ABSTRACT

BACKGROUND: The consent of physicians is an important factor for the successful acceptance of switches. This consent is not part of the official over-the-counter-switch (OTC-switch) procedure in Germany. Physicians’ views on potential switches have never been sought in Germany before.

OBJECTIVES: The aim was to identify potential switch candidates and indications that would be supported by physicians in Germany.

METHODS: Physicians in Germany were invited to complete a survey distributed via the online survey tool of the physician’s journal “Ärztezeitung” asking their opinions on the OTC-switching of further therapeutic groups and active substances. The survey was comprised of 8 questions. Besides some basic parameters the questionnaire included a list of proposals for new switch candidates, a vote on the general acceptance as well as economic and health professional expectations regarding further switches.

RESULTS: In the survey 540 physicians participated within the period from 22 December 2017 to end of January 2018; 43% of responses came from general practitioners. 51% of respondents supported more OTC-switches and agreed that community pharmacies can provide the necessary advice. Just over half of participants (51%) agreed pharmacy-based self-medication was advantageous for patient care. The highest support was for modern non-sedating antihistamines (64%) and nasal glucocorticoids (46%) for treatment of hay fever, proton pump inhibitors (57%) for reflux disorders, as well as triptans (84%) for migraine treatment.

CONCLUSION: Doctors in Germany who responded to the survey are supportive of further switches. Especially for active substances within indications which have already one substance available as OTC. Furthermore, in the opinion of many physicians surveyed, more OTC medicines are an advantage for patient care.
INTRODUCTION

Currently one can see an internationally increasing activity of switches. Germany is part of this trend. The German medicine distribution system has three classifications. First there are the prescription only drugs (Rx), second pharmacy only drugs (Apothekenpflichtig, in this text OTC is used for pharmacy only) and third the products which are commonly offered in a pharmacy but also available in GSL (General Sales List - freiverkäufliche Arzneimittel). To switch Rx to OTC, the consent of physicians has rarely been sought in Germany so far, even though it is an important step for the successful acceptance of OTC-switches. So, the motivations for initiating a non-substance-specific study of this kind were complex. On the one hand, the recent experience with newly switched, now pharmacy-only medicines was positive, at the same time, the burden on the medical profession is constantly increasing, and this puts pressure on physicians. Here, more pharmacy-only medicines could fill a gap between demand and supply. The existing discrepancy is caused by a shortage of physicians on the one hand and a restricted scope of recommendation options for pharmacists on the other hand. Moreover, modern switches bring therapeutic advances directly to the patient. The low-threshold access to medicines in pharmacies enables easy and rapid access to well-established medicines. Additionally the time expended for patients can be less. Besides, there are economic advantages. Both European and German studies show that further OTC-medicines could reduce the burden for healthcare systems.

Although large parts of the European pharmaceutical legislation have been harmonized, the decision whether a medicinal product is only available with a prescription, directly without a prescription in pharmacies or even in mass markets, is – except for centrally approved medicines - purely a decision for EU member states (MS). MS have implemented quite different rules for reclassifications, for the transition from the prescription-only to the pharmacy-only status (‘Rx-to-OTC-switch’ or ‘switch’). An overview of the relevant provisions in the various European countries and the procedure in Germany has been published recently.

In general, the German switch architecture is influenced by the principle ‘safety first’. To meet this principle, it must be critically analysed and discussed before a switch whether the active substance has an acceptable safety profile, allowing the exemption from medical supervision. For this, the simplicity of use is just as important as the easy recognition of a disease by the patient. The safety-first principle leads to a more restrained approach of German authorities to OTC-switches. However, this restraint might be responsible for a remarkable success. During the entire 40 years of the German switch procedures there have been only three ‘reverse’ switches to prescription-only status for safety reasons (terfenadine, astemizole and topical forms of ketoprofen). This means that the switches conducted so far have been perceived to be safe.

