SWITCH

Prescription to nonprescription medicines switch

WSMI

WORLD *self*-MEDICATION INDUSTRY

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Executive summary

“Through prescription to nonprescription switches, hundreds of millions of consumers around the world have benefited from wider and more convenient access to appropriate self-treatment options.”

Medicines available without a prescription are called nonprescription or ‘Over-the-Counter’ (OTC) medicines. There are many different nonprescription medicines, many of which have been available for a long time and have long track records of safety and efficacy. Examples are nonprescription medicines used in cases of mild to moderate pain, cough and cold, minor skin problems, and heartburn. Other nonprescription products are newer, and started out as prescription medicines which have been ‘switched’ to nonprescription status. Examples are the triptans for migraine, proton pump inhibitors for prevention of acid indigestion, anti-virals for cold sores and antihistamines for hay fever.

This booklet is about this ‘switching’ – the conversion of prescription medicines to nonprescription status, increasing access to safe and effective medicines which patients and consumers can use without always having to go to a healthcare professional.

In some countries, such as Australia, New Zealand, Finland, France, Sweden and the UK, there is a graduation in the level of availability of nonprescription products. There can be some sub-divisions in the nonprescription category such as a “behind the counter” class – where there is a need for pharmacist assistance; pharmacy “self-selection”, or “general sale” through any retail outlet. Although this booklet focuses on the switch of prescription to nonprescription status for medicines, the term ‘switch’ may also be used for reclassification in terms of access in countries where these categories exist.

Responsible self-medication with nonprescription medicines is the most prevalent form of medical care in the world. An increasing number of 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. An estimate in 2002 was that over 92% of people had used at least one nonprescription medicine in the previous year, and 55% had used more than one. Through prescription to nonprescription switches, hundreds of 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 increasingly important as better self-care is essential to prevent the coming global epidemic of chronic non-communicable diseases.

In determining whether a condition is suitable for self-treatment, and switching of prescription medicine 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, as consumers can treat more of their everyday health conditions without the costs associated with the formal system. Future switches can enable doctors to spend more of their time and attention on more involved illnesses and 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.

This booklet reviews the history of switch and its public health aims and benefits, using actual examples and country case studies, and explores the conditions and regulations needed to create a successful country switch programme.

Switch and the global emergence of nonprescription medicines

Section I

“In the public health domain, citizens are increasingly taking greater control of their own healthcare… they are becoming more demanding and more pro-active in their choices and becoming advocates of their own life.[1] ”

Although there has been increased recent attention to global switches, the reclassification trend is not altogether new. Many prescription-to-nonprescription switches now have a long record of bringing new self-medication opportunities to people, and a solid track record of safety in use. Older switches with a long safety record include:

- Acetaminophen / paracetamol – switched in the 1950's.
- Nasal decongestants and antihistamines – switched in the 1970's.
- Athlete's foot products – switched in the 1970's.
- Ibuprofen – switched in the 1980's
- Nicotine Replacement Therapy (NRT) – switched in the 1990's

U.S.A

In the United States prescription and nonprescription medicines were differentiated for the first time in 1951 with the Durham-Humphrey Amendment. This amendment defined the criteria for prescription drugs, to be used only under a doctor's supervision. All other medicines were eligible to be sold over the counter. In 1962, the Kefauver-Harris Drug Amendments were introduced to tighten controls – manufacturers now had to prove not only safety, but also effectiveness for the product's intended use. The requirement was applied retrospectively from 1938. During a substantial process of medicines evaluation in the USA, FDA staff and other stakeholders again recognised that there were some medicines that were safe to use without a doctor's supervision.

1 European Commission DG Health and Consumer Protection Future Challenges, Paper 2009-2014.

Europe

Until 1980, the conditions generally considered as suitable for people to treat themselves without the intervention of a doctor were quite limited. They included mild to moderate pain, coughs and colds, constipation and minor skin problems such as cuts and bruises. In the last 20 years however, people in Europe have shown a growing willingness to take responsibility in health-related matters. This attitudinal change was reflected in a gradual change in European health policies, with governments recognising the importance of developing and taking advantage of the potential offered by this change in behaviour on the part of their citizens. Governments actively encouraged this increased individual responsibility for health, in the early part of the 1990s, approving the move of a growing number of ingredients from prescription-only to nonprescription status.

In 2001, the European Commission funded a research project for Industry entitled "Development of an information policy for medicinal products[2]". The principal objective was to examine the information needs of both the public and healthcare professionals in case the range of conditions that can be treated with nonprescription medicines was to be extended to categories currently not available for self treatment. This project identified the necessary stages in the development of a policy geared towards a citizen-centred approach to public health that would give individuals more responsibility for the management of their own health.

The principles of switch have also been supported by the World Health Organization (WHO) in a study of self-medication in Europe. The conclusion of the studies was for a framework of orderly development including reforms in pharmacy professional education and practice[3].

[2] http://www.aesgp.be/ResearchProject/FinalReport.pdf

[3] Lund L, Dukes G, eds. The role and function of the pharmacist in Europe. Report of a WHO working group. Groningen: Styx Publications

Worldwide

An increasing number of governments have recognized that switches can make a major contribution to public health. In Mexico in 1998, the Ministry of Health authorised 31 ingredients for switching to nonprescription status. An international comparison of the prescription/nonprescription status of the ingredients was the main element in the decision.

In China, between 2004 and early 2006, the SFDA classified 4542 drugs as nonprescription, including 3548 Chinese herb-formulated medicines and 994 chemical medicines. In March 2006, it was estimated that 25% of the marketed drugs in China were nonprescription medicines.

In Australia, a list of schedules denoting the level of access permitted for various 'drugs and poisons' has been officially published since 1986. Drugs, or substances for therapeutic use, are included in Schedules 2, 3 and 4. Of these, medicines containing substances from either Schedule 2 or 3 are considered to be nonprescription, but can only be purchased from a pharmacy. Nonprescription medicines containing substances exempt from scheduling are available as general sale items and may also be purchased from non-pharmacy retail outlets.

Since 1986:

- Approximately 65 substances have been switched from prescription to Schedule 3 status – these medicines may only be bought in a pharmacy following consultation with a pharmacist
- Over 30 substances have been switched from prescription to Schedule 2 status – these medicines may only be bought in a pharmacy
- There have also been a number of reverse switches to prescription status

Over the years, many schedule entries have been 'fine-tuned' or substances have been shifted between the various nonprescription schedules or exempted from scheduling, thereby enabling the medicine to be purchased from retail outlets other than pharmacy. It should be noted that 'switches', whether to a higher or lower schedule, may be undertaken for either specific indications/pharmaceutical dosage forms/dosages of a substance, or for a substance in general.

In Japan, the Ministry of Health and Welfare issued in 1967 a notice on the classification of medicines, dividing them into prescription and nonprescription. In 1983, the first prescription to nonprescription switch was approved. Switching was further encouraged in 2002, with the publication of the Interim Report on the Linearization of OTC by the Ministry of Health, Labour and Welfare (MHLW). In 2007, the MHLW announced the introduction of a prescription to nonprescription switch scheme and a review by the Pharmaceutical Society of Japan of 20 switch candidates, including anti-allergy drugs, NSAIDs, glucose absorption inhibitors and ACE inhibitors. With further responses from other stakeholders including doctors' representatives, the MHLW in August 2008 invited pharmaceutical manufacturers to consider seven ingredients to be switched.

In Canada, there has been a gradual evolution of the switch process over the past few decades. During the 1980's a number of ingredients (e.g. benzoyl peroxide, hydrocortisone, ibuprofen) were switched after wide consultations with stakeholder groups following initial recommendations from expert advisory committees formed by the federal department 'Health Canada'. Since the 1990's, all prescription to nonprescription switches in Canada have been initiated by sponsoring companies through the preparation of Supplemental New Drug Submissions. Once a decision to remove the requirement for a prescription is made by Health Canada, the National Drug Scheduling Advisory Committee – an advisory group to the provincial governments – makes a recommendation on the place of sale for the switched ingredient (i.e. Schedule II – behind the dispensary in licensed pharmacies, Schedule III – front shop of licensed pharmacies, or Unscheduled – sale through any outlet). In early 2009, the Natural Health Products Directorate of Health Canada began consultations on a list of eleven prescription drugs, including l-tryptophan, l-carnitine and lovastatin, which it proposes to switch to nonprescription natural health product status.

