Medicines Dictionary

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INTRODUCTORY REMARKS

Innovative medicinal products, clinical research, medicine co-payments and the availability and advertising of medicines are topics that we all, whether as healthcare professionals or patients, are aware of. They are part of a comprehensive drug policy created and continuously regulated through a number of legislative and non-legislative documents in the CR and the EU. Since the drug policy is rather broad, it is so often difficult to understand it.

This is why, we, together with healthcare professionals, have created for you the Medicines Dictionary. It provides basic terminology, shows the process of clinical trials and medicine registration, explains the price and reimbursement regulation of medicinal products and how medicine co-payments are calculated and defines highly innovative medicinal products. The Medicines Dictionary also focuses on medicinal product re-exports and medicinal product advertising regulation. I believe that the Medicines Dictionary will help you to better understand the highly regulated area of medicinal products.

MUDr. Pavel Sedláček,
chair of the Board of Directors of the Association of Innovative Pharmaceutical Industry

It is a long way from a laboratory to a physician or patient, during which a medicinal product must undergo a complicated clinical trial, registration, pricing and reimbursement. All healthcare professionals and especially Czech legislators should understand this complex issue that is also affected by the European Union. Deputies and senators, who work on legislation related to medicinal products, will find in the presented Medicines Dictionary, which was created in cooperation with the Association of Innovative Pharmaceutical Industry, the definitions of individual terms and process and time sequences related to the drug policy. I believe that this small, yet comprehensive, brochure can become the first "syllabary" and a good helper in understanding the fascinating "world of medicines".

MUDr. Roman Kraus, MBA,
chair of the Health Committee of the Senate of the Parliament of the CR

As the chair of the Health Committee of the Chamber of Deputies of the Parliament of the Czech Republic and as a physician and a human being, I know that health issues are topical at all times. A high-quality drug policy is crucial for the stable and sustainable functioning of the Czech healthcare system. I am therefore very pleased that you are holding the Medicines Dictionary, which explains in detail the parameters and terms that all politicians should know since it is about ensuring an available and affordable healthcare for Czech patients as well as about reining in budgetary expenditures. We live in a time of an enormous upswing of the most advanced, but also expensive, medicines that health insurance needs to cover. It is up to us when and under what conditions they will be available to our citizens.

doc. MUDr. Bohuslav Svoboda, CSc.,
chair of the Health Committee of the Chamber of Deputies of the Parliament of the CR

BASIC TERMS

MEDICINAL PRODUCTS

The Pharmaceuticals Act defines a medicinal product as a **substance or combination of substances with therapeutic or preventative properties**, or a substance or combination of substances that can be used to restore, modify or affect physiological functions through pharmacological, immunological or metabolic effects, or to make a medical diagnosis.

It doesn't matter whether we use the term medicinal product, drug or medicine. They all mean the same thing.

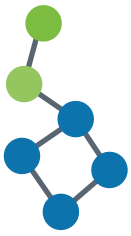
A medicinal product does not only consist of the active ingredient. It also contains **excipients, binders, colorants**, etc., which, for example, help hold the tablet together, ensure that the drug is released at the right time in the right place, or that the color and taste are as pleasant as possible to the patient. These substances may have other functions, but in principle they do not impact the effect of the medicinal product.

ORIGINAL AND GENERIC MEDICINAL PRODUCTS

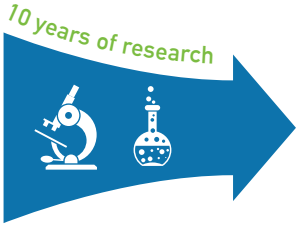
ORIGINAL MEDICINAL PRODUCTS

An original medicinal product (sometimes also referred to as a **"reference medicinal product"**) is the first authorized drug containing a new active ingredient not yet contained in any other medicinal product.

The active ingredient and possibly the manufacturing process (know-how) are typically protected by a patent. The authorized original medicinal product is protected by a period during which no copy can be marketed. The manufacturer is this compensated by the sale of the newly authorized medicinal product for the costs invested into its development.



10.000
molecules
tested



1 drug

Did you know that...

*...the authorization of a medicinal product is preceded by many years of research, development and testing? At the beginning of research there may be roughly **10,000 substances** that are examined in detailed to determine whether they have any therapeutic potential. Many of them are found to be insufficiently effective during scientific research, analysis and testing. Others have side effects that are too serious or are otherwise unsuitable to continue to the human testing stage (clinical trials). Statistics show that out of **10,000 molecules there may be only one that is successful enough** to pass all the tests required to be registered as a new medicinal product. And this is all after roughly 10 years of hard work by teams of scientists and doctors. It may not surprise us, then, that the entire development of a drug, mostly funded by private companies, often costs more than one or two billion dollars.*

GENERIC MEDICINAL PRODUCTS (GENERICS)

Generics are products that have the same qualitative and quantitative composition with respect to active ingredients, and the same pharmaceutical form as a reference medicinal product. They are also shown to be released (and excreted from the body) in the same way as the reference product. At the end of the protective period, during which only the original drug can be on the market, generic products containing the **same active ingredient** in the same pharmaceutical form (e.g. tablets or injections) arrive very quickly. Generics may contain other excipients. The launch of a generic drug is also preceded by research, but in some parameters it is considerably simpler and is not associated with the business risk of complete failure and futile investment.

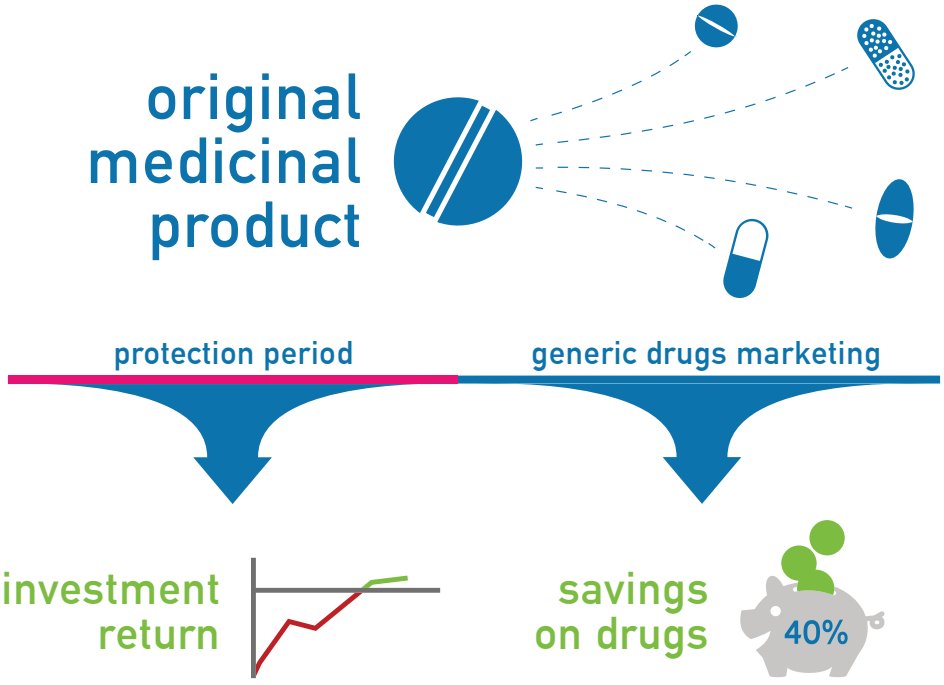
All medicinal products, including generics, must be authorized by the competent drug oversight agencies. During the authorization procedure, however, generics require fewer documents to be submitted (and some in simplified form) than original medicinal products. It is most important to demonstrate that they have the same attributes as the original, i.e. the same effect, including speed of onset, duration of effect etc.

EXAMPLES:
Acetylsalicylic acid (aspirin) is one of the oldest drugs in the modern history of medicine that is still being used today. We are all quite familiar with it. We use it when we have a fever or are in pain, for example, when we have the flu. The original medicinal product of the German pharmaceutical company containing this active ingredient has been on the market for over 100 years. But over time, hundreds of generics have also appeared.

A similar situation exists for the active ingredient ibuprofen, which was discovered over fifty years ago and which we most often use for pain relief. It also has an anti-inflammatory effect. In addition to the original product there are many generics.

Did you know that...

...generic medicinal products are brought to market at a price that is on average 20 to 40 % lower than original products? ***Generics thus bring savings to patients and also health insurance companies*** *that reimburse medicines for their policyholders.*



DIFFERENTIATING PRODUCTS ACCORDING TO MANNER OF DISPENSING

PRESCRIPTION DRUGS

A prescription is understood as a **prescription** or **request**. Requests are used to deliver drugs from pharmacies to health care facilities – to be administered to patients and for use in outpatient clinics. The majority of us only come into contact with prescriptions written by our doctors that we then take to the pharmacy. **Doctor's prescriptions are used to prescribe drugs** which **require a doctor's supervision** for use or to make a diagnosis. There may be various reasons for this. Most often it is so that the patient will only use the drug if it will actually help him (within the approved indication) and the doctor can check whether the treatment is proceeding properly, whether there are side effects or unexpected effects and whether the patient is taking the medicine as he should.

Whether a drug will be subject to doctor's prescription is a decision made in each country by the competent **drug agency** (in the CR this is the **State Institute for Drug Control – SÚKL**). These drug agencies primarily take into account the technical data and data on the safety and efficacy of the given drug. If sufficient safety data are not known, it will always choose to require a prescription to keep the patient under supervision. If the patient pays for the medicine himself, then it does not matter which doctor prescribes the prescription drug. Any physician, such as a general practitioner, can prescribe any prescription drug to a patient. The physician is responsible for ensuring that the drug has been prescribed within the approved indication for the drug. Otherwise, it would be a use outside the approved indication – known as **off-label use**. This is permissible in certain limited circumstances, but in such case the doctor (or medical facility where he/she works) will be liable for any harm the patient suffers as a result of using the product.

