a particular drug, but prescribe it without criticism under the influence of the pharmaceutical industry, are a typical example of medical conflict of interest.

The conflict of interest is the dichotomy between the professional responsibility and the personal interest of a person in a position of trust. Conflict of interest is typically characterized by a set of circumstances where conflicts arise between two duties (two value systems). These would include: (a) primary, professional duty (in medicine for patients and general public welfare), and (b) secondary, personal interest (as a rule economic, but also professional, including expert recognition, scientific project support, or academic advancement funding). In such circumstances, a physician may decide in accordance with their personal rather than the general interest, which usually depends on the assessment of the likelihood of the secondary interest affecting and damaging the professional duty [17].

The management of conflicts of interest includes several points. First, transparency should be paramount through a straightforward declaration of conflict of interest. So, if the pharmaceutical company pays the physician directly or indirectly for medical research, this should be disclosed in any publication containing relevant research findings [15]. Any potential conflict of interest should be disclosed in case of financial support connected to professional activities, including lectures, presentations, publications, or development of clinical services. Secondly, sponsoring research and educational programs should involve the existence of several sponsors in order to avoid direct payments to individuals. Thirdly, accommodation, trip expenses, and other comparable activities related to educational/scientific programmes should be modest; however, small value gifts can be allowed.

Because pharmaceutical companies invest significant financial resources to promote new products to medical doctors (by means of gifts, free samples, educational seminars, entertainment, consulting arrangements, etc.), an adequate control by relevant professional associations is required [18]. Professional associations should provide their members with assistance and guidance at any times, on matters

such as the suitable level of cash benefits, gifts, etc. It would also be beneficial to establish a relevant public registry. After all, the public must be better informed about the influence of the pharmaceutical industry on the medical profession and advocate the necessary adjustments [14].

IV. Marketing drugs and ethical standards – the promotion

In reaction to the changing business environment, the pharmaceutical industry has made notable efforts to ensure that their marketing and promotion routines are compliant with ethical standards [19]. Marketing can be any information, activity, practice, or communication intended to increase the prescription rate, supply, sale, or consumption of a medicinal product [20]. The promotion *per se* presents the composition, effect, and administration of a medicinal product, and it is only performed for and by healthcare professionals who are qualified to prescribe and sell medicinal products [20]. The most frequent promotions come in the form of written or verbal information on drugs. Written drug information refers to information communicated in written words, pictures or sound, via all media, whereas verbal drug information covers information transmitted in person by representatives of pharmaceutical companies [21]. This means that such information can be provided in combination with personal visits, visits to clinics, symposia, training seminars, conferences, and different other meetings.

The most common way of passing relevant information on a specific drug is detailing. The traditional function of detailing is to provide a physician with medical information, which ranges from simple awareness-building to detailed technical information [22]. Professionals involved in the promotion process should comply with the highest ethical standards and maintain objectivity based on medical facts. The selection and elucidation of scientific facts relating to a particular pharmaceutical or other medicinal product should be at the highest level. For example, this aspect is clearly reflected in the assessment of the benefit versus risk ratio in the specific drug prescribing process, especially if a drug with a significant number of potential adverse reactions is prescribed. This is why any promotion must support the rational use of drugs by objectively presenting them without amplifying their properties [23]. In other words, without a

justified reason, the marketing must not use the word *safe* or imply that the product has no adverse effects, or that its use is not linked to the risk of addiction [24].

In order to enable physicians to build their own opinion on the therapeutic worth of the medicinal product of interest, the information and documentation supplied with the medicinal products during marketing practice must be exact, balanced, fair, objective, and suitably complete. The information must be based on the state-of-the-art assessment of scientific evidence [20]. It must be ensured that any material used in the promotion does not conflict with the existing national advertising regulations of a particular country. This means that marketing must enclose neither violence, sexual behaviour, criminal actions (or any reference to them), nor offensive or tasteless expressions [24].

The distribution of free drug samples is a well-known method of promotion. Free samples of pharmaceuticals can only be disseminated to individuals eligible to prescribe or dispense them, who actually prescribe the drug of interest, consequently benefiting from the chance of becoming familiarized with the pharmacological product [24]. Several conditions must be fulfilled during this process [15, 23]. Namely, free samples are only provided on an exceptional basis and for the purpose of gaining experience with such a product; each sample cannot be larger than the smallest product presentation on the market; each sample must be marked with *free medical sample - not for sale*; and, finally, each sample must be accompanied by a copy of the summary of product characteristics (SmPC).

When promoting a new pharmaceutical product, the balance between interesting and attractive promotion must be found in relation to the medically-based accuracy of the information and messages delivered. It is necessary to ensure that the public, doctors, pharmacists, and patients always have accurate information on the medicine since non-critical drug prescribing always carries the risk of depriving drugs from patients who actually need health care. Accordingly, the extension of previously-established pharmacological indications to mild or transient disorders or the identification and classification of new clinical entities without scientific evidence should be avoided. The distribution of medicines over the Internet, especially those that avoid the legal frameworks adopted, should be under continuous control. Moreover,

mailing lists must be always updated, and any request from physicians to be removed from promotional mailing lists must be promptly answered [23]. When conducting market research, particular attention must be paid to protecting the privacy of all the participants who participated in the research, and the questions asked must respect the principle of objectiveness. This also implies that market research should not affect individual patients' treatment [24].

