Prescription to Nonprescription Medicines Switch

Q&A

GLOBAL SELF-CARE FEDERATION

WHAT IS **RECLASSIFICATION** OF MEDICINES?

The process of making prescription medicines available without prescription is called widening access or switching and is a normal part of medicines regulation in most developed countries. Most nonprescription or 'Over-the-Counter' (OTC) medicines contain ingredients which have been used for a long time and have long track records of safety and efficacy. Other nonprescription medicines started out as prescription medicines and have been reclassified or 'switched' to nonprescription status after their safety has been established and they are deemed suitable for people to use without medical intervention.

Through prescription to nonprescription switches millions of consumers around the world have benefited from wider and more convenient access to appropriate self-treatment options. This empowerment of individuals in managing their own health will become more important as better self-care is essential to prevent the coming global epidemic of chronic non-communicable diseases.

Worldwide surveys have shown that people are confident in self-diagnosis of minor conditions and have the ability to appropriately treat themselves with nonprescription medicines, with or without intervention from healthcare professionals. Research conducted in the United States shows that 81% of adults use OTC medicines as a first response to minor ailments. [1]

Safety of consumers is paramount for industry, regulators and all stakeholders and there is consensus that in determining whether a condition is suitable for self-treatment and widening access to nonprescription status is appropriate various questions may be asked:

- **Can the symptoms of the condition be recognised by the patient?**
- **Is the illness self-limiting?**
- **Are there any underlying conditions that might be masked by self-treatment?**
- **Does the product have a wide safety margin?**
- **Can the product be used safely without medical supervision?**
- **Could the use of the product lead to misuse, abuse or dependence?**
- **Could the product present a hazard to the community if used unsupervised?**

For the future, prescription to nonprescription switches hold promise for governments by helping to ease pressures on the formal healthcare system. Consumers can treat more of their everyday health conditions without the costs associated with the formal system. Doctors can spend more of their time and attention on more involved illnesses. Pharmacists and other healthcare professionals can utilize their communication skills and clinical knowledge by helping consumers in the area of self-care and self-medication.

WHAT MEDICINES ARE AVAILABLE FOR PEOPLE TO USE **WITHOUT** A MEDICAL PRESCRIPTION?

The Global Self Care Federation and the Association of European Self-Medication Industry (AESGP) websites (www.selfcarefederation.org and www.aesgp.eu) include a comparison of over 200 ingredients and their legal classification status in 39 countries. Opportunities still remain in many countries to provide citizens with better access to nonprescription medicines. Of the 224 ingredients on the AESGP list, available in some form without a prescription, only 5 out of 39 countries list more than 50% of them as nonprescription medicines. Furthermore, 11 out of 36 country markets have less than 30% of these ingredients available without a prescription. [2]

WHAT ILLNESSES CAN PEOPLE **SELF TREAT** WITHOUT MEDICAL INTERVENTION ?

Progress from a situation where all illnesses are taken to a doctor to a position where people can manage many for themselves is an evolutionary one. It begins with the treatment of self-limiting illness through self-treatment of chronic or recurring illness that may need a medical diagnosis in the first instance to treatments that prevent illness.