There are some critical factors for the successful performance of a switch. One crucial prerequisite is the assessment of possible OTC-switches from the medical perspective.
MATERIALS AND METHODS

2.1 How was the proposal list generated?

The proposal list was generated from active substances and groups of active substances that are already available without a prescription in at least one other country in the world, mostly a country of the European Union. These were identified from the AESGP (Association of the European Self-Medication Industry) database. As antihistamines have in the meantime become OTC in many countries, the list focused on modern second-generation antihistamines, giving desloratadine, levocetirizine and fexofenadine as examples that have already been switched in other countries. Relating to the treatment of hay fever, the assessment of nasal glucocorticoids was examined. In this group the two active substances mometasone and fluticasone have been switched in Germany during 2016. Internationally, other agents from this group, such as triamcinolone (in Germany only available as OTC in topical form for oral ulcers) and budesonide were switched recently. For several years, OTC-preparations for emergency treatment such as salbutamol or epinephrine/adrenaline for acute asthma attacks have been discussed. Due to the switch of a sildenafil-containing preparation in Poland in 2016, medicines for erectile dysfunction (ED) have become the focus of many discussions. A corresponding preparation had previously been switched in 2014 in New Zealand (NZ) and was afterwards switched in the United Kingdom (UK) in 2018. In some countries, antibiotics have also been switched in recent years. In NZ and Australia chloramphenicol for use in eye infections was switched in 2009 and 2010 and trimethoprim for the treatment of urinary tract infections (UTI) in 2012 in NZ. Besides that, topical forms of erythromycin are available as OTC products in Belgium and Poland. The survey explored the application of topical presentations of antibiotic agents for bacterial eye infections, as well as oral presentations for UTIs. Recently, some vaccines for administration by pharmacists have become available without requiring a prescription in many countries. In the UK, this step was completed in 2002, followed by Ireland (2011). Likewise, pharmacists have also been allowed to administer vaccines in most cantons of Switzerland since 2015, when the pharmacist has undergone a special training. In NZ, vaccines for influenza, cholera and traveller’s diarrhoea, meningococcal infections, tetanus-diphtheria-pertussis, and herpes zoster vaccines may be dispensed by pharmacists without a prescription. Finally, survey questions covered preparations against various dermatological, typically chronic relapsing diseases such as herpes cold sores, acne and rosacea. Other candidates were proton pump inhibitors (PPIs), for example lansoprazole and rabeprazole. A second list of proposals contained medicines for the treatment of chronic diseases or long-term medication. The first group included oral hormonal contraceptives (OC), which currently still require a medical prescription in all major European OTC markets, such as UK, France or Germany. Exemptions have only been implemented in some individual State or Provincial jurisdictions of the United States, Canada and in NZ. As a further group of agents for the treatment of chronic diseases the triptans for the treatment of migraine were put on the list, one of the most common and stressful forms of headache. In Germany, so-called ‘attack packs’ with two tablets...
of naratriptan or almotriptan have been available without a prescription since 2006 and 2009, as first in world switches. Further active substances in this group are available as OTC medicines in other countries.

2.2 Design of the nationwide survey/ final questionnaire

The survey comprised a total of eight questions, as detailed below. Besides some basic demographic parameters (e.g. age, medical qualification group, localisation in a score from metropolitan to rural areas) the questionnaire included a list of proposals for new switch candidates, a vote on the general acceptance as well as economic and health professional expectations regarding further switches. As the advice provided by pharmacists is essential for many modern switch products, physicians were asked if from their perspective community pharmacists were qualified to advise the patients properly. In addition, the assessment of the influence of more OTC-switches on the doctor-patient relationship and the patient’s care situation was also undertaken. To gain the most comprehensive picture possible, only drug names and indications, but not specific products, were used.

This final questionnaire was distributed and advertised with help of the physician’s journal ‘Ärztezeitung’ and their online survey tool. The participants had the chance to fill in the questions directly online or to send the extra sheet from the journal back via fax. The online version of the questionnaire was put up at 22nd of December 2017. The extra sheet was sent to the subscribers within the journal edition of 21st January 2018. Due date of all filled in forms was 2nd February 2018.

