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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?

The authority responsible for applying and enforcing the regulatory framework in relation to drugs, biologicals and medical devices is the Ministry of Public Health (MSP), which is part of the Executive Branch.

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

The regulatory framework for the authorization of drugs, biologicals and medical devices is mainly comprised of Law 9,202 (MSP Organic Law), Law 15,443 (Drugs Law), Decree 521/984, Decree 324/999 and Decree 12/007 (Drugs), Decree 3/008 (Medical Devices) and Decree 38/015 (Biologicals). These regulations are supplemented by other decrees, resolutions and ordinances published by the MSP.

Price control in the private sector is not regulated.

In Uruguay, there is no reimbursement in the private sector.

Notwithstanding, the National Resources Fund (FNR), an institution created by Decree-Law 14,897 as a non-state public entity, provides financial coverage for some highly specialized medical procedures and high-cost drugs to the users of the National Integrated Healthcare System. Also, the National Reference Center on Congenital Defects and Rare Diseases (CRENACEDER), which is part of the Social Security Institute (BPS), provides drugs for treatment of rare diseases.

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

Pursuant to Law 15,443 and Decree 521/984 manufacturers or importers must obtain an authorization of the MSP in order to test, develop, import and market products (authorizations are granted for product category, e.g. drugs, biologicals, medical devices, homeopathic, etc.).

In order for a company to obtain authorization as a manufacturer or importer, the company must be incorporated in Uruguay, have a responsible technician holding a Uruguayan accredited degree, a warehouse (either own or outsourced) and a manufacturing plant (in the case of manufacturers). Likewise, the company must submit documentation such as facilities authorizations (e.g. Municipality, National Fire Department, Hygienic and Environmental, Potable Water, etc.), operational procedures, list of products to be manufactured/imported, outsourced agreements if any (e.g. technical service for medical devices, product testing, storage). The companies' authorization proceedings may take

approximately between four and eight months if no objections are raised and considering it is the company's first request for authorization.

Also, in order to sell products in the Uruguayan market, manufacturers or importers must obtain a marketing authorization -granted by the MSP- for each particular product.

MARKETING AUTHORIZATIONS

Requirements and timeframes vary among drugs, biologicals and medical devices. Each category of product has its own regulation indicating the requirements (documentation and information) for registering the product and obtaining marketing authorization.

For drugs and biological, qualitative and quantitative tests must be performed in finished products. In the case of the import of finished products, before registration, the importer must submit to the MSP:

(i) a power of attorney granted to the importer by the foreign manufacturer authorizing the importer to distribute the products in Uruguay and; (ii) a GMP/CPP evidencing that the foreign manufacturer is authorized by its country's regulatory authority.

DRUGS

Decree 324/999 states that in order to register a drug, the manufacturer or importer must inform and submit to the MSP, among others:

(a) name proposed for the drug
(b) qualitative – quantitative formula
(c) monograph of active or inactive raw materials
(d) pharmaceutical form
(e) methodological analytics of the finished product
(f) description of the characteristic of the pharmaceutical form
(g) qualitative analysis of active raw materials in the finished product
(h) quantitative analysis
(i) hygienic control of the non-sterile finished product
(j) sterility control of pyrogenics and safety, as applicable
(k) stability study of active raw material/s
(l)updated pharmacoloical basis of the foreseen therapeutic effect of active raw material/s. The submision of further documentation might be necessary -for demonstrating interchangeability and bio-comparability- depending on whether raw materials are already present in other registered drugs or drugs pending registration or whether they have been approved or not by FDA or EMA
(m) draft prospectus
(n) labeling design.

The approval timeframe depends on the type of proceedings followed:

(i) expedited: 30 days approx.
(ii) standard: 12-18 months approx.

BIOLOGICALS AND BIOSIMILARS

Decree 38/015 sets forth the requirements to grant the marketing authorization for biologics and biosimilars. Besides the information and documentation for drugs set forth by Decree 324/999, the following must be submitted, among others:

Biologicals

(i) GMP of the active ingredient's manufacturer
(ii) evidence of marketing in other countries, in the case of imported products

(iii) information on active ingredient/s
(iv) information on the pharmaceutical product
(v) preclinical information: pharmacodynamics studies, pharmacokinetic studies, toxicity
(vi) clinic information: phase I, II, III and IV studies (if applicable), immuno genicity studies
(vii) pharmacovigilance and risks managing plan.

Biotechnological similar drugs

(i) GMP of the active ingredient's manufacturer
(ii) evidence of marketing in other countries, in the case of imported products
(iii) information on active ingredient/s
(iv) information on the pharmaceutical product
(v) quality comparability protocol
(vi) preclinical comparability protocol
(vii) clinical comparability protocol: pharmacokinetic and pharmacodynamics studies, including confirmatory clinical trials to demonstrate the similarity of efficacy between the biosimilar and the reference biologic
(viii) efficacy studies
(ix) security studies
(x) immunogenicity studies.

The approval timeframe for biologicals and biosimilars takes approx. 12-18 months.

MEDICAL DEVICES

Decree 3/008 sets forth the information and documents to be filed before the MSP in order to obtain a marketing authorization for medical devices, which are, among others:

(i) MSP Form
(ii) copy of the company's approval at the MSP
(iii) in the case of imports, Free Sale Certificate at the country of origin
(iv) complete dossier with technical information on the product.

The approval timeframe takes approx. 6 months.

4. What are the approximate fees for each authorization?

MSP fees for the company authorization (as manufacturer or importer) depend on the area of the premises and number of employees of the company. In case of an importer with an outsourced storage, fees amount to 1 Readjustable Unit (USD 35 approx.)

