

# OFF-LABEL USE OF MEDICINAL PRODUCTS

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## 1. INTRODUCTION

Legal regulations concerning the use of medicinal products are an extremely significant issue for at least three groups of entities that are involved in a broadly understood process of providing medical services: patients, physicians and pharmaceutical drugs producers. A mistake made in the real legal norms regulating this field may have far-reaching consequences for the appropriate exercise of rights and obligations of each of those entities; in particular, it may have a considerable impact on the appropriateness of the process of treatment. Such a risk occurs especially in case of untypical situations and these include the use of medicinal products for an indication that is not contained in the Summary of Product Characteristics (SPC), i.e. off-label.

The article aims to present the legal state in the field of admissibility of off-label use of medicinal products for indications not contained in the SPC. In accordance with currently binding regulations, the issue raises many doubts and there is no uniform opinion on the requirements for lawfulness of the use or prescription of off-label products. In my opinion, such activities are legal, if general rules of healthcare services provision are complied with.

The first part of the article explains a few issues constituting a basis for further discussion of the possibility of administering/prescribing medicinal products not contained in the SPC. Opinions on the issue expressed so far are presented in the next section. In the third part, I present my view on the issue and try to justify it.

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## 2. EXPLANATION OF BASIC ISSUES

The first concept that requires explanation is “medicinal product”. It is defined in Article 2(32) of the Act of 6 September 2001: Pharmaceutical law.<sup>1</sup> In accordance with its content, a “medicinal product” means a substance or a mixture of substances advertised as one having the characteristics that allow preventing and treating illnesses that people or animals suffer from or administered in order to diagnose or to restore, improve or modify physiological functions of an organism by means of pharmacological, immunological or metabolic activities. The definition raises a series of doubts and has been subject to numerous judgements, including ones issued by the European Court of Justice.<sup>2</sup> However, an analysis of them would go beyond the scope of this article and is not necessary to understand the subject matter. It is also worth pointing out that in accordance with Article 26(1) of the Act of 6 September 2001: Provisions introducing Act: Pharmaceutical law, Act on medical products and Act on the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products,<sup>3</sup> in the event pharmaceutical drugs or medicines are referred to in the binding regulations, they should be understood as medicinal products laid down in Pharmaceutical law. A similar provision is found in Article 2(10) of the Act of 12 May 2011 on reimbursement of medicines, foods for special medical purposes and medical devices,<sup>4</sup> in accordance with which the concept of “medicine” used in statute means a medicinal product as defined in the Pharmaceutical law. In accordance with the definition laid down in Pharmaceutical law, the terms “medicinal product” and “medicine” are used as synonyms in the article.

Another concept that needs explanation is the “Summary of Product Characteristics”. The term is also used in Pharmaceutical law. In accordance with Article 10(2.11), the Summary of Product Characteristics is an element of documents submitted in the process of applying for authorisation for marketing a medicinal product. Article 11(1) lays down the data that must be contained in the document. Giving up an analysis of details, one should point out that this is any thorough information about a medicinal product, including its characteristic features that make it possible to determine in what situations and in what way it should be used and what consequences it may have. The data are determined based on clinical trials.<sup>5</sup> It should be mentioned that it is not information about any possible applications of a given medicinal product but only those that are listed in an application for marketing authorisation. An applicant may decide not to apply for authorisation for marketing a given medicinal product for all possible indications because of various reasons (unprofitability of a given therapy, marketing medicines for particular illnesses, a lack of sufficient clinical data at the moment of an application submission, reimbursement of medicines only for some indications).

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<sup>1</sup> Uniform text, Journal of Laws [Dz.U.] of 2017, item 2211; hereinafter: Pharmaceutical law.

<sup>2</sup> See, M. Krekora, M. Świerczyński, E. Traple, *Prawo Farmaceutyczne*, Warsaw 2012, p. 39 ff.

<sup>3</sup> Journal of Laws [Dz.U.] of 2001 No. 126, item 1382, as amended.

<sup>4</sup> Uniform text, Journal of Laws [Dz.U.] of 2017, item 1844.

<sup>5</sup> W. Masełbas, A. Członkowski, *Stosowanie produktów leczniczych poza wskazaniami rejestracyjnymi*, Przewodnik lekarza No. 3, 2008, p. 82.

