Chapter 25

Pharmaceuticals

1. General

Following Romania's accession to the European Union, Romanian healthcare legislation was generally harmonized to European legislation, the main EU enactments in the pharmaceutical field being transposed into national legislation. However, certain matters such as pricing, reimbursement and taxation are specifically regulated at a national level by the Romanian competent authorities.

The legal regime of medicinal products in Romania is widely regulated, and important pharmaceutical related aspects are set forth under secondary legislation issued by the competent Romanian authorities. Unpredictable changes may therefore occur in pharmaceutical legislation, depending on the actual economic circumstances and public policies decided by the Romanian authorities, which may have an immediate impact on companies acting on the pharmaceutical market.

2. Main Regulations

- Law No. 95/2006 on health care reform, as republished on 28 August 2015 and subsequently amended and supplemented (the "**Health Law**");
- Government Decision No. 400/2014 for the approval of service packages and of the Framework Agreement on the conditions of medical assistance provision within the social health insurance system for 2014-2015, as subsequently amended and supplemented;
- Government Decision No. 206/2015 for the approval of national health programs for 2015 and 2016, as subsequently amended and supplemented;
- Government Decision No. 720/2008 for the approval of the List of International Non-proprietary Names (DCIs) of Medicines out of which insured persons benefit with or without personal contributions, based on medical prescription, within the social health insurance system, and of the International Non-proprietary Names of Medicines granted under the national health programs, as subsequently amended and supplemented (the "**DCI List**");
- Order of the President of the National Health Insurance House No. 615/2010 for the approval of the computation method of the reference price for medicines with and without personal contributions, prescribed in the ambulatory treatment, as subsequently amended and supplemented;
- Ministry of Health Order No. 1605/2014 for the approval of the computation method, of the lists of trade names, and of the reimbursement prices of medicinal products which are granted to the patients under the national health programs, and the computation method thereof, as subsequently amended and supplemented;
- Ministry of Health Order No. 75/2009 for the approval of the Norms regarding the calculation of the price of medicinal products for human use, as subsequently amended and supplemented;

- Ministry of Health Order No. 904/2006 for the approval of the Norms relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

3. Competent public authorities

3.1 The Ministry of Health

The Ministry of Health (the "MoH") is the central authority in the healthcare system with the following main attributes in the pharmaceutical area:

(i) issues general healthcare policies, strategies and regulations;

(ii) controls the implementation of healthcare politics, strategies and programs;

(iii) ensures, in collaboration with local and central public administration institutions, the necessary financing for the function of public healthcare institutions;

(iv) issues, implements and coordinates national health programs;

(v) organizes national tenders for the acquisition of medicinal products; and

(vi) approves the maximum prices of medicinal products applicable in Romania.

3.2 The National Health Insurance House

The National Health Insurance House (the "NHIH") is a specialized public institution which sets the regulations for the functioning of the social health insurance system, and has, *inter alia*, the following main roles and responsibilities:

(i) drafts and approves regulations related to the collection, management and control of social health insurance funds;

(ii) drafts the national framework agreement regarding medical assistance in the social health insurance system;

(iii) regulates certain aspects in connection to the reimbursement of medicinal products;

(iv) administers, together with local health insurance houses, the social health insurance funds;

(v) monitors and controls the release of reimbursed medicinal products; and

(vi) coordinates the activity of local health insurance houses.

3.3 The National Agency for Medicines and Medical Devices

The National Agency for Medicines and Medical Devices (the "NAMMD") is a public authority subordinated to the MoH, set up by the merger in 2010 of the National Medicines Agency and the Technical Office for Medical Devices. The NAMMD has the following relevant attributes and responsibilities in connection to medicinal products:

(i) drafts various norms, instructions and regulations in connection with the authorization, marketing, manufacturing, import and distribution of medicinal products;

(ii) issues marketing authorization for medicinal products;

(iii) issues wholesale distribution licenses;

(iv) issues manufacturing and import licenses;

(v) authorizes clinical trials carried out in Romania;

(vi) supervises and controls the quality of medicinal products;

(vii) supervises the activity of wholesale distributors of medicines;

(viii) implements the mechanism of health technology assessment;

(ix) regulates and controls the pharmacovigilance activity; and

(x) approves advertising materials used for the promotion of medicines.

4. Marketing authorization procedure

Any medicinal product for human use marketed in Romania requires a valid marketing authorization (the "MA").

The MA is issued by the NAMMD with respect to medicinal products whose approval for marketing is sought only in Romania (national procedure), or for those medicinal products whose approval for marketing is simultaneously sought in several EU Member States, amongst which is Romania (the decentralized procedure). An MA may be acknowledged by NAMMD, in cases where medicinal products have already been approved for market placement in one or several EU Member States, and the subsequent approval for placement on the Romanian market is subsequently sought (the mutual recognition procedure). Likewise, a valid MA may be issued by the European Medicines Agency, within the centralized procedure regulated by EC Regulation No. 726/2004.

NAMMD grants the MA only to the applicants established in Romania or in another EU Member State. Therefore, pharmaceutical companies located in countries outside the European Union should firstly set up an entity in Romania, or in another EU Member State in order to be entitled to apply for a MA.