Today, many classes of ingredients have been switched in a variety of countries, with the authorities in the UK, Germany, Australia and the US taking a lead (Box 1).

Box 1 Some examples of worldwide switches include:

- Non steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, diclofenac, naproxen. These can be used for rheumatic pain, migraine, mild to moderate pain and dysmenorrhoea and sore throats
- Antihistamines such as acrivastine, cetirizine and loratadine for prevention and treatment of hay fever.
- H2 antagonists such as cimetidine and ranitidine for acid indigestion and heartburn
- Proton pump inhibitors such as omeprazole and pantoprazole for heartburn and acid indigestion
- Vitamin D_3 analogues such as calcipotriol for psoriasis
- Levonorgestrel for emergency hormonal contraception
- Antifungals such as fluconazole for vaginal thrush; amorolfine for nail infections and terbinafine for athlete's foot
- Antivirals such as penciclovir and aciclovir for cold sores and oseltamivir for influenza
- Simvastatin for lowering cholesterol and prevention of coronary heart disease
- Triptans for migraine
- Antimicrobials such as chloramphenicol for bacterial conjunctivitis and azithromycin for chlamydia
- Orlistat for weight management and obesity

The WSMI and the Association of European Self-Medication Industry (AESGP) websites www.wsmi.org and www.aesgp.be include a comparison of over 200 ingredients and their legal classification status in 37 countries (see Appendix). Opportunities still remain in many countries to provide citizens with better access to nonprescription medicines. The Appendix illustrates that of 224 ingredients available in some form without a prescription, only 5 out of 36 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.

Public health aims and benefits of switches

Section II

General benefits of switches

People benefit in several ways if medicines are available 'over the counter', without a prescription. They can visit a pharmacy rather than wait for an appointment with their doctor. They can treat common and troublesome conditions that have easily recognizable symptoms, such as hay fever and cold sores, and reduce the time from the onset of symptoms to the treatment. They can more easily obtain time-critical products such as emergency hormonal contraception which has to be taken early to be most effective.

Interestingly, the significant problem of people treating themselves with prescription drugs (in countries where enforcement of the prescription requirement is insufficient), is reduced by wider availability of nonprescription medicines. A study in Mexico showed a 20% decrease in the degree of self-prescription in the 10 years between 1989 and 1999. This was attributed to the significant number of switches authorised by the Mexican Ministry of Health between 1995 and 1998.[4]

This observation is supported by the statement in the World Health Organization's (WHO) principal guidelines on nonprescription medicines: "*... in some countries a large number of medicinal products originally intended primarily for use under medical supervision are in fact widely sold without prescription. In such instances, recognition of the real self-medication situation and the introduction of appropriate safeguards (e.g. adapted package sizes and texts) may be more in the public health interest than the maintenance of a merely theoretical prescription status. The possibility of considering the reclassification of products to non-prescription status on the basis of experience in other countries should be borne in mind.*[5]"

From the perspective of healthcare professionals, switching medicines means that doctors no longer need to spend time on a surgery full of people with minor self-treatable conditions, or write prescriptions for minor ailments. Pharmacists can make better use of their professional skills by recommending appropriate self-care actions and responsible use of nonprescription medicines.

4 Bolaños, H. Responsible Self-Medication in Latin America. *Drug Information Journal*, 2005, 39: 99.

5 WHO. Guidelines for the Regulatory Assessment of Medicinal Products for use in Self-Medication. WHO Geneva 2000, p21.

People generally pay directly for the medicines that they buy over the counter and the spending on medicines by insurers and governments can be redirected or lowered.

Switch in support of better self-care behaviours

"Healthcare systems in all regions are under pressure and cannot cope if they continue to focus on disease rather than patients; they require the involvement of individual patients who adhere to their treatments, make behavioural changes and self-manage.[6] *"*

Health systems around the world have evolved to focus on the treatment of communicable diseases, being based on a 'biomedical model' (Box 2)[7]. They are, in essence, 'sickness services'.

Box 2 Characteristics of the biomedical model of health systems.

- Diseases come from outside, or originate as internal involuntary physical changes – patients are passive 'victims'
- Focus on treatments for illness rather than the prevention of illness
- Treatments with medicines, vaccines, surgery etc are designed to change physical state of body in response to illness
- The medical profession is solely responsible for treatment
- The psychological and social components of illness are not considered significant.
- Self-care and responsible self-medication are not considered important
- The self-imposed risk factors of chronic diseases – tobacco use, obesity, insufficient physical exercise etc are not given major attention.

6 International Alliance of Patients Organisations, 2007

7 Jane Ogden. Health Psychology. McGraw Hill 2007, p. 2

Health systems have not evolved to take into account the main future causes of death and disability – chronic non-communicable diseases. However, non-communicable (chronic) diseases (cardiovascular diseases, cancer, chronic respiratory diseases and diabetes) are now emerging as the primary source of disease burden in both developed and developing countries (see below). The key feature about these diseases is that they are substantially *preventable* through appropriate self-care behaviours. Current health systems – sickness services – are not appropriately oriented towards disease prevention and better self-care.

Research has shown that good health behaviour, including better self-care, is influenced by a complex combination of individual psychological factors together with knowledge and social, environmental and economic factors. One of the environmental factors is the availability of effective nonprescription medicines, which help to give people a sense of control over their individual health situation. Switch programmes can therefore help tackle the emerging public health threat of chronic disease through empowering people to look after themselves better, rather than simply being passive recipients of care from overstretched health systems.

Addressing global chronic diseases through switch

"Without action, an estimated 388 million people will die from chronic diseases in the next 10 years. Each of us has a choice: whether to continue with the status quo, or to take up the challenge and invest now in chronic disease prevention.[8] *"*

Globally, of the 58 million deaths in 2005, approximately 35 million will be as a result of chronic diseases such as heart disease, stroke, cancer, chronic respiratory disease and diabetes. This is double the number of deaths from all infectious diseases (including HIV/AIDS, tuberculosis and malaria), maternal and perinatal conditions, and nutritional deficiencies combined. Four

out of five chronic disease deaths are in low and middle income countries.[8] In fact, common, *modifiable* risk factors underlie the major chronic diseases. They include **tobacco use**, **obesity** and **raised cholesterol levels**. Switching some medicines to nonprescription status can make a significant contribution to tackling these risk factors by empowering people to look after themselves through better self-care behaviours.

Treatment of tobacco dependence with NRT

"I finally managed it! After all those years on 20 a day. I was about to get my usual pack of cigarettes at the petrol station but on the spur of the moment I bought NRT instead. That was two years ago and I haven't had a puff since..."

British woman, aged 47, 2008.

Tobacco smoking is one of the leading causes of death throughout the world, accounting for approximately 5.4 million deaths per year currently and for a predicted 8 million deaths per year within 20 years.[9] Quit rates vary – for example in Europe, only 21% of smokers manage to quit each year, while every day 80,000-100,000 young people around the world become addicted to tobacco. Yet only just over one-third (37%) of smokers have ever used the nonprescription medicine NRT (Nicotine Replacement Therapy)

NRT is a class of nicotine delivering medicines which helps people to stop smoking by acting at brain nicotine receptors, thereby reducing withdrawal symptoms. It is a 'clean' form for delivering nicotine, which is not accompanied by the main carcinogens and other toxic substances found in tobacco products and produced by their combustion. There are various methods for delivering NRT such as trans-dermal patches, which delivers a relatively steady level of nicotine during the time it is worn, and several acute dosing systems, including chewing-gums, inhalators, sprays, tablets and lozenges.

[8] WHO. Preventing Chronic Diseases. A vital investment. WHO 2005.