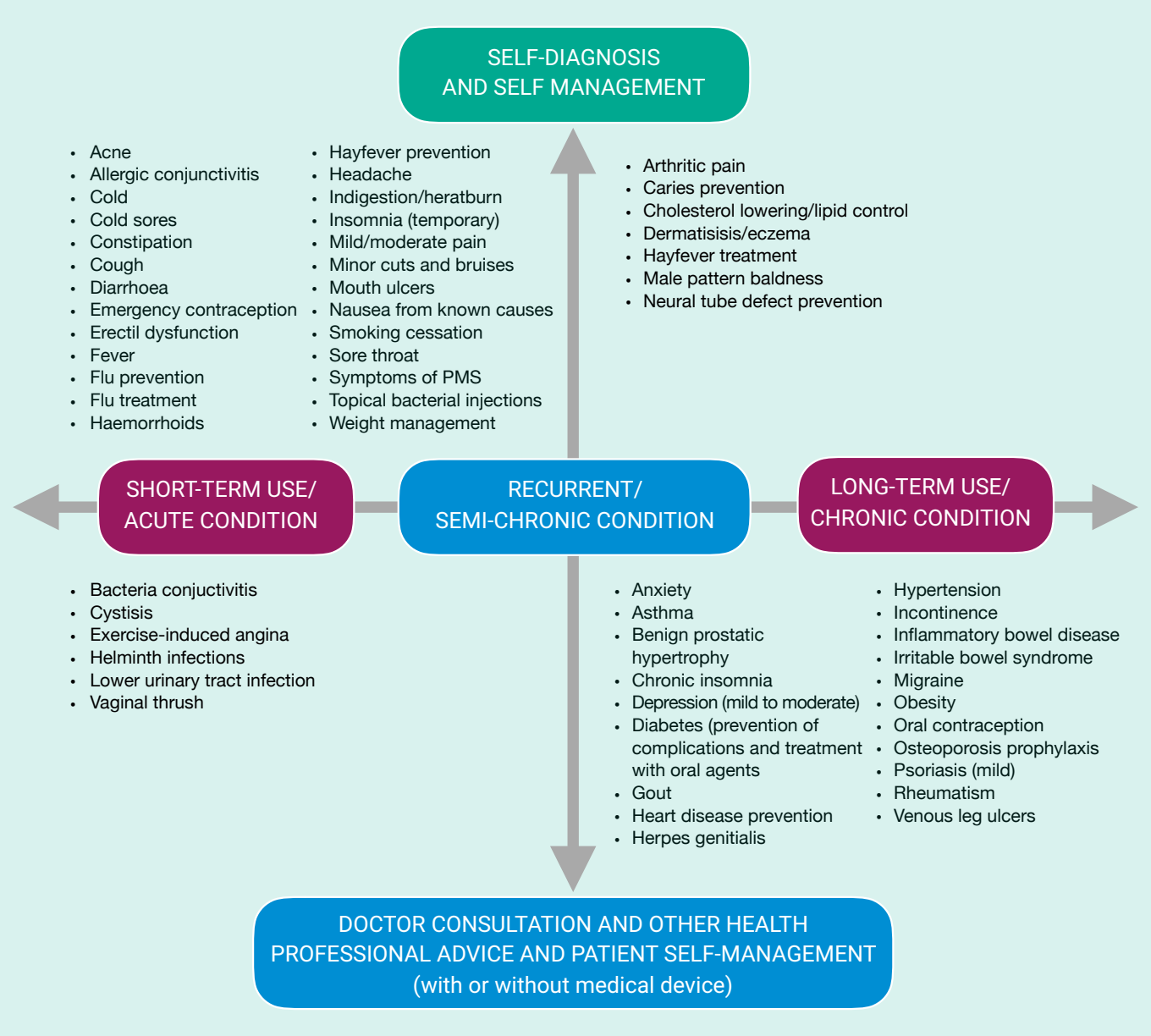
In 2001, a task force supported by the EU and including industry representatives of the European umbrella organizations of medical doctors, pharmacists, and consumers as well as national associations of medical doctors and pharmacists, and regulatory authorities developed a chart in which indications were mapped according to the following two dimensions:

- **Is it an acute condition requiring short-term use of a medicinal product, or a semi-chronic condition requiring recurrent use of a medicinal product or a chronic condition requiring long-term use of a medicinal product.**
- **Is it a condition that can easily be self-diagnosed and self-managed or a condition that requires prior consultation of and diagnosis by a medical doctor? Is there a test which can be administered by the consumer himself?**

Figure 1 on next page, presents the results of this exercise, mapping both the range of indications which are currently suitable for self-medication in the top half of the chart, and identifying other indications for consideration.