The MA procedure is in line with the procedure set forth under Directive 2001/83/EC on the Community code relating to medicinal products for human use (the "Directive 83/2001"), while the content of the MA application filed with the NAMMD is similar to the one required under the European centralized procedure.

The relevant legislation stipulates the national MA procedure to be finalized within 210 days from the date of submission of the complete application file (including the proof of payment of applicable taxes), provided that no supplementary request for completion is made by NAMMD. The MA is valid for an initial 5 years period, which may subsequently be extended. Further to the issuance of the initial MA, any additional

strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions to the relevant medicinal product must be authorized by the NAMMD.

The Health Law provides a period of exclusivity of data of 10 years for innovative medicinal products, thus, generic medicinal products authorized based on the results of pre-clinical tests and clinical trials of a reference (innovative) medicinal product cannot be placed on the market until 10 years have elapsed from the initial authorization of the respective reference product.

5. Distribution

Romania observes the principles of EU legislation also in connection with the distribution of medicinal products for human use. Thus, the distribution of medicines to hospitals, pharmacies, distributors or other competent entities may be only performed by entities authorized as wholesale distributors of medicinal products.

Wholesale distribution authorization is required not only for the sale or purchase of medicines, but also for the warehousing, handling, delivery and export related activities. Entities holding a manufacturing authorization in Romania are deemed as authorized wholesale distributors of the medicinal products covered by said authorization.

Since 2008, a wholesale distribution authorization is issued by the NAMMD, previously the competent authority being the MoH. The authorization procedure should not exceed 90 days from the day the NAMMD receives a valid application and complete documentation, a term in which the NAMMD is required to carry out an inspection of the distributor's warehouse or premises, as the case may be.

While the main wholesale distributors generally own the medicine's warehouses, a company may also apply for a wholesale distribution authorization without owning a warehouse, provided it has concluded an agreement for warehousing services with an entity holding an authorized warehouse for medicinal products. Likewise, a wholesale distributor may execute agreements with other authorized entities with respect to other logistic services (*e.g.* transportation, handling, delivery). Once issued, the wholesale distribution authorization is valid for an unlimited time, unless revoked by the competent authority in case the authorized distributor no longer observes the authorization requirements.

According to the Health Law, a company holding a wholesale distribution authorization for medicinal products may not also hold an authorization for dispensing medicines to patients. Thus, wholesale distribution and retail distribution activities should be performed by separate entities.

The distribution of medicinal products in Romania must be carried out with the observance of the applicable guidelines on good distribution practice of medicinal products for human use, issued by the MoH, otherwise they may be subject to certain significant sanctions set forth by the Health Law. The said guidelines are generally consistent with the guidelines on good distribution practice issued by the European Commission and the World Health Organization.

Both the marketing authorization holders and the wholesale distributors have a general obligation to supply the local market with continuous and sufficient stocks of medicines, in order to cover the needs of Romanian patients, this being qualified by the law as a 'public service' obligation.

6. Pricing

While prices of over the counter medicinal products released without medical prescription are generally set independently, and just notified to the MoH, the prices of medicinal products subject to medical prescription must be approved by the MoH.

The manufacturer price of a medicinal product must be lower or at the most equal to the lowest price of the same medicinal product within a list of twelve European countries specified by the MoH. The conversion of the relevant foreign prices into RON is made by taking into account the relevant foreign exchange rates used for the calculation of the state budget for the current year. By Law, the proceedings for the approval of the manufacturer price should not exceed 90 days from the date when the MoH is provided with the complete application file by the relevant MA holder or the representative thereof. The manufacturer price is approved for a limited period of 1 year. Within 90 days prior to the expiry of the 1-year deadline, the MA holder or its representative should submit to the MoH new pricing documentation, in order to obtain re-approval of the medicines' prices.

Further to the approval of the manufacturer price, the maximum wholesale and retail prices are calculated according to a special formula, by taking into account the maximum applicable wholesale and pharmacy margins set forth by the applicable regulations.

A specific matter regulated by Romanian law is that the maximum price of a generic medicinal cannot exceed 65% of the price of the reference innovative medicinal product. According to a new rule, set forth by the MoH Order no. 703/3015, which amended Order no. 75/2009, the prices of innovative medicinal products proposed by an MA holder / its representative for Romania, might in the future be impacted by the generic reference price, in the sense that the price of innovatives which have generics on the market should not exceed the generic reference price.

7. Reimbursement

NHIH and local health insurance houses reimburse the cost of certain medicinal products which are included in the reimbursed DCI List, which contains the INNs (DCIs) of the medicines that may be reimbursed by the State at a specific price.

The reimbursement procedure is mainly regulated in Romania by the framework contract regarding the conditions for granting medical assistance in the social health insurance system, approved by the Romanian Government. NHIH and MoH further detail the reimbursement rules within the methodological norms to the said framework contract. Basically, the specific INNs within the DCI List are included in specific sub-lists, where the percentage of reimbursement is, as the case may be, 20, 50, 90 or 100 of the reference price. Medicinal products used for the treatment of diseases included in the national health programs are subject to certain special reimbursement conditions, regulated through the Government Decision on national health programs as well as the technical norms thereto, jointly issued by the MoH and the NHIH.