Overview of questions (translated from German):

1. In the past several Rx-to-OTC-switches have already been implemented. Do you basically support further switches?

2. The following list contains active substances that are available without a prescription at least in one other country. Should these substances from your personal perspective also be reclassified from prescription-only to pharmacy-only status in Germany?

   - Anaphylaxis: epinephrine auto-injectors
   - Acne: other topical agents
   - Short-time treatment of dyspnoea: inhaled β2-agonists (e.g. salbutamol)
   - Erectile dysfunction: PDE-5 inhibitors (sildenafil, vardenafil, tadalafil)
   - Acute urinary tract infections: oral antibiotics
   - Short-term treatment of minor eye infections (conjunctivitis): topical antibiotics
   - Vaccines: (in particular influenza vaccine, vaccination would be performed in pharmacies)
   - Oral herpes: systemic or oral famciclovir
   - Short-term treatment of reflux disorders: further proton pump inhibitors (rabeprazole, lansoprazole)
• allergic rhinitis and urticaria: oral second-generation antihistamines (desloratadine, fexofenadine, levocetirizine)
• allergic rhinitis and urticaria: further nasal glucocorticoids (e.g. budesonide, triamcinolone)
• Short-term treatment of rosacea: topical metronidazole

Active substances for the treatment of chronic diseases or contraception:

• Migraine: further triptans (sumatriptan, rizatriptan, zolmitriptan)
• Lipid-lowering agents: (simvastatin)
• Hormonal contraception: oral contraceptives
• Urinary incontinence (muscarine receptor antagonists)

3. Switch products require additional advices in pharmacies. Can pharmacists provide the necessary advice?
4. Do you see an advantage or disadvantage in an expansion of pharmacy-based self-medication for medical practices?
5. Do you see an advantage or disadvantage in expanding the pharmacy-based self-medication for the patient’s care situation?
6. What impact do you see for the doctor-patient relationship?
7. Do you see in expanding the pharmacy-based self-medication rather a strengthening or weakening of medical competence?
8. Statistic information about
   • age,
   • medical profession and
   • locality of the physician’s office.

RESULTS AND DISCUSSION

3.1 Aim:
The first aim was to involve those who deal daily with pharmaceuticals and patients in such processes. Therefore, a first Germany-wide, prospective survey was conducted within the medical profession. The second aim of the present study was, to identify potential switch candidates and indications that would be accepted by physicians for OTC.

3.2 Results:
In the survey 540 physicians participated within the period from 22 December 2017 to end of January 2018. Fax response was provided by 234 participants. The remaining 306 answers were
given via online tool. The journal ‘Ärztezeitung’ has 49,000 subscribers. That makes a response rate of 1.10%.

The largest subset (232, 43%) of the participants were general practitioners, followed by 65 specialists of internal medicine (12%) and many other qualifications (Figure 2). 163 participants (30%) belonged to other specialist groups not pre-defined, and 40 (7%) did not reveal their qualification. The age distribution of the participants revealed the typical high age of the German physicians, especially those working as general practitioners. 45% of the participants are 60 years or older, another 30% in the age group of 50-59 years (Figure 3). 10% of all participants were younger than 40 years.

Figure 2: Distribution of physicians’ specialist groups - the most dominant group are the general practitioners

Figure 3: Age?
Figure 4: In the past several Rx-to-OTC switches have already been implemented. Do you basically support further switches?

Source: Survey of ‘Arztezeitung’ in cooperation with the University of Kaiserslautern and the German Medicines Manufacturers’ Association (BAH). Survey period: December 2017/January 2018. 540 Participants.

Approximately half of the surveyed physicians support further OTC-switches (Figure 4). 51% of the participants chose the options ‘yes’ or ‘yes, with restrictions’. This reflects a general acceptance by the physicians. The other half of the physicians, 45%, seemed to be more sceptical and answered with ‘rather no’ or ‘no’, 4% did not specify anything. If you take a closer look at the groups of supporters and opponents of further switches you will see, that the supporters are mostly at age under 49 (73% of group under age 49). The ‘opponents’ group is mostly older than sixty (53% of group older than 60).