FIGURE 1: CONDITIONS MAPPED ACCORDING TO SELF MANAGEMENT POTENTIAL AND CHRONICITY

This chart has provided a good basis for discussion between stakeholders as to potential indications for switch. Most countries recognise the indications in the top left as the base for self-medication. More developed countries with the appropriate infrastructure have allowed products to be nonprescription when they treat recurring illnesses which may need a diagnosis in the first instance. There is also growing acceptance of the role of nonprescription medicines for prevention of illness. [3]



Stichting AESGP Foundation, Development of an information policy for medicinal products, January 2002

HOW DO PEOPLE SELF-CARE FOR RECURRING OR CHRONIC CONDITIONS – WHAT IS **COLLABORATIVE CARE**?

Collaborative care is the term used for self-care of conditions which need an initial diagnosis. This means that people usually go to the doctor when presenting symptoms of these conditions for the first time. Once the doctor has established a medical diagnosis, people are capable of recognising the symptoms when they recur and will treat the condition with a medicinal product available without a prescription. In this setting, the pharmacist can also provide valuable information and advice on appropriate treatment and the need to consult a doctor again in certain circumstances that will vary according to the condition.

Nonprescription treatments for conditions such as irritable bowel syndrome and vaginal candidiasis allow far more people to have access to effective medicines to manage conditions that reduce quality of life and can be debilitating. Experience has shown that people are well able to manage these conditions provided they have the right information and appropriate diagnosis and assistance from a health professional.

In 2013 the FDA approved Oxytrol for overactive bladder having been presented with evidence that showed women were able to correctly select and use the product in accordance with pack directions. In the UK the MHRA approved tamsulosin for benign prostate hypertrophy (BPH) provided patients were encouraged to check the diagnosis with a doctor. In New Zealand sildenafil became available without prescription in 2014 from pharmacies whose staff have had special training to help identify at-risk men including smokers, men with self-reported high cholesterol, diabetics and men with a previous coronary problem. [4]

These examples show that the doctor is not excluded from self-care. Wider access to nonprescription medicines has not only enabled people to self-treat it has encouraged them to seek medical advice for a diagnosis at the appropriate time. Perhaps even more importantly, these changes are bringing effective treatments to the knowledge of the public for conditions that often go untreated because people are not aware that products exist or that conditions can be managed.

WHO has endorsed this approach to widening the indications for self-treatment. In its guidelines on self-medication, WHO considered that “if prescription status has been considered preferable because a physician can perform certain diagnostic or sensitivity tests before selecting the product, ensure good patient compliance, or take steps to avoid adverse effects or interactions, it is important to know whether in practice physicians can and do perform these tasks. If commonly they do not, the provision of the medicinal product in self-medication form with appropriate warning instructions may provide at least as great a measure of safety for the user. [5]

HOW ARE MEDICINES **EVALUATED** FOR THEIR SUITABILITY FOR USE IN SELF CARE ?

Virtually all applications for reclassification from prescription to nonprescription status are submitted by the manufacturer who will go on to market the product. The type of application can range from simple products with long established drugs for short term use in through to switches involving new drugs for established indications or even new drugs for new indications so decisions have to be made on a case by case basis. It is simply not possible to define precisely what data are required in each and every case.

A significant new tool for evaluating the suitability of medicines for self- care has been developed and published by Brass et al. [6] It sets out an approach based on a systematic review of benefits of a potential switch as well as the possible safety concerns.

