Owner/responsible party:
Legal Status of Supply Committee

MEDICINES EVALUATION BOARD

Policy document MEB 37

Legal Status of Supply

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1 Contents

2 Abbreviations and definitions

GS	General Sales
NR	*Niet-Receptplichtig* (the Dutch term for over the counter)
OTC	Over the counter
RegGW	Medicine Law Regulation
PH	Pharmacy Only
PDO	Pharmacy and Drugstore Only
PO	Only on Prescription from Doctor or Specialist

3 Introduction

The legal status of supply of medicinal products is divided into two main categories: medicinal products that are Only on Prescription from Doctor or Specialist (PO) and medicinal products that can be obtained without a prescription (Over The Counter: OTC). Over-the-counter medicinal products are better known as OTC medicinal products. These OTC medicinal products are further subdivided into three subcategories, namely Pharmacy Only (PH), Pharmacy and Drugstore Only (PDO) and General Sales (GS).

The legal status of supply ensures a balance between the availability of a medicinal product and the minimisation of risks. Medicinal products with a high relative potential risk fall into the PO category, medicinal products with a mild relative potential risk fall into the PH category, medicinal products with a low relative potential risk fall into the PDO category and medicinal products with a very low potential risk fall into the GS category.

Assigning the legal status of supply when awarding a marketing authorisation is a legal duty of the Board, as is changing the legal status of supply of registered medicinal products. This is an important tool with which the Board can manage the risks associated with the use of registered medicinal products. This means allocating medicinal products on the continuum of GS, PDO, PH and PO is part of the Board's risk-management task.

Classification in a specific category can be changed at the Board's initiative if new scientific insights or changed use/misuse of the medicinal product gives cause to do so (Section 59(1) of the Medicines Act). Naturally, it can also be changed following an application to change the legal status of supply from the marketing authorisation holder.

4 Categories of legal status of supply

4.1 Only on Prescription from Doctor or Specialist

The classification of medicinal products in PO is primarily decided based on European legislation. Article 71 of Directive 2001/83/EC sets out the criteria for the PO legal status of supply. These criteria are implemented in the Netherlands at the national level through Section 57 of the Medicines Act. However, establishing the legal status of supply involves a national decision, meaning the legal status of supply can differ between Member States.

Pursuant to Section 57(1) of the Medicines Act, the Board will decide on the classification of a medicinal product as a PO medicinal product if it:

a) can directly or indirectly pose a risk, even under normal use, if used without medical supervision;
b) can pose a direct or indirect risk to health when used frequently and very extensively not in accordance with the user instructions;
c) is based on a substance or means of preparing that substance that, due to its being new, requires further study of its effectiveness or adverse reactions;
d) is intended for parenteral administration.

According to the notes to the Medicine Law Regulation (published in the Government Gazette), PO status is awarded if normal use (i.e. according to the adopted prescription) could result in health risks if the product is used without medical supervision. This includes: direct risk (toxicity, interactions, adverse reactions), indirect danger (such as masking underlying diseases, development of resistance), the need for a physician to make a diagnosis or the need for a medical intervention to administer the agent (injection or infusion).

PO status is also assigned if there are indications that the medicinal product will be used improperly on a large scale or if there is insufficient experience with the medicinal product in actual practice.

4.2 Over the counter

The classification of OTC (over the counter) medicinal products makes a distinction between PH, PDO and GS legal status of supply.

Classification as an OTC medicinal product means the user can determine the condition (illness) themselves and can purchase the medicinal product without mandatory intervention of a physician.

Medicinal products in the PH category may exclusively be sold by pharmacies, medicinal products in the PDO category may exclusively be sold by pharmacies and chemists and medicinal products in the GS category are generally available.

Generally available means that the relevant medicinal products are available not just at pharmacies and chemists but also at other points of sale, such as supermarkets or gas stations. It involves a graduated system: medicinal products that are generally available can also be purchased at pharmacies and chemists.