[9] http://www.who.int/selection_medicines/committees/expert/17/application/NRT_inclusion.pdf

Most countries are today party to the WHO Framework Convention on Tobacco Control (FCTC) which supports commitment to demand reduction measures including facilitating access for pharmaceutical treatment of tobacco dependence. Article 14 of the WHO FCTC requires parties to implement measures for the management and treatment of tobacco dependence, including pharmaceutical products such as NRT. Yet the accessibility of NRT varies greatly according to country – from being available in pharmacies, grocery stores, via specialist stop smoking clinics, practice nurses and doctors, through to being only available on prescription. Ready accessibility of NRT is critical – it has been shown that a significant proportion of attempts to stop smoking are unplanned and yet have a good chance of succeeding.[10]

NRT has been available in many high-income countries for many years and has been studied intensively for its effectiveness, safety, adverse effects, cost and cost–effectiveness. There is strong, consistent evidence that use of NRT increases the rate of success in quitting smoking and is cost–effective. The Cochrane Library contains systematic reviews conducted since 1994 on the effectiveness of NRT for the general population. The seventh update was released in 2008 and concluded that all commercially available forms of NRT can increase people's chances of stopping smoking.

Thanks to the nonprescription availability of NRT, the use of the medicines increased by 152% in the first year after the prescription-to-nonprescription switch. That translated into an estimated 114,000 to 300,000 new former smokers annually in the US.[11] Switching NRT products for use in smoking cessation in Australia resulted in an estimated 68,750 premature deaths being prevented in the 10 years NRT has been available as a nonprescription medicine in Australia[12].

Little wonder that in 2009 the WHO and the 17th Expert Committee on the Selection and Use of Essential Medicines approved the inclusion of NRT into the 16th Model List of Essential Medicines (the 'Essential Drugs List').

[10] West R, Sohal T. Catastrophic pathways to smoking cessation: findings from national survey. *BMJ* 2006, 1 February: 332.

[11] Shiffman S et al. Public Health Benefit of Over-the Counter Nicotine Medicines. *Tobacco Control* 306 1997.

[12] Bittoun R. Brain and Mind Research Institute, University of Sydney, Australia. A decade of over-the-counter therapeutic nicotine in Australia. Its contribution to improving quit rates and saving lives. May 2007

Treatment of obesity with orlistat

"I was tired of the lectures from my doctor, and tired of the weight loss programmes which started off well but were hard to keep up. With orlistat from the pharmacy to help me I can keep up with the programmes – and with my doctor!"

British female in a patient's forum, 2009

Obesity and weight management is an area that has recently been added to the self-medication arena. Being overweight or obese increases risk for hypertension, coronary heart disease, diabetes and premature death. Major commercial weight loss programs have reported disappointing results. It has been shown in particular that individuals failed to lose and sustain a weight loss of 5%, the recommended loss for a "distinct health benefit". Studies have pointed to the need for more effective and safe adjunctive approaches, such as pharmacotherapy. In most countries around the world, weight-loss drugs have however been limited to prescription-only. The recent switch in a number of countries of orlistat for use when combined with a modified diet has filled an important weight management gap.

In Australia and New Zealand, orlistat has been categorized as a Schedule 3 drug, which means it is available without a prescription, but with the proviso that consumers should receive counseling. Orlistat is now also available as a nonprescription medicine in China, the Philippines, Singapore and the US. In 2009 orlistat was approved as the first ever centralized switch in Europe by the European Medicines Evaluation Agency to help tackle the increasing prevalence of heart disease, making it the first licensed weight loss aid available without prescription throughout Europe.

Treatment of raised cholesterol with simvastatin

Simvastatin has been reclassified as a pharmacy only medicine in the UK for people currently at moderate risk of a heart attack in the next 10 years. Efficacy data considered by the UK regulatory agency for the switch demonstrated that the product can significantly reduce the 'bad' (low density lipoprotein, LDL) cholesterol in the body by around 27% after 4 weeks. Reductions of this order reduce the risk of a major coronary event (death or non-fatal myocardial infarction) by about one third after 3 years of treatment. The level of absolute risk reduction depends on the starting level of risk.

In the UK, the pharmacist will advise consumers about whether the product is appropriate for them, provide information on their individual coronary heart disease risk factors and offer appropriate lifestyle advice. Individuals who are at moderate risk of a heart attack in the next 10 years will benefit from reducing their cholesterol level irrespective of the starting point. Consumers in the UK are therefore not required to have a cholesterol test before starting to take simvastatin. After 5 years of nonprescription use, data collected from pharmacovigilance activities do not show any significant problems associated with this switch.

The examples of NRT, orlistat and simvastatin illustrate how switching some medicines to nonprescription status can make a significant contribution to tackling the major risk factors confronting populations in most countries, by helping people lower the risk factors of chronic diseases.

Some other notable switches

"Like many people, I suffer from migraines and triptans are the only medication which I know will work when I have a migraine or feel one coming on. For me, triptans are nothing short of miraculous and I am mystified as to why other countries still do not have them available without a prescription."

German consumer, 2009

Over the past 10 years, the self-medication situation in many countries has been transformed by the introduction of new products offering different delivery systems such as patches and instant dissolving tablets, new combinations, new treatments such as dimeticone for existing indications such as head lice, triptans for migraine, new indications such as irritable bowel syndrome, and proton pump inhibitors for prevention of acid indigestion. In many nonprescription categories today, the most-used product is one which has been switched from prescription control.

Examples of notable switches include **chloramphenicol** eye drops. Topical chloramphenicol is available in the UK, Belgium and Portugal for topical treatment of acute bacterial conjunctivitis. The reclassification of chloramphenicol eye drops from prescription-only to nonprescription medicine enables pharmacists to provide an effective medicine that is regarded as the drug of choice for treating bacterial conjunctivitis.

In 2008, **azithromycin** became the first oral antibiotic to be available from a pharmacist without a doctor's prescription to treat asymptomatic chlamydia in the UK. Azithromycin is available to people of 16 years and over if they have tested positive for the infection and have no symptoms, and for their sexual partners. Chlamydia is the most common sexually transmitted disease in the UK. Up to 70% of people who have chlamydia have no symptoms and could, therefore, remain undiagnosed. This gives a huge risk of serious long-term health complications, including infertility and ectopic pregnancy. Symptom–free people diagnosed with chlamydia and their partners are now able to get convenient effective treatment from their local pharmacy after a diagnosis of chlamydia is confirmed by a simple urine test.

Emergency hormonal contraception containing **levonorgestrel** is now available in many countries as a nonprescription product, on the basis that the safety of the drug is well-documented and that emergency contraception to avoid unplanned pregnancy is clearly an area where timely access matters. A survey carried out by the UK Office for National Statistics between 2000 and 2002 concluded positively that nonprescription availability of emergency hormonal contraception did not raise the proportion of women using emergency hormonal contraception more than once during a year. Women preferred obtaining emergency hormonal contraception this way rather than from a doctor, with uptake being high and giving corresponding savings in time and resources for the health service. Making emergency hormonal contraception available over the counter in the UK did not lead to an increase in its use, to an increase in unprotected sex, or to a decrease in the use of more reliable methods of contraception.[13]

[13] Marston *C et al.* Impact on contraceptive practice of making emergency hormonal contraception available over the counter in Great Britain: repeated cross-sectional surveys. *BMJ* 2005, July 30: 331.

Oral **fluconazole** has been switched to nonprescription status for the treatment of vaginal candidiasis (thrush) and associated candidal balanitis in many countries. Vaginal candidiasis and candidal balanitis occur commonly and present with easily recognizable symptoms. Vaginal candidiasis is one of the most common infections seen by doctors. Up to 75% of women suffer an episode of thrush at some point in their lives and about half have more than one episode. People are readily able to treat the condition with a nonprescription medicine. Availability as a nonprescription medicine reduces delay in initiation of treatment and can reduce embarrassment for the patient.

"Well, I'm allergic to literally everything: dust, trees, grasses, molds, cockroaches, dust mites – you name it. And I've learnt the hard way that taking a daily antihistamine, in my case cetirizine, is a necessity year round. What a relief when cetirizine finally became available without a prescription at the end of last year! It did not make sense to me why I had to visit the doctor for which medicine to take when I knew my symptoms so well and had been happy with cetirizine for ages."