Individuals and institutions responsible for protecting the general population's health should not become an extended hand of drug manufacturers. It is therefore necessary that the legislation be continuously a key element in the management of all irregularities related to: (a) the process of drug registration (for example, lack of necessary information); (b) intentionally slowing down the registration process in order to obtain additional funding from suppliers; (c) bias in the selection of members of drug registration commissions and other regulatory bodies; and (d) theft and fraud in the drug distribution chain, including health facilities. In order to prevent the above irregularities, it is necessary to stimulate legislative reforms aimed at the formation and active implementation of anti-corruption laws, as corruption can radically affect the well-being and everyday lives of millions of people worldwide [17].

V. Advertising drugs and ethical issues - the general public

Only non-prescription drugs can be marketed to consumers, with the exception of distributing public information on vaccination campaigns [24]. Generally speaking, marketing communication is any activity and provision of information that is directly relevant to the business of a company, irrespective of the form and means in which it is delivered and performed in order to influence the attitude and conduct of the communication addressee [20]. For example, recent Canadian legislation supports two types of advertisements to the general public: (a) reminder ads, which include only the brand name without mentioning health claims or product use; and (b) disease-oriented ads, which discuss a specific condition, but unclear treatment [25].

An advertisement for a pharmaceutical must contain the following information [24]: (a) the name of the medicine along with the name of the pharmacologically active substance (if the drug of interest contains only one active ingredient), all in accordance with the national

legislation on medicines and medical devices; (b) indications for use; (c) the information necessary for the correct and safe use of the medicine, as well as any special precautions, interactions, and adverse effects; (d) a clear, readable, and comprehensively written, drawn or spoken warning to the patient or user to carefully read the instructions , and to consult a physician or pharmacist about the potential risks, as well as adverse reactions; and (e) the name of the marketing authorization holder, importer or marketer.

Marketing practice involving the general public must always implement the highest ethical standards [20]. This means that marketing practice will: (a) never discredit the pharmaceutical industry; (b) be executed with a focus on the particular nature of a medicinal product and the professional standing of the recipient; (c) not be abusive, offending, decisive, or aggressive; (d) be concise and consistent with the grammatical rules and orthography, as well as proper style of the language used; (e) be easily understood by consumers for whom the advertising is intended; and (f) be subject to reasonable self-control and moderation.

When advertising a drug or medical device, the general public should not be led to the impression that: (a) the drug does not have adverse reactions; (b) it is not necessary to consult a physician before taking the medicine; (c) medical examination, advice, or surgical intervention may be avoided by using the drug; (d) taking the medicine guarantees success in treating the disease; (e) particular medicine is better than another drug; (f) medicine should be taken even when there are no signs of illness, implying that it improves health; (g) the health of individuals not taking the medicine will be impaired, (h) because of its natural origin, the medicine is harmless and effective; (i) the medicinal product represents food, cosmetics, or other objects of general use; and (j) the recommended drug may be replaced by another drug [20, 24].

Currently, the United States and New Zealand allow advertising of prescription drugs [26]. On the other hand, the European Union restricts all advertising of prescription drugs, including television and print advertisements [27]. In particular, it should be forbidden to advertise the following drugs to the general public: (a) medicines that are issued with prescription; (b) the medicines issued at the expense of the health insurance fund; (c) drugs containing opioid or psychotropic substances; (d) drugs for tuberculosis; (e) drugs for sexually-transmitted

diseases; (f) drugs for infectious diseases; (g) medicines for chronic insomnia; and (h) medicines for diabetes and other metabolic diseases.

Finally, in advertising medicinal products to the general public is not permitted if it displays children taking medicine without the presence of adults. Moreover, advertising of the medicinal product to the general public should not be exclusively or mainly directed at children. Furthermore, it is not permitted to collect and disseminate personal data on the disease of a particular person, diagnoses, therapeutic procedures, especially medicines that have been used.

VI. Advertising drugs and ethical issues - the professional public

A worldwide and important ban related to advertising pharmaceuticals or introducing a new use of an existing medicine, is that the drug cannot be promoted before the regulatory marketing authorization was issued [1]. It is broadly accepted that advertising materials for the professional public must be labelled with the wording "solely for the professional public." Moreover, marketing must be based on the most recent summary of product characteristics (SmPC), which encompasses the factual basis for information on the drug [2, 24]. Nonetheless, doctors should not rely merely on promotional literature from pharmaceutical representatives for information on specific drugs, but should seek independent and evidence-based sources of information on the benefits and risks before actually prescribing them [15]. It is certain that patients can only benefit from medical doctors who are aware of the recently-approved and clinically-effective treatments that can, for example, induce fewer adverse reactions or improve adherence [28].