The criteria for classification as PH or GS medicinal products are set out in Sections 4.1 and 4.2, respectively, of the Medicine Law Regulation (RegGW) (see §4.2.1).
The *PH legal status of supply* is assigned when the intervention of a pharmacist is necessary from a medication monitoring, information or supervision perspective.
The *GS legal status of supply* is justified when this is a responsible option, taking into account the active ingredient, the dosage and the package size, from a safe use perspective. The *PDO legal status*

of supply is used when the medicinal product does not fall into either the PO category or the GS category.

4.2.1 PH and GS criteria

Pursuant to Section 4.1 of the Medicine Law Regulation, the Board will classify a medicinal product as a **PH medicinal product** if:

a) monitoring of the use of the medicinal product by a pharmacist is necessary in connection with the chance of significant interactions with other medicinal product or of important adverse reactions;
b) the provision of information or supervision is necessary during the dispensation, with regard to providing information about the medicinal product or providing advice on the correct choice and safe and correct use of the medicinal product; or
c) supervision of the use of the medicinal product is necessary to prevent off-label use.

Pursuant to Section 4.2 of the Medicine Law Regulation, the Board will classify a medicinal product as a **GS medicinal product** if:

a) the Community or the United States of America has at least five years of experience with the active ingredient of the medicinal product as an active ingredient of a medicinal product that is available over the counter;
b) the risk of damage resulting from use of the medicinal product is negligible;
c) there are no indications of abnormal use;
d) the number of units in each package is relatively limited; and
e) the packaging and the patient information leaflet provide a warning for any potentially high-risk situations;
f) the availability of verbal advice from a pharmacist or chemist is not necessary.

Whether a medicinal product is eligible for GS legal status of supply will exclusively be determined after a marketing authorisation holder has made an application to this end.

A medicinal product will only be eligible for classification in the GS category if it meets all six criteria for GS status simultaneously. The MEB will consider the six criteria in combination with each other, rather than separately, taking into account the use of and experiences with the product.

4.2.2 Distinction between PH, PDO and GS

The most important distinction between **PH and PDO** is the required intervention of the pharmacist in the dispensation of PH medicinal products. The reason for this is that a form of supervision and care provision is necessary for PH medicinal products, which a chemist is neither equipped nor required to provide. This mostly concerns medication monitoring and the provision of information or supervision during dispensation that the patient information leaflet cannot provide or cannot provide to a sufficient extent. For PH medicinal products, the provision of information or supervision

is crucial (Section 4.1 RegGW), and the pharmacist must provide this, regardless of whether the patient requests this.

Classification as a **PH medicinal product** is appropriate if pharmacotherapeutic knowledge that a pharmacist can provide and a chemist cannot, is required for monitoring of the use of the product and/or the provision of information or supervision. The pharmacotherapeutic knowledge of the pharmacist may be necessary if:

- in case of a specific condition, a choice must be made between different types of medicinal products; or
- the use of a medicinal product is sufficiently complex that information in the patient information leaflet may not suffice and incorrect use may lead to damage or lack of efficacy; or
- an interaction has been found through medication monitoring and adjustment of the medication is necessary; or
- adverse reactions may occur that necessitate an adjustment of the medication.

PDO medicinal products require a pharmacist or chemist to be able to provide advice. The responsibilities of chemists when dispensing PDO medicinal products are laid down in Section 62(2)(b) of the Medicines Act (Gmw) and are as follows:

> 'any person who is provided with a PDO medicinal product must be clearly informed of what they must reasonably know about the nature and purpose of the medicinal product, the consequences to be expected and the associated risks to their health, unless they have indicated that they have no need for this;'

When dispensing medicine, chemists and pharmacists only need to provide information or advice if the patient requests this. It is therefore up to the patient to clarify their need for information. This means that, for PDO medicinal products, the information in the patient information leaflet should be sufficient to guarantee safe and effective use.

The main distinction between **PDO and GS** is that the possibility of advice by a chemist or pharmacist is missing for GS medicinal products. The characteristics of the product as indicated in the product information (patient information leaflet and packaging) must be such that responsible self-care is possible.