More than half of the participating physicians (59%) expect an improvement of their position as the point of contact for relevant health problems through more self-medication or expected no impact on the doctor-patient relationship.

The results reveal modest support for further OTC-switches by physicians. 51% of respondents supported more OTC-switches and were convinced that community pharmacies can provide the necessary advice. And half of the participants (51%) agreed on pharmacy-based self-medication as advantageous for patient care (Figure 6).

Figure 6: Do you see an advantage or disadvantage in expanding the pharmacy-based self-medication for the patient’s care situation?

Source: Survey of ‘Arztezeitung’ in cooperation with the University of Kaiserslautern and the German Medicines Manufacturers’ Association (BAH). Survey period: December 2017/January 2018. 540 Participants.
The survey also identified promising candidates for further switch applications from the perspective of physicians (Figure 5). The highest consent scores were obtained for non-sedating antihistamines for hay fever, and topical preparations for acne. Nasal glucocorticoids for treatment of hay fever, proton pump inhibitors for treatment of reflux, and triptans for migraine treatment had support that was a little lower – from just under half of respondents for additional nasal glucocorticoids and triptans to nearly 60% support for additional PPIs for reflux. Oral contraceptives and erectile dysfunction agents had support from just under half of physicians. Statins were supported by nearly a third, vaccines and UTIs around a quarter of respondents.

In general, it can be said that the general practitioners are somewhat more restrained compared to the rest of the specialist groups. For example, considering the indications of acne and vaccines. 58% of general practitioners are positive for OTC-switches in the area of acne and among the remaining groups 66% agreed with ‘yes’ or ‘yes, with restrictions’. The vaccinations show a similar picture. Here, 23% of general practitioners are positive and 32% of the remaining groups of physicians.

### 3.3 Discussion

The study breaks new ground as the first survey of doctors in Germany about potential switch candidates, to our knowledge. One published study explored the opinions of physicians on certain active substances before and after a switch. Several studies have explored the opinions of general practitioners in the UK. The present study however examines the interest in Germany.
Some notable issues arise. There is a valuable discussion to be had on whether easy access to vaccines, e.g. flu vaccination, can be a strategy to persuade the population to accept the offer of a preventive vaccine, and thus achieve the medically desirable higher immunization coverage. In the US, the American College of Physicians and American Society of Internal Medicine supports the idea of pharmacist-administered vaccinations27, so it is interesting to see a different perspective from Germany. Maybe the German physicians fear the consequences and that they might lose their position within the healthcare system.

Further switches are sometimes discussed for the indication of acute UTIs, although the possible switch of antibiotics is also associated with the concern that use in self-medication without medical control by a physician could promote resistance to the active substances28. Nevertheless, antibiotics such as fosfomycin, which was especially mentioned in the survey and is taken orally for cystitis, act only locally in the urinary tract and the bladder29 and hence are unlikely to promote resistance. These could then be a possibility for affected women, in order to initiate an effective therapy quickly. Due to the high proportion of recurrence in this indication, the infection can be easily recognized by the patient30 which is a prerequisite for a proper self-medication. Controlled pharmacist-supply in New Zealand with trimethoprim for cystitis was not associated with overall increased use of antibiotics31. It may be that more information could be provided to doctors to reassure them.

The queries also covered preparations against various dermatological, typically chronic relapsing diseases such as herpes cold sores, acne and rosacea. The advantage of such indications is that they can be easily recognised by the patient, which makes them ideal for OTC. These diseases represent a significant burden for the patient. Substances with sufficient evidence for their efficacy and safety profile are available. So, the patient would have fast low-threshold access to qualified help, and most doctors agreed with a switch for acne. However, their enthusiasm for famciclovir for cold sores, and metronidazole topical for rosacea was limited.