In general, every medicine authorised for marketing in the territory of the Republic of Poland<sup>6</sup> must have officially approved characteristics, including indications registered for its use.

The off-label use of medicinal products may be defined in at least two ways: a narrow and a broad one. As it was indicated in the Introduction, it refers to the use of medicines for indications that are not registered. It is the narrow meaning of the term off-label and this is how it will be used in the article. However, it should be mentioned that there is a broad use of the term, closer to the English meaning, which also covers the use of a medicinal product that is not in compliance with the provisions of the SPC other than just indications, e.g. prescription regardless of special warnings, a different method of administration or a different dosage.<sup>7</sup>

Another issue that should be explained is connected with the rules physicians should follow in their practice. In accordance with Article 2 of the Act of 5 December 1996 on the profession of a physician and a dentist,<sup>8</sup> the practice of a physician's profession consists in the provision of healthcare services, in particular: examining a patient's health, diagnosing illnesses and preventing them, treatment and rehabilitation of patients, providing medical advice and issuing medical opinions and certificates. The term "healthcare services" is defined in the Act of 15 April 2011 on medical activities.<sup>9</sup> Article 2(1.10) of the Act defines healthcare services as activities serving to maintain, rescue, restore and improve health and other medical activities resulting from the process of treatment or other provisions laying down the rules for their performance. It is indicated in jurisprudence that it is an activity concerning a person's health and undertaken with the use of methods and techniques recognised in medical science as those serving to achieve specified medical aims.<sup>10</sup> Undoubtedly, the concept covers the administration or prescription of medicinal products aimed at improving or maintaining (not worsening) a patient's state of health. Thus, prescribing medicines should be treated as one of the aspects of a physician's job.<sup>11</sup> By the way, it should be highlighted that the act of prescribing medicines does not constitute the substantive provision of healthcare services. The substantive provision of healthcare services includes medicinal products as material things (in accordance with civil law) that most often a healthcare entity provides to a patient and not the process of a therapeutic decision-making concerning their use.<sup>12</sup> However, for the purpose of this article, the latter is most important.

Article 4 of the Act on the profession of a physician and a dentist imposes a particularly important duty on a physician. Pursuant to it, a physician is obliged to

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<sup>6</sup> I omit the issues concerning the way in which a medicinal product is authorised for marketing and the use of unauthorised products, which are of minor importance for the discussion in this article.

<sup>7</sup> O. Luty, *Zaniechanie zlecenia produktu leczniczego poza zarejestrowanym wskazaniem a odpowiedzialność cywilna lekarza – part I*, *Prawo i Medycyna* No. 1, 2014, p. 106.

<sup>8</sup> Uniform text, *Journal of Laws [Dz.U.]* of 2017, item 125 as amended.

<sup>9</sup> Uniform text, *Journal of Laws [Dz.U.]* of 2018, item 160.

<sup>10</sup> B. Janiszewska, *Pojęcie świadczenia zdrowotnego*, [in:] M. Safjan, L. Bosek (ed.), *System Prawa Medycznego*, Vol. 1, *Instytucje Prawa Medycznego*, 2018, p. 1064.

<sup>11</sup> Compare, *ibid.*, p. 1035 ff.

<sup>12</sup> *Ibid.*, p. 1060.

practice following the indications of the current medical knowledge, with the use of available methods and preventive, diagnostic and treatment measures, in compliance with the principles of professional ethics and due diligence. This means that every practicing physician is obliged to permanently broaden his/her knowledge and to study the current developments in the knowledge within the practice. Moreover, this knowledge must be used in the job practice.<sup>13</sup> Current medical knowledge means present standards adopted in the contemporary medical science. Being current means that this knowledge is subject to constant updating resulting from the progress in science.<sup>14</sup> It is not only the state of medical knowledge in Poland but the whole global scientific output available in publications (mainly medical books).<sup>15</sup> At present, the Evidence-Based Medicine is the doctrine that plays an essential role in determining the scope of current medical knowledge. In accordance with its principles, when taking therapeutic decisions, a physician follows reliable and up-to-date results of scientific research.<sup>16</sup> Generally, a randomised clinical trial is recognised as reliable research.<sup>17</sup> In order to get access to current results, physicians must read recognised medical journals. Thus, the obligation to practice following the indications of the current medical knowledge means a requirement to use the latest achievements of medical science as well as a ban on using obsolete methods or those recognised as erroneous.<sup>18</sup> As a result, a physician having the knowledge of new, better methods of treatment should use them in his/her practice. The obligation is limited by availability of methods and means. Thus, a physician shall not be obliged to use a method of treatment, even if it is recognised as a standard procedure, in the event a healthcare institution in which he provides services does not possess the medical equipment necessary to use the method. In such a situation, he should provide a service with the use of the best available methods. However, the norm is not only a limitation of the obligation to act following the indications of the current medical knowledge to the available methods but also (and probably mainly) an obligation to use all available methods and means of treatment. This means that, having a possibility of implementing a better medical procedure, a physician is obliged to use such an opportunity.