In the case of a product covered by state health insurance, reimbursement may also be conditional on having the drug prescribed only by a doctor with a certain specialization. But more about that in later sections.

As of January 1st, 2018 doctors are obliged to only write prescriptions in electronic form. These are called e-prescriptions. Only in exceptional cases, especially when it is not possible to access the central database of e-prescriptions (e.g. during an Internet outage), can a doctor write a classic "paper" prescription.

After a doctor prescribes a drug on a device connected to the Internet, he will be sent an e-prescription code from the central database. The doctor may send this code to the patient via e-mail, text message, through an application in the patient's mobile phone or table, or it may be handed over as a paper print out.

When dispensing the drug at the pharmacy, the pharmacist scans the identification code provided by the patient and obtains information from the central e-prescription database about what drug was prescribed, at what strength, pack size, information on the number of packs prescribed and on drug dosage. Information about dispensing the drug to the patient is sent by the pharmacy to the central e-prescription database.

The e-prescription is also associated with other functions, in particular the patient's drug record, which allows the treating physician, the dispensing pharmacist and the patient to monitor the safety of treatment, especially with regard to possible use of drugs with the same active ingredient or undesirable drug interactions. The patient's drug record also includes an electronic vaccination record.

There is also a special **"restricted prescription"** mode. This is intended for particularly sensitive cases where it is appropriate that the drug be prescribed only by specialists who have experience with the disease for which the drug is authorized. Like decisions regarding prescription drugs in general, limited prescriptions are determined according to current laws by the authorization authority (in the Czech Republic, SÚKL).

Restricted prescription drugs may pose an increased threat to the patient due to misuse or abuse. Supervision by a relevant specialist is therefore necessary, or even direct administration of the drug by a specialist in the hospital. There are only a few such drugs today. They include, for example, the **abortion pill** (several registered products with this effect) or **medical cannabis**.

OVER-THE-COUNTER DRUGS

If a medicinal product is not issued exclusively through a prescription, it is categorized as an over-the-counter drug that can be dispensed without a prescription. In general, it must be a medicinal product for **such illnesses** patients can diagnose by themselves that **do not need to be treated under the regular supervision of a doctor**. Once a drug is classified as over-the-counter, it is suitable for self-medication and a sufficient amount of professional counseling will be provided by the pharmacist. The patient should also become familiar with the information given in the package leaflet included in every pack. It is therefore not necessary to consult a doctor. The vast majority of drugs for less serious illnesses, such as the flu or colds, are included in this category.

Even in this category there is a special category of **"over-the-counter medicinal products with restrictions"**. These are medicinal products that can **only be dispensed in consultation with a pharmacist and in limited amounts** each time. A typical example are products **containing pseudoephedrine.** These products which, unfortunately, can be abused by drug addicts, and cannot be purchased in unlimited amounts but only amounts corresponding to approximately one week's treatment.

Did you know that...

...SÚKL manages a drug database where you can find the most up-to-date and complete infor-mation about medicines? The database is publicly available and contains information about all medicinal products authorized in the Czech Republic and it is updated daily.

TERMINOLOGY

Rx

A medicinal product dispensed according to a doctor's prescription.

OTC (over the counter)

A drug that can be dispensed without a doctor's prescription, a drug that can be freely sold.

BEFORE AND AFTER MARKETING

CLINICAL TRIALS

After the research phase and positive results from animal or cell culture tests, the drug is tested on volunteers. A **clinical trial** is conducted according to a predetermined approved schedule in several phases, from healthy individuals to the patients for whom the drug is intended. The aim of the clinical trial is to demonstrate the safety and tolerability of the drug, to verify its therapeutic effects and behavior in the human body, and to find out what its side effects are.

I In **phase I**, healthy volunteers are tested to see if the active ingredient is dangerous to the human body and at what doses it is tolerated. The trial starts with low doses, which are gradually increased, and the maximum tolerated dose is sought. Research on healthy volunteers is not performed if administration of the substance to a healthy person is highly inappropriate (e.g. cytostatics).

II **Phase II** already involves testing on patients. Therapeutic effects are demonstrated in a small number of patients, and only if good efficacy is demonstrated that outweighs the risk of adverse reactions does the trial proceed to the next phase.

III In **phase III**, the efficacy, safety and appropriate dosage of the drug are tested on hundreds to thousands of patients. Based on the results of this phase, an application for marketing authorization is submitted. .

IV In **phase IV**, which takes place after marketing authorization and post-marketing experience, long-term adverse reactions in patients and possible interactions with other drugs are monitored.

The results of the clinical trial define the use of the drug (concrete indication for groups of patients) and determine the most suitable dose for patients with a minimal risk of side effects.

389

clinical trials approved in 2019

Oncology and immunology have recorded a significant growth in total number of trials compared to 2015, specifically 56 % (oncology) and 45 % (immunology).

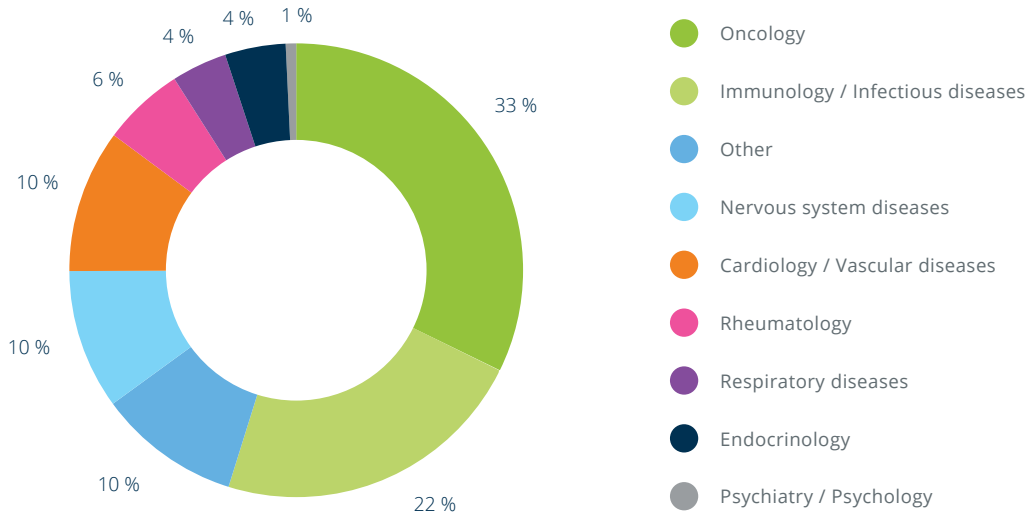
In general, clinical trials of medicinal products can only be conducted in the EU (and Czech Republic) if the rights, safety, dignity and quality of life of patients participating in such trials are adequately protected. At the same time, each clinical trial must be designed to result in reliable and robust data on the efficacy and/or safety of the medicinal products investigated.

The implementation of clinical trials to be carried out in the Czech Republic is subject to a permitting procedure, which is regulated uniformly within the EU from 31 January 2022 (although in certain cases it is still possible to proceed under the previous regulations until the end of January 2023 or the end of January 2025). Submitted materials are assessed on behalf of the Czech Republic by the State Institute for Drug Control (SÚKL) and ethical supervision is performed by the ethics committee, which is one of its bodies. If the application for a permit is rejected by SÚKL, it is not possible to conduct a clinical trial in the Czech Republic. All information related to the clinical trial (including the results of the clinical trial) is stored in a single EU database.

Did you know that...

*...the nature of clinical trials in the Czech Republic has been changing over the long term. We have seen a **shift from general trials to trials focused on highly specified diagnoses and personalized treatment.** This is reflected in the **increase in trials in the areas of oncology and immunology,** where research is focusing on rarer diseases or diseases that require a personalized approach.*

The structure of conducted clinical trials by therapeutic area in 2019



Each clinical trial has three important participants: the **sponsor**, which is the company or institution (most often the pharmaceutical company that is developing the drug) that is responsible for commencing, managing and also funding the clinical trial, the **investigator** or doctor responsible for conducting the clinical trial, and the **trial subjects**, which are healthy volunteers or patients.

Each patient and healthy volunteer signs an **informed consent**, which confirms their willingness to take part in the clinical trial after being informed of all aspects. Participation in a clinical trial is not only an opportunity to obtain a newly developed drug that is not otherwise available, but it also means the participant accepts the responsibilities and obligations associated with taking part in the clinical trial. Consent to participate in a clinical trial can be revoked at any time during the clinical trial. It is important to note that clinical trials are conducted during drug development periods when there is insufficient information about its effects. It is not uncommon for the benefit of treatment to be found to be below expectations during the study, in which case the clinical trial is terminated.

Clinical trials of new drugs are usually randomized and double-blind. Randomization is the random separation of subjects into either the group receiving the test drug or the control group. The control group can be given either a placebo (an inactive substance administered like the drug) or a drug with which the test drug is compared. This is the case, for example, when administering a placebo instead of an active drug could harm the patient. The purpose of randomization is to reduce bias and increase the validity of the data obtained. Objective results are also obtained through double blinding, a procedure where neither the examining physician nor the trial subject knows which group they are in.

Doctors are motivated to participate in clinical trials because it is an opportunity to get a new drug for their patients free of charge and get acquainted with new treatment options. Patients are drawn by the opportunity to be treated with state-of-the-art drugs several years before they become generally available, especially in situations where current drugs are no longer sufficiently effective for them.