For **GS legal status of supply**, the risk when using the medicinal product is considered negligible. The Notes to the Medicine Law Regulation (published in the Government Gazette) state the following in this regard: '*For this criterion as well, it is considered in combination with the other criteria and against the background of the use of the medicinal product. The entire social context of the experience with and the knowledge of the product is relevant to the question of whether the risk of damage is negligible, and the effects of wide-spread and easy availability are also considered in this context. This way, a product with an ingredient that is not harmless on its own can be acceptable for the GS category if the social use is such that the practical risk of damage is negligible.'*

The notes to the Medicine Law Regulation subsequently also discuss the implementation of 'negligible risk' and 'very low relative risk' (in the passage, '*In the latter case (very low relative risk), the risk when using the medicinal product is considered negligible*').

The answer to the question of whether a specific medicinal product is subject to a negligible risk cannot be found in nationally or internationally recognised or suggested cut-off points or models from which a 'negligibility' can be derived, but rather is the result of a broad consideration, taking into account numerous factors that need to be considered in combination. These range from the cohesion with the other criteria and experience with and knowledge of the product to the person to whom and the circumstances in which the medicinal product is made available. The balance between advantages (for each indication) and disadvantages (adverse reactions) and whether risks can be minimised, and if so how, are important in this regard. For each legal status of supply assessment, the MEB will weigh up the potential risks to determine whether the risk is negligible. A risk profile of the medicinal product and authorised indications are determined based on all relevant aspects. In the event of a very low relative potential risk, the risk is deemed negligible pursuant to Section 4.2(b) of the Medicine Law Regulation.

4.2.3 GS list

The GS legal status of supply will only be awarded to the marketing authorisation holder/applicant if this is explicitly requested and the GS criteria have been met. To simplify the award of GS legal status of supply, the Board has drawn up a list of active ingredients that are eligible for general sales under certain conditions. This list is referred to as the GS list and is published on the MEB website.

The Board determines which active substances are included in the GS list and whether conditions apply (for example, in relation to indication, pharmaceutical form, package size or strength).

4.2.4 Package size

OTC medicinal products are medicinal products for situations where people can determine the illness themselves and can purchase the medicinal product without mandatory intervention by a physician. In principle, OTC medicinal products are intended for short-term use. When determining the legal status of supply, safety is always the main priority. The safety risk is determined not only by the active ingredient but also by different circumstances, such as the dosage, the package size and the target group for the medicinal product. With regard to the package size for GS products, criteria b and d of Section 4.2 of the Medicine Law Regulation are of particular importance:

b. the risk of damage resulting from use of the medicinal product is negligible;
d. the number of units in each package is relatively limited;

The notes to Section 4.2 RegGW state that:

'*When determining the legal status of supply, the medicinal product factors must be taken into account. The number of units per package and the strength of the dosage will be determining factors for the decision in which category the relevant product will be placed. Products in the PH category may have a relatively higher dosage strength and a larger number of units per package, whereas products in the GS category will be permitted to have a lower dosage strength and fewer units per package. When determining the legal status of supply, the user factors will also be taken into account. The packaging and the patient information leaflet of products in the PDO category, and*

especially those in the GS category, should contain warnings for specific high-risk situations, including specific user groups, in so far as necessary, in order to encourage safe and effective use of the medicinal product.'

(…)

'*For medicinal products in the PDO and GS categories, the packaging and the patient information leaflet should be adapted to relatively widespread availability. The Board is aware that unnecessary requirements for package size should be avoided for cost and efficiency reasons. In many cases, it will be possible to use the existing trade packs. If a product may potentially be harmful, or it is not intended for a specific user group or a specific age group, the packaging and patient information leaflet should clearly include a warning for use [in case of pregnancy/for children up to [...] years of age/age group [...]].'*

It follows from the above that medicinal product factors and user factors (see §5 for further explanation) are also determining factors for the further requirements to which a medicinal product is subjected, including package size.

With regard to the package size in the GS category, the starting point is that these medicinal products should have a relatively low dosage strength, and each package should only contain a small number of units. This is based on the principle that medicinal products with GS legal status of supply should generally be for short-term use.

Limiting the package size for GS products is an additional risk minimisation measure the Board has at its disposal. Limiting the package size for GS products can contribute to limiting off-label use; after all, the physical possibility of off-label use is reduced. However, this is no guarantee (someone could still buy several packages at the same time or in short succession) and can therefore at best function in supplement to other measures (including the information in the patient information leaflet and on the packaging).