American 40 year-old male, 2008

Switch economic benefit studies

The true cost of obtaining a prescription drug actually includes the cost of the doctor. Although some insured patients may have higher out of pocket costs in paying for nonprescription medicines, evidence from the most recent switches from prescription to over the counter shows that most patients benefit overall from nonprescription availability.[14,15]

[14] Cohen JP, Paquette C, Cairns CP. Switching prescription drugs to over the counter. *BMJ* 2005 330: 39

[15] Sullivan PW. Switching prescription drugs to over the counter: Consumers may benefit financially. *BMJ* 2005, 330, 904.

Studies in the US,[16] Europe,[17] the UK[18] and elsewhere have consistently shown that there are substantial net economic benefits from the switch of some prescription-only drugs to nonprescription status. These benefits arise from an increase in incremental consumer benefit, savings in terms of doctor time and in terms of travel time to and from the doctor's office.

Research has been conducted on the nature and amount of economic benefits of nonprescription medication in Australia[19]. It examined the benefits obtained from the use of nonprescription products such as reduced pressure on professional care, the incremental consumer benefit and additional general benefit on Australia's external balance of trade. In an early study, it was estimated that the potential benefits of further switches of prescription drugs to nonprescription status could be as high as AD$200 or AD$300 million.

A study published in Sweden concluded that the benefits of switching more ingredients to self-medication status clearly outweigh the possible drawbacks.[20] The research showed that a switch to nonprescription cut the number of medical visits by up to 15-24% and prescriptions by anything between 6 and 70%, resulting in lower healthcare costs.

Cough and cold: Research between 1976 and 1989 showed that $750 million per year were saved from the switch of all cough and cold ingredients in the US[21] . On average, doctor visits for this purpose fell by 110,000 a year. The cost of a visit to the doctor includes the consultation, transportation and the time spent traveling and waiting. The total cost of a visit to the doctor in 1989 was $42. There were 16,500 fewer consultations for colds than fifteen years before; a difference that was attributed to the FDA's switch policy. As a result, the total resource saved in 1989 was $70 million. The study concluded that, in a more recent 14 year period, with a 5% greater population and a 20% price increase for doctor visits, cough and cold product nonprescription availability generated savings of nearly $1billion.

An updated study by researchers at Northwestern University USA found nonprescription medicines to treat common upper respiratory infections could save $4.75 billion a year. The savings come from improving work productivity, reducing unnecessary doctor visits, and taking prescription medicines only when appropriate.[22]

Heartburn: In 2009 a study showed that switching nonprescription heartburn therapies saved patients an average of $174 in office visits and medication costs each year. Additionally, some $757 million in annual savings to the U.S. healthcare system was attributed to the reduction of doctor visits. The overall findings reflect the evolution of heartburn treatments as the availability of over-the-counter treatment options have expanded over the past 15 years to include antacids, H2-blockers, and proton pump inhibitors.[23]

Vaginal candidiasis: In the US, vaginal antifungal products became available in January 1991. Research showed a 15% decline in the number of doctor visits over a 4-year period for treatment of vaginitis, attributed to the availability of nonprescription antifungal preparations[24]. The decline in doctor visits resulted in approximately $45 million in direct cost savings for the insurers, and another $18.75 million in indirect savings for the patient by reducing time lost from work.

In summary, aside from the positive benefits to people's health care, economic studies confirm the substantial contribution to reducing system costs following a variety of different switches.

[16] Temin P. Costs, benefits, and politics in switching drugs from prescription to over-the-counter in the United-States. *J. Social Admin. Pharmacy*, 1984, Suppl. 1: 189.

[17] AESGP. The Economic and Public Health Value of Self-Medication. Brussels, June 2004, 74 pp.

[18] Ryan M, Yule, B. "Switching drugs from prescription to OTC availability; economic benefits in the UK" *Health Policy* 1990, 16: 233.

[19] Johnson LW. School of Business, Bond University, Gold Coast, Queensland, Australia.

[20] Swedish Institute for Health Economics (IHE). On the Economic benefits of switching medicinal products to OTC status. March 2008.

[21] Temin P. Realized benefits from Switching Drugs. *J. Law & Economics* 1992, XXXV: 351

[22] Lipsky M *et al.* An Economic Analysis for Treating Viral Upper Respiratory Tract Infection in the United States. Paper presented to the World Self-Medication Industry Asia Pacific Regional Conference, October 28 2004.

[23] http://www.chpa-info.org/media/resources/r_5333.pdf

[24] Lipsky MS *et al.* Impact of Vaginal Antifungal Products on Utilization of Health Care Services: Evidence from Physicians Visits. *J. Am Board Fam. Pract.* 2000, 13: 178

Future switches | Section III

“For patients, the trend towards more switches will take self-care to a new level, focused increasingly on chronic prevention of serious illness.[25]”

In the past, a prescription medicine has become a switch candidate for availability without a prescription if it is used for a condition that has easily recognised symptoms and a high margin of safety under conditions of wide availability.

Today, years of safe experience in many countries with many ingredients, and increased patient and consumer interest and knowledge about self-care and self-medication provides a good basis for extending prescription to nonprescription switching. Evolving trends in switching has meant expansion of indications suitable for self-treatment into the arena of longer term use, chronic conditions, and situations in which an initial diagnosis is made by a doctor. As a result, more diseases are now being considered for switch to self-care with nonprescription medicines.

Identifying new areas for switch

In 2001, supported by the European Commission, the European Self-Medication Industry Association (AESGP) led a task force to examine how a possible expanded role for self-medication products could be achieved. The task force included 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. The task force looked at a way to review indications or conditions that might be considered for self-medication in the future.

One result was a chart in which indications were mapped according to the following two dimensions:

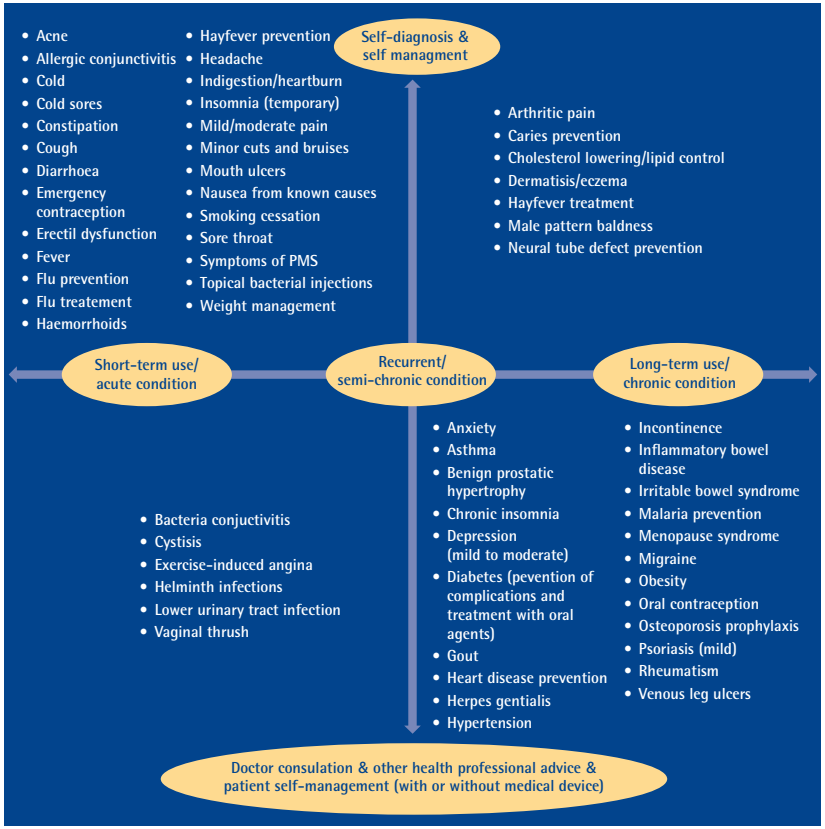
- Is it an acute condition requiring short-term use of a medicinal product, or a semi-chronic condition requiring recurrent use of a medicinal product, or a chronic condition requiring long-term use of a medicinal product?