In 2019 a total of 16,854 patients were included in clinical trials. This number has been steadily declining over time. In 2015 the number was 26,267, in 2017 it was 21,530. This decline need not necessarily be interpreted negatively, as the shift to more personalized trials means that fewer patients are needed for a single trial than in more general clinical studies.

Saved treatment costs

1.5–1.6 bil. CZK

At the same time, member companies generated public savings on treatment costs amounting to 305 mil. CZK. This value is of course only given for some of the trials listed. **When extrapolating this value according to total number of patients, the overall costs savings thanks to the inclusion of patients in clinical trials is approximately 1.5 bil. CZK – 1.6 bil. CZK.** The resulting value is equivalent to 0.6 % of all funds spent by health insurers for health care in 2017.

MARKETING AUTHORIZATION

If a new drug successfully passes stage three clinical trials, all of the trial results can be submitted to the drug authority for marketing authorization. The main purpose of authorization is to assess the foreseeable risks associated with marketing the given drug and to evaluate whether such risks outweigh the demonstrable benefits of the product – therefore the **quality, efficacy and safety** of the medicine are always assessed and whether a favorable benefit-risk balance is demonstrated. The marketing authorization and post-marketing processes are constantly evolving in response to scientific progress.

THE MARKETING AUTHORIZATION PROCEEDINGS CAN TAKE PLACE IN DIFFERENT WAYS:

Centralized authorization – the assessment is performed by the European Medicines Agency (**EMA**) and the marketing authorization granted by the European Commission is valid **in all EU member states**, Norway and Iceland. This procedure is mandatory for biotechnologically manufactured products, new drugs indicated for AIDS, diabetes, oncology, neurodegenerative, autoimmune and viral diseases, and products for the treatment of rare diseases that affect only a very limited number of patients.

Other types of authorization are granted by the drug agency of the country where the company wants to market the product. The rules for granting authorization are the same for EU countries. In the Czech Republic these rulings are issued by SÚKL.

MRP authorization – The procedure for mutual recognition is intended to authorize drugs that have already been registered in a member state. This country is referred to as the "reference country". The reference country prepares a report summarizing the information submitted for marketing authorization. The agencies of other member states in which the drug is to be registered assess the report and decide whether to authorize the drug in their country or not.

DCP authorization – Decentralized authorization is intended for a medicine that is not yet registered in

any country and is to be registered in more than one country at the same time. The applicant chooses a "reference country" which prepares an assessment report giving a positive or negative opinion on authorization. The other states assess the report and decide whether or not to agree with it.

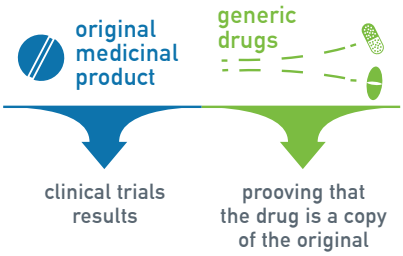
National authorization – is only possible for those drugs that are not yet registered in the EU, and registration is requested in only one country (e.g. in the Czech Republic). This type of registration is being used less and less.

As already mentioned, the marketing authorization requirements for medicines are harmonized in all EU member states. The basic requirements include documentation of drug safety and efficacy, individual production steps, and measures to control the quality of raw materials and the final product. It is necessary to prove that the drug complies with stability tests and that production is carried out according to standards guaranteeing the quality of the drug (good manufacturing practice). However, the requirements for documented data and the marketing authorization dossier vary according to the type of drug:

- **Authorization of an original drug** – for approval it is necessary to submit the results of tests and clinical studies lasting a number of years, the goal of which is to obtain sufficient information on the use of the drug and to assess the risks and benefits.

- **Authorization of a generic drug** – for approval it is necessary to submit a bioequivalence study demonstrating that the given drug behaves identically in the body as the original.

In addition to these most common types of registration there are also other types of registration for traditional herbal preparations, homeopathic medicines and drugs that have long been used with well-established therapeutic applications that have specific requirements adapted for these categories.



BIOLOGICALS

The most modern and fastest developing group of drugs are **biological drugs**. Unlike conventional drugs produced by chemical synthesis, biological drugs are prepared using living organisms (cells) into which specific genetic information stored in DNA has been inserted in a controlled manner. The natural processes in the host cell result in diverse spatial shapes of the molecule. The structure of these drugs cannot be precisely defined. They are large and complex molecules of proteins or polypeptides, which are further modified during the extraction, purification, formulation and storage of the biological drug.

After the end of patent protection of original biological drugs it is possible to market **biosimilars**. These are biological medicinal products that are only **similar** to the original products. They are never absolutely identical because the biological origin and manner of production always make them unique. Considering their natural variability, biosimilars should not be called biogenerics because they are the product of living cells and their structure cannot be precisely defined. Due to the effect on the immune system, their interchangeability with the original biological product is not possible without the assessment of a doctor and there must be medical reasons for any change in the product used. Unlike conventional generic products, preclinical and clinical studies comparing biosimilars to the original product are required in the registration process to assess the efficacy and safety of biosimilars.

The main advantage of biological drugs is the ability to bind to specific places in the body (e.g. cancer cells). **This makes it possible to precisely target treatment, improve therapeutic effect and reduce the likelihood of side effects.** Biological therapy also differs from conventional therapy in terms of financial cost, as the development and production of these products is quite demanding.

The authorization process also determines the manner of dispensation (whether the drug must be prescribed by a doctor or can be dispensed over the counter). Documents are created to provide information about the drug to the public. For the professional community (doctors and pharmacists) there is the **Summary of Product Characteristics** – SPC. This is a relatively extensive document containing all important information related to the use of the drug, its dosage, indication, interactions, adverse effects, pharmacological and pharmacokinetic attributes as well as information about the marketing authorization holder (hereinafter the "holder"). For patients there is the **Patient Information Leaflet** – PIL, which in a comprehensible manner provides information about the drug that is important from the patient's perspective. A patient information leaflet is included in every drug pack and patients are advised to read it carefully before first using the medication and again whenever necessary.

At the end of the registration process, a marketing authorization decision is issued, based upon which the holder (usually the manufacturer or its representative) **can market the given drug**. The drug continues to be monitored. During this post-authorization monitoring its side effects and interactions are assessed, the method of storage is specified, new indications are added, and so on. This is to ensure that the basic goal is met – i.e. that the drugs legally available in the Czech Republic have an adequate level of quality, efficacy and safety.

An authorized drug may be marketed, but without additional procedures patients would have to pay for both prescription and over-the-counter drugs entirely by themselves. For some drugs that costs tens or hundreds of crowns this need not be a problem and the law clearly anticipates this. But for many other medicinal products full payment by patients could represent a problem. This concerns very expensive drugs, and even some cheaper ones if used for chronic illnesses where patients are expected to use them for many months or years.

Therefore, there is a possibility that a health insurance company will contribute to covering the patient's medicine, and this is a constitutionally guaranteed right of every citizen of the Czech Republic to free health care, under the conditions stipulated by law. Ensuring this, however, is not easy at all. Not every medicine can be covered by health insurance, not every patient will be entitled to reimbursement and not all doctors will be able to prescribe such a medicine. But first things first.

WHAT KINDS OF DRUGS DO HEALTH INSURERS COVER?

Health insurance coverage depends on whether a medicinal product is provided during **outpatient or inpatient care**.

When providing inpatient care the health insurer fully reimburses the least expensive version of medicinal products depending on the degree and severity of the illness. **The patient will never pay for medicinal products provided during inpatient care regardless of whether these are prescription or over-the-counter drugs.**

During **outpatient care** medicinal products are covered by the insurer for the amount **and under the conditions mostly set out by rulings of the State Institute for Drug Control** as described below.

However, the law explicitly provides for several exceptions to this procedure.

During outpatient care insurance companies do not cover medicinal products that do not require a prescription (over-the-counter drugs), **unless all health insurance companies agree to reimbursement for reasons of public interest. Health insurers also do not cover auxiliary or supplementary medicinal products, birth control, impotence drugs and others.**

In principle, health insurers do not cover such drugs – patients must pay for these by themselves. The price is determined by the manufacturer, while distributors and pharmacies can add on any surcharge they deem fit. **The price is subject only to market competition.**

If a medicinal product does not fall into a category that excludes reimbursement by an insurer, **the marketing authorization holder may request reimbursement** (here we are still talking about outpatient care) from the health insurance system. The **amount** of patient reimbursement and the **conditions for such** are decided in administrative proceedings by SÚKL.

PRICE AND REIMBURSEMENT REGULATIONS IN OUTPATIENT CARE

At the present time, it is formally **up to the marketing authorization holder** to decide whether to **request** that its drug be fully or partially **reimbursed by public health insurance**. The holder therefore need not necessarily request coverage of drugs that would otherwise be eligible for reimbursement. It can market the medicine immediately after authorization, but patients would then pay the full price at the pharmacy. This price not only includes the price of the manufacturer for supplying the medicine, but also the profit margins of distributors and pharmacies. At the same time, none of these prices would be regulated. The price would be freely determined by the market.

In reality, marketing authorization holders are often motivated to request that their drug be reimbursed. Why? Without reimbursement they would not be competitive. For drugs that do not have an alternative (generic), there would be no risk that patients would buy another drug, but the price would most likely be so high that almost no one could afford to pay for it. In order to ensure the availability of the medicine, the holder tries to ensure that the patient pay as little as possible and that the health insurer pay as much of the price as possible. The situation is all the more striking for drugs that have an alternative. If competitors are covered by health insurance, it is essential that the new drug also be reimbursed by health insurance, otherwise patients would only request the drug that is covered.

