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# Guidelines for the Regulatory Assessment of Medicinal Products for use in Self-Medication



**World Health Organization**

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# Guidelines for the Regulatory Assessment of Medicinal Products for use in Self-Medication



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# 1. Introduction

Self-care can be defined as the primary public health resource in the health care system. It consists of the health activities and health-related decision-making of individuals, families, friends, colleagues at work, and so on. It includes self-medication, non-drug self-treatment, social support in illness, and first aid in everyday life.

The reclassification of medicinal products from sale on prescription only to non-prescription (over-the-counter, or OTC) sale is of great current interest in many countries. Drug regulatory and health authorities have to consider the types of medicinal products for which reclassification is appropriate, safe and rational in the interest of public health.

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 socioeconomic status in many countries form a reasonable basis for successful self-medication. New drugs with specific pharmacological action, such as histamine H<sub>2</sub>-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. Regulatory assessment of a change from prescription to non-prescription status should be based on medical and scientific data on safety and efficacy of the compound and rationality in terms of public health.

The purpose of the present guidelines is to suggest criteria and methods which drug regulatory authorities can employ in determining the suitability of medicinal products for use in self-medication. The term "assessment" is used rather than "clinical evaluation",

since in many cases the process will involve a review of existing data and experience and not the performance of new clinical trials or investigations, though the latter may occasionally be necessary. The guidelines are also intended for use by marketing authorization holders applying for the classification of a prescription medicinal product to be changed to non-prescription sale. Lastly, they provide guidance on documentation for new active substances which have not been marketed as prescription medicines to accompany applications for marketing authorization in self-medication.

The initiative for the review of prescription products or any new product that might reasonably be released for self-medication has generally been taken by the pharmaceutical industry in the form of documented proposals to national drug regulatory authorities. Occasionally, such authorities have themselves taken steps to reclassify medicinal products to make them available for self-medication. In some cases, moreover, products have been changed back from self-medication to prescription drug status because new safety issues have arisen. This underlines the fact that it is of crucial importance carefully to monitor the use of medicinal products and post-marketing data on adverse effects to be able to respond adequately and quickly to possible harmful developments.

## 2. General Principles

### **2.1 Scope of the guidelines**

These guidelines address the criteria for regulatory assessment of safety and efficacy of self-medication products, including new active substances that have not been marketed as prescription medicines, drugs that have hitherto been available only on prescription, and those for which new information requires the re-evaluation of safety. These guidelines do not address homeopathic medicines, in vitro diagnostic products or other medicinal preparations such as vitamin and mineral supplements, and some medicines of plant origin that are not well characterized.

### **2.2 Definition of medicinal products for self-medication**

Medicinal products for self-medication may for the present purpose be defined as those which do not require a medical prescription and which are produced, distributed and sold primarily with the intention that they will be used by consumers on their own initiative and responsibility, when they consider such a use appropriate. The term "over-the-counter (OTC) medicines" is widely used to describe this class of product. The packing, package size, labelling and product information (package insert, leaflet, directions folder or other accompanying text) will generally be designed and written to ensure appropriate self-medication.

It should be realized that the distinction between self-medication products and prescription medicines is not a sharp one; differences in dosage and/or in indications can lead to differences in classification. For example, ibuprofen is sold only on prescription at high dose for treatment of arthritis and over the counter at low doses for treatment of headaches and other minor pain. It is sometimes the practice that smaller packages are available as self-medication.

## **2.3 Basic criteria for a self-medication product**

A medicinal product for self-medication should fulfil at least the following three criteria:

- (1) Active ingredient: The active ingredient at the intended dose should have low inherent toxicity (e.g. no reproductive toxicity or genotoxic or carcinogenic properties relevant to human use, unless such hazard can be appropriately addressed by labelling).
- (2) Intended use: The intended use should be appropriate for self-medication. Use of the product should not unduly delay diagnosis and treatment of a condition requiring medical attention.
- (3) Product properties: The product should not have properties that make it undesirable. For example, it should not have an unfavourable adverse event profile; require a physician's supervision for monitoring during drug therapy; represent a significant risk of dependence or abuse; or display other limiting characteristics such as interaction with commonly used medicines or foods that may result in serious adverse reactions.