It is also necessary to draw attention to Article 45 of the Act on the profession of a physician and a dentist. It imposes an obligation on a physician to prescribe only medicines that are authorised for marketing in the territory of the Republic

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<sup>13</sup> L. Ogiełto, *Art. 4 Ustawy o zawodach lekarza i lekarza dentystry*, [in:] L. Ogiełto (ed.), *Ustawa o zawodach lekarza i lekarza dentystry. Komentarz 2015*, 2<sup>nd</sup> edition, System Informacji Prawnej Legis.

<sup>14</sup> D. Bach-Golecka et al., *Prawa Pacjenta*, [in:] M. Safjan, L. Bosek (ed.), *System Prawa Medycznego*, Vol. I, *Instytucje Prawa Medycznego*, 2018, p. 819.

<sup>15</sup> Obviously, a physician is not obliged to know all publications or research findings. However, it is important what sources he uses in order to solve medical problems he encounters in his medical practice. Compare, R. Jaeschke, D.J. Cook, G.H. Guyatt, *Evidence based medicine (EBM), czyli praktyka medyczna oparta na wiarygodnych i aktualnych publikacjach (POWAP). Wprowadzenie*, *Medycyna Praktyczna*, Special issue 1/1999, pp. 3–10.

<sup>16</sup> W. Masełbas, A. Członkowski, *Stosowanie produktów...*, p. 83.

<sup>17</sup> R. Jaeschke, D.J. Cook, G.H. Guyatt, *Evidence based...*, pp. 6–8.

<sup>18</sup> E. Zielińska, *Komentarz do art. 4 ustawy o zawodach lekarza i lekarza dentystry*, [in:] E. Zielińska (ed.), *Ustawa o zawodach lekarza i lekarza dentystry. Komentarz*, LEX, 2014.

of Poland. Article 45(3) of the regulation allows the prescription of a medicine authorised for marketing in another country but only in exceptional, specially justified situations.

### 3. ARGUMENTS FOR LIMITATION OF ADMISSIBILITY OF OFF-LABEL USE OF MEDICINAL PRODUCTS

Both in the literature and in practice, various opinions are formulated concerning lawfulness of application of off-label medicinal products. There are voices that this activity is inadmissible, admissible under some conditions and those treating off-label administration of medicines as a physician's standard practice.

According to J. Zajdel, off-label prescription of medicines is not in compliance with the binding regulations.<sup>19</sup> This author recognises the data from the officially approved SPC as the only admissible indications to use a medicinal product. As a result, almost every application of a medicine in a different way exposes a physician to liability for infringing law. The legal risk a physician prescribing an off-label medicine faces and the importance of the decision approving the SPC are, in J. Zajdel's opinion, the main arguments against application of medicinal products in the way that is not contained in the registered indications. She says that such an activity may be legal, provided that the following conditions are met:

- all available medicinal products registered for the given indication have already been used in the treatment process;
- the applied therapy has been inefficient;
- the treatment results are insufficient.<sup>20</sup>

J. Zajdel recognises any other instance of off-label treatment as action in the circumstances of a medical experiment and in order to make such action legal, it is necessary to meet the requirements for such an experiment.

There is also an opinion in the literature that, in accordance with the regulations currently in force, off-label application of medicines should be recognised as either a medical experiment or medical service carrying an increased risk.<sup>21</sup> That results from the fact that such treatment is never confirmed by an adequate administrative decision as scientifically proved and authorised to be used. Therefore, the off-label prescription of medicines would be an action carrying a greater risk than in a standard medical procedure.