The holder is therefore forced to request reimbursement of its drug from public health insurance for many reasons. However, the law notes another circumstance. In situations where a drug is to be fully or partially reimbursed by public health insurance, the law requires that it be subject to price regulation at all levels - for manufacturers, distributors and pharmacies, or for a select groups of drugs, only at the level of mark-up. This means that the price is not set freely by the market, but is subject to certain restrictions.

The rules and processes that regulate pricing at all levels of the distribution chain (from manufacturers to distributors to pharmacies) are called **price regulations**. The rules and processes that regulate reimbursement from public health insurance, including the determination of the amount of reimbursement and the conditions under which the drug will be reimbursed, are called **reimbursement regulations**. Price and reimbursement regulations are partially intertwined.

Price regulations are directed towards drug suppliers and govern the procedure of limiting the price at which they will sell the drug. **Reimbursement regulation** is much more complex. It is not directed towards drug suppliers, but establishes the public right of the patient to obtain a reimbursed drug if she meets the conditions for its reimbursement. At the same time, its mechanisms affect a number of relationships, not only between the patient and her health insurance company, but also between the health insurance company and the prescribing doctor or health care provider.

PRICE REGULATION

Price regulation in the area of mass-produced drugs is directed separately at both the originator (usually the marketing authorization holder or person marketing the drug) and the distributors and pharmacies. We thus speak of two components of this regulation, **the price regulation of the originator and price regulation of the distributors and pharmacies** (i.e. regulation of mark-up). Both components are founded on a slightly different principle, but are mutually related.

PRICE OF THE ORIGINATOR

The price of the originator is regulated through the maximum price determined by SÚKL in administrative proceedings, or possibly by material guidance of the originator price (only applied in select cases).

Regulated prices in the CR are not set as fixed, they only represent ceilings, i.e. the price limit that can be requested by the originator of a medicinal product and the mark-up limit for a distributor and pharmacy. The originator may not exceed the maximum price, but it may supply a medicinal product for a lower price. Distributors and pharmacies have a shared mark-up limit. How they choose to divide this mark-up is subject to mutual agreement.

If there is sufficient competition in a group of mutually interchangeable medicinal products, the Ministry of Health may determine that there shall be no price regulation of the originator's price in such group. The originator's price for such medicinal products is then "deregulated" (i.e. determined by the market) and price regulation is applied only to the mark-up. The originator's price is then subject only to a notification obligation, where the originator must report changes in its price to SÚKL within set deadlines, but the price itself is created through free competition.

TERMINOLOGY

Price regulation of the Ministry of Health

A legal regulation issued by the Ministry of Health of the Czech Republic, which contains, for instance, the definition of the price regulation basic terms, the method of regulation using maximum price or material price regulation and the setting of a maximum commercial mark-up.

Price decision

A legal regulation issued by the Ministry of Health that contains a list of active substances that – in a specific drug form – are not subject to the originator's price regulation. The price is only announced, and only the mark-up is subject to price regulation.

AHP

An agreement on the highest price concluded between the health insurance company and the manufacturer of the medicinal product in the public interest; the manufacturer may not exceed the agreed price when supplying the medicinal product to the Czech market.

MAXIMUM ORIGINATOR PRICE

The maximum originator price is determined by SÚKL in an administrative proceeding according to the Public Health Insurance Act. The price of the medicinal product is generally determined based on the price of the given medicinal product in the countries of the "reference basket". The reference basket, i.e. the countries in which SÚKL ascertains the price of the drug being assessed, is exactly specified by law. The reference basket includes all countries of the European Union with the exception of Bulgaria, the Czech Republic, Estonia, Luxembourg, Austria, Romania, Greece, Cyprus and Malta. Of the 27 EU countries, 9 are excluded. There are several reasons for excluding these countries from the reference basket. In the case of the Czech Republic it is obvious, because we cannot determine the maximum Czech price based on the Czech price, SÚKL would be chasing its tail as it were. In other countries the reason is usually because the country either does not have price regulations or the source of pricing (database of drug prices in the given country) is not public, or possibly because the market of the given country is fundamentally incompatible with the Czech market.

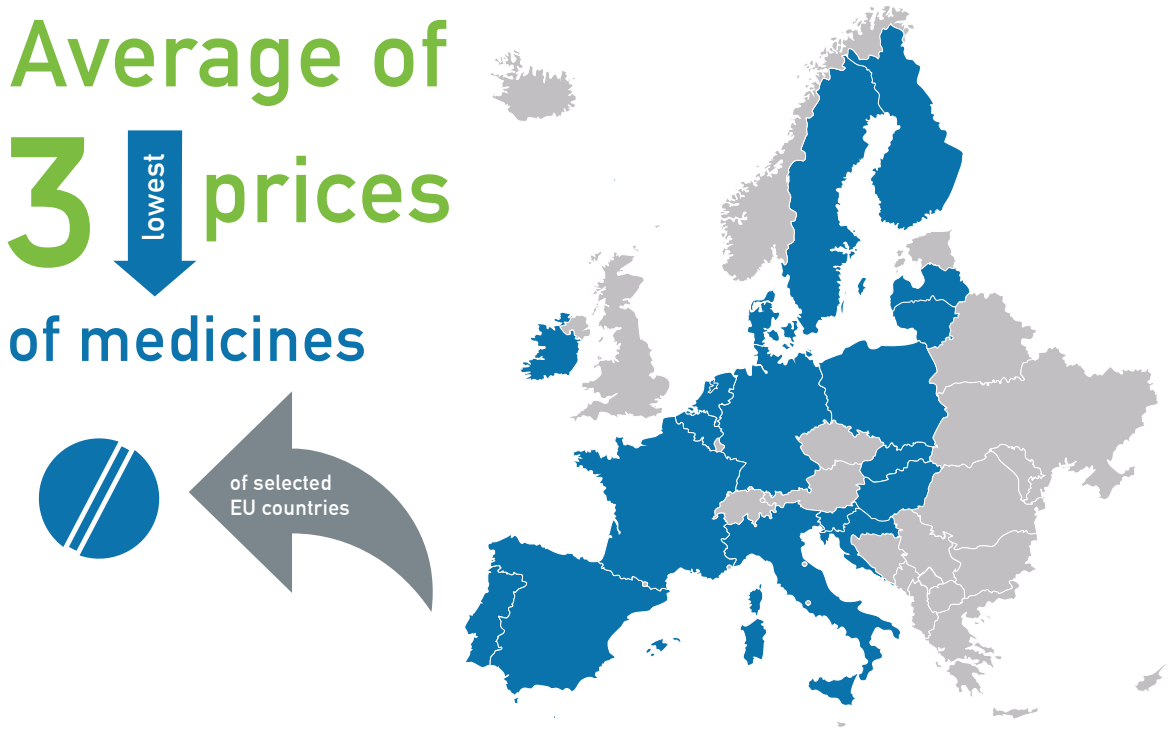
TERMINOLOGY

Maximum manufacturer price

Manufacturer regulation setting the maximum price that the manufacturer cannot exceed when marketing the given drug. This is determined in administrative proceedings and calculated by a mechanism which is precisely specified by law. The price is decided by SÚKL.

Manufacturer's announced

if a competitive environment is ensured, the manufacturer can choose the market price of the medicinal product itself. Then it will simply notify SÚKL. The given price can only be changed by re-notifying SÚKL, within the given deadlines and always once per calendar quarter.



The maximum price is **set as the average of the three lowest prices of the given drug in the countries of the reference basket**. This means that SÚKL will search for the price of the drug being assessed in all 18 countries of the reference basket where it is marketed. It will select the three lowest prices, calculate the average, and use this price as the maximum price for marketing the drug in the Czech Republic.

If the medicinal product does not exist in at least three countries of the reference basket, its price may be determined based on a contract between the marketing authorization holder and the health insurance company. Such a contract is called the **highest producer price agreement (DNCV)**.

If no agreement has been reached with health insurance companies, the last option is to set a maximum price, **based on the price of the nearest therapeutically comparable product**. In this variant, the maximum price is no longer set according to the price of the **same medicinal product** (as it was when working with the countries of the reference basket), but another drug is sought that is therapeutically closest to the product being assessed. The closest therapeutically comparable product is one that contains, in relation to the product under assessment, the closest active ingredient, pharmaceutical form (tablet, capsule or solution for injection, etc.), strength (active ingredient content in one tablet or other unit) and pack size (number of tablets or other dosage units), with these criteria being assessed in that order.

The price is therefore primarily determined based on the lowest price of the closest therapeutically comparable product in the Czech Republic, the price of which was determined based on the average of 3 prices in the reference basket. If none of these occurs in the Czech Republic, then the determination will be based on the lowest price of the closest therapeutically comparable product in the countries of the reference basket.

If no product is found that meets all the quality criteria, then the individual criteria are successively abandoned. It is therefore not necessary to look for a product with the same pack size, it may not even be of the same strength, and if no such drug can be found, a different pharmaceutical form is sought, and ultimately a different drug with the most similar possible active ingredient (within the anatomical-therapeutic-chemical classification).

A simple and shorter procedure is intended for medicinal products that are similar products. Generics and biosimilars, for example, are **similar products**. If a company want to enter a generic in the public health insurance system a does not request a higher maximum price or higher reimbursement or wider reimbursement conditions than the original product, the maximum price and reimbursement will be set within 30 days.

This measure is aimed at facilitating the entry of competing medicinal products in the reimbursement system, since it is competition that leads to reduced prices and reimbursements, and thus **savings for both health insurers and patients**. The law therefore stipulates that when requesting a price (and reimbursement) for the **first similar product in a reference group**, then compared to the original product the maximum price and reimbursement is reduced :

- by 40 % if a generic is being marketed,
- by 30 % if a biosimilar is being marketed,
- by 15 % in other cases.