[25] Cohen JP et al. Switching prescription drugs to over the counter. *BMJ* 2005, 330, 39-41.

– 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?

Figure 1 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. This chart provides a good basis for discussion between stakeholders as to potential indications for switch.

Figure 1 Conditions mapped according to self management potential and chronicity



Traditional self-medication arena

For the indications that are listed in the top half of the chart, i.e. the traditional self-medication area, the following questions are typically asked to determine whether the indication is suitable for self-treatment:

– 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?

Collaborative care indications

The conditions that are listed in the bottom left-hand quadrant are becoming gradually available for self-medication in certain countries, often in a "collaborative care" setting. This means that people often go to the doctor when presenting symptoms of these conditions for the first time. Once the doctor has established a medical diagnosis, people are often 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.

Indications that may be suitable for self-medication in the future

The bottom right-hand quadrant of the chart includes the conditions identified by the task force as possible new areas for treatment in this collaborative care setting. According to the task force, there is a need to ask the following additional questions to determine if these new indications would be suitable for self-treatment:

- Is the illness life threatening?
- Can the management of the condition/disease be enhanced by greater access of medicinal products available without a prescription?
- Can patients adequately self-monitor (e.g. through the use of a device) and self-treat asymptomatic diseases?
- Is the illness stable over the recommended treatment period?
- Is the treatment regimen simple and easy to follow or does it require dose titration?
- What is acceptable compliance/non-compliance for treatment of the disease?

An illustrative case study of a future candidate for switch – urine urge incontinence – is given in Box 3.

Box 3 Case study: Urge incontinence as a future candidate for switch

Overactive bladder/urge incontinence is a common condition that affects millions of people and negatively impacts their quality of life. Nearly half of all sufferers have to change their lifestyle in order to deal with the condition, and consider it a significant problem. Many sufferers do not seek help because they are embarrassed or because they are not aware that help is available; close to a quarter of people have never discussed their condition with their doctor. Bringing the condition into the self-care, self-medication arena would raise public awareness of the condition, and inform sufferers that there is something that can be done about it.

Urge incontinence is easily discernable by the consumer. It is reasonable to expect that the consumer can differentiate "urge" incontinence from "stress" incontinence (urine leakage when laughing, coughing or sneezing), through informative labeling information. Adequate labeling can also help identify those people with other conditions. Oxybutynin and tolterodine, drugs commonly used for the treatment of this condition, have demonstrated an efficacy and safety profile that lend themselves for potential nonprescription use.

In discussing suitability for nonprescription status, in the core document on regulation of medicines for self-medication, the WHO states the following:[26]

"The potential benefit/risk characteristics of the medicinal product in self-medication should be set against its benefit/risk characteristic as a prescription product; it cannot be assumed that prescription status necessarily provides a greater guarantee of safety than non-prescription status. Where for example 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. Similarly, in some countries a large number of medicinal products originally intended primarily for use under medical supervision are in fact sold widely without prescription. In such instances, recognition of the real self-medication situation and the introduction of appropriate safeguards (e.g. adapted package sizes and texts) may be more in the public health interest than the maintenance of a merely theoretical prescription status."

In summary, in future a country's citizens may expect to benefit switches for chronic, progressive, recurring and symptomless conditions. Of course it must be recognised that each potential switch raises specific questions which need to be evaluated, and every country varies in its conditions in terms of patient and consumer education, healthcare professional support, and so on. The country conditions necessary for efficient switching are the subject of section IV.

[26] WHO. Guidelines for the Regulatory Assessment of Medicinal Products for use in Self-Medication. WHO Geneva 2000, p21

Country conditions for switching

Section IV

Switching prescription medicines to nonprescription status presents clear opportunities for countries to improve public health, as detailed in sections II and III. A number of basic conditions are important for switching, including an appropriate regulatory classification system, government (political) support, information availability to patients and consumers, supportive healthcare professionals and recognition and reward for companies developing new switches.

Switches, even those which in the past might have been thought to be unsuitable for nonprescription status, can be undertaken safely and successfully provided industry, government, pharmacists and doctors work together to provide the information and educational support consumers need to make informed decisions for self-care and self treatment choices.

The regulatory classification system

A pre-requisite for a switch is the existence of a clear differentiation between prescription-only medicine and nonprescription medicine at the regulatory level. In a market where prescription products and nonprescription products are not differentiated, the switching of ingredients makes little sense.

Spain provides an illustration of this point. A new Medicines Law to implement the provisions of the EU's 2004 pharmaceutical revision was adopted in 2006 as the *Law on the Guarantees and Rational Use of Medicines*. The law distinguished prescription and nonprescription medicines and brought a number of changes to the distribution system for medicinal products. In particular, when supplying prescription-only medicines, the presentation of a prescription was essential and enforced – the supply of a prescription medicine without a prescription treated as a serious infringement. Following this stricter regulation, various ingredients were switched to nonprescription status in early 2007, including topical ketoconazole, terbinafine, etofenamate, ketoprofen, loratadine, azelastine, and NRT.

In some countries, such as Australia, New Zealand, Finland, France, Sweden and the UK, there is graduation in the level of availability of nonprescription products. There are some sub-divisions in the nonprescription category such as a "behind the counter" class – where there is a need for pharmacist assistance; pharmacy "self-selection", or "general sale" through any retail outlet. Although this booklet focuses on the switch of prescription to

nonprescription status for medicines, the term switch may also be used for the reclassification of nonprescription medicines from "behind the counter" to "general sale" status, in countries where these categories exist. For example, in Australia, a number of athlete's foot remedies have been switched from schedule S2 (self-selection in pharmacies) to general sale since 2006. In Finland, NRT products were moved from pharmacy only to general sale distribution as from February 2006. In Sweden, the sale of NRT products was allowed outside of pharmacy as of March 2008.

Government support

An important reason for differences in the switching procedures for prescription-only to nonprescription medicines in different countries is the leadership of government in individual countries. For example, in different ways the USA, China, Japan, Mexico and the UK have all demonstrated interest and support for the processes of switching (see Box 4 for the UK example).

Box 4 UK Reclassification Strategy Group

At the launch of the new reclassification procedure in May 2002, a Reclassification Strategy Group (RSG) composed of representatives from the Medicines and Healthcare products Regulatory Agency (MHRA), the Department of Health, the Royal Pharmaceutical Society of Great Britain (RPSGB), the Proprietary Association of Great Britain (PAGB) and the Association of the British Pharmaceutical Industry (ABPI) was set up to look at switch opportunities.

Between 2002 and 2008, over 50 products have been switched from prescription to general sale, as well as from prescription to pharmacy. Recent switches include oral naproxen and diclofenac, omeprazole, simvastatin, sumatriptan, antibiotics such as topical chloramphenicol, and azithromycin.

New regulations to lift the advertising restrictions on some therapeutic areas for nonprescription medicines to the public came into force in June 2004/November 2005. Furthermore, a provision from the '2001 Review' of European medicines legislation, to give one year's data/market exclusivity for significant clinical or preclinical tests or trial results used for reclassification, came into force in the UK on January 2005.[27]

[27] MHRA website: http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Legalstatusandreclassification/index.htm

The EU switching guideline is an example of supra-national political support. In 1996, the Council of Health Ministers and the European Parliament each adopted a Resolution on the outlines of an industrial policy for the pharmaceutical sector in the European Union. Both Resolutions called for a tightening of the classification system for medicinal products and the establishment of transparent switching procedures. In response, the Commission in September 1998 adopted detailed guidance with a view to harmonizing the conditions for switching prescription-only medicines to nonprescription status for use in self-medication.[28] The guideline came into effect on 1 January 1999.