It should also be pointed out that there are opinions in the doctrine indicating the initial unlawfulness of off-label therapy and its later legalisation by the construct

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<sup>19</sup> J. Zajdel, *Stosowanie produktów leczniczych „off-label” – eksperyment medyczny czy działanie zgodne z prawem?*, *Gazeta Lekarska* No. 12, 2010, p. 36.

<sup>20</sup> *Ibid.*

<sup>21</sup> See, T. Szafrąński, A. Szafrąńska, *Przechadzki po polu minowym – uwagi dotyczące stosowania leków niezgodnie z charakterystyką produktu leczniczego*, *Postępy Psychiatrii i Neurologii* No. 21(2), 2012, pp. 107–115.

of the state of necessity.<sup>22</sup> In such a case, human health or life is the interest protected by law, and the obligation to use a medical product in accordance with the SPC is the interest sacrificed. The obligation must result from the norms of Pharmaceutical law.<sup>23</sup>

W. Masełbas and A. Członkowski suggest assuming that a medicine may be applied in a way different than indicated in the SPC in two situations (apart from clinical trials and a medical experiment):

- if a given indication was mentioned in the SPC of another product containing the same active substance, or
- a given indication was confirmed in reliable clinical trials and described by a competent scientific society or in recognised literature.<sup>24</sup>

It should be noted that these are criteria for recognising a given therapy as part of current medical knowledge rather than an indication of a norm of legal admissibility of off-label product application.

#### 4. ARGUMENTS FOR FULL LAWFULNESS OF OFF-LABEL THERAPY

Eventually, the last group of opinions, in general, recognises the off-label application of medicinal products as fully legal and equivalent to the on-label one from the legal point of view.<sup>25</sup> In my opinion, it is a right stand and, thus, the discussion to follow aims to support it and, at the same time, criticise other opinions.

The first issue on which I would like to focus is the nature of the administrative decision, which is the authorisation for marketing a medicine. In accordance with Article 3(1) Pharmaceutical law, medicines given this authorisation can be marketed. Article 3(3) stipulates that the President of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products must be an authority competent to issue a decision concerning the matter. In accordance with Article 23(2) Pharmaceutical law, the approval of the SPC, i.e. an official confirmation of the data contained in it, is an element of this authorisation. As a result of the decision, a medicine can be marketed in the territory of the Republic of Poland. Article 65(1) of the Act stipulates that medicinal products marketing must follow the rules laid down in statute.

Pharmaceutical law does not define the concept of “marketing”, however, the analysis of regulations makes it possible to assume that it refers to civil law transactions, in particular all forms of ownership transfer (also free of charge) and physical activities such as storing medicinal products.<sup>26</sup> Obviously, the term covers operations of pharmaceutical industry, wholesalers, importers and pharmacies. There are no doubts, however, that the definition does not cover a physician’s

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<sup>22</sup> J. Kanturski, *Leczenie off-label: eksperyment medyczny czy stan wyższej konieczności?*, Prokuratura i Prawo No. 10, 2012.

<sup>23</sup> *Ibid.*

<sup>24</sup> W. Masełbas, A. Członkowski, *Stosowanie produktów...*, p. 85.

<sup>25</sup> O. Luty, *Zaniechanie zlecenia...*

<sup>26</sup> M. Krekora, M. Świerczyński, E. Traple, *Prawo Farmaceutyczne...*, p. 392.

activities consisting in the prescription of medicinal products because it is not part of production- and trade-related activity but part of a process of providing healthcare services.

The above-presented findings show that the authorisation for marketing medicinal products and all the regulations concerning it are not applicable to the process of treatment. They only determine the rules of production, storage and sale of medicines and are binding on entities involved in that activity.

One should mention Article 1 Pharmaceutical law determining the subject matter of the regulation. In accordance with the provision, the Act determines:

- 1) the rules and mode of authorisation for marketing medicinal products, including in particular requirements for quality, efficiency and safety of application;
- 2) conditions of medicinal products clinical trials;
- 3) conditions of medicinal products production;
- 4) requirements concerning medicinal products advertising;
- 5) conditions of medicinal products marketing;
- 6) requirements concerning pharmacies, wholesalers and out-of-pharmacy sale;
- 7) organisation and rules of functioning of the system of supervising and monitoring safe application of medicinal products;
- 8) tasks of the Pharmaceutical Inspection and its bodies' competences.