The main reasons for limiting the package size under GS (as included in the GS list) are:

- inherent risk of the substance (e.g. ibuprofen, iodine, loratadine, ceterizine);
- risk of overdose (e.g. paracetamol, tocopherol);
- risk of sensitisation (e.g. bug bite relief products);
- underlying threat of acute illness (e.g. loperamide).

4.2.5 Product information

The patient information leaflets of OTC medicinal products (GS and PDO products in particular) must contain advice on responsible use as well as warnings for high-risk situations, including high-risk situations for specific user groups, to encourage safe and effective use of the medicinal product (see also §5.1.2). The information in the SmPC is guiding in this regard.

Unless otherwise stated in the SmPC, the patient information leaflet of an OTC medicinal product must recommend contacting a physician after 14 days if the symptoms are not improving or are getting worse.

As of September 2016, the MEB implements national policy on the shelf life of OTC medicinal product with resealable packaging after opening. See MEB 5 'Package leaflet of pharmaceutical products' and MEB 6 'Labelling of pharmaceutical products' for more information as well as standard sentences for the patient information leaflet and the packaging.

The QRD template standard text for OTC must be followed for patient information leaflets of OTC medicinal products.

Any indications and contraindications (as stated in the patient information leaflet) must be included on the packaging of an OTC medicinal product. The dosage may be included on the packaging. Other than that, the use of an abbreviated indication is permitted on the main side of the packaging, provided that the full indication is listed elsewhere on the packaging. See MEB 21 'Expression of "abbreviated indications" on packaging of OTC products' for more information.

5 Basic principles when determining the legal status of supply

5.1 Medicinal product factors and user/patient factors

When it comes to medicinal products, a distinction must be made between the product and the use. The Board registers a medicinal product if this product has a positive balance in terms of its effectiveness and the harm it causes. By supporting careful use, based on correct information, the objective is to minimise the potential risks for patients. Classifying medicinal products on the GS, PDO, PH and PO continuum ensures a balance between the availability of the product and minimising the risks and is part of the Board's duty to manage risks.

People are not always sufficiently aware that medicinal products in and of themselves are never (and can never be) entirely safe: all medicinal products have adverse reactions. Moreover, improper use of medicinal products can be harmful. That is why medicinal products should always be used in accordance with the user instructions. The starting point for all OTC medicinal products is that they are not unsafe when used normally, in accordance with prescribed use.

The patient/consumer is responsible for this. Dealing with the risks of OTC medicinal products is no different for users than dealing with the risks of other activities or products, such as pesticides and food supplements. Each user is therefore ultimately personally responsible for actually using the product according to the instructions in the patient information leaflet.

Patients at all times have the option of obtaining an OTC medicinal product at a pharmacy in connection with individual additional risks, for example. In this context, it is crucial that individual users are able to assess the individual risks based on the information provided when purchasing the

medicinal product. This can be made possible by means of additional information on the packaging and in the patient information leaflet, which is included in the packaging.

The MEB in fact has access to two pathways, which are not strictly separate, through which it can arrive at an effective classification of the legal status of supply, based on 1) medicinal product factors and 2) individual or other user or patient factors.

5.1.1 Medicinal product factors

Medicinal product factors are inherent risks of the active ingredient in the pharmaceutical form. These are taken into account when determining the legal status of supply. The number of units per package (see also §4.2.4) and the strength of the dosage will be determining factors for the decision in which category the relevant product will be placed. Products in the PH category may have a relatively higher dosage strength and a larger number of units per package, whereas products in the GS category will often have a lower dosage strength and fewer units per package.
A single medicinal product can have more than one legal status of supply, specifically in cases where different package sizes require different classifications. An example of this is the 500 mg paracetamol tablet, which is eligible for GS legal status of supply when it is sold in packages of a maximum of 20 tablets. For higher numbers of tablets per package, it is assigned PDO legal status of supply. The different package sizes (with the same strength) fall under the same marketing authorisation (the same RVG number). The text of the patient information leaflets will of course be identical.
Medicinal products with an OTC and PO indication in the product information (SmPC and patient information leaflet) are furthermore subject to the rule that the strictest legal status of supply (PO) is assigned.