Another noteworthy development in recent years has been the additional political support from the EU Council for the expansion of switches in indications previously not available for self-medication. The EU Health Council said in its Community Programme on health promotion: *"after initial diagnosis and prescription, self-medication is possible with the doctor delegating control while retaining an advisory role such as in the case of diabetes and asthma."*

The World Health Organisation (WHO), in their core guidelines on nonprescription medicines states: *"The reclassification of medicinal products from sale on prescription only to nonprescription sale is of great current interest in many countries...It has become widely accepted that self-medication has an important place in the health care system. Recognition of the responsibility of individuals for their own health and awareness that professional care for minor ailments is often unnecessary have contributed to this view. Improvements in people's general knowledge, level of education and socio-economic status in many countries form a reasonable basis for successful self-medication. New drugs with specific pharmacological action, such as histamine H2-receptor antagonists, nonsteroidal anti-inflammatory compounds (NSAID) and nicotine preparations for cessation of smoking, have been successfully reclassified from prescription to non-prescription status in many countries.[29]"*

[28] Guideline on changing the classification for the supply of a medicinal product for human use of 29 September 1998

[29] WHO. Guidelines for the Regulatory Assessment of Medicinal Products for use in Self-Medication. WHO Geneva 2000. p4.

Information availability

Self-care and responsible self-medication gives people more choice and responsibility, but also involves helping to ensure that they are equipped to make appropriate choices. The trend towards self-medication must be accompanied by a strengthening of information measures – for example the special role of labels and leaflets on nonprescription medicines, a focus on the usability of information, recognition of people's limitations as well as strengths, and recognition of the role of advertising.

Good nonprescription medicines labeling (labels and/or leaflets), specially designed for consumers, is a fundamental requirement in responsible self-medication. By definition, the information consumers need to use nonprescription medicines correctly and without professional supervision must be on the label or in the leaflet which comes with the product.

The outer packaging is the appropriate place for information to patients and consumers in self-medication. Information on the outer packaging allows consumers to quickly and easily make a choice about the appropriateness of the medicine for their needs at the point of sale. The leaflet placed inside the pack allows the consumer to find and appropriately use instructions for using the medicine safely and effectively after they have purchased the product. Additional information for consumers can be provided via booklets and website links.

For nonprescription medicines the aim is that the information on the label is presented in such a way that consumers can:

- Choose an appropriate medicine on their own.
- Use the medicine safely and effectively.
- Readily find the information they need, understand it and act on it appropriately.
- Access further information if they want to know more about the medicine.

Giving the people more choice and responsibility must also involve ensuring that they are equipped to make sensible choices. Ultimately, the more informed and educated the consumer is, the more extensively the limits of self-medication can be drawn.

As expressed by the WHO: *"Adequate information on the appropriate use of medicinal products should always accompany the product. Further guidance for self-medication can be provided by health care professionals. An important consideration is whether the medicinal product and its uses are such that accompanying texts (information, advice and warnings) can be devised that will be sufficiently clear and complete to enable the consumer to use the product safely, effectively and in a rational way.*[30]"

In contrast to labeling, advertising – as a lower involvement, less targeted communication medium – is ill-suited to carrying detailed information. Nevertheless advertising can have an important role in communicating to the patient or consumer the existence of a condition, and the availability of a relevant nonprescription product. Advertising is therefore an important part of the package of information that should not be subjected to unnecessary restrictions.

Healthcare professional support

> *"With their education, training and ready accessibility, pharmacists are an excellent source of information and advice about nonprescription medicines."*

It would be entirely wrong to think that self-care and self-medication does not require or involve the support of healthcare professionals, and indeed this is particularly the case for some of the more progressive switches. As illustrated in sections II & III, an increase can be expected in situations where an initial diagnosis and self-medication treatment options are determined by a doctor and discussed with the patient. On recurrence of the same symptoms the patient can then respond and treat themselves as necessary, without visiting the doctor on every occasion. Evolving trends in switching has thereby meant expansion of indications suitable for self-treatment into the arena of longer term use and chronic conditions.

[30] WHO. Guidelines for the Regulatory Assessment of Medicinal Products for use in Self-Medication. WHO Geneva 2000. p21.

More generally, doctors can and should play a very important part in encouraging and supporting self-care activities. People need much encouragement and support, not least in reducing the avoidable risk factors for chronic diseases, as described in section III.

Although doctors will continue to have an important role in encouraging self-care and responsible self-medication, the opportunities for pharmacists with new switches is even greater. Pharmacists can represent a reliable and convenient source of advice, not least about newly-switched medicines. The community pharmacist has close patient contact, and consumers seek their advice. Suitably-trained pharmacists are well placed to provide information and education about nonprescription medicines. Pharmacists are trained to identify possible interactions with other products an individual may be taking, to educate and advise on appropriate usage and possible side effects, and other pertinent aspects of nonprescription medicines usage. It is likely that the pharmacist (and their staff) will play a greater role in self-medication in future, and indeed their support is likely to be essential for future successful switches.

Recognition and reward for innovation

Support of innovation is as important to nonprescription medicines as it is to the development of new prescription drugs. Advancing new medicines to nonprescription status requires a significant initial capital investment, and investment in research. But chemical entities that comprise nonprescription medicines are commonly not protected by intellectual property patents on the basic molecule. In many countries, switch applications are ingredient-related and not product-related. This means that all products containing a particular ingredient could benefit from the successful switch application of one manufacturer, which is unfair to the company investing in the switch.

Innovation in nonprescription medicines is also based upon the development of new therapeutic claims for established products and therefore needs recognition and reward. In developed markets this typically comes in the form of data protection, market exclusivity and brand protection. A minimum of 3 years of data protection or market exclusivity is appropriate for innovators granted approval for novel indications on existing self-care products, and for the switch of a product from prescription to nonprescription status.

In the USA the Hatch-Waxman Act specifies a three-year data exclusivity period for submissions requiring clinical trials, which would include new indications for existing products. Similar rules are in effect in Japan. The European Union Directive 2004/27/EC specifies that where an application is made for a new indication for a well-established substance, a period of one year of data exclusivity shall be granted, provided that significant pre-clinical or clinical studies are carried out in relation to the new indication. Further details of data protection legislation are given in section V, page 40.

More generally the value of self-care *brands* should be recognised. A well known brand, supported by informative and responsible advertising, makes it much easier for consumers to decide if the product is what they need, and to be confident in trying it. A trusted brand name is therefore an important vehicle to encourage self-care behaviour.

The use of so-called "umbrella branding", where a known brand widens its products to treat related ailments, is also important for promoting consumer confidence in a new product. This includes allowing the same trade name for different forms of nonprescription medicines and for medicines moved from prescription to nonprescription status.

Given the value to patients and consumers of brand recognition, protection for a brand against copying or 'passing off' (where a company misrepresents its products as being the products of another, usually the brand leader), should be appropriately implemented and enforced.

Switch regulation issues

Section V

Switch regulations

As illustrated in this booklet, various countries have led the world in switching prescription products to nonprescription status, and they have been very thorough in the review process, recognizing that consumer safety is the highest priority. When deciding if a medicine should be reclassified to make it available over the counter, regulatory authorities must balance the benefits of easier access against the potential harm from unsupervised or inappropriate use. While no product, medicine or otherwise, can be completely safe, regulatory authorities in these countries have demanded from applicants appropriate evidence of a wide margin of safety, along with convincing evidence of effectiveness, before transferring the product to nonprescription status. The safety profile has in the case of switch products been established and documented through years of experience and extensive use as a prescription medicine.

It is unnecessary and inappropriate that every country around the world repeats the experience of other countries. International comparison is therefore the important first step for switching products which have a long history of safe and effective use. Fundamentally, nonprescription products do not need to be subject to the same extent of regulation as a new prescription medicine at the point of making a switch application, or in its ongoing usage. Several potential regulatory strategies can optimise the safety of nonprescription medicines. Regulators can for example further reduce the potential for harm by specifying the concentration, dose, or pack size that a pharmacist can supply without prescription.

In general, it is important that the assessment of a product or ingredient be based only on benefit/ risk criteria. The drug should be safe for self-supervision and the condition to be treated should be self-diagnosable or with a previous diagnosis from their doctor for some of the more complex switches. No other issues such as reimbursement status or professional monopolies should be the subject of an assessment. In order to concentrate resources in industry and the authorities, a clear timetable is also necessary as well as clear communication

by all parties and agreed action to be taken to achieve a switch in the desired timeframe. A clear, transparent and a well-grounded switching procedure is a basic requirement for successful switch regulation. Box 5 gives details of the specific switch regulations for various countries.