Therefore, the Act does not regulate the process of providing healthcare services, prescription of medicinal products or application of medicines.

As a result, there is a lack of whatsoever justification of the above-mentioned opinions about an obligation to apply medicines in accordance with the SPC seemingly laid down in Pharmaceutical law. The Act is not applicable to any stages of healthcare services provision, including in particular the prescription of medicinal products. Thus, J. Kanturski is wrong to draw a rule saying that a physician cannot be at variance with the indications in the SPC from Pharmaceutical law<sup>27</sup> because there is no (and should not be) such a rule in this legal act. The Act regulates other matters. Thus, J. Kanturski's considerations concerning the possibility of applying the above norm because of the state of necessity, i.e. the necessity of saving a patient's health or life with the use of off-label therapy, are groundless, because considering a possibility of avoiding a legal norm that does not exist and sacrificing an interest that does not exist is groundless.

Assigning the SPC a special power as an official authorisation for a given therapy or the confirmation of admissibility of the application of a medicine for given indications should also be critically assessed. Although the SPC is subject to approval in the course of authorisation for marketing a medicine, the President of the Office for Registration is not an authority responsible for defining standards of medical procedures. In accordance with Article 2 of the Act of 18 March 2011 on the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products,<sup>28</sup> the President of the Office is an authority competent in matters connected, inter alia, with authorisation for marketing medicinal products and clinical trials.

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<sup>27</sup> J. Kanturski, *Leczenie off-label...*, p. 96.

<sup>28</sup> Journal of Laws [Dz.U.] of 2011, No. 82, item 451, as amended.

His competences do not include any one concerning issuing recommendations for the application of medicines. The President's activities in the course of registration procedure concern marketing a medicine, not its application.

It should be highlighted that the authority acts, as a rule, on the motion filed by a party (Article 9(1) Pharmaceutical law). In accordance with Article 8 Pharmaceutical law, it verifies an application for authorisation for marketing a medicinal product (including the SPC) but only within the scope of the motion and does not examine all the possible applications of that medical product. Simply speaking, if an applicant wants a medicine X to be authorised for sale as a medicine for flu, the President of the Office examines whether the medicine X may be marketed as a medicine for flu. He does not check whether the medicine X might be also marketed as a medicine for tonsillitis, pneumonia, etc. One can even state that it is not examined whether it is admissible to prescribe a medicine for a given indication, but admissibility of marketing for a given indication. The assessment of admissibility of application for a given indication is a physician's task each time. Of course, this last distinction is in some sense theoretical, however, it is worth making in order to explain the real role of the President of the Office.

As a result, in my opinion, it should be recognised that the above-mentioned views assigning a decision of authorisation for marketing a special legal power to recognise a therapy with the use of a given medicine as legal are erroneous. It must be added that the decision of the President of the Office not only depends on the motion but also comes later than the findings of the latest clinical trials.<sup>29</sup> Therefore, assigning the SPC a binding power on the choice of therapy by a physician would often mean permission for non-application of the latest inventions in medical science. The decision of the President of the Office is binding on entities involved in marketing medicinal products, not on people involved in the provision of healthcare services. One should also highlight a general principle of administrative law in accordance with which a decision is binding on the parties to the proceedings (in this case, a responsible entity that is an applicant) and not on an indefinite group of addressees, because it constitutes adjudication in an individual case concerning the parties.<sup>30</sup> Therefore, there are no grounds for stating that the Act is binding on a physician, also because of the nature of this Act.

It is also worth pointing out that there are categories of products that can be marketed without the need to obtain any official authorisation. One can mention made-to-order medication prepared by a pharmacist based on a physician's prescription (Article 3(4) Pharmaceutical law). What clearly results from it is that the legislator assumes that medical professionals are competent to independently decide what substances their patients should be given.

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<sup>29</sup> O. Luty, *Zaniechanie zlecenia...*, p. 114.

<sup>30</sup> J. Borkowski, A. Krawczyk, *Postępowanie zwykłe. Przedmiot postępowania zwykłego*, [in:] R. Hauser (ed.), *System Prawa Administracyjnego*, Vol. 9, *Prawo procesowe administracyjne*, 2017, p. 188.