Applicable legislation – Act No. 48/1997 Coll., on Public Health Insurance, as subsequently amended.

TERMINOLOGY

Price regulation of the Ministry of Health

A legal regulation issued by the Ministry of Health of the Czech Republic that contains, for example, definition of basic price regulation terms, the manner of maximum price regulation or guidance, and determination of the maximum mark-up.

Price ruling

A legal regulation issued by the Ministry of Health of the Czech Republic that contains of list of active ingredients not subject in the given drug form to originator price regulation. This is only announced and only mark-up is subject to price regulation.

DNCV

Highest producer price agreement concluded in the public interest between a health insurer and marketing authorization holder. The holder may not exceed tis price when marketing the drug in the Czech Republic.

MAXIMUM MARK-UP

We now already know how the maximum price is determined. But this is not the price we pay for the drug in a pharmacy or which is paid in full or in part by a health insurance company. The key to pharmacy pricing is the actual price of the originator, i.e. the price at which the originator actually introduced the medicinal product to the Czech market (typically the price on the invoice between the originator and the first distributor of the product in the Czech Republic).

We must then add the mark-up to the actual originator price. The amount of this mark-up is also regulated, as a set maximum which can be added to the originator price. In this case we speak of the **maximum mark-up**. The mark-up is intended to cover business costs and is **shared by all subjects that take part in selling the drug** – distributors, pharmacies, and possibly also the originator if it directly shares in business operations. Each commercial subject is obliged to notify the next distributor or pharmacy of the amount of mark-up already used up. When selling medicinal products to patients the pharmacy may not exceed the maximum mark-up.

The maximum mark-up is stipulated in the price regulation of the Ministry of Health of the CR. In addition to the amount of mark-up expressed as a percentage of the actual originator price, the price regulation also determines the manner of calculating this. **The base for calculating the mark-up is the price of the actual originator price, not the maximum price or announced price.**

If the maximum price is 500 CZK but the originator actually markets the drug for 400 CZK, then the percentage amount of the maximum mark-up is not calculated from 500 CZK, but from the actual price of 400 CZK. The mark-up of individual distributors is added together along with the pharmacy mark-up. Together, the distribution and pharmacy chain may not exceed the maximum mark-up.

The percentage rate of the maximum mark-up is conceived to be degressive, as the originator price increases (the base for calculating mark-up) the maximum amount of mark-up shared by all commercial subjects decreases. Added to the amount calculated by percentage rate we must also add the surcharge, a fixed amount corresponding to zone and base amount (see table below).

As of 1. 1 .2020 the amount of maximum mark-up is:

Zone	Base from (in CZK)	Base up to (in CZK)	Rate	Surcharge (in CZK)
1	0.00	150.00	37 %	0.00
2	150.01	300.00	33 %	6.00
3	300.01	500.00	24 %	33.00
4	500.01	1 000.00	20 %	53.00
5	1 000.01	2 500.00	17 %	83.00
6	2 500.01	5 000.00	14 %	158.00
7	5 000.01	10 000.00	4 %	658.00
8	10 000.01	9 999 999.00	2 %	858.00

The table shows that if the originator markets the drug at a real (not maximum) price of 100 CZK (excluding VAT), then distributors and the pharmacy can add a maximum of 37 CZK excluding VAT (37% of 100 CZK) to this price. VAT will be added to the result (which is currently 10% for medicines) so the final price in the pharmacy cannot exceed 150.70 CZK.

We then generally know the maximum price or announced price of the originator, and we know how to add the maximum mark-up. Every patient can then verify what the theoretical maximum final price in the pharmacy would be, comprised of the maximum price, maximum mark-up and VAT.

SÚKL is required to post maximum prices and announced prices on its website. Every patient can then check whether the price of the medicinal product in the pharmacy corresponds to the maximum price for the end user, which is determined by adding the maximum price (or announced price), the maximum mark-up and VAT.

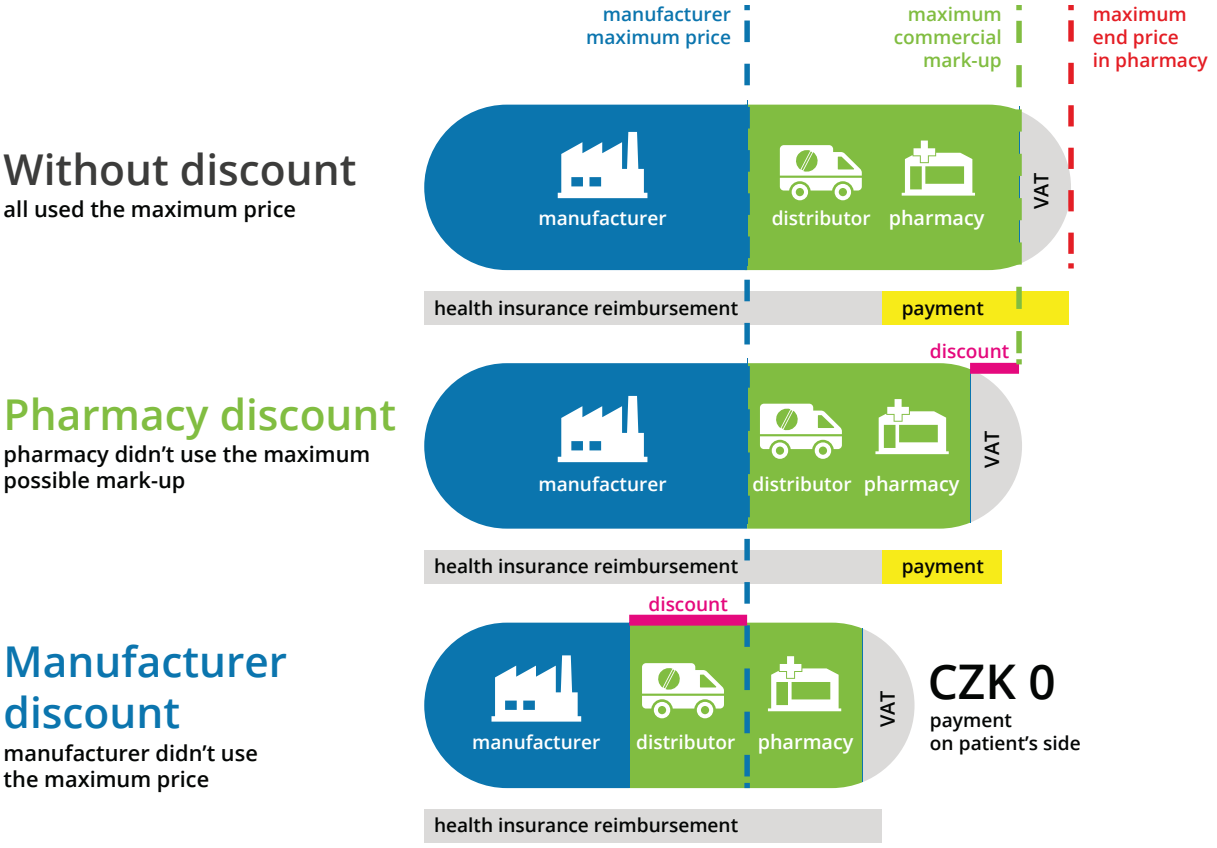
If the price of the medicinal product exceeds such calculated price, this need not necessarily indicate a pricing offense on the part of the manufacturer or distributor or pharmacy. Clearance sales may also come into consideration.

If the maximum price decreases after a drug is placed on the market (SÚKL issues a new decision reducing the maximum price), then it is not necessary to immediately adjust the prices of all products in stock to correspond to the newly set maximum price. The price ruling gives distributors and pharmacies the option of clearance sales at the original price within a maximum of 3 months after such reduction in the maximum price takes effect. Therefore, the new, lower maximum price may be published in the publicly available database, but packs may still be available on the market at the original higher price.

TERMINOLOGY

List of reimbursed medicinal products and foodstuffs for special medical purposes (LP / PZLÚ)

A list published by SÚKL which contains, among other things, the maximum price, the maximum final price of the drug, the amount of reimbursement from public health insurers and the amount of co-payment for the drug, which is counted towards the patient's protective limit for co-payments and regulatory fees.



REIMBURSEMENT REGULATION

SÚKL again decides on reimbursements for **outpatient care**. For innovative medicines this involves a very complex and long-lasting administrative procedure, in which the drug is comprehensively evaluated in terms of its future standing in clinical practice, its efficacy and safety in comparison with other drugs already reimbursed, its benefit and other qualitative and quantitative parameters .

Reimbursement of a medicinal product is determined according to the **basic reimbursement of the reference group**. The reference group is the group of essentially therapeutically interchangeable medicinal products with similar efficacy and safety and similar clinical use. A **list of reference groups** is given in the Decree on the list of reference groups issued by the Ministry of Health of the Czech Republic.

Reimbursement for the reference group is determined at the level of basic reimbursement. **Basic reimbursement is the reimbursement** for a single typical daily therapeutic dose. The cornerstone of reimbursement regulation in the CR is the principle of equal reimbursement for equal effect, which means that if there are several drugs that are therapeutically interchangeable, then their reimbursement is compared at the level of standard daily therapeutic dose intended to achieve the same effect. From the perspective of expenditures by a public health insurer it should not matter which particular drug is given to the patient, reimbursement for the same effect should be the same. In addition to the mutual therapeutic interchangeability of individual drugs, administrative proceedings also determine the dose at which individual drugs have the same effect for a day of therapy.