5.1.2 User/Patient factors

User or patient factors are connected to the risks that are influenced or caused by the use of the medicinal product (the behaviour of the user/patient).

Possible risks resulting from the use by the patient (user or patient factors) are:

- off-label use;
- addiction/dependence;
- development of resistance to the medicinal product;
- interactions;
- relatively serious adverse reactions.

If relevant, medicinal products with GS or PDO status will include warnings regarding potentially high-risk situations on the packaging and in the patient information leaflet, recommending users to contact a physician or pharmacist for advice before use. Possible high-risk situations can be caused by:

- serious organ function impairment (kidney/liver);
- comorbidity (for example, diabetes, cardiovascular diseases, depressive disorders);

- comedication (for example, coumarins or other products with a narrow therapeutic window, such as digoxin);
- the masking of conditions that require different treatment, such as the use of painkillers when antibiotics or surgical intervention are necessary;
- specific patient groups:
    - children below a certain age;
    - pregnant people and people hoping to get pregnant;
    - people who are lactating;
    - elderly people above a certain age;
- a heightened chance of certain adverse reactions (serious or otherwise) occurring as a result of the patient's deviating genetic characteristics (for example, a deficiency of certain proteins or enzymes);
- long-term treatment, even though GS and PDO products are intended for short-term treatment.

The packaging and the patient information leaflet of products in the PDO category, and especially those in the GS category, must contain warnings for such high-risk situations, including those for specific user groups, in so far as necessary, in order to encourage safe and effective use of the medicinal product. The Board also takes this into account when determining the legal status of supply.

5.2 Risk profile

When determining the risk profile and whether a medicinal product meets the legal status of supply criteria set, the Summary of Product Characteristics is used as the starting point for the assessment because this is a summary of all data included in the authorisation dossier and reflects the current state of knowledge. In addition to the SmPC, other specific sources available to the MEB are also consulted, including recent publications, the Netherlands Pharmacovigilance Centre Lareb database and the EudraVigilance (European database).

Sections 4.1 to 4.9 of the SmPC in particular contain the most important information for effective use: 4.1 indications; 4.2 posology and method of administration; 4.3 contraindications; 4.4 warnings and precautions (for specific patient groups); 4.5 interactions; 4.6 pregnancy and breastfeeding; 4.7 influence on the ability to drive; 4.8 adverse reactions; 4.9 overdose. The information in the patient information leaflet is taken directly from the SmPC and contains all the information patients need for safe and effective use. Each package with medicinal products contains a patient information leaflet, meaning this information is available to the user. Any risks and how to prevent and limit damage resulting from these risks is described in this leaflet.

The main elements with regard to risks are assessed based on a decision tree. For each decision, it is decided whether the intervention of a physician or medication monitoring is necessary and whether additional verbal explanation is necessary for responsible use. This concerns a consideration of safe and effective use as well as off-label use (frequency and seriousness of the consequences). With regard to contraindications and warnings, for example, it is considered whether these can be recognised and whether it is safe to assume that a user would know they suffered from a specific condition for which use of the medicinal product is contraindicated or for which the warning applies. The interactions that might occur are assessed, as well as the frequency, how serious they are and

how they might be prevented. Possible interactions with a PO medicinal product are also included in this assessment. Whether there might be specific user groups and what the possible risks are for, for example, children and pregnant women is also assessed.

Any possible influence on the ability to drive is considered as well, taking into account, among other things, what the various classification systems indicate about the effects of the active ingredient on reaction capacity and the influence on the ability to drive.

Attention is also paid to the possible occurrence of adverse reactions (taking into account both seriousness and frequency).