The Polish legislator, as a rule, does not lay down legal norms regulating standards of medical procedures.<sup>31</sup> Their determination is the competence of science and appropriate professional self-governments or scientific societies.<sup>32</sup> Thus, it seems there is no reason justifying the assignment a binding character to the decisions of the President of the Office in the process of treatment, especially as there is no legal norm in the system of law that would justify it.

The SPC most often constitutes a fragment of current medical knowledge because the data included in it are based on the findings of randomised clinical trials.<sup>33</sup> However, it is not a complete reflection of the current medical knowledge in relation to the specified substance, but only its fragment, in addition, one that has been up-to-date at least a few months before the date of issue of its authorisation decision.<sup>34</sup> Therefore, it is worth looking at the current medical knowledge as a certain collection, of which the SPC is just one (of course, very important) element. We will find research results, articles and course books, which do not have their reflection in the characteristics. A complete review of all these elements may constitute grounds for a physician's therapeutic decision. The determined content of the SPC cannot limit a physician's obligation to act following the current medical knowledge.

Also the suggestion that the necessity of using medicines in accordance with the SPC seemingly results from an attempt to limit physicians' liability cannot be recognised as right. Obviously, one must agree that a physician faces a lesser risk using a medicine on-label than using one off-label. In a situation like this (in case of a therapy failure caused by inappropriate working of a medicine), it would be much easier to prove a producer's liability based on the Civil Code regulations concerning liability for hazardous products and exclude a physician's liability.<sup>35</sup> However, there is a reservation that it concerns a situation in which, in the light of the current medical knowledge, both therapies offer identical opportunities to succeed as well as potential threats. If off-label therapy offers more therapeutic advantages, a physician should choose it. Otherwise, he may be liable for omission to use it.<sup>36</sup>

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<sup>31</sup> Some exception should be pointed out here, e.g. regulations concerning perinatal care, the nature of which raises controversies, and their content was amended many times. See, inter alia, D. Karkowska, *Nowe standardy opieki nad matką i dzieckiem w kontekście prawnej organizacji opieki okołoporodowej w Polsce*, Warsaw 2013.

<sup>32</sup> Stanowisko Nr 67/15/P-VII Prezydium Naczelnej Rady Lekarskiej z dnia 16 października 2015 r. w sprawie projektów rozporządzeń Ministra Zdrowia: 1) w sprawie standardów postępowania medycznego przy udzielaniu świadczeń zdrowotnych z zakresu opieki profilaktycznej nad dziećmi i młodzieżą, 2) w sprawie standardów postępowania medycznego w dziedzinie patomorfologii. Compare, K. Kordus, R. Śpiewak, *Lekarz wobec ordynacji „off-label”*, *Przegląd Lekarski* No. 1, 2015, pp. 40–41.

<sup>33</sup> W. Maselbas, A. Członkowski, *Stosowanie produktów...*, p. 82.

<sup>34</sup> O. Luty, *Zaniechanie zlecenia...*, p. 116.

<sup>35</sup> O. Luty, *Zaniechanie zlecenia produktu leczniczego poza zarejestrowanym wskazaniem a odpowiedzialność cywilna lekarza – part II, Obowiązek zlecenia leku off-label i konsekwencje jego niewykonania*, *Prawo i Medycyna* No. 2, 2014, p. 138.

<sup>36</sup> *Ibid.*

Also, it cannot be assumed that off-label application of a medicine always excludes the liability of its producer or a responsible entity. A medicine remains a definite chemical substance with specific characteristics. Thus, if, in accordance with the current medical knowledge, such a substance works in a certain way, even if it is not contained in the SPC, a producer is liable for its failure to work this way, provided that it results from the product characteristics.

It is worth drawing attention to Article 35a(4) Pharmaceutical law, which stipulates: "A responsible entity, a producer, an entity authorised for wholesale or retail marketing, a physician or other persons authorised to prescribe or provide a medicinal product in accordance with other regulations are not subject to civil or disciplinary liability for the effects of a medical product administration other than medical indications laid down in the authorisation or for the effects of the application of a medicinal product without such an authorisation if such application is connected with authorisation for marketing a medicinal product for a limited period determined by a competent minister of health in accordance with Article 4(8)" (Article 4(8) is applicable in case of natural disasters). Thus, if in case of application of a medicine for not registered indications required in accordance with the decision of the Minister of Health, the statutory provision clearly excludes liability of the entities listed above, it can *a contrario* lead to the conclusion that in other situations the entities can be made liable.