If a new chemical entity or a prescription product meets the three basic criteria, the following additional criteria may favour consideration of change of status to non-prescription sale:

- (1) The use of the product has been sufficiently extensive or in high enough volume.
- (2) The product has been marketed on prescription for at least five years. The time considered appropriate for a product to have been on prescription varies widely, e.g. no time specified in the European Union, three years in New Zealand, six years in Japan, and up to 10 years in the Philippines.
- (3) Its adverse events give no cause for concern, and their frequency has not increased unduly during the marketing period.

The reason for requiring five years of prescription marketing is that withdrawals from the market because of adverse events or the need for major changes in product information have usually occurred during the first three to five years after the start of marketing in countries with effective systems of safety monitoring. A high level of use permits detection of relatively rare but serious adverse effects, and sometimes the detection of an increased frequency of particular adverse events. High use also is likely to mean that the drug has been used in a broad range of people with a wide variety of concomitant diseases, concomitant drugs and risk factors for adverse events. It should be noted that the period of use may vary in countries with well-developed pharmacovigilance systems.

The criteria outlined above are based on the normal stepwise widening of exposed patients in three consecutive stages of drug development:

- (1) Investigational use prior to marketing authorization, with limited controlled exposure of a relatively small group of people in clinical trials who are monitored closely for adverse effects.



(2) Prescription marketing, entailing exposure of potentially large numbers of people, though limited to those who go to a physician and for whom the physician considers the drug has a positive benefit/risk balance in the treatment of a disease.

(3) Marketing and commercial promotion for self-medication – involving the increasing exposure of potentially enormous numbers of people – when concomitant diseases and other medications used may vary, and other risk factors such as pregnancy, lactation, working conditions (driving), sport, alcohol use, and potential interaction with climate, sun or food may be present. It should be noted that systems to monitor adverse reactions to self-medication products may not always exist.

Only for a few drugs will information from the clinical trials prior to use be enough to support general availability in self-medication form, because such trials are conducted in selected populations monitored intensively for efficacy and safety. However, experience from marketing elsewhere in the world may provide suitably detailed data on exposure under conditions of use that are sufficiently similar to the situation in a particular country. Additional clinical studies may sometimes be necessary in the target consumer population where the product is expected to be used.

It should be borne in mind that consumers may consider that a medicinal product not subject to a medical prescription is less harmful than the same product when subject to a medical prescription. In such cases, labelling directed to the consumer should clearly communicate both the benefits and the risks of using the product for self-medication.

## **2.4 Characteristics of self-medication**

Self-medication involves the use of medicinal products by the consumer to treat self-recognized disorders or symptoms, or the intermittent or continued use of a medication prescribed by a physician for chronic or recurring diseases or symptoms. In practice, it also includes use of the medication of family members, especially where the treatment of children or the elderly is involved.

In order to use a non-prescription product safely and effectively, the consumer must perform a number of functions normally carried out by a physician treating a patient with a prescription drug. These functions include accurate recognition of the symptoms, setting of therapeutic objectives, selection of a product to be used, determination of an appropriate dosage and dosage schedule, taking into account the person's medical history, contraindications, concomitant diseases and concurrent medications, and monitoring of the response to the treatment and of possible adverse effects.

In the case of non-prescription medicinal products, all of the information required to permit safe and effective use must come from the labelling material, patient information texts, the individual's previous personal experience, various sources of information in the media, advertising, and advice given by health care professionals.

Pharmacists in particular can play a key role in giving advice to consumers on the proper and safe use of medicinal products intended for self-medication. It is important, therefore, to take this role into account both in their training and in practice.