When considering whether a product can be awarded GS status, whether the adverse reaction (rare or otherwise) is reversible plays a major role. In general, the occurrence of adverse reactions resulting in permanent serious damage with normal use cannot be reconciled with GS legal status of supply. When determining the legal status of supply, the frequency with which adverse reactions occur must also be considered. An adverse reaction that is serious but very rare may still be reconcilable with the GS status. The crucial factor in this regard is whether the legal status of supply (PO/PH/PDO or GS) can prevent the occurrence of the rare adverse reaction. For example, the occurrence of very rare and unpredictable but in some cases serious adverse reactions, often immunological/allergic adverse reactions (such as Stevens-Johnson syndrome, bronchospasms, etc.), is unavoidable. The patient will only visit a physician once such an adverse reaction actually occurs. These adverse reactions will occur regardless of how the patient obtained the product (PO/PH/PDO or GS). This means a different legal status of supply will not contribute to minimising the risk in relation to this adverse reaction, which could in principle occur with any medicinal product and is difficult to 'regulate' due to how rare and unpredictable it is. A product that might cause such an adverse reaction could therefore still be awarded GS status.

When considering whether a product should be given GS legal status of supply, the duration plays an important role. GS medicinal products are generally intended for short-term use. Medicinal products intended for chronic use or for long-term prevention purposes are unlikely to qualify for GS legal status of supply. The MEB believes that chronic use is hard to reconcile with GS status. Products containing nicotine (indexed for use to help people quit smoking) and products containing disodium cromoglycate (indexed for use in cases of allergic rhinitis or allergic conjunctivitis), for example, are exceptions. With regard to OTC medication and the duration of treatment, a physician should generally be consulted if the symptoms get worse or continue for longer than 14 days, regardless of the legal status of supply GS, PDO or PH (see also§4.2.5).

5.3 Combination products

The legal status of supply of a combination is the same as that for the component with the strictest legal status of supply. However, it should be checked whether possible interaction of the components gives cause to change the legal status of supply of the combination, for example because the components strengthen each other, as a result of which the combination presents a greater risk.

5.4 Classification system for the legal status of supply of NSAIDs

For the legal status of supply of NSAIDs in self-care, the Board applies a classification system as a risk minimisation tool. This can be consulted on the MEB website. The classification focused on three determining factors: the active ingredient, the dosage and the package size.

The classification system is determined using the level of the active ingredients and is based on the latest scientific insights. Regarding the anti-inflammatories studied, the Board has noted that the dosage, both per time and per day, is the key factor in reducing the risks of adverse reactions and interactions with other medicinal products. Additionally, the MEB aims to minimise possible health risks by limiting the package size.

If the product information (SmPC and patient information leaflet) also includes a PO indication, the PO indication will be imposed for the relevant NSAID (see also §5.1.1).

In 2009, the MEB determined the classification system for NSAIDs and aspirin. In the period thereafter, various other decisions were made relating to combination preparations containing NSAIDs, new strengths and new pharmaceutical forms.

5.5 Classification system for the legal status of supply of paracetamol

For the legal status of supply of paracetamol in self-care, the Board applies a classification system based on strength and package size as a risk minimisation tool. This classification system can be consulted on the MEB website.

The previous decisions and considerations regarding risk minimisation in the classification of the NSAIDs in self-care were taken as the starting point for this. With this classification system, the package size of paracetamol is limited under GS and PDO. For the time being, no limit has been imposed for the PH legal status of supply of paracetamol.

If the product information (SmPC and patient information leaflet) also includes a PO indication, the PO legal status of supply will be imposed for the relevant paracetamol (see also §5.1.1).

6 Procedural aspects

6.1 Determining the legal status of supply for new registration applications

When it receives an application for a marketing authorisation, the Board also decides on the legal status of supply. First, it assesses whether the product should be prescription only. If the product does not need to be prescription only, the Board assesses whether the medicinal product qualifies for PH or PDO legal status of supply. If one or more PH criteria apply, the PH legal status of supply

will be awarded. This assessment is based on a substantiation (based on the PH criteria) by the applicant.

In this context, the basic principle is that two comparable medicinal products with the same risk profile (the same active substance, the same strength, the same pharmaceutical form and the same indication) cannot have a different legal status of supply (with the exception of GS; see below).

If the applicant desires GS legal status of supply, the applicant must always explicitly indicate this. Two situations can be distinguished in this context: 1) the active ingredient is included in the GS list and the conditions of the GS list have been met, 2) the active ingredient is not included in the GS list or the conditions of the GS list have not been met. In the latter case, the applicant must submit a substantiation based on the six GS criteria. If GS status is awarded following the assessment, the Board may decide to adapt the GS list to reflect this.