The basic reimbursement for the standard daily therapeutic dose is determined based on four criteria, with SÚKL choosing the criterion that leads to the **lowest amount of basic reimbursement**. The first criterion is the **external price reference**, i.e. the procedure where the basic reimbursement is determined based on the prices of medicinal products in any EU country. The basic reimbursement is then determined **according to the lowest price of the manufacturer for the standard daily therapeutic dose**. The second criterion determines the basic reimbursement based on the **daily costs of a comparatively effective and cost-effective therapy**, if this amount is lower than the reimbursement determined based on an external price reference. The law further determines the basic reimbursement according to the price stated in the **agreement on the highest manufacturer price** (third criterion) or a **reimbursement agreement**, i.e. an agreement concluded with all health insurance payers specifying the highest possible reimbursement for the product (fourth criterion), provided that this amount is less that the basic reimbursement determined based on external price reference or cost of a comparatively effective therapy.

Formulas given in the implementation guidelines for the Public Health Insurance Act are applied to the basic reimbursement to calculate the reimbursement for individual drugs.

TERMINOLOGY

Reference group

A group of essentially therapeutically interchangeable medicinal products with similar or near efficacy and safety and similar clinical use.

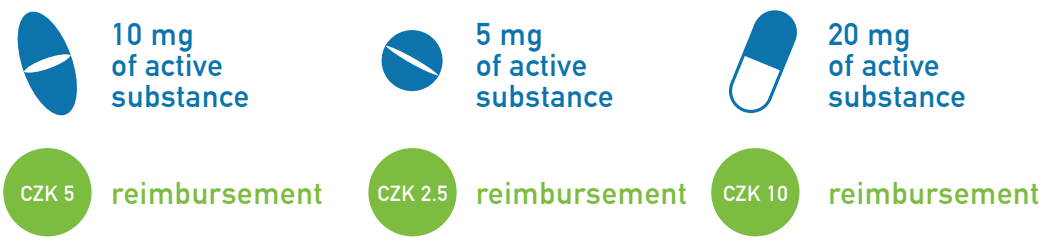
Basic reimbursement

Identical reimbursement for the entire reference group for the standard daily therapeutic dose.

ODTD (standard daily therapeutic dose)

The amount of drug per day for a normal patient, used to compare the efficacy in a common indication for a group of therapeutically interchangeable drugs .

Usual daily dose



SÚKL can also establish conditions under which medicinal products will be covered, if required by professional or safety aspects associated with the treatment, or if this is necessary to ensure the efficient and economical use of medicinal products.

There are two basic types of conditions for reimbursement, **prescription and indication restrictions**. **Prescription restrictions** determine which physician with specialized qualifications can prescribe a medicinal product for reimbursement from public health insurance funds. The reimbursement decision may state that the medicinal product may only be prescribed by a doctor of a particular specialization or by another doctor authorized by a specialist authorized to prescribe the medicinal product.

At the same time, SÚKL may set **indication restrictions** that determine the group of patients or illnesses for which the medicinal product may be covered by public health insurance. Indication and prescription restrictions for individual medicinal products are given in the **List of reimbursed LP/PZLÚ or in the auxiliary code lists published on the SÚKL website**.

The institute may also stipulate that a specific product will not be reimbursed when dispensed at a pharmacy, but only when medical services are provided at an outpatient clinic of a medical facility or during hospitalization – these are called specially billed medicinal products (ZÚLP). Drugs that are very expensive and intended for specialized therapy constitute a special category of ZÚLP. These products may only be prescribed (used) and above all reported by health service providers with special contracts for such specialized therapy – typically these are specialized treatment centers for oncological or other serious diseases. Such centers are then reimbursed by the health insurance company only if the reimbursement of a specific medicinal product is agreed between the health insurance company and the specialized center based on a special contract.

During each procedure to determine or change the basic reimbursement of a group of essentially therapeutically interchangeable medicinal products, the State Institute for Drug Control must examine whether there is full reimbursement (i.e. no patient surcharge) of at least one medicinal product in the group of medicinal products listed in **Annex 2 to the Public Health Insurance Act**. Annex No. 2 to the Public Health Insurance Act currently contains 195 groups of therapeutic substances. Thus, only in these groups of therapeutic substances does the law impose the obligation to have a fully reimbursed medicinal product.

Not all groups of medicinal products are placed in one of the groups of Annex no. 2. The commonly held view that at least one product in each reference group must be fully reimbursed does not apply.

TERMINOLOGY

Annex no. 2

An annex to the Public Health Insurance Act, which specifies the groups of medicinal products in which at least one product must be fully reimbursed.

Full reimbursement of a medicinal product

The obligation to provide a fully reimbursed medicinal product in the group of medicinal products belonging to Annex no. 2. This obligation is not specified for each group of therapeutically interchangeable medicinal products (reference group).

The State Institute for Drug Control must first find out whether the given reference group belongs to a group in Annex no. 2. If it does not, then there is no obligation to ensure full reimbursement of a medicinal product in that particular group. If the reference group is one of the groups listed in Annex no. 2, SÚKL must examine whether the full reimbursement of at least one medicinal product is ensured.

Assuming that full payment is ensured, SÚKL shall not further modify the basic payment calculated according to the four criteria above. If the full reimbursement of at least one medicinal product in a group listed in Appendix no. 2 is not ensured, the State Institute for Drug Control is obliged to adjust the basic reimbursement so that the least expensive medicinal product is fully reimbursed. In such case, the basic reimbursement is based on the price of such medicinal product in the Czech Republic.

In certain cases, it is possible to request a **bonus** for reimbursement of the product compared to the basic reimbursement, or it is possible to **devalue** a specific product, i.e. to set a reimbursement lower than the basic reimbursement. This occurs when a specific product has a better or worse efficacy or safety than the product used to determine the basic reimbursement in the reference group (reference product). It is also possible to provide a bonus (but not devalue) a product that enables better patient cooperation, has a more suitable pharmaceutical form, or requires a bonus with respect to public interest. In no case may the bonus constitute more than 30 percent of the basic fee.

An **additional increased reimbursement** may also be provided for a medicinal product that can be used to treat patients in an indication where the reference product used to calculate basic reimbursement cannot be used. The procedure described above shall be used to determine additional increased coverage. **Such product will thus have two reimbursements**: one according to the basic reimbursement (for indications identical to the reference product), the other separately with increased reimbursement for indications which differ from the reference product.

TERMINOLOGY

Eligible co-payment

A co-payment that can be counted towards the protection limit for the amount of the lowest co-payment for a medicinal product containing the same active ingredient with the same route of administration as the dispensed medicinal product.

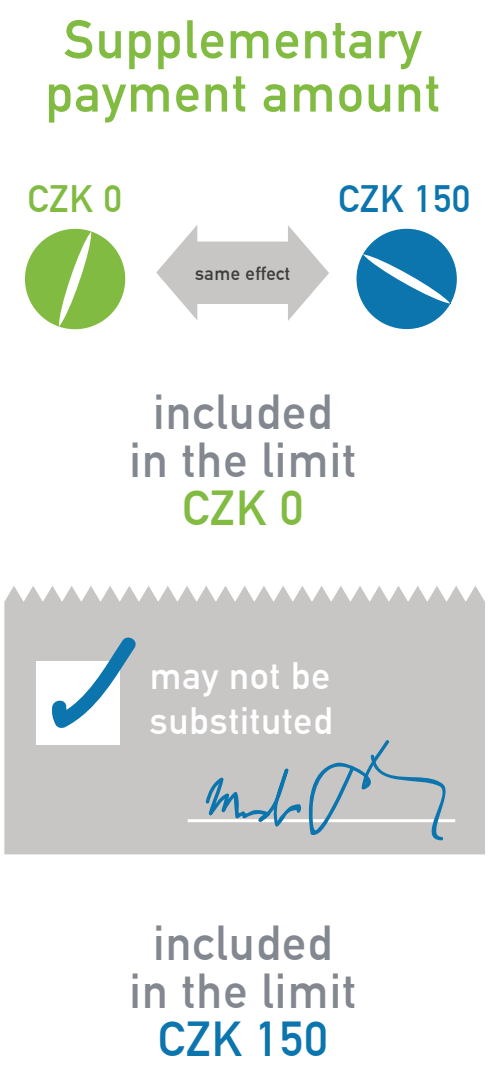
CO-PAYMENTS

The difference between the price of the medicinal product and reimbursement from public health insurance is paid by the patient (during outpatient care) in the form of a **co-payment**. As the price of the medicinal product is not fixed, the co-payment of the patient may differ at different pharmacies.

The Public Health Insurance Act protects patients from high co-payments through the **protective limit on co-payments for medicinal products**. Counted towards this protective limit are co-payments for drugs amounting to the lowest co-payment for a product containing the same active ingredient given through the same route of administration as the medicinal product dispensed. **Therefore, if at least one medicinal product containing the same active ingredient and administered in the same way as the dispensed medicinal product is fully covered by the health insurance company, the co-payment counted towards the protective limit is 0 CZK, regardless of the patient's actual co-payment.**

An exception is the situation where the prescribing doctor indicates on the prescription that the prescribed medicine cannot be replaced. In this case, the actual co-payment will be included in the protection limit. The amount of the eligible co-payment can be found for each reimbursed medicinal product from the **List of Reimbursed LP / PZLÚ**. Co-payments for medicinal products containing active ingredients intended for supportive and supplementary treatment are not included in the protection limit. There is an exception for patients over 65 years of age. **A list of therapeutic substances intended for supportive and supplementary treatment is given in the Decree of the Ministry of Health of the Czech Republic. The protection limit is set at 5,000 CZK per year, 1,000 CZK for persons under 18 and over 65 and 500 CZK for persons over 70 and disabled pensioners in the third degree of disability (if other conditions are met).**

It is not necessary to personally monitor whether the protective limit for co-payments has been exceeded. This is done directly by health insurers who are required to do so by law. The insurance company is obliged to return the amount by which the limit was exceeded to the insured within 60 days after the end of the quarter in which the limit was exceeded.