It must be remembered that a producer or a responsible entity has liability for a medicinal product and a physician for the process of treatment. At the same time, physicians should not forget that they have tools that enable them to use adequate legal protection, also in case of application of medicines for not registered indications. It includes obtaining a patient's written consent for a given therapy after the provision of adequate information about it. There are no obstacles to informing a patient that a medicine will be used off-label (of course, the term must be explained in a proper way) and presenting scientific arguments for the choice. In case of a lack of adequate data in the SPC, it is worth finding additional documented grounds for such a therapeutic decision by appropriately justifying it and attaching (if possible) scientific articles or research findings. Of course, first of all the on-label treatment is fully understandable and approved of, provided that it has at least the same value in a given clinical condition as the off-label one.

There is no doubt that off-label prescription of a medicine often matches the conditions of a medical experiment. However, under no circumstances, can one assume this in advance. It depends on the fulfilment of statutory requirements laid down in Article 21 of the Act on the profession of a physician and a dentist. Thus, a therapy should have the features of a new and only partly tried diagnostic, medicinal or therapeutic method. The prescription of a medicine that is not for registered indications, which is confirmed by numerous clinical trials and sufficiently described in medical literature, cannot be recognised as such. A physician choosing such a treatment does not act as an experimenter but has sufficient knowledge that lets him choose that therapeutic method. Thus, if the off-label treatment can be recognised as part of current medical knowledge, it certainly cannot be treated as a medical experiment.

In addition, one can point out that in some situations the off-label therapy may be subject to reimbursement. Therefore, if the legislator admits funding of this type of treatment from the state budget, it is hard to recognise it as banned at the same time. In accordance with Article 40 of the Act on reimbursement of medicines, the Minister of Health may, if it is necessary to save patients' life and health, and there is a lack of other procedures to be used and financed from public funds, issue a decision to reimburse for a medicine used for indications other than laid down in the SPC. It must be remembered, however, that it is an exception that can take place under certain conditions and is only applicable to healthcare services funding. Thus, one cannot draw too far-reaching conclusions based on that. However, together with the above-presented arguments, it supports full admissibility of off-label prescription of medicines following the same rules as the on-label one.

## 5. CONCLUSIONS

The arguments for inadmissibility of prescribing medicines for non-registered indications presented in the article, in my opinion, have no grounds in the legal regulations in force. One cannot also say that clinical practice or a patient's interest support this stand because it would limit a patient's access to some therapies. If we take into consideration the arguments I presented, we must draw a conclusion that off-label application of medicines is admissible and should follow the same rules as the prescription of medicines in accordance with the SPC. Each case should be individually analysed by a physician and a decision made after taking a patient's interest into consideration. The directive to act in compliance with the indications of the current medical knowledge cannot be limited in a way that is different from clearly expressed legal norms, which does not take place in this case. Thus, a physician should take decision based on it and not on administrative acts concerning the registration of medicinal products.

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## OFF-LABEL USE OF MEDICINAL PRODUCTS

## Summary

The aim of the article is to present the Polish regulations concerning off-label application of medicinal products as well as a critical review of opinions of the doctrine on this matter. The author analyses and makes comments on the most important arguments raised in the discussion and makes conclusions that the off-label application of medicines is originally lawful. His justification for the presented opinions is based on the literature and arguments offered for the first time.

Keywords: off-label, application of medicinal products for non-registered indications, medical law

## STOSOWANIE PRODUKTÓW LECZNICZYCH OFF-LABEL

## Streszczenie

Artykuł ma na celu ukazanie polskich regulacji prawnych dotyczących problematyki stosowania produktów leczniczych poza zarejestrowanymi wskazaniami (*off-label*), jak również krytyczny przegląd poglądów doktryny na ten temat. Autor analizuje i komentuje najważniejsze argumenty podnoszone w dyskusji, a następnie wyprowadza wnioski o pierwotnej legalności stosowania leków *off-label*. Uzasadnia to twierdzeniami zarówno już podnoszonymi w literaturze, jak i wskazanymi po raz pierwszy.

Słowa kluczowe: *off-label*, stosowanie produktu leczniczego poza zarejestrowanymi wskazaniami, prawo medyczne

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