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01 REGULATORY, PRICING, AND REIMBURSEMENT OVERVIEW

1. What are the regulatory authorities with jurisdiction over drugs, biologicals, and medical devices in your country?

Within Luxembourg, the regulatory authority in charge of the matter of drugs, biologicals, and medical devices is the Ministry of Health ("***Ministère de la Santé***"), in particular the National Health Directorate ("***Direction de la Santé***"), composed of six departments among which:

- the Pharmacy and Medication Department ("***Division de la Pharmacie et des Médicaments***") is in charge of the regulatory framework concerning drugs and biologicals; and
- the Curative Care and Healthcare Quality Department ("***Division de la Médecine curative et de la Qualité en santé***") is in charge of the regulatory framework concerning medical devices.

2. What is the regulatory framework for the authorization, pricing, and reimbursement of drugs, biologicals, and medical devices?

For an easiest reading, drugs and biological will be referred hereafter as "***medicinal products***" except otherwise mentioned.

I. MEDICINAL PRODUCTS

The main regulations governing the authorization of medicinal products, compiled in the Health Code ("***Code de la Santé***") are:

- the law of 4 August 1975 relating to manufacturing and import of medicinal products as amended;
- the law of 25 November 1975 relating to the delivery to the public of medicinal products, as amended;
- the law of 11 April 1983 on the regulation of the marketing authorization and advertising of medicinal products as amended;
- the law of 6 January 1995 relating to the wholesale distribution of medicinal products as amended;
- the Grand-Ducal regulation of 15 December 1992 relating to the marketing of medicinal products as amended; and
- the Grand-Ducal regulation of 19 November 2004 relating to the manufacturing, the distribution and the brokerage of medicinal products, as amended.

Regarding the pricing, and reimbursement of medicinal products, the Social Security Code ("***Code de la Sécurité Sociale***") and the statutes of the National Health Fund ("***Caisse Nationale De Santé***" or "***CNS***") would apply.

II. MEDICAL DEVICES

The regulatory framework for the authorization, pricing, and reimbursement of medical devices is:

• the law of 16 January 1990 on medical devices as amended, which constitutes the main regulation for medical devices and the Grand-Ducal regulations related thereto.
• the Social Security Code and the statutes of the CNS for pricing and reimbursement.

3. What are the steps to obtaining authorization to develop, test, and market a product?

I. MEDICINAL PRODUCTS

Manufacturing authorization:

Pursuant to the law of 4 August 1975 relating to manufacturing and import of medicinal products as amended, in order to obtain authorization to develop and test new medicinal products, the manufacturer should apply and obtain a prior authorization of manufacturing from the Ministry of Health, except if there is specific exemptions in the law.

The application for the granting of the authorization is subject to investigations and a report established by the relevant authority ("***Inspection des Pharmacies***").

The decision taken by the Ministry is notified to the applicant and must contain the grounds of the decision.

As foreseen in the Grand-Ducal regulation of 19 November 2004 relating to the manufacturing, the distribution and the brokerage of medicinal products as amended, the application for a prior authorization of manufacturing must contain information such as the contact details of the applicant, the place where manufacturing operations are performed, list of medicinal products manufactured.

According to article 4 of the law of 4 August 1975 relating to manufacturing and import of medicinal products as amended, the manufacturing of the medicinal products is made under the supervision of a pharmacist duly agreed by the Ministry of Health.

Marketing authorization:

Before the launching of a new medicinal product on the market, the manufacturer must have obtained a marketing authorization.

• In case of a national marketing authorization, the manufacturer should apply for a prior authorization from the Ministry of Health. According to article 2 of the Grand-Ducal regulation of 15 December 1992 related to the marketing of medicinal products as amended, the complete application must be submitted to the Ministry of Health in electronic format in accordance with the requirements of the European file format.

Details regarding the medicinal product and the applicant should be included in the application, including (without being exhaustive) the name or company name and the domicile or the registered office of the person responsible for the marketing and name of the medicinal products.

• In case of the filing of an application for an EU marketing authorization from the European Medicines Agency ("***EMA***"), several steps regulated at the EU level have to be duly followed.

In this case, there is no need for a marketing authorization within Luxembourg. However, prior to the sale of the medicinal product, a file has to be provided to the Ministry Health containing a copy of the European Commission's decision with all the annexes.

In addition, a request for the price to the public of the medicinal product has to be filed at the Ministry of Social Security.

Lastly, for the potential reimbursement of the medicinal product, if any, a request to the CNS has to be filed in order to be mentioned on a list called "liste positive", i.e. the list of the medicinal products for which a part of the price to the public will be reimbursed by the CNS, the rate of the reimbursement depending on the type of medicinal product.

