The Pharma Legal Handbook

Italy

Regulatory, Pricing and Reimbursement Overview · Preclinical and Clinical Trial Requirements · Marketing, Manufacturing, Packaging and Labeling Advertising · Traditional Medicines and OTC Products · Product Liability · Patents and Trademarks · Regulatory Reforms

PHARMA BOARDROOM

Italy

The Pharma Legal Handbook answers essential questions about this environment for pharmaceuticals in Italy.
It is a must have for any company operating in the country or looking to enter the market.

Prepared in association with DLA Piper, an international law firm, it should answer any questions linked to Regulation, Pricing, Clinical and Preclinical Trials, Marketing, Manufacturing, Trademarks and Patents.

*** THIS REPORT WAS ORIGINALLY PUBLISHED IN JANUARY 2020 AND THE INFORMATION CONTAINED WITHIN IS SUBJECT TO CHANGE.**

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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?

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

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

4. What are the approximate fees for each authorization?

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

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

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

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?

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

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

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

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

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?

01 REGULATORY, PRICING, AND REIMBURSEMENT OVERVIEW

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

The Italian Medicines Agency (Agenzia Italiana del Farmaco – "AIFA") is the national authority vested with jurisdiction over medicinal products (including biologics).

The Ministry of Health (Ministero della Salute) is responsible for the regulation and monitoring of medical devices and has jurisdiction in relation to certain aspects pertaining to the regulation of non-prescription medicines (e.g., promotion).

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

a. Authorization

Italian legislative decree 219/2006 on medicinal products for human use ("Italian Medicines Code"), implementing Directive 2001/83/EC, and Regulation (EC) 726/2004 set forth the main regulatory framework for the authorization of medicinal products (including biologics) in Italy.

Legislative decree 46/1997 on medical devices, legislative decree 507/1992 on active implantable medical devices, and legislative decree 332/2000 on in vitro diagnostic medical devices, respectively implementing Directive 93/42/EEC, Directive 90/385/EEC and Directive 98/79/EC, establish the main regulatory framework for the authorization of medical devices in Italy.

The aforementioned legislative framework for medical devices will soon be replaced by the new Regulation (EU) 2017/745 on medical devices and Regulation (EU) 2017/746 on in vitro diagnostic medical devices, which will become fully applicable on 26 May 2020 and 26 May 2022 respectively.

b. Pricing and reimbursement

All medicinal products available on the Italian market are classified into one of the following four reimbursement categories:

- **Class A:** includes essential medicines and medicines for chronic diseases. Class A medicines are generally fully reimbursed by the Italian National Health Service (Servizio Sanitario Nazionale) ("SSN").
- **Class H:** includes hospital-use only medicinal products. These are also reimbursed by the SSN.
- **Class C:** not reimbursed by the SSN.
- **Class C(nn):** separate class for centrally approved medicinal products which pricing and reimbursement decision in Italy has not yet been taken. These are not reimbursed by the SSN.

The price of Class A and Class H medicinal products is negotiated between the marketing authorization holder and AIFA (Italian law 326/2003). Prices

are negotiated on the basis of the criteria set out by Resolution 3/2001 of the Inter-ministerial Committee for Economic Planning. ("CIPE's Resolution 3/2001"). CIPE's Resolution 3/2001 will be lifted pursuant to a decree adopted by the Ministry of Health and Ministry of Economy and Finance in July 2019. However, as such decree has not yet been published in the Official Journal (as of October 2019), CIPE's Resolution 3/2001 is still valid and in force.

The price of Class C medicines is freely set by the marketing authorization holder. The marketing authorization holder may only increase the price of Class C products every two years (in January of each odd-numbered year).

For medicinal products belonging to classes A and H, the price negotiation involves a two-phase procedure. Phase I requires the marketing authorization holder to submit to AIFA the following information:

- a risk / benefit assessment;
- an evaluation of the economic impact on the NHS;
- a comparison with the price and consumption of the medicine in other EU member states.

Phase II involves negotiations with AIFA, with the support of the prices and reimbursements committee (Comitato Prezzi e Rimborso) and the national observatory for the use of medicinal products (Osservatorio Nazionale sull'Impiego dei Medicinali).

The above provisions do not apply to medical devices.

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

a. Medicinal products

New medicinal products must undergo an evaluation of their quality, safety and efficacy before being placed on the Italian market. The process is mainly regulated by the Italian Medicines Code and legislative decree 211/2003 on clinical trials, implementing Directive 2001/20/EC, and monitored by AIFA.

The main steps are the following:

- **Pre-clinical tests**: not regulated under the medicinal product regulatory framework.
- **Clinical trials:** the investigational medicinal product is tested on human beings. This is subject to regulatory and ethical review in accordance with legislative decree 211/2003.
- **Marketing authorization application**: once the pharmaceutical company has gathered sufficient quality, safety and efficacy data, it can include all such data in a dossier and apply for a marketing authorization to either AIFA or the European Medicines Agency ("EMA").

The marketing authorization holder may place the new medicinal product on the market once it has (i) obtained a marketing authorization from either AIFA or the European Commission, and (ii) the product has been included in one of the reimbursement categories and a price has been set.

b. Medical devices

Medical devices do not require a prior authorization from the Ministry of Health to be placed on the market in Italy. However, the manufacturer is responsible for ensuring that the medical device complies with the essential requirements set forth by legislative decree 46/1997 and it has been subject to appropriate tests to verify such conformity.

All medical devices require a "CE mark" to be placed on the market. In order to affix the CE mark, the manufacturer must follow a conformity assessment procedure. For Class I devices, the manufacturer draws up the EC declaration of conformity after having verified compliance with the applicable requirements. For Class IIa, IIb, or III devices, the manufacturer must involve a Notified Body – i.e., a private legal entity designated by the competent regulatory authority to exercise conformity assessment procedures. The Notified Body issues the declaration of conformity required for the manufacturer to affix the CE mark.

If the manufacturer (or its EU authorized representative) is established in Italy, it must register with the Ministry of Health and communicate a description of the medical devices before it may lawfully place the devices on the Italian market.

In respect of Class II and III medical devices, Italian law requires the manufacturer (or its EU authorized representative) to inform the Ministry of Health of certain data allowing the identification of such devices when they are put into service in Italy, including the labels and instructions for use.

4. What are the approximate fees for each authorization?

The fees to apply for a marketing authorization of a medicinal product vary depending on the procedure, the pharmaceutical form and the presentation, among other factors. The fees for marketing authorization application are published on AIFA website and, according to the latest update (March 2019), they amount approximately to:

- 67,000.00 euros in case of national procedure, decentralized procedure or mutual recognition procedure where Italy acts as Concerned member state;
- 80,000.00 euros in case of decentralized procedure or mutual recognition procedure where Italy acts as Reference member state;
- 40,000.00 – 50,000.00 euros for homeopathic medicinal products;
- 20,000.00 – 30,000.00 euros for herbal medicinal products.

Once an authorization is obtained from AIFA, an annual fee of Euro 1,000.00 applies to each marketing authorization (AIFA Order No. 21 of 30 May 2012).

In relation to Class IIa, IIb and III medical devices, each Notified Body sets its own fees system for the conformity assessment procedure.

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

The initial marketing authorization for a medicinal product has a duration of five years. The holder of the marketing authorization may apply for a renewal by submitting to AIFA an application at least six months before the expiry of the marketing authorization. The application must contain an updated version of the dossier filed with the original application in order to enable a new