The rapid development of new technology, and especially the Internet and related communication systems, has opened up new possibilities for searching for information. This may eventually offer important new channels for the dissemination of knowledge on medicinal products, their characteristics and proper use in self-medication, although the quality of information may vary. It should be emphasized, however, that there are marked differences in opportunities to obtain access to this information between people with different socioeconomic and educational backgrounds and in different countries. Well-tested labelling designed for a particular cultural milieu can help to reduce these differences. However, it should not be used in a way that would limit the availability of the OTC product.

### **2.4.1 Potential benefits**

The social and economic benefits of self-medication reflect the fact that it is voluntarily chosen by consumers for conditions where it seems preferable to them. It will usually be selected for use in symptoms and conditions which the user regards as sufficiently troublesome to need medicinal treatment but not to justify consulting a physician. Only if the condition fails to respond, persists or becomes more severe will professional medical help be sought. Accordingly, good self-medication should offer the individual consumer:

Efficacy: i.e. the product does what it is claimed to do;

Reliability and safety: the individual will often choose a product which experience has shown to be suitable. The scope and duration of self-medication can be kept within safe limits by appropriate selection of approved indications, labelling texts, dosage strengths and forms, and package sizes;

Product safety when used as recommended in the instructions;

Acceptable risk, even when used for a longer duration, at a higher dose, or somewhat differently than recommended in the instructions;

Wider availability of medicines;

Greater choice of treatment;

Direct, rapid access to treatment;

An active role in his or her own health care;

Self-reliance in preventing or relieving minor symptoms or conditions;

Educational opportunities on specific health issues (i.e. stop-smoking aids and products to treat heartburn);

Convenience;

Economy, particularly since medical consultations will be reduced or avoided;

At the community level, good self-medication can also provide benefits such as saving scarce medical resources from being wasted on minor conditions, lowering the costs of community-funded health care programmes (including prescription reimbursement systems), and reducing absenteeism from work due to minor symptoms.

### **2.4.2 Potential risks**

Self-medication has a number of potential risks. In particular, the ordinary user will usually have no specialized knowledge of the principles of pharmacology or therapy, or of the specific characteristics of the medicinal product used. This results in certain potential risks for the individual consumer:

Incorrect self-diagnosis;

Failure to seek appropriate medical advice promptly;

Incorrect choice of therapy;

Failure to recognize special pharmacological risks;

Rare but severe adverse effects;

Failure to recognize or self-diagnose contraindications, interactions, warnings and precautions;

Failure to recognize that the same active substance is already being taken under a different name (products with different trademarks may have the same active ingredient);

Failure to report current self-medication to the prescribing physician (risk of double medication or harmful interaction);

Failure to recognize or report adverse drug reactions;

Incorrect route or manner of administration;

Inadequate or excessive dosage;

Excessively prolonged use;

Risk of dependence and abuse;

Risks at work or in sport;

Food and drug interactions;

Storage in incorrect conditions or beyond the recommended shelf-life;

At the community level, improper self-medication could result in an increase in drug-induced disease and in wasteful public expenditure;

It is important to realize that many of these risks are not unique to self-medication: they can also occur in the prescription situation, particularly, if the patient consults several physicians for the illness or lacks counselling during therapy;

In selecting the types of medicinal products that can be used for self-medication, the aim should be to exploit the benefits listed above and to minimize the risks.

# 3. General basis for regulatory assessment

The basic criteria for a self-medication product are outlined in paragraphs 2.3 and 2.4 above.

## 3.1 Established properties

A basic principle is that the pharmacokinetics, pharmacodynamics, indications, safety and efficacy, and toxic or allergenic potential of a medicinal product should have been reasonably well established and documented in humans before its eligibility for use in self-medication can be assessed.

Where a new active pharmaceutical substance that has not been marketed as a prescription medicine is being considered for use in self-medication, the previous studies will have been conducted largely in animals. The clinical trials and investigations with such a substance should as much as possible reflect the self-medication situation, and subsequent collections of post-marketing data on long-term safety and efficacy may be necessary. These data must be sufficient to meet the criteria for self-medication.