II. MEDICAL DEVICES

Manufacturing authorization:

No prior authorization is required for the manufacturing of medical devices.

However, the manufacturer should fulfill the requirements related to the manufacturing provided for under the different Grand-Ducal regulations related to medical devices, among which there are requirements related to conception and production of the device.

Marketing authorization:

No prior authorization is required for the marketing of the medical devices.

However, the manufacturer should fulfil two conditions foreseen under the different Grand-Ducal regulations related to medical devices:

- the medical devices may only be marketed and/or put into service provided that they are duly supplied and are correctly installed, maintained and used according to their intended purpose; and
- the medical devices may only be marketed and/or put into service provided that the label EC is mentioned, this label indicating that their conformity with EC requirements has been validated.

4. What are the approximate fees for each authorization?

I. MANUFACTURE AUTHORIZATION:

For a new medicinal product, the manufacture authorization fee is determined on a case by case basis depending on the scope of the investigations carried out by the Inspection des Pharmacies.

II. MARKETING AUTHORIZATION:

Pursuant to the Grand-Ducal regulation of 24 December 1993 fixing the fees due for the marketing authorization of medicinal products as amended, the marketing authorization fee amounts:

- to 600.€ (six hundred euros), when the medicinal product has already been granted with an authorization delivered in a Member State of the European Union, in accordance with the relevant directives;

- to 12,500.€ (twelve thousand five hundred euros), when such authorization is lacking.

The fee has to be paid per form and dosage.

5. For how long are marketing authorizations/registrations valid? How are marketing authorizations/registrations renewed?

Pursuant to the law of 11 April 1983 on the regulation of the marketing authorization and advertising of medicinal products as amended, the marketing authorization is valid for 5 years.

It can be renewed every 5 years by a request of the authorization's holder, presented within 3 months before the expiration of the marketing authorization.

6. How does the authorization process differ between brand-name products and generic products? Are there differences for local manufacturers versus foreign-owned manufacturers?

According to article 1-1 of Grand-Ducal regulation of 15 December 1992 relating to the marketing of medicinal products as amended, for generic versions of medicinal products, the applicant shall follow the general authorization process.

Nevertheless, the applicant doesn't need to provide the results of the pharmaceutical, preclinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product that is or has been authorized since eight years.

Instead, he can provide an appropriate scientific bibliographical documentation concerning the above tests.

There is no difference for local manufacturers versus foreign-owned manufacturers.

7. How are combination products (drug + drug, drug + biologic, drug + device, biologic + device, drug + biologic + device) regulated?

There is no special regulation about combination products between several medicinal products.

In case of combination products between medicinal products and devices, according to article 1 (3) of Grand-Ducal regulation of 11 August 1996 on medical device as amended, if a device is marketed in such a way that the device and the medicinal product form a single integrated product that is intended to be used exclusively in the association given and which is not reusable, this product is regulated by EU Directive 2001/83/EC as a medicinal product.

8. How is compliance with regulations monitored and evaluated? Is the regulatory regime comparable with the U.S. Food and Drug Administration or the European Medicines Agency expectations and requirements?

Compliance with regulations is monitored and evaluated by the Pharmacy and Medication Department / Ministry of Health.

It has authority over questions related to medicinal products and it controls the manufacturing, marketing, advertising, distribution, import and export of these products.

The Pharmacy and Medication Department / Ministry of Health also carries out inspections to make sure that the distribution sites are compliant with the requirements of good practices.

The regulatory regime is comparable with EMA expectations and requirements.

9. What is the potential range of penalties for noncompliance?

For non-compliance:

- with the provisions related to the manufacturing and import of medicinal products (article 14 of the law of 4 August 1975 relating to manufacturing and import of medicinal products as amended):
  - o 8 days to 6 months of imprisonment and/or
  - o a fine of 251 to 10,000 euros.
- with the provisions related to the marketing authorization and advertising of medicinal product (article 20 of the law of 11 April 1983 on the regulation of the marketing authorization and advertising of medicinal product as amended):
  - o 8 days to 6 months of imprisonment and/or
  - o a fine of 251 to 10,000 euros.
- with the provisions related to medical devices (article 4 of the law of 16 January 1990 on medical devices as amended):
  - o 8 days to 1 month of imprisonment and/or
  - o a fine of 2,501.- to 1,000,000.- Luxembourgish Francs (to be converted into euro / no updated version of the article available in the Code de la Santé).

10. Is there a national healthcare system? If so, how is it administered and funded?

The national health care system is administered by the National Health Fund ("***Caisse nationale de santé***" or "***CNS***").
The CNS is a public institution endowed with the civil personality and placed under the supervision of the Ministry of Social Security, acting through the General Inspectorate of the Social Security ("***Inspection générale de la sécurité sociale***" or "***IGSS***").