HIGHLY INNOVATIVE MEDICINAL PRODUCTS

Reimbursement for highly innovative products is determined in a somewhat different manner.

Medicines used to **treat extremely serious diseases** can be classified as highly innovative. **An extremely serious disease is a disease requiring permanent or long-term hospitalization, a disease leading to frequent re-hospitalizations for several years or disability, a disease that results in permanent serious damage to health, complete or almost complete loss of sight, hearing, speech or movement, or a disease that shortens life expectancy by more than 20%.** The available data on such a highly innovative medicinal product must then sufficiently substantiate its contribution to the treatment of a highly serious disease in the manner described in more detail in the law. These highly innovative medicines, for which in most cases there is not yet enough data to pass the standard health insurance reimbursement process described in the previous chapters, can be set up as **temporary reimbursement**. This is set for 3 years, with the possibility of being re-established for another 2 years (a maximum of 5 years in total). During this time, sufficient data on the efficacy or cost of therapy should be collected to establish permanent reimbursement.

Innovative medicines often save lives or improve quality of life for patients. These are very expensive treatments provided only at specialized centers that have concluded contracts with health insurers, so they are the "center drugs" listed above.

Costs to public health insurers to reimburse highly innovative medicinal products provided to policyholders during temporary reimbursement may not exceed the amount specified in the budget impact analysis used as the basis for the SÚKL decision. Otherwise, the marketing authorization holder is obliged to cover the amount by which costs exceeded the amount specified in the budget impact analysis. To this end, each health insurance company shall conclude a contract with the marketing authorization holder, which shall include an agreement on how to reimburse the costs that health insurance companies would incur if the costs of reimbursing the highly innovative medicinal product during temporary reimbursement exceed the expected amount.

If **after temporary reimbursement expires** the highly innovative medicinal product is not permanently reimbursed, **the insured person** treated with the highly innovative medicinal product under temporary reimbursement **shall have the right be treated with this medicinal product at the expense of the marketing authorization holder** until switched over to a comparatively effective and safe treatment covered by health insurance and suitable for such insured person, **but for a maximum period of 24 months**.

The cost of health insurance in 2019 for all center medicines, not just highly innovative drugs, amounted to 20.4 billion crowns. The number of patients treated with innovative drugs is constantly growing. However, resources devoted to treatment are not merely consumed. They also represent an investment because treatment not only helps to prolong life but also prevents or delays disability, keeping patients productive (if treatment is provided in a timely manner, patients remain active instead of becoming disabled like before, survival can be extended by up to decades).

MEDICINAL PRODUCTS INTENDED TO TREAT SEVERE ILLNESSES

Effective as of January 1st, 2022, there is a new rule for reimbursing **products to treat rare diseases**, i.e. products granted this status by the European Medicines Agency for the entire EU. Simply put, these are medicines that are used to treat life-threatening or chronically debilitating diseases that affect a very small number of patients (no more than five in 10,000 people in the EU) that are unlikely to be developed and marketed without a special regimen (given their high cost and small number of patients). At the same time, there is no [other] satisfactory treatment for such diseases and the medicinal product can be expected to bring significant benefits to those affected.

Thanks to this new reimbursement rule, patients have the opportunity to obtain reimbursement for medicinal products that undisputedly provide medical benefits but which, due to their cost and small number of patients, would probably never be covered by health insurance (therapy per patient is very expensive compared to "normally covered" therapy). This is a groundbreaking change. In contrast to the normal reimbursement process, **relevant professional societies and patient organizations are also directly involved in the administrative process**, allowing professionals and patients to directly influence the outcome of such proceedings through their arguments and statements. In addition, applications are submitted to the advisory body of the Ministry of Health of the Czech Republic after a basic assessment by SÚKL, which evaluates the application in terms of the **social security system and societal impacts of the possibility of treating such rare diseases**, which are parameters that SÚKL does not, in principle, assess when determining reimbursement in the usual way. On this basis, the Ministry will issue a binding opinion on the application, which SÚKL must follow when ruling on the application.

Even in this case, the marketing authorization holder is obliged to reimburse health insurance companies for costs incurred to reimburse medicinal products intended to treat rare diseases in excess of the costs stated in the budget impact analysis, which was the basis for the SÚKL decision. To this end, each health insurance company enters into a contract with the marketing authorization holder specifying how the health insurance companies will be compensated if the costs incurred to reimburse the medicinal product exceed the expected amount.

EXCEPTIONAL REIMBURSEMENT FROM HEALTH INSURANCE

For special situations where the patient cannot be treated with medicines that are covered by health insurance **due to his/her state of health**, an exceptional method of reimbursement is introduced in Section 16 of the Public Health Insurance Act. In the event that all options for reimbursed treatment have been exhausted for a particular patient, and a drug that is not covered is the **only treatment option** in terms of the insured's health condition, the health insurance company will also cover treatment with an otherwise unreimbursed medicinal product.

The health insurance company decides whether the conditions for extraordinary payment according to Section 16 are met. The applicant, who is either the patient or his healthcare provider, must document in the application what treatment the patient has already received and justify why the required medication is the only treatment option for that patient. Most often, this is a drug that is new and not yet reimbursed by health insurance, or a drug used to treat a disease for which it is not registered, but where there is scientific justification for its use in this particular patient, or a situation where other treatments are not effective or the patient cannot undergo them for health reasons. Alternatively, it may be a situation where the health insurance medicine is only reimbursed for a certain period of time, however, a particular patient may benefit from continued treatment. The insurance company must give its prior consent to this procedure, and if it does not do so within 15 days of receiving

the application, it must decide on the application according to the Administrative Procedure Code.

This may possibly concern a situation where the drug is only covered by health insurance for a certain period of time, however, a particular patient may benefit from continued treatment. The insurance company must give its prior consent to this procedure, and if it does not do so within 15 days of receiving the application, it must decide on the application according to the Administrative Procedure Code – it is therefore possible to take legal recourse against rejection or failure to act by an insurer in the same way that legal recourse may be taken against any other administrative ruling.

The reason for approving a request for exceptional coverage must always be the medical condition of the patient. Other conditions such as the economic situation of the patient or the patient's wishes or refusal of treatment cannot be taken into account.

The prior consent of an insurance company to exceptional reimbursement is not required in the case of urgent care, i.e. care designed to prevent or limit emergencies that are immediately life-threatening or could lead to sudden death or serious health risks or cause sudden or intense pain and sudden changes in the behavior of a patient who is endangering himself or his surroundings. In such situations, the doctor may provide the patient with care in accordance with Section 16 without further notice and shall then immediately inform the health insurance company of this fact.

REIMBURSEMENT DECREE

An important part of the public health insurance system is the reimbursement decree, which each year establishes the **principles for regulating the reimbursement of health care services provided by all segments of health care**. Among other things, the decree sets the rules for calculating the various limits of reimbursement from health insurance for individual areas of specialization, e.g. for general practitioners, outpatient specialists and dentists, but also for hospital care and laboratories.

For various fields of medicine the decree stipulates the **method for calculating regulatory limits** for medicinal products prescribed by individual doctors or reported in the provision of care. It also lists the cost limits for center medicines for individual diagnostic groups - the reimbursement limit for center medicines is then contracted by a specific provider with a health insurer within the center medicines budget.

In the event that a doctor, hospital or specialized center **exceeds the limit set by the decree**, the health insurance company will only provide **partial reimbursement** for such care or medication, or in very exceptional cases it will not pay at all. At the same time, however, if the medical facility is able to agree with the health insurance company on the rules of reimbursement and conclude a contract, such contract takes precedence over the rules of the reimbursement decree, so that it is possible to individually take into account a specific situation to which the rules are not applicable.

AVAILABILITY OF MEDICATIONS FOR PATIENTS

Probably every one of us has once visited a pharmacy and requested a drug that they do not have. If this is a drug for which generics exist, then it is usually not a serious problem since the patient can get a generic and "only" has to get used to the different name and appearance of the drug she is taking. However, the situation is different in the case of a drug for which there is no generic. The patient has to go back to her doctor and find an alternative – a medicine with another active ingredient which may or may not suit the patient as well as the original medicine (to be sure, a pharmacist may help find such an alternative, but doctor approval is essential here).

There are a number of reasons why a medication may not be available in Czech pharmacies. The most common include problems with the drug's own production, which usually causes only a temporary supply outage. The intensity of measures taken to address it this outage depend on the length of such a failure, the severity of the disease being treated with such drug, and the number of patients in dire need of it.

The legal regulations governing pharmaceuticals stipulate that in the Czech Republic, only registered medicines for which safety and efficacy have been verified may be used to provide health care. At the same time, however, these regulations introduce certain tools for situations where a registered drug is not available and cannot be replaced by another registered drug in that situation.

If short-term unavailability of a drug is expected or this drug is only for a small group of patients, the situation may be resolved by importing an unregistered drug from abroad. Such drug may only be prescribed by the attending physician by writing "unregistered medicinal product" on the prescription. This must be a drug that is registered in another country - usually it is imported from a neighboring country (e.g. Germany, Slovakia). A problem may be that such medicine is not covered by any health insurance company in the Czech Republic - either the patient has to pay for it himself or he can request special reimbursement if the conditions of Section 16 are met (see the section on Exceptional Reimbursement).