When the release for self-medication of a medicinal product hitherto used only on prescription is being considered, it should first have been properly investigated as described above, and then employed for a number of years on a considerable scale in prescription medicine. The older the original product, however, the more likely it is that the original studies will prove to fall short of present-day investigational standards, and the more necessary it will be to rely on subsequent evidence, e.g. from incidental studies, adverse reaction reporting and general experience in the field.

Similarly, where the future status is being considered of a product already in use for a long time for self-medication, there is commonly a lack of formal prospective clinical studies matching present-day standards. Again it will often be necessary to draw conclusions from practical and circumstantial data, but if the medicinal product has been used on a large scale this may be possible.

Where the suitability of a fixed-combination product for use in self-medication is being considered, the basic principle will apply that the combination should be therapeutically rational, including only ingredients necessary for the treatment and containing no active ingredients that are superfluous to the treatment of the conditions in which efficacy for self-medication is to be claimed.

### **3.2 Approaches to regulatory assessment and supervision**

In the assessment of a medicinal product's suitability for use in self-medication, at least the following five complementary aspects need to be considered:

- (1) The active substance and the rationality of its indications;
- (2) One or more specific routes of administration, dosage forms and formulations;
- (3) Other specific safeguards;
- (4) Suitability for self-medication status; and

(5) Labelling and package inserts and other information forming a basis for advertising and promotion.

Other aspects may require more specific additional consideration in the light of the pharmacological properties of the medicinal product, the intended indication, type of use, adverse effects or other characteristics, such as those relating to the social and environmental circumstances.

### **3.2.1 Consideration of the active substance and its indications**

This will involve deciding whether the active compound itself is suitable and rational for self-medication. It should include the following aspects:

The purpose for which the product is indicated, i.e. whether the indication can be regarded as appropriate for self-diagnosis, self-medication and self-monitoring. Generally, such indications are widely experienced symptoms or disorders that are readily recognizable by ordinary consumers, or that are initially diagnosed by a doctor and are often self-limiting in nature;

Provision of reliable and consistent relief of symptoms;

Favourable benefit/risk ratio of the product; if the indications are minor, as they generally will be in self-medication, the benefit will be quickly outweighed by potential adverse effects that are other than minor;

The general toxicity, reproduction toxicity, genotoxicity and carcinogenicity of the compound with regard to its use in self-medication. In general, the drug must have a wide margin of safety, even if used incorrectly;

Its potential risks in comparison with prescription drugs that are commonly used in the same patient group;



Its mode of action and pharmacokinetics. In particular, the absorption, metabolism and excretion of the compound should not be affected by other commonly used drugs or display marked fluctuations between individuals because of concomitant diseases, interactions with food, or genetic or environmental factors (working conditions, climate, and so forth);

Low and well-documented risks in specific patient groups, for example in elderly people, during pregnancy and lactation, and in patients with impaired liver or kidney function;

The potential impact of widespread use on the levels of microbial resistance to antimicrobial medicines in the general population;

Low risk of masking symptoms of underlying serious disease, resulting in delays in proper diagnosis and treatment;

Acceptable level of risk from inappropriate use;

Low or well-characterized incidence of adverse effects or side-effects, and contraindications for which advice or counselling is easily available;

Drug dependence and abuse potential of the drug;

The existence of other dosage forms of the same active ingredient that have already been approved for OTC sale.

### **3.2.2 Consideration of one or more specific routes of administration, dosage forms and formulations**

Since no active therapeutic substance is likely to be ideal in every way, it will usually be necessary to consider which specific presentations or formulations might be best suited to self-medication, since these can affect the medicinal product's safety, efficacy and suitability in such use. For example, only preparations that can be administered in a

manner not requiring technical expertise, assistance or patient training can be considered suitable for self-medication; thus, oral or topical preparations will generally be suitable, but injections will usually not. It may be desirable to avoid certain types of excipient, where they are known to affect certain patient groups adversely.