It is managed by a Council of Administration with a tripartite organisation comprised of representatives of the workforce, the employers and a State representative as chairman of the Committee.

Funds come from the payment of the mandatory social contributions (the general principle is that one part of these social contributions is paid by the employers and one part is paid by the employees).

11. How does the government (or public) healthcare system function with private sector healthcare?

Many people subscribe to a private health insurance with a professional company affiliated with the Ministry of Social Security. The advantage of having an additional insurance is to cover unforeseen medical costs and/or unexpected hospitalization not covered by the CNS.

12. Are prices of drugs and devices regulated and, if so, how?

In addition, many employers offer supplementary coverage as a benefit of employment. This additional coverage pays the portion of medical fees that isn't covered by the CNS and may offer extended coverage.

I. MEDICINAL PRODUCTS

Prices of medicinal products are regulated by the Ministry of Social Security, according to article 22ter of the Security Social Code and the Grand-Ducal

regulation of 1 December 2011 determining the criteria, conditions and procedure relating to the pricing of medicinal products for human use as amended.

As mentioned above, a request for the price to the public of a medicinal product has to be filed to the Ministry of Social Security before the launching of the product on the market.

According to article 4 of the Grand-Ducal regulation of 1 December 2011 determining the criteria, conditions and procedures relating to the pricing of medicines for human use as amended, the prices of medicinal products approved by the Minister of Social Security are published in the official Gazette (the "Memorial") each year in January on the list of prices of commercialized medicinal products ("Liste des médicaments commercialisés"). Changes of price during the year are published monthly at the Memorial.

II. MEDICAL DEVICES

To our knowledge, prices of medical devices are freely determined.

13. How are the drugs and devices used by patients paid for? What roles do public and private payers play?

I. MEDICINAL PRODUCTS

There is a third party payment system for medicinal products. The CNS is in charge of the national reimbursement system for medicinal products.

As mentioned above, before the launching of a medicinal product on the market, for the potential reimbursement of the medicinal product, if any, a request to the CNS has to be filed in order to be mentioned on a list called "liste positive", i.e. the list of the medicinal products for which a part of the price to the public will be reimbursed by the CNS, the rate of the reimbursement depending on the type of medicinal product (there are three rates of reimbursement, depending on the category of the medicinal product: 40%, 80% and 100%).

As a result, the CNS will cover the reimbursable part of a medicinal product according to this list, and the patient will pay for the rest of the price, if any.

II. MEDICAL DEVICES

The CNS is also in charge of the reimbursement of medical devices.

Similarly, before the launching of a medical device on the market, for the potential reimbursement of the medical devices, if any, a request to the CNS has to be made in order to be grouped into specific files from "Fichier B1" to "Fichier B7" in CNS Statutes, i.e. the files of the medical devices for which a part of the reference price will be reimbursed by the CNS, the rate of the reimbursement depending on the type of medical devices (there are three rates of reimbursement, depending on the category of the medical devices: 40%, 80% and 100%).

Therefore, the CNS will cover the reimbursable part of a medical device according to the files, and the patient will pay for the rest of the price, if any.

14. Who dispenses drugs and devices to patients and how are those dispensers compensated?

According to articles 3 of the law of 25 November 1975 concerning the deliverance of medicinal products to the public as amended, medicinal products can only be dispensed to the public in pharmacies, except in cases where they

can also be delivered by the pharmacist, under specific conditions, to patients accommodated in the following establishments:

- centers, homes and services for the elderly;
- geriatric or accommodation centers of services for authorized people according to the law of 8 September 1998 regulating relations between the State and organisations working in the domain of social, family and thera peutic as amended.

Pursuant to the statutes of the CNS, the CNS is in charge of the payment of the fees due to the pharmacists according to the reference tariff and the rate (80% or 100%) as provided for in list n° 11, appendix D of the statutes of the CNS. In case the fees due to the pharmacists exceed the part taken in charge by the CNS, the remaining part of the fees is paid by the patients.

15. What are the professional and legal responsibilities of those who dispense drugs and devices? What role do they play in providing patient care, information, and safety?

Pursuant to the law of 28 October 2016 on the recognition of professional qualifications, pharmacists who dispense medicinal products and devices have the obligation to dispense safe and effective medicinal products of the required quality and to provide information and advice on medicines including their proper use.

In addition, they have also ethical obligations towards other healthcare profession and the public as provided for in the Code of Ethics of Pharmacists, such as the obligation of professional secrecy.

Any breach of these obligations might lead to their common civil liability and/or disciplinary penalties such as warning, reprimand and fine, in accordance with article 20 of the law of 8 June 1999 on the Medical College ("Collège médical")