From a global perspective, many other countries have at least one of the questioned active substances as OTC. These include examples which were rated in the present study as not safe and not qualified for OTC-switch. For example, Sildenafil in New Zealand. Men can buy it in community pharmacies after having a short consultation with the pharmacist. Qualitative interviews revealed that the pharmacists are pleased with the controlled pharmacist-supply of sildenafil and they are thinking it is positive for their patients32. Another example could be oral contraceptives. In a study among pharmacists in the Philadelphia area, as stated above, they were evaluated as safe for OTC33. In comparison to the present German study this is a completely different result. The findings from the Philadelphia study may be caused by the availability through pharmacists without a prescription in other individual State jurisdictions of the US33. Additionally, today oral contraceptives are non-refundable by official or private payers in Germany. Consequently, a switch would bring no additional costs for the patients, unless an additional consultation fee is charged. Our finding of low support for a simvastatin switch echoes that of a survey of UK general practitioners23. However,
general practitioners in the UK in 2004 were considerably more positive about chloramphenicol for eye infections and trimethoprim for UTIs than in our survey. Possibly by not stating the agent in our survey the physicians were more cautious in their response. It is possible that UK GPs are more positive about switch, or perhaps increasing antibiotic resistance concerns since 2004 have changed the perspective of physicians.

The potential of further switches is obvious. By offering a wider range of pharmacy-only OTC products, patients could consult the community pharmacist for minor ailments, physicians would be relieved accordingly, and appointments could be more targeted and effective for acute and severe cases. Economic savings for the health system is another potential. This would not change the patient’s relationship with the doctor. The doctor remains the central contact point especially for severe health issues. This opinion is also shared by many of the physicians interviewed. 51% recognize an advantage for patient care through an expansion of pharmacy-based self-medication.

The evaluation of the proposals on the list by the medical profession reveals many parallels with a previous similar survey of German pharmacists, and a further survey among patients. These three questionnaires contained almost the same questions and revealed almost the same outcomes. The patients are also very supportive for further switches, particularly for the indication bladder infection. The most supported indication from the point of view of both health professions is the indication hay fever, closely followed by acne and reflux symptoms/heartburn. In all these indications there are OTC products already on the German market, thus all participants have experience in the correct handling and correct recommendation. This acquired safety in handling could be a reason for the broad support of further switches in these indications. Similarly, physicians and pharmacists agreed on rejecting switches for statins, vaccines and oral antibiotics UTIs. These products should, in the opinion of the participating physicians, continue to be subject to prescription. But there were also some differences between the two surveys of physicians and pharmacists. For example, the rejection of a switch of oral contraceptives was higher in the pharmacist survey (65%) than in the survey of physicians (51%). A similar picture shows within the indication of eye infections. Almost 70% of the pharmacists surveyed were positive for a switch but only 39% of physicians voted positive.

The aim of the present study was to identify potential switch candidates and indications that would be accepted by the physicians. Multiple interesting and important aspects emerged from this endeavour, which should be further supported and developed in the future.

In terms of orientation and scope, this survey is unique in the world, especially when compared with the previous survey of pharmacists. The participating physicians were obviously pleased to be interviewed on this topic. The observed consent for further OTC-switches was not expected. 51% of respondents supported more switches and were convinced that community pharmacies can provide the necessary advice. Different meaning is showed whether switches would bring any benefit or disadvantage to their practices. There are almost the same numbers of supporters who
see a relief and division of labour in the foreground, and opponents who fear poorer patient care.

3.4 Strengths and limitations:

The strengths of the survey were the number of participants, 540, and the range of doctors responding, rather than simply general practitioners, considering there was no incentive given for participation within the survey. If you look at the other mentioned surveys, they are all examining only a few indications, active substances or areas. So, another strength is, that the survey was available for a large group of physicians all over Germany and many different indications and active substances were evaluated.

Figure 1: Distribution of physicians’ specialist groups - an overview in per cent out of 540 answers.

The primary limitation of the survey was the low response rate; physicians not responding might differ from those responding. Additionally, some groups of doctors are very small (Figure 1). Besides that, the sample deviates from the totality of German physicians in age distribution. In 2017 there were about 19% physicians under 35 years old in Germany. But only 10% of the survey participants were under 40 years old35.

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Ethical Statement: This article does not contain any studies with human participants or animals performed by any of the authors.

Results: Detailed information and results can be obtained from the authors.
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