### **3.2.3 Consideration of other specific safeguards**

The suitability of a substance for use in self-medication can be further affected by the feasibility of providing other specific safeguards, e.g. those related to:

- (1) Dosage: Restricting the maximum single dose or maximum daily dose may protect against danger when the medicinal product is used either correctly or incorrectly. However, it is necessary to confirm that the dose retains the necessary efficacy.
- (2) Dosage strength: For children, specific dosage strengths suitable for paediatric use are preferable. For the adult population, consideration should be given to the need for several strengths, bearing in mind different uses and characteristics, though this should be balanced against any problem that may be encountered in selecting the proper dose.
- (3) Dosage schedule: The recommended duration of treatment should prevent unnecessary prolonged use. If the symptoms fail to respond adequately or persist, medical attention/consultation is necessary.
- (4) Package size: The package size should be limited to a reasonable number of doses in relation to the recommended duration of the treatment. This is necessary to safeguard against misuse, particularly overdose or undue delay in seeking medical attention. There may occasionally be a need for larger packages as an option in specific, designated situations or for prolonged use.
- (5) Packing material and form: Medicinal products should have a container which as far as possible prevents children gaining access to the medicine if they get hold of the container.

### **3.2.4 Suitability for self-medication status**

The potential benefit/risk characteristics of the medicinal product in self-medication should be set against its benefit/risk characteristics 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 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.

### **3.2.5 Consideration of labelling and package inserts**

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.

When package inserts or leaflets are required by governments, manufacturers or distributors should ensure that they reflect only the information that has been approved by the country's drug regulatory authority. If package inserts or leaflets are used for promotional purposes, they should comply with the WHO Ethical Criteria for Medicinal Drug Promotion set out later in this section.

In addition to approved package inserts and leaflets wherever available, the preparation and distribution of booklets and other informational material for patients and consumers should be encouraged as appropriate. If such material is promotional, it should comply with the WHO Ethical Criteria mentioned above.

Information for the consumer should be easily understandable and in accordance with national legislation; for self-medication products it is particularly important that the written text is comprehensible to the lay person. In general, it is helpful for sufficient information to appear on the outer packaging to allow consumers to make a decision about suitability of the product before purchase. This is of particular importance where advice from health care professionals is not readily accessible. The following aspects of labelling and package inserts should be considered:

The consumer information should be simple and not open to misinterpretation;

The fact that the item is a medicinal product should be clearly indicated;

The composition of the product (generic name of active substance) should be stated;

The uses for which the product is intended should be indicated;

The mode of use should be specified, including the route of administration (systemic or local), maximum single dose, maximum daily dose and duration of the treatment;

It should be clearly indicated whether the product is intended for children or adults;

The most important precautions, contraindications and adverse effects should be clearly presented in lay terms;

Specific warnings and information should be provided for use during pregnancy or lactation, by the elderly, or in patients with renal or hepatic failure, where appropriate;

The circumstances in which medical advice should be sought and the duration of use should be described if appropriate;

Information on storage conditions and shelf-life should be provided;

It may be helpful to describe other measures the patient should take to control symptoms (e.g. for a histamine H<sub>2</sub>-receptor antagonist, other ways to reduce heartburn);

Inactive ingredients, which may be allergenic, should be listed;

It may be useful to provide information on the expected benefit when the drug is properly used;

The use of pictograms should be considered.

A model list of drug information for a self-medication product is provided in Annex 1.

### **3.2.5.1 Advertising and promotion**

Approval of product information relating to a medicine is an important part of the assessment of suitability for self-medication. Advertising and promotion should always be consistent with this approved information. However, the compliance of advertising with product information can normally be judged only after self-medication status has been approved.

Although these do not constitute guidelines for the classification of medicinal products, the following extracts from the WHO Ethical Criteria are included for reference purposes.