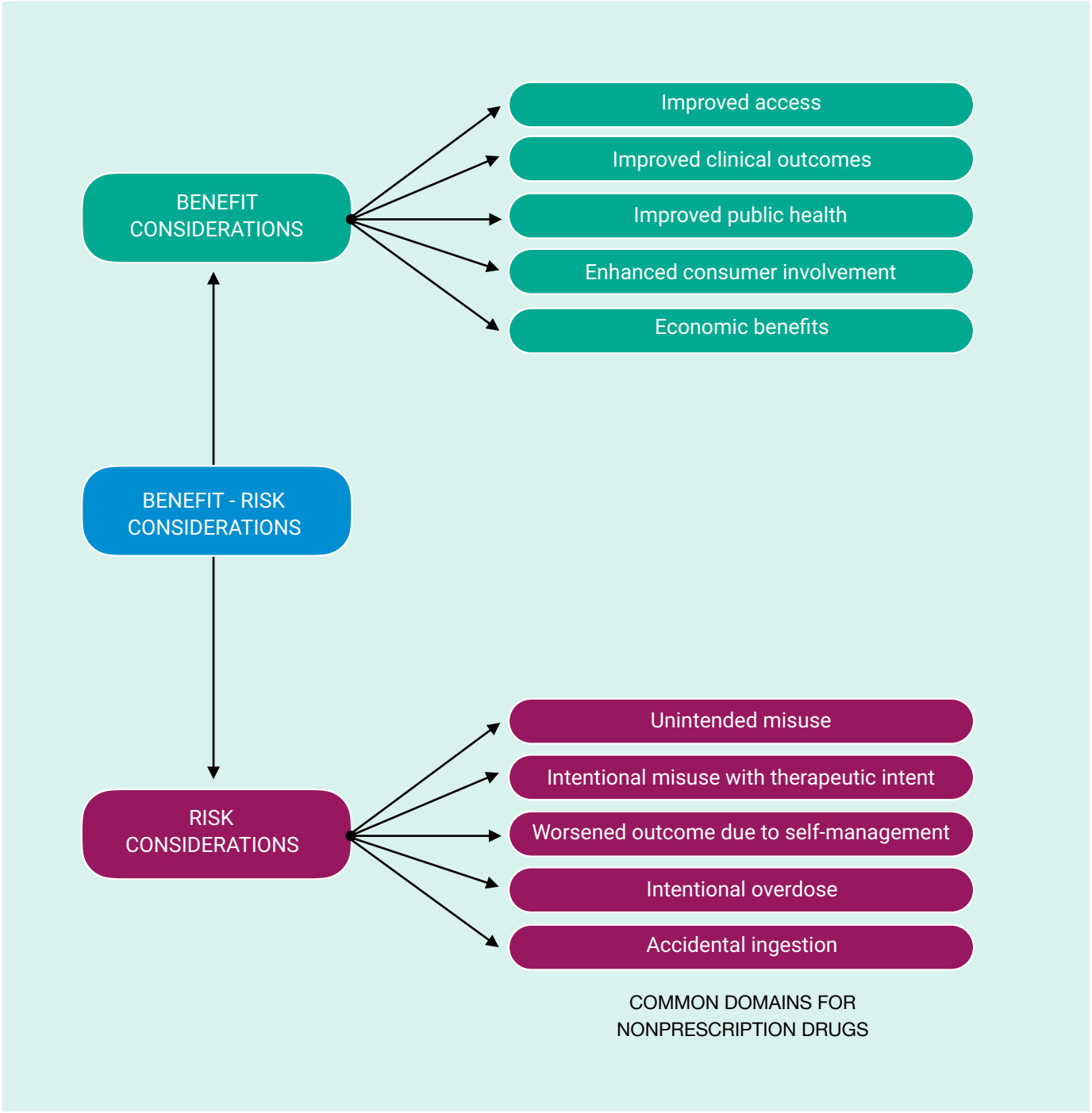
The model is based on the premise, established by WHO, that the safety profile of a molecule when used in the same or similar demographic groups is the same whether it is prescription or non-prescription. It focuses the safety and efficacy review on differences relating to the management of the illness or inappropriate use of the medicine and also takes into account other products in the same therapy area and associated benefits such as early treatment, speed of action and convenience.

The model encourages dialogue between the manufacturer sponsoring a switch and the regulatory agencies and expert committees who have the task of reviewing and approving it. It has been incorporated into guidelines produced by the United Kingdom, New Zealand, Finland, Australia and Canada.

Effective dialogue between regulator and manufacturer before a dossier is prepared will identify any gaps in the information available and agreement on ways of filling those gaps. Most countries with a switch programme involve scientific committees to provide advice to the regulatory agencies.