Professional associates (advertisers with usually a degree in medicine, dentistry, pharmacy, or veterinary medicine) can promote the medicinal product to the professional public. Advertisers must receive special training in basic and clinical pharmacological knowledge on the medicines they promote. The pharmaceutical company is obliged to provide continuous education for the professional associates who perform the promotion. And *vice versa*, the advertisers promoting the medicinal product are obliged to provide all information concerning any reported adverse effects on the medicinal product to the pharmaceutical company. Importantly, sales representatives should not

use any incentive or tactic to get an interview with a doctor; furthermore, under no circumstances, should they pay for access to a healthcare professional [15]. While promoting a product to the professional public, it is neither allowed to encourage prescribing, issuing, or purchasing specific medicines, nor to offer money in cash, high-value gifts, or to promise or provide privileges or rewards. In case the relationship also involves medical research, the doctor must make sure that the relationship with the pharmaceutical company neither affects the study itself, nor its design or the interpretation of any obtained findings. This relationship should be reported to the relevant ethics committee, and explicitly quoted in future publications, and at the relevant scientific meetings [15].

As for scientific meetings, pharmaceutical companies have substantial financial resources for payments to medical doctors in the form of meals, gifts, and educational materials, as well as speaker and consulting fees. These payments usually compensate physicians for their clinical and scientific input and support them in educational meetings, but they are also used for promotional purposes [28]. Many national codes cover issues related to the support of healthcare professional attendance at medical conferences. In particular, the main purpose of the meeting must be scientific and professional in nature, and any conference packs/meals/conference gifts provided must be secondary to that purpose. The venue itself should encourage the scientific or educational purpose of the meeting [1, 5]. In other words, the main focus of the event must be on research and pharmaceutical information, or other relevant medical training, meaning that participants should spend most of the time in the scientific programmes/sessions/trainings offered. The event must not be organized in venues celebrated for entertainment or luxury [24]. Thus, the choice of the location must be rational with regard to the purpose of the meeting, and leisure resorts, as well as places known for their exclusivity, must be avoided [2]. Finally, any hospitality associated with an event shall be reasonable and restricted to the economical travel arrangements, meals, simple accommodation, and genuine registration fees [23, 29].

There is a considerable ethical concern that gifts from the pharmaceutical industry to individual healthcare providers could compromise their objectivity and integrity associated with their primary

ethical duty of putting the interests of patients first [16]. Although physicians may generally express negative to neutral attitudes towards pharmaceutical representatives, in addition to creating the so-called reminder effect, a constant interaction develops a routine of benevolence between a sale representative and the medical doctor, which may be later translated to a positive physician prescription performance [22]. This is not surprising, as the recipient of a gift often experiences three types of responsibilities towards the giver: (a) grateful conduct (i.e., acceptance of the gift and expression of gratitude); (b) grateful use (i.e., in accord with the giver's intention), and (c) reciprocation [16]. Moreover, one should bear in mind that gifts place people in binding personal relationships that generate vague and undefined moral obligations [16]. For all preceding reasons, doctors should not accept gifts (including hospitality) from pharmaceutical or other commercial companies, excluding reasonable fees for any work they do as part of a contractual arrangement with a company [15]. Moreover, providing low-value promotional aids (pens, pads, etc.) has long been a routine of pharmaceutical advertising, and international rules still permit inexpensive promotional aids, provided they are applicable to the practice of the healthcare provider [1].

VII. Conclusion

Instead of the classical concluding remarks, we would like to list the eight principles of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) which, in our opinion, reflect the minimum standards of many worldwide codes regardig the pharmaceutical industry's ethical interaction during the drug marketing process [30]. The eight principles are as following: (1) The health-care and well-being of patients are the first priority of pharmaceutical companies; (2) Pharmaceutical companies shall comply with high standards of quality, safety, and efficacy as determined by regulatory authorities; (3) Pharmaceutical companies' interactions with stakeholders must always be ethical, appropriate, and professional; nothing should be offered or provided by a company in a manner or on conditions that would have an inappropriate influence; (4) Pharmaceutical companies are responsible for providing accurate, balanced, and scientifically-valid data on products; (5) Promotion must be ethical, accurate, balanced, and must not be misleading; information

in promotional materials must ensure proper assessment of the risks and benefits of the product and its appropriate use; (6) Pharmaceutical companies shall respect the privacy and personal information of patients; (7) All clinical trials and scientific research sponsored or supported by companies will be conducted with the intent to develop knowledge that will benefit patients and advance science and medicine; pharmaceutical companies are committed to the transparency of industry-sponsored clinical trials in patients; and (8) Pharmaceutical companies should adhere to the applicable industry codes in both spirit and letter; to achieve this, pharmaceutical companies will ensure that all relevant personnel are appropriately trained.

Acknowledgements

The Ministry of Education and Science of the Republic of Serbia and the Fogarty International Centre at the U.S. National Institutes of Health (NIH) supported this article through grants 175073, and 2 R25 TW008171-06A1, respectively.

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