For registration applications through the centralised, mutual recognition or decentralised procedure, it is assessed whether the medicinal product qualifies for PO legal status of supply during the European stage of the procedure. If OTC legal status of supply is awarded, it will be assessed during the national (implementation) stage whether the medicinal product qualifies for PH or PDO legal status of supply (based on substantiation by the applicant). After all, for determining PH or PDO legal status of supply, it is important that the information in the patient information leaflet is already fixed (for example, the warnings, interactions and adverse reactions included in the patient information leaflet). When submitting the Dutch translation of the established product information, the applicant must indicate (preferably by means of an accompanying letter) the desired legal status of supply. This must be accompanied by a substantiation based on the PH or GS criteria.

For registration applications through the centralised procedure, the marketing authorisation is awarded by the European Commission. The European Commission determines whether PO or OTC legal status of supply is awarded (based on the CHMP's recommendation). The Board decides the subcategory for OTC medicinal products.

6.2 Changing the legal status of supply

6.2.1 At the marketing authorisation holder's initiative

No variation procedure has been defined in the classification guideline for a national change to the legal status of supply. The Board has determined that a change from PO to OTC (or vice versa) or from PH to PDO (or vice versa) requires a type II variation application. Category C.I.z can be used. As part of the type II variation, a scientific substantiation based on PO and/or PH criteria must be provided as described in Section 57(1) of the Medicines Act and Section 4.1 of the Medicine Law Regulation.

The Board has determined that changing the legal status of supply to GS requires a type II or type IB variation.
If the active substance is included in the GS list and the conditions of the GS list have been met, the change can be applied for through a type IB variation category C.I.z. This involves an administrative procedure without a substantive assessment.

If the active substance is not included in the GS list, or if the conditions of the GS list have not been met, the change must be applied for through a type II variation category C.I.z. In this case, scientific substantiation based on the GS criteria must be provided as described in Section 4.2 of the Medicine Law Regulation.

6.2.2 At the Board's initiative

Based on new information
Section 59(1) of the Medicines Act states the following:

> '*The Board, taking into account the criteria referred to in Sections 57 and 58, will again take a decision relating to the classification of a medicinal product if new information has been brought to the Board's attention, which information indicates that the classification must be changed.'*

The information, based on which the Board will reclassify the medicinal product, must therefore be new, meaning that the information only became available subsequent to the previous classification decision. If the legal status of supply is changed at the Board's initiative, this usually means it is being tightened. The marketing authorisation holder will be informed of the proposed decision to change the legal status of supply of the relevant medicinal product and will be given the opportunity to share its views. The views of the marketing authorisation holder will be taken into account in the definitive decision.

Based on the changed legal status of supply of a comparable product
After the legal status of supply of a medicinal product has been changed at the request of the marketing authorisation holder, the Board will initiate the process of changing the legal status of supply of comparable medicinal products. After all, in this context, the basic principle is that two medicinal products with the same active substance, the same strength, the same pharmaceutical form and the same indication cannot have a different legal status of supply. GS legal status of supply is an exception to this. The GS legal status of supply will exclusively be awarded after a marketing authorisation holder has made an application to this end.

The Board will inform the marketing authorisation holder(s) of the proposed decision to change the legal status of supply of the relevant medicinal product. The marketing authorisation holder will be given the opportunity to share its views. The views of the marketing authorisation holder will be taken into account in the definitive decision.

6.2.3 Adjustment period following a change to the legal status of supply

The Health and Youth Care Inspectorate (IGJ) gives manufacturers, wholesale suppliers, pharmacies and chemists a maximum of 12 months – following a change to the legal status of supply of a medicinal product (OTC or otherwise) – to align their practice with the changed status.

The transition period is necessary because:

- manufacturers cannot immediately change the packaging of the medicinal products prepared by them;
- wholesale and retail may still have packaging with the ‘old’ legal status of supply lying around.

The transition period is a general starting point that can be deviated from in specific situations. For example, with a view to public health interests, the changed legal status of supply may need to be implemented immediately.