In the UK, applications to reclassify medicines are evaluated by the Medicines and Healthcare products Regulatory Agency (MHRA), with advice from a suitable expert committee e.g. the Commission on Human Medicines (CHM), or Expert Advisory Groups (EAGs) as necessary. Where it is considered that the proposed reclassification may safely be made, wide public consultation by the MHRA takes place. Interested organisations are notified when a new consultation has been issued. Responses to the consultation are evaluated by the MHRA and advice is sought from the CHM only if a new safety issue is raised during consultation. Following a successful reclassification proposal, the change of legal status takes place. All other products with the same active substance need to make a separate application to follow suit.

In Germany, the procedure for a change of classification status is clearly defined in the German Medicines Law (AMG). In the last few years, a considerable number of switches have been recommended by the German Expert Committee for the Classification of Medicines and subsequently enacted within nine months. The responsibility to decide on classification lies with the Federal Ministry of Health. Although applications can in principle be made by anybody, it is usually the manufacturer who initiates a switch application.

In Australia there are guidelines for the National Drugs and Poisons Schedule Committee (NDPSC) which specify the nature of the switch process in the rescheduling of medicines with respect to items such as the committee procedures, the evaluation process, guidelines for application and information requirements.

Box 5 Guidelines on switch-related regulations from around the world

European Union: *Guideline on changing the classification for the supply of a medicinal product for human use:*
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-2/c/switchguide_160106.pdf

UK: *MHRA Guidance Note 11. Changing the Legal Classification in the United Kingdom of a Medicine for Human Use:*
http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Legalstatusandreclassification/index.htm

Australia: *Guidelines for the National Drugs and Poisons Schedule Committee:*
http://www.tga.gov.au/ndpsc/ndpscg.htm

NDPSC scheduling/rescheduling template:
http://www.tga.gov.au/ndpsc/schedule-template.htm

Guidelines for brand advertising of substances included in Schedule 3 of the Standard for Uniform Scheduling of Drugs and Poisons (SUSDP):
http://www.tga.gov.au/ndpsc/ndpsc3a.htm

Canada: Factors for listing drugs in Schedule F (Rx status)
http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/pol/schf_annf_fact_pol-eng.php

In a few instances, the introduction of a new nonprescription ingredient does not come via the prescription to nonprescription switch route, but comes directly to the market as a nonprescription medicine. For example, some of the strengths and dosage forms of products to treat vaginal yeast infections were originally introduced as nonprescription products in the US; as was triclosan as an antigingivitis ingredient. Bentoquatum for poison ivy protection in the US is another example. In the UK, dimeticone was introduced directly as a nonprescription product for treatment of head lice, providing an alternative to chemical insecticides. In Japan, minoxydil was introduced directly as a nonprescription product for treatment of hair loss in men.

While the introduction of a product on nonprescription status without prescription experience is fairly rare, the main point is that the data on safety and effectiveness should drive such a decision, not an arbitrary time-on-the-market limitation. Direct nonprescription status without prior prescription experience should not, therefore, be automatically prohibited.

Data protection

'Data protection' means that for a defined and limited period a regulatory authority must not refer to the data of one party to grant registration or approvals for another party, without the agreement of the owner. Data protection recognizes the significant investment necessary to generate and provide data to meet ever increasing regulatory requirements. It encourages product development and maintenance, innovation and access to products by providing for a defined period of exclusive data protection.

Data protection encompasses both data exclusivity (the exclusive right to use proprietary information in support of an application, for a defined period) and market exclusivity (the exclusive right to market a product). The exclusivity period generated by data exclusivity legislation is usually longer than the one generated by the market exclusivity legislation. For example, if a country has data exclusivity legislation a generic applicant would be able to use the registration files of the original application only after (say) three years. This means that the originator effectively has a market exclusivity of three years *plus* the time it would take the regulatory authorities in that country to approve the generic application. In the case of market exclusivity legislation, a generic applicant would be allowed to use data on the registration file of the original drug *prior to* the expiration of three years in order to secure immediate entry into the market at the time of expiry of the market exclusivity.

The period of data exclusivity should begin when the product is placed on the market and not when the marketing authorisation is issued. Currently, data exclusivity starts when a marketing authorisation is issued for the reclassification, but many of the processes – such as finalising labelling and advertising – cannot begin until the marketing authorisation is issued. Months may pass before the product is marketed, resulting in limited commercial benefit.

In the US, a switch is eligible for three years of data exclusivity if the "new drug application" (or "supplemental new drug application") for the switch contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application, and the investigations are conducted or sponsored by the applicant.[31] Similar rules are in effect in Japan.

The European Union has passed an amended Directive, in which the data protection period was originally set at 3 years, but this was reduced to 1 year at the final stages of approval.[32] The wording is: *"Where a change of classification of a medicinal product has been authorized on the basis of significant pre-clinical tests or clinical trials, the competent authority shall not refer to the results of those tests or trials when examining an application by another applicant for or holder of marketing authorization for a change of classification of the same substance for one year after the initial change was authorized."*

However, there is little indication that a 1 year period of data protection is sufficient incentive to encourage companies to invest in the necessary work to bring new switches to market. Further, it is important to note that the one year period of data protection would start from the date of the grant of the authorization or variation which affects the reclassification, not the date on which it is first placed on the market. The legal clarity of the EU Directive and subsequent amendments has been affected by political considerations and as a consequence, there are a number of incomplete formulations. The real value of the current system is therefore a crucial issue for the future.

Current provisions in most other countries' legislation do not provide any data exclusivity. To encourage switch applications a similar approach to the US's of granting a three-year period of market exclusivity would be appropriate.

[31] US Federal Food, Drug and Cosmetic Act, section 505: New Drugs

[32] Article 54 of EU Directive 2004/27/EC amends Directive 2001/83/EC wording, inserting a new Article 74a

Safety scrutiny

Once medicines have been reclassified, they remain subject to 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:[33]

"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."

The first points of reassurance are that nonprescription medicines are those which have been shown to be safe and effective for their intended purpose, are sold with explicit directions for their use, and are manufactured to a high quality according to the principles of Good Manufacturing Practice (GMP). 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 nonprescription medicines, nongovernmental systems, poison control centers, and published case studies in medical literature serve a similar function.

[33] WHO. Guidelines for the Regulatory Assessment of Medicinal Products for use in Self-Medication. WHO Geneva 2000, p14

Regulatory authorities need to accept that any additional requirements from companies must be proportional to the data already gathered over decades of safe use by the public before being switched. It is not reasonable to expect manufacturers to provide, as a routine for every single switch application, additional post-marketing surveillance studies regardless of the type of molecule, especially as there are no data or market exclusivity provisions allowed for this.

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.

Nonprescription Ingredients Classification Tables

Appendix

Nonprescription Ingredients Classification Tables

The following tables are specimen *examples* of the AESGP/WSMI Nonprescription Ingredients Classification Tables. The complete tables are available through WSMI's website at: http://www.wsmi.org/otc.htm and the AESGP website at: http://www.aesgp.be/publications/otcIngredientTables.asp

Table 1. Legal classification status of selected ingredients (acid disorder products) in the European Union of 15

Table 2. Legal classification status of selected ingredients (dermatologicals) in 10 new EU and non EU countries

Table 3. Legal classification status of selected ingredients (analgesics) in 12 countries worldwide

Notes on the Tables

The acronym "OTC" means that at least one dosage or form of the ingredient has the legal status of nonprescription medicine in the country concerned. Where available, the first move of the ingredient from prescription to nonprescription status is indicated by the "year" in which this switch took place. A year therefore also equals "OTC". Footnotes provide additional information and can be accessed with the complete Tables through the websites.

Table 1. Legal classification status of selected ingredients (acid disorder products) in the European Union of 15.