If a drug is not available for a long period of time, the Ministry of Health of the CR will cooperate with SÚKL to call for applications for a Specific Treatment Program (SLP). Based on this, an applicant, most often a drug manufacturer or distributor, can deliver an unregistered medicinal product to the Czech Republic until the registered product is available again. Such drug is dispensed in pharmacies in packs marked with the words "specific treatment program" and may be reimbursed by the health insurance.

In recent years we have increasingly seen a lack of medications available to patients in pharmacies, even though manufacturers have no problem with producing and exporting these drugs to the CR. This situation is caused by re-exports, when drugs imported to the CR are sent back abroad by distributors.

RE-EXPORTS

Re-exporting occurs when the Czech price of drugs is lower than the price elsewhere. So if a re-exporter in the CR purchases drugs at the lower (officially set) price and is able to sell them abroad at a much higher price, the difference between prices after deducting re-export costs is profit.

The manner of determining the maximum price is described in a previous section, including the reasons why it is in the interest of the Czech Republic to set this price at a relatively low level to ensure the financial sustainability of the health insurance system. The downside of successfully reducing maximum prices is precisely the danger of re-exports. The greater the difference between the price in the Czech Republic and the price in other countries (just one is enough), then the more attractive such drug becomes for re-export. This not only applies for the Czech Republic, but for any country. A number of European countries are faced with re-exporting to varying degree.

At first glance it may appear that the simplest solution would be wholesale prohibition of re-exporting drugs to other countries. This, however, is not possible because the principle of free trade between individual countries is one of the basic pillars of the EU and under normal circumstances this also applies to medications. Another solution might appear to be a uniform European price that would entirely eliminate re-exporting. However, this would remove pressure for the lowest possible price that virtually every country wants to achieve. In addition, the financial strength of individual health systems varies significantly. If prices increased without a corresponding increase in reimbursements from health insurance, it could happen that medicines will be on the market, but will be unavailable to patients due to high co-payments.

Restrictions or prohibition of re-exporting may only be carried out for particular drugs. Every such ban must be justified by the fact that a lack of the drug would jeopardize the health of patients in the country. SÚKL evaluates information about the supply and consumption of available drugs, and assesses the risk of insufficient inventory of individual drugs in the Czech Republic. This is always with regard to the replaceability of a particular drug by by another. Medications with a realistic risk of unavailability will be placed by the Ministry of Health of the Czech Republic on a list of medicines for which planned exports abroad must be reported in advance to SUKL by distributors.

If based on the mandatory reports of drug manufacturers, distributors and pharmacies SÚKL determines that a drug planned to be re-exported and listed by the Ministry of Health of the CR will not be available for patients in the Czech Republic, the Export Ministry will restrict or entirely prohibit such re-export, but only while the reasons for such ban persist.

ADVERTISEMENT OF MEDICINAL PRODUCTS

As evident from the preceding sections, drugs are a commodity this is regulated by strict rules from the moment development begins to registration and during the entire time they are marketed. The purpose of these regulations is to ensure the protection of public health and the health of individuals. It is therefore no surprise that drug advertising is also regulated by law.

Advertising is, very simply put, any activity intended to increase the sale of goods (in our case, medications). Of course, distinguishing the difference between providing information about treatment options and advertising a drug is not at all easy.

The purpose of regulation is to ensure that advertising provides objective, current and complete information to persons who decide to use medicines. In previous sections, we explained that the method of dispensing drugs is always determined during their registration, i.e. whether they can only be issued with a prescription or can be sold freely over the counter. While over-the-counter drugs need not be supervised by

a physician, the patient makes the decision regarding their purchase (possibly after consulting a physician or pharmacist), while for prescription drugs a doctor decides on the prescription and subsequent use.

In practice, this means that advertising for prescription drugs may only be addressed to the professional public (doctors and pharmacists), while advertising for over-the-counter drugs can also target the broader general public. We will explain in greater detail how the advertising we all see is regulated, i.e. the advertising for over-the-counter medications.

Do you know that...

...the only medical prescription drugs that can be advertised to the general public are vaccines? Such advertising, which is intended to increase the vaccination rates of populations, must be carried out within guidelines approved by the Ministry of Health of the Czech Republic. This must always be an advertisement for optional vaccination, where everyone can decide (after consulting a doctor) whether to get vaccinated (like influenza vaccinations).

The law establishes two types of requirements for advertising – general, which apply to any kind of drug advertising (regardless of the person it is intended for) and special requirements depending on whom it is targeting.

General requirements:

- the advertising must only be for a **registered drug**,
- all information in the ad must **correspond to the Summary of Product Characteristics** (the public document approved during registration). Of course, advertising tends to be more concise, but all information in advertising must also be found in the Summary of Product Characteristics,
- the advertising must **objectively** introduce the drug without exaggerating its attributes, thus promoting its **rational** use.

Advertising targeting the general public must meet a number of special requirements, such as the obligation to indicate that it is a medication, the name of the drug, information on proper use of the product and an appeal to read the patient information leaflet. Advertising must not indicate that the effects of the drug are guaranteed, that they are not associated with any side effects, or that they are better than or equivalent to the effects of other treatments. Advertising must also not refer to the recommendations of scientists, health professionals or persons with social status.

Drug advertising must not be focused solely on children under 15 years of age, because they are generally unable to use drugs without supervision and advertising must not encourage them to seek out and use them. The law contains a number of other requirements to protect patients and guarantee that the information given in advertising is understandable and clear, and cannot cause misleading or deceptive impressions.

The manner of disseminating advertising is not regulated. Advertising for over-the-counter drugs can be found in newspapers, magazines, on television or the radio or on the Internet.

If the law establishes rules and restrictions, there must also be someone who ensures compliance. It is not possible to rely only on the responsibility and conscientiousness of entities in the pharmaceutical industry. The body monitoring compliance for all advertising outside television and radio broadcasting is the State Institute for Drug Control. The Radio and Television Broadcasting Council monitors radio and television advertising. In the event that one of these authorities determines and then demonstrates in administrative proceedings that certain advertising violates the rules of the law, then it imposes a fine. In practice, fines range from tens of thousands to hundreds of thousands of crowns depending on the severity of the violation.

BORDERLINE PRODUCTS – NOT EVERYTHING SOLD IN A PHARMACY IS A DRUG

In addition to drugs, pharmacies also offer other categories of products that are typically called **health and beauty products**. These include **medical devices, dietary supplements and cosmetics**. The attributes or presentation of certain products may fall under multiple categories. It is useful to know how these categories differ and what we can expect from them so we can make the right decisions based on our needs.

DRUGS

Previous sections describe in relatively great detail the regulations of drugs, how they are monitored and the demanding process that each drug must pass through to be marketed. In brief, we may summarize that if something is labelled a *medicinal product*, then this is a drug that had to pass through a clinical trial and registration process, during which it had to demonstrate its **efficacy and safety**. All information given on the pack and in the patient information leaflet correspond to what has actually been demonstrated for the drug. It is necessary to realize that the entire regulation of pharmaceuticals is quite demanding financially and that the resources invested into development must necessarily be reflected in the price of the drug.

The regulation of other categories is not that strict.

DIETARY SUPPLEMENTS

Dietary supplements are the category that we most often mistakenly consider medication and expect a therapeutic effect without carefully reading the package text. Although visually dietary supplements look very similar to over-the-counter medicines, in terms of regulated claims these are very different categories.

The difference ensues from the very definition of a dietary supplement, which is a **foodstuff, the purpose of which is to supplement a normal diet**, and which is a **concentrated source** of vitamins and minerals or other substances with nutritional or physiological effect, contained in a food separately or in combination. Such food is intended for direct consumption in small measurable quantities. Typically this concerns tablets or drops.

Dietary supplements need not demonstrate their efficacy but only safety. Legal regulations determine what substances may be contained in dietary supplements and which are prohibited.

There is also a common European list of health claims that can be **made by dietary supplements or in advertising for them**. No other claims may be made by dietary supplements. Only a small percentage of claims that have been made in the past for dietary supplements have been approved. These are claims that have been demonstrated by the results of clinical studies.

The most common health claim is that a supplement "*contributes to normal functio*n" or "*condition*". It follows that dietary supplements are not intended to remedy a state of disease, but are intended to maintain normal condition. As an well-known example, we can mention vitamin C. There are a total of 15 health claims approved for vitamin C, fourteen of which mention that it “contributes” (to normal function of the immune system, to normal energy metabolism, to normal collagen formation). The final claim is that it increases iron absorption.

Dietary supplements thus cannot be directly presented as having therapeutic or preventative attributes. In practice, however, we see celebrities promoting dietary supplements on TV by saying that they use a product that is, for example, “for joints”. Then the person is shown running up stairs. The viewer watching such advertisement often gets the impression that the celebrity is able to move so well because they use the product being promoted, even though no such information is given. Or the pack provides information about a particular disease and a person gets the impression that the product is intended to treat this illness, even though no such claim is made.

The fact that a dietary supplement contains the same or similar ingredient as a drug does not mean that it acts the same way or has a similar effect in the human body. The effect of any substance in the body is a complicated process affected by a number of factors, such as the size of the molecule and the excipients. That is why a generic must demonstrate its bioequivalence (see the corresponding section). When choosing a suitable medication in a pharmacy we must always be aware of what we can reasonably expect from the particular category of product with respect to the obligations that must be met before it can be marketed.

Dietary supplements serve an important role when for whatever reason a person is lacking a sufficient amount of vitamins, minerals or nutrients from their diet – either due to increased consumption or insufficient uptake (illness, season). In such case the lacking substance should be supplemented. Dietary supplements should not serve as a replacement for a sufficiently varied diet and they should not be used long-term.

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