8. Advertising and promotion

The advertising and promotion of medicinal products in Romania must be carried out with the observance of the Health Law and the NAMMD and MoH specific norms.

The Health Law defines advertising as any form of door-to-door information and any form of promotion which stimulates the prescription, supply, sale or consumption of medicinal products. The Health Law refers in particular to the following forms of advertising:

(i) the advertising of medicinal products to the general public;

(ii) advertising of medicinal products to persons qualified to prescribe or supply them;

(iii) visits by medical sales representatives to persons qualified to prescribe medicinal products;

(iv) the supply of samples;

(v) the inducement to prescribe or supply medicinal products by granting, offering or promising any benefits, whether in money or in kind, except when these have a symbolic value;

(vi) sponsorship of promotional meetings attended by persons qualified to prescribe or supply medicinal products; and

(vii) sponsorship of scientific congresses attended by persons qualified to prescribe or supply medicinal products, and in particular payment of their travel and accommodation expenses in connection therewith.

The Health Law prohibits any advertising of a medicinal product in respect of which an MA has not been granted for Romania.

The advertising of medicinal products to the general public is allowed for medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the intervention of a medical practitioner for diagnostic purposes, or for the prescription or monitoring of treatments, which are not released only on the basis of medical prescription, and which do not contain psychotropic or narcotic substances.

NAMMD is the competent authority to monitor the advertising of medicinal products, including without limitation to approve advertising materials designed for the general public in the case of non-prescription medicinal products and, in case of medicinal products subject to medical prescription, to review the advertising materials designed for persons qualified to prescribe or supply such products.

As a rule, all the advertising materials designed for the general public have to include the following minimum information: the name of the medicinal product, as well as the non-proprietary name if the medicinal product contains only one active substance; the information necessary for correct use of the medicinal product; an express, legible invitation to read carefully the instructions on the package leaflet or on the outer packaging, as the case may be.

The advertising of a medicinal product to persons qualified to prescribe or supply such products must include, as a rule, essential information compatible with the summary of product characteristics, and the release classification of the medicinal product.

The pharmaceutical companies should adequately train their medical representatives, so that they will have sufficient scientific knowledge to be able to provide precise and complete information about the medicinal products which they promote.

As a rule, in the case of promotional activities designed for the persons qualified to prescribe or supply the respective medicinal products, no pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons, unless they are inexpensive and relevant to the practice of medicine or pharmacy. Nevertheless, hospitality in the case of professional and scientific events is permitted, provided that it is strictly limited to the main scientific objective of the event, and must not extend to persons other than healthcare professionals.

Detailed rules and requirements concerning the advertising and promotion of medicines are set forth in the specific Norms issued by the MoH, and also in the industry codes.

According to the latest amendments to the Health Law, manufacturers, MA holders or their representatives in Romania, as well as wholesale distributors of medicinal products should disclose to MoH and to NAMMD the sponsorships and other expenses borne for physicians, medical assistants/nurses, professional organizations, patient organizations and any other type of organization in the health field. Such a disclosure obligation is applicable also for the relevant beneficiaries of the sponsorships.

9. Clinical trials

Clinical trials are defined under Romanian law as investigations in human subjects intended to discover or verify clinical, pharmacological and/or other pharmacodynamic effects of one or more investigated medicinal product(s), and/or to identify any adverse reactions to one or more investigated medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigated medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy.

Clinical trials should be authorized by the NAMMD and the National Ethics Committee (*i.e.*, the National Bioethics Committee for Medicinal Products and Medical Devices), which verifies the fulfilment of the requirements under the applicable regulations issued by the MoH and the NAMMD, including those concerning the protection of clinical trial subjects.

The clinical trial authorization procedure should not exceed 60 days from the day on which the NAMMD and the National Ethics Committee receive the complete application files from the sponsor, except for trials involving medicinal products for gene therapy, somatic cell therapy including xenogeneic cell therapy, and all medicinal products containing genetically modified organisms, for which an extension of a maximum of 30 days is allowed. In the case of these latter medicines, the 90-day period may be extended by a further 90 days in the event of consultation of a group or an expert committee.

After the commencement of a clinical trial, the sponsor may make amendments to the relevant protocol. The amendments which are substantial, significant or likely to have an impact on the safety of the trial subjects, or may change the interpretation of the scientific documents in support of the conduct of the trial, must be approved by the NAMMD and by the competent ethics committee.

During the performance of a clinical trial, the sponsor shall ensure that all relevant information about serious unexpected adverse reactions is recorded and reported to the NAMMD, and to the competent ethics committee, and, as the case may be, to the competent authorities in the concerned states.

If the NAMMD has objective grounds for considering that the conditions in the application for authorization submitted by the sponsor are no longer met, or has information raising doubts about the safety or scientific validity of the clinical trial, it may suspend or prohibit the clinical trial and notify the sponsor thereof.