Ingredient	Austria	Belgium	Denmark	Finland	France	Germany	Greece	Ireland	Italy	Netherl.	Portugal	Spain	Sweden	UK
A. ALIMENTARY TRACK AND METABOLISM														
A01 Stomatological preparations														
Fluoride (sodium)	OTC[1]	OTC	Rx	OTC	OTC	1986[2]	OTC	OTC	OTC	OTC	OTC	1995	OTC	OTC[3]
Hexetidine	OTC	OTC	N.R.	N.R.	OTC	OTC	OTC	OTC	OTC	OTC	OTC	1992[4]	N.R.	OTC
Triamcinolone (oral)	Rx	N.R.	Rx	2003[5]	Rx	2003[6]	N.R.	Rx		Rx		Rx	Rx	OTC[7]
A02 Drugs for acid-related disorders														
Aluminium hydroxide	OTC	N.R.	OTC	N.R.	OTC	OTC	N.R.	Rx	N.R.	N.R.	N.R.	1982	Rx[8]	1994
Calcium carbonate	OTC	OTC[9]	OTC	<1965	OTC	OTC	OTC	OTC	OTC[10]	OTC	OTC	1982	OTC	OTC
Carbenoxolone	OTC[11]	N.R.	N.R.	N.R.	N.R.	Rx	N.R.	OTC[12]	N.R.	N.R.	OTC	Rx	N.R.	OTC[13]
Cimetidine	OTC[14]	Rx	1989	Rx	1997[15]	Rx	Rx	Rx	1993[13]	1996	Rx	1996[17]	Rx[18]	1994[19]
Famotidine	Rx	N.R.	1996[20]	1996[21]	1997[22]	1999[23]	Rx	1996[24]	OTC[25]	1996	2002	1996[26]	1995[27]	1994[28]
Lansoprazole	N.R.	Rx	Rx	Rx	Rx	Rx	Rx	Rx		N.R.		Rx	2004[29]	Rx
Nizatidine	Rx	Rx	Rx	N.R.	Rx	Rx	Rx	1999[1]	Rx	Rx	Rx	Rx	N.R.	1996[31]
Omeprazole	Rx	Rx	Rx	Rx	Rx	Rx[32]	Rx	Rx	Rx	2008	Rx	Rx	1999[33]	2004[34]
Pantoprazole	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx		Rx		Rx	OTC	Rx
Ranitidine	OTC[35]	2003[36]	1989	1996[37]	1997[38]	1999[39]	Rx	1999[40]	Rx	1996[41]	Rx	1998[42]	1995[43]	1994[44]
Sucralfate	OTC[45]	Rx	1989	1985	1994	Rx	Rx	Rx	OTC[46]	OTC	Rx	Rx	Rx	Rx
A03 Drugs for functional gastrointestinal disorders														
Dicyclomine (Dicycloverine)	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	OTC[47]	Rx48	N.R.	Rx	Rx	N.R.	OTC[49]
Dimeticone	OTC	OTC	OTC	OTC	OTC	OTC	OTC	OTC	OTC	OTC	OTC	1982	OTC	OTC

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Table 2. Legal Classification status of selected ingredients in 10 new EU and non EU countries.

Ingredient	Bulgaria	Croatia	Czech Republic	Hungary	Lithuania	Norway	Poland	Slovak Republic	Slovenia	Switzerland
D. DERMATOLOGICAL										
D01 Antifungals for dermatological use										
Amorolfine *(topical)*	N.R.		Rx	Rx		Rx	Rx	Rx	Rx	Rx
Bifonazole	Rx	Rx	2002	Rx	N.R.	OTC[1]	2002[2]	OTC	OTC	N.R.
Butenafine	N.R.	N.R.	N.R.	N.R.	Rx	N.R.	N.R.	N.R.	N.R.	N.R.
Ciclopirox olamine	Rx	N.R.	Rx	OTC[3]	N.R.	N.R.	Rx	N.R.	Rx	Rx
Clotrimazole *(topical)*	Rx	Rx	OTC	OTC	Rx	OTC[4]	OTC[5]	OTC	OTC[6]	OTC[7]
Croconazole	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.
Econazole	Rx	Rx	OTC[8]	Rx	Rx	OTC[9]	Rx	Rx	OTC[10]	OTC[11]
Fenticonazole *(topical)*			Rx			N.R.			N.R.	
Haloprogin *(topical)*	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.
Isoconazole *(topical)*	N.R.	Rx	N.R.	N.R.	Rx	N.R.	Rx	N.R.	N.R.	Rx
Ketoconazole *(topical)*	OTC[12]	Rx	OTC	OTC[13]	Rx	OTC[14]	OTC	OTC	OTC	1998[15]
Miconazole *(topical)*	N.R.	Rx	Rx	Rx	N.R.	OTC[16]	OTC[17]	OTC	OTC[18]	OTC[19]
Miconazole & Hydrocortisone *(topical)*	N.R.	N.R.	N.R.	N.R.	N.R.	OTC[20]	Rx	N.R.	N.R.	Rx
Naftifine *(topical)*	Rx	N.R.	Rx	Rx	Rx	N.R.	Rx	N.R.	N.R.	Rx
Natamycin *(topical)*	N.R.	N.R.	Rx	Rx	N.R.	N.R.	Rx	Rx	N.R.	Rx
Nystatin	Rx	Rx	OTC[21]	N.R.	Rx	Rx	Rx	OTC	Rx	Rx
Oxiconazole	N.R.	N.R.	1998[22]	N.R.	Rx	N.R.	N.R.	OTC	N.R.	OTC[23]
Selenium sulfide	N.R.	N.R.	N.R.	N.R.	N.R.	OTC	OTC[24]	N.R.	N.R.	OTC[25]
Sulconazole nitrate *(topical)*	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	OTC[26]

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Table 3. Legal classification status of selected ingredients in 12 countries worldwide.

Ingredient	Argentina	Australia	Canada	Chile	China	Japan	Korea	Mexico	New Zealand	Philippines	Singapore	USA
Oxybuprocaine	Rx	Rx	OTC	Rx	Rx	Rx	Rx	Rx	Rx	N.R.	OTC	Rx
Pramocaine	Rx	N.R.	OTC	N.R.	N.R.	N.R.	OTC	N.R.	Rx	Rx	N.R.	OTC
Prilocaine	N.R.	1993[1]	OTC	Rx	Rx	Rx	OTC	OTC	OTC[2]	N.R.	OTC	Rx
N02 Analgesics												
Acetylsalicylic acid	2003[3]	OTC[4]	OTC	OTC	OTC[5]	OTC	OTC	OTC	OTC[6]	OTC[7]	OTC	OTC
Diflunisal	N.R.	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx	N.R.	Rx	Rx
Dihydrocodeine	Rx	OTC[8]	Rx	Rx	Rx	OTC	Rx	N.R.	Rx	N.R.	N.R.	Rx
Naratriptan	N.R.	Rx	Rx	Rx	N.R.	Rx	Rx	N.R.	Rx	N.R.	Rx	Rx
Paracetamol	OTC	OTC[9]	OTC	OTC	OTC	OTC	OTC	OTC	OTC[10]	OTC[11]	OTC	1955
Paracetamol + dihydrocodeine	Rx	OTC[12]	Rx	N.R.	Rx	N.R.[13]	Rx	N.R.	Rx	N.R.	N.R.	Rx
Sumatriptan	Rx	Rx	Rx	Rx	Rx	Rx	Rx	OTC	Rx	Rx	Rx	Rx
Zolmitriptan	N.R.	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx
N05 Psycholeptics												
Chlorproethazine (topical)	N.R.	N.R.	N.R.	N.R.	N.R.	N.R.	Rx	N.R.	N.R.	N.R.	N.R.	
Hydroxyzine	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx	Rx
Prochlorperazine	N.R.	200014	Rx	Rx	N.R.	Rx	OTC	N.R.	OTC[15]	N.R.	Rx	Rx
N06 Psychoanaleptics												
Pyritinol	N.R.	N.R.	N.R.	N.R.	Rx	N.R.	N.R.	Rx	N.R.	N.R.	N.R.	
N07 Other nervous system drugs												
Nicotine (gum)	OTC	1988[16]	1992[17]	Rx	2008	2001	OTC	OTC	OTC[18]	N.R.	2002[19]	1996[20]
Nicotine (nasal spray)	N.R.	OTC[21]	2003	N.R.	N.R.	N.R.	N.R.	N.R.	OTC	N.R.	N.R.	Rx

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