In May 1988, in resolution WHA41.17, the Forty-first World Health Assembly endorsed in 1988, WHO's Ethical Criteria for Medicinal Drug Promotion. It also appealed to pharmaceutical manufacturers and distributors, the promotion industry, health personnel involved in the prescription, dispensing, supply and distribution of drugs, universities and other teaching institutions, professional associations, patient and consumer groups, the professional and general media (including publishers and editors of medical journals and related publications), and the public:

(1) to use these criteria as appropriate to their spheres of competence, activity and responsibility;

(2) to adopt measures based on these criteria as appropriate, and monitor and enforce their standards.

### **3.2.5.2 Advertisements in all forms to the general public**

14. Advertisements to the general public should help people to make rational decisions on the use of drugs determined to be legally available without a prescription. While they should take account of people's legitimate desire for information regarding their health, they should not take undue advantage of people's concern for their health. They should not generally be permitted for prescription drugs or to promote drugs for certain serious conditions that can be treated only by qualified health practitioners, for which certain countries have established lists. To fight drug addiction and dependency, scheduled narcotic and psychotropic drugs should not be advertised to the general public. While health education aimed at children is highly desirable, drug advertisements should not be directed at children. Advertisements may claim that a drug can cure, prevent, or relieve an ailment only if this can be substantiated. They should also indicate, where applicable, appropriate limitations to the use of the drug.

15. When lay language is used, the information should be consistent with the approved scientific data sheet or other legally determined scientific basis for approval. Language which brings about fear or distress should not be used.

16. The following list serves as an illustration of the type of information advertisements to the general public should contain, taking into account the media employed:

- the name(s) of the active ingredient(s) using either international nonproprietary names (INN) or the approved generic name of the drug;
- the brand name;
- major indication(s) for use;
- major precautions, contraindications and warnings;
- name and address of manufacturer or distributor.

Information on price to the consumer should be accurately and honestly portrayed.

### **3.2.5.3 Free samples of non-prescription drugs to the general public for promotional purposes**

21. Countries vary in their practices regarding the provision of free samples of non-prescription drugs to the general public, some countries permitting it, some not. Also, a distinction has to be made between provision of free drugs by health agencies for the care of certain groups and the provision of free samples to the general public for promotional purposes. The provision of free samples of non-prescription drugs to the general public for promotional purposes is difficult to justify from a health perspective. If this practice is legally permitted in any country, it should be handled with great restraint.

# 4. Collection and regulatory assessment of evidence for medicinal products intended for self-medication

When drug regulatory authorities assess applications for marketing authorization, three types of situation need to be distinguished:

- (1) Assessment of new active substances, not marketed as prescription medicines and designed specifically for use in self-medication.
- (2) Assessment for self-medication of medicinal products hitherto available only on prescription.
- (3) Assessment of existing self-medication products that have not previously been evaluated.

## **4.1 Assessment of new active substances not marketed as prescription medicines and designed specifically for use in self-medication**

The material should comprise pharmaceutical, pharmacological (preclinical and general pharmacological characterization of the compound), toxicological, clinical pharmacological (clinical trials) and long-term therapeutic data (efficacy and safety) obtained in appropriate experimental animals and humans. It will then need to be submitted to the regulatory authority for review. The clinical trials must address the



specific issue of the use of the medicinal product in a representative self-medication population. Sufficient clinical experience of the use of a new active substance must be gained before marketing authorization of the product for self-medication can be granted.

#### **4.2 Assessment for self-medication of medicinal products hitherto available only on prescription**

From previous sections it is clear that the evidence for or against the proposed use of a medicine in self-medication may be obtained from many different sources worldwide and analysed in a manner somewhat different to the material normally presented when a new pharmaceutical product is submitted for official approval by a national regulatory authority. The object should be to form an opinion on the basis of selected evidence. The material will generally comprise:

(1) The original regulatory data (chemistry, manufacturing, pharmaceutical, pharmacological, toxicological, clinical pharmacological and clinical trial data, and data on therapeutic efficacy and safety).