MSP fees for product registration are:

DRUGS

Depends on the proceedings to be followed:

(i) expedited: 50 Readjustable Units (USD 1,750 approx.) plus 5 Readjustable Unit (USD 175 approx.) per active ingredient in the product or
(ii) standard: 30 Readjustable Units (USD 1,050 approx.) plus 5 Readjustable Unit per active ingredient in the product. MSP has discretionary powers to decide whether or not to accept expedited requests and a maximum of 5 expedited requests is being accepted per registering party.

BIOLOGICS AND BIOSIMILARS

5 Readjustable Units (USD 175 approx.).

MEDICAL DEVICES

30 Readjustable Units (USD 1,200 approx.).

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

Marketing authorizations are valid for five years. Marketing authorizations must be renewed every five years. Non-compliance with filing the renewal request before the end of the five year term will cancel the registration and a new registration process shall need to be followed.

For renewal, applicants must evidence compliance with good manufacturing practices, safety and efficacy standards, pharmacovigilance, labeling standards and all other applicable provisions.

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

In general terms the differences are that for brand-name products it is necessary to evidence safety and efficacy and for generic products it is necessary to evidence interchangeability and bio-comparability.

There are no differences between local manufacturers versus foreign-owned manufacturers in the authorization processes.

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

There is no regulation related to combination products. Combination products must obtain marketing authorization from MSP. Given their particular features, combination products can be classified either as drugs (drug/biologic) and/or medical devices (drug/device). Requirements and application timeframes differ in each case. Depending of the nature of the combination product, it may require separate drug or biologic and medical device approvals or not.

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

MSP is the authority responsible of monitoring and assessing compliance with regulations. MSP has a permanent pharmacovigilance program based on information on possible adverse effects of drugs, provided, among others, by:

(i) doctors and physicians
(ii) pharmaceutical companies that manufactured or imported the products and those who conduct clinical trials, who must both report any health risks.

Under the Health Law Regulations, MSP's monitoring is focused on ensuring, among other things:

(i) compliance with good manufacturing practices and standard operating procedures

(ii) that activities do not exceed the limits set by the authorization and do not differ from those activities which have been authorized

(iii) performance of validation analysis of the manufacturing processes and systems involved.

Although the regulatory regime is comparable to the U.S. Food and Drug Administration or the European Medicines Agency expectations and requirements, the MSP does not undertake such an active control as the one undertaken by these agencies and, in practice, sanctions applied by the MSP are different.

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

MSP is empowered to make on-site visits at any time to inspect premises and verify compliance, and can initiate ex officio administrative proceedings to sanction non-compliance. Ultimately, these administrative proceedings can result in warnings, confiscation of products, revocation of the marketing authorization, ordering partial or total suspension of activities, closure of establishment and sanctions ranging between 30 to 1,000 Readjustable Units (USD 1,050 to 35,000 approx.)

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

Laws 18,131 and 18,211 regulate the National Integrated Healthcare System.

Within the framework of such system, a National Healthcare Fund (FONASA) was created, which is managed by the National Health Board (a body which is part of the MSP).

FONASA receives mandatory contributions from employed personnel, both private and public, employers, independent professionals, personal services one-person businesses providers and retired workers.

FONASA finances the National Healthcare Insurance through which employed personnel, independent professionals, personal services one-person businesses providers and retired workers have the right to health coverage for themselves and for their families at any of the healthcare providers which are part of the system.

Healthcare providers charge FONASA a price per insured person which is called healthcare fee.

The healthcare fee is comprised of two elements:

(i) capita: an amount adjusted to the coverage risk which varies according to the age and gender of the insured person, in accordance to certain criteria set by the government,

(ii) goal: this part of the price is only charged when the healthcare provider fulfills the quality and sanitary objectives set by the National Integrated Health System.

The public healthcare sector normally implements measures to limit costs, for example, by pressing for price reductions in public bids and encouraging competition.

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

Both, public healthcare system and private healthcare providers are part of the National Healthcare Insurance, so users may decide to join any of them.

Likewise, users who are not part of the Insurance (for example, because they are unemployed and do not have a family member under whom they are provided coverage) may be assisted either at the public or private sector. In these cases, such coverage has a cost.

Free healthcare coverage is only granted to persons who do not reach a certain level of income.

There currently exist complementation agreements between public and private institutions with the aim of complementing their services.

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

Prices of drugs and devices are not regulated in Uruguay.

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

Users of public and private healthcare services providers can access certain drugs and medical examinations by paying a certain price, whose maximum amount is set by the government as "moderating rates".

The MSP issues a list (Drug Therapeutic Formularium) which determines the drugs which healthcare providers must provide under the moderating rates regime.

This allows for healthcare providers to purchase large volumes of drugs which gives them significant negotiating powers.

Moreover, users also have the possibility of acquiring drugs at pharmacies by paying the corresponding amount (this amount is set freely by pharmacies).

As regards medical devices, companies which manufacture, import, store, distribute or are involved in their maintenance or repair must obtain prior approval of the MSP. Likewise, medical devices must be registered in order to be marketed.

Also, the FNR provides financial coverage for some highly specialized medical procedures and high-cost drugs to the users of the National Integrated Healthcare System.

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

Pharmacies authorized by the MSP. Healthcare institutions have the possibility of having their own pharmacy in order to dispense drugs to their users.

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?

The MSP investigates dispensing errors that are reported to it.
Law 15,703 states that Technical Directors of Pharmacies are legally responsible for the correct dispensing of drugs and devices.

Healthcare professionals who prescribe drugs or devices could be responsible vis-à-vis patients for the prescribed treatment and for the information provided in relation to such treatment.