Increasingly manufacturers are encouraged to involve medical opinion leaders in the development of the application and their views are shared with the regulatory agency. Where this has happened the potential for last minute concerns to be raised are minimised. Early advice would allow the necessary information to be generated before a switch is submitted and allow consideration and testing of additional safeguards where this is necessary such as restriction of sale through pharmacy or behind the counter for a period of time, additional warnings and information on the pack or a programme of post marketing surveillance. Such restrictions should of course be required only where there is a risk which justifies it.

FIGURE 2: PRE REVIEW EXAMPLE OF VALUE TREE [6]



HOW IS THE **SAFETY OF NONPRESCRIPTION MEDICINES** ESTABLISHED AFTER MARKETING?

Once medicines have been reclassified, they remain subject to ongoing safety review, although in approving a switch, a country is in effect making a balanced judgment on the benefit/risk ratio of individual ingredients, and for self-medication as a whole. As expressed by the WHO:

> *"It is not assumed, and it cannot reasonably be assumed, any more than in other fields of pharmacotherapy, that benefit will always be assured or the risk will be entirely eliminated. Since the risk factors vary in degree from one individual to another and one situation to another, there may be patients who will suffer inconvenience or harm. However, provided that in the population as a whole the degree and incidence of such harm are not disproportionate to the benefits offered, the risk will be acceptable."* [7]

The basic safeguards that are implemented include the selection of the most suitable and safe substances, doses and dosage forms, the provision of special information or public education, the control of advertising and package texts, and the definition of distribution channels.

For pharmacovigilance, safeguards are in place for switches, via global signal detection by manufacturers and regulators, supplemented by consumer reporting of adverse effects. One method for tracking what is known about ingredients is through such adverse event reporting systems.

Even where reporting systems are not formally required by a government for well-known, established non-prescription medicines, nongovernmental systems, poison control centres, and published case studies in medical literature serve a similar function.

Only long-term experience with sufficient high exposure of the population can uncover rare or delayed adverse events. As science advances and more is known about an ingredient, if new evidence develops leading authorities to believe an ingredient on nonprescription status can no longer be considered safe or effective for nonprescription use, they can return it to prescription status or even remove it from the marketplace altogether. The fact that very few ingredients have required such reverse switches is testimony to the careful evaluation given to applications for switch. In the UK, for example, the antihistamines terfenadine and astemizole were reclassified from prescription-only to pharmacy status but in 1997 were switched back to prescription only when the possibility of causing torsade de pointes was appreciated. In general, however, there is very little evidence to show that current switches and switch policies have caused public health problems in any country.

WHAT REGULATIONS **CONTROL THE CLASSIFICATION** OF MEDICINES?

Most developed countries have regulatory processes in place to control the classification of medicines as prescription or nonprescription. The Global Self-Care Federation strongly supports the development of effective switch programmes which have a clear and transparent regulatory framework including:

- **A definition of a prescription or nonprescription medicine and criteria to be applied**
- **An understanding of which conditions are suitable for self-care in their populations,**
- **A list of prescription or nonprescription ingredients,**
- **A framework for developing a dossier to support an application for switch,**
- **A benefit risk approach to the evaluation of switches**
- **Encouragement of innovation through data protection**
- **Use of the same branding for prescription and nonprescription versions of a product with advertising to the public part of the information mix**

As nonprescription medicines are no longer under patent there is a lack of intellectual property rights for switch even though the development of a switch medicine can be time consuming and require the generation of new trials and studies.

The Global Self-Care Federation calls for data protection to cover any aspects of a switch reclassification programme which is an essential part of the benefit: risk evaluation of the product including the following:

- **Clinical trials which are relevant to the dose and/or indication for which the product is to be used including meta analyses and review of original trial materials**
- **Review of company-held adverse reaction reports undertaken to establish safety and efficacy when the product is going to be used without medical advice**
- **Patient and consumer studies to support the formulation and/or dose to be reclassified**
- **Label comprehension studies**
- **User studies or real life trials to establish safety when used without medical advice**
- **Risk management and evaluation studies both pre- and post-marketing**

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