Much of this will be relevant only if the product as currently proposed for self-medication is in all respects identical to the original product. Human data will weigh much more heavily than animal data. If any of the original animal investigations suggested severe risks (e.g. carcinogenicity), the risks should be reassessed in the light of subsequent experience in humans.

(2) Clinical data obtained after the approval of the drug:

Trials performed according to current standards and relating closely to the proposed use in self-medication should be accorded the greatest weight.

(3) Drug utilization and consumption data:

These can be helpful in determining the way in which the medicinal product has hitherto been employed by physicians (volume of use, major indications in practice, precautions normally taken), and particularly in interpreting alleged risks.

(4) Reported adverse events/reactions and interactions:

These should be examined with respect to their profile, frequency and severity. Sources in which the evidence is critically assessed (especially in well-controlled clinical studies or epidemiological studies) are preferable to those in which unevaluated observations of possible adverse reactions are accumulated. Data from sources that have collected adverse drug reaction data from different countries for long periods of time may be useful, in particular, information from WHO's International Drug Monitoring Programme Telephone: +46 18 656060, Facsimile: +46 18 656080. (Uppsala, Sweden).

(5) Current scientific data:

The pharmaceutical form and packaging should be considered; any available clinical studies, field data and market-related studies on consumer use of the product for self-medication should be examined.

### **4.3 Assessment of existing self-medication products that have not previously been evaluated**

When it proves necessary to reassess the status of an existing self-medication product, the following steps are recommended:

- (1) Review of the rationality of the product (single active ingredient or combination) its efficacy, adverse effects, patterns of use, and labelling, particularly in the hands of lay consumers.
- (2) Assessment of the benefit/risk ratio of the product.
- (3) Consideration of steps to be taken to deal with emerging problems. When steps have been taken already, e.g. the publication of warnings or imposition of limitations on package size or distribution, the effect of such measures should be assessed.

### **4.4 Assessment of new strengths, formulations, doses, indications or combinations**

Careful assessment is also necessary when it is proposed to make the medicinal product available without prescription in a new strength, in a new formulation, at a new dose, using a new route of administration, for a new age group or for a new indication, particularly if the indication has not previously been approved without a medical prescription. In addition to an assessment of the rationality of such a proposal, the safety and benefit/risk of a medicinal product in the new circumstances should be evaluated.

A medicinal product containing a new combination of two or more active substances, which are available in two separate products, neither of which is subject to a medical prescription, will not automatically be classified as a non-prescription product. The applicant needs to demonstrate that the combination offers an advantage over the separate active substances, and that the risk is acceptable.

# Annex

Model list of drug information (leaflet, product information) for a self-medication product

Various types of information are needed by consumers to ensure the safe, effective and rational use of drugs in self-medication. The advice to the consumer/patient should describe the use of the product without medical supervision and the circumstances when referral for medical advice is necessary. The following list is a sample that should be adjusted to meet the needs and abilities of the consumer. This information will also be of value to health care professionals.

1. International Nonproprietary Name (INN) of each active substance in the product.

2. A brief and simple description of pharmacological effects and mechanism of action.

3. Clinical information:

(a) Indications: whenever appropriate, simple diagnostic criteria should be provided;

(b) Dosage regimen:

- average dose and range for adults and children;
- dosing interval;
- average duration of treatment;
- special situations, e.g. renal, hepatic, cardiac, or nutritional insufficiencies that require either increased or reduced dosage or special precautions.

(c) Contraindications for use;

(d) Precautions and warnings (in relation to pregnancy, lactation, age of patient, etc.);

(e) Adverse effects (quantify by category if possible);

(f) Drug interactions, including the effects of alcohol use.

#### 4. Pharmaceutical information:

(a) Dosage forms;

(b) Strength of dosage form;

(c) Excipients, including substances causing allergic reactions;

(d) Storage conditions and shelf-life (expiry date);

(e) Pack sizes;

(f) Name and address of manufacturer(s).

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