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

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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 Baker Mckenzie. an international law firm, it should answer any questions linked to Regulation, Pricing, Clinical and Preclinical Trials, Marketing, Manufacturing, Trademarks and Patents.

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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?

In Italy, the regulatory authorities with jurisdiction over drugs, biologicals, and medical devices are:

- the Ministry of Health ("MoH"), which generally governs the Italian healthcare system and has a more specific role in relation to the regulatory framework concerning medical devices; and
- the Italian Medicine Agency ("AIFA"), a public entity under the supervision of the MoH, which is responsible, amongst other things, for the manufacturing, distribution, import, promotion, advertising, pricing and reimbursement of medicines, including biological drugs.

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

I. Medicinal products

As regards medicinal products, including biological drugs, the relevant legislative and regulatory framework mainly consists of:

- Regulation (EC) No. 726/2004 laying down EU procedures for the authorization and supervision of medicinal products;
- Legislative Decree No. 219/2006 (the "Pharma Code") implementing Directive 2001/83/EC relating to medicinal products for human use;
- Law No. 326/2003 with entrusts the AIFA with the task of negotiating the cost of medicines reimbursed by the National Healthcare System ("NHS") and, more generally, monitoring prices of medicinal products;
- Decree of the MoH dated August 2, 2019 setting forth the criteria and methods according to which the AIFA establishes, through negotiation, the prices of medicinal products reimbursed by the NHS; and
- Law Decree No. 87/2005 governing the price of medicinal products not reimbursed by the NHS.

II. Medical Devices

With respect to medicinal devices, the relevant legislative and regulatory framework mainly consists of:

- Regulation (EU) No. 2017/745 on medical devices and active implantable medical devices ("MDR");
- Regulation (EU) No. 2017/746 on in vitro diagnostic medical devices ("IVDR");
- Legislative Decree No. 46/1997, implementing Directive 93/42/EEC on medical device;
- Legislative Decree No. 507/1992, implementing Directive 90/385/EEC on active implantable medical devices; and

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• Legislative Decree No. 332/2000, implementing Directive 98/79/EC on in vitro diagnostic medical devices.

In Italy, there are no specific provisions of law governing the pricing and reimbursement of medical devices. Rather, medical devices are directly purchased by the NHS in the context of tender procedures governed by Italian public procurement laws. These laws set forth specific rules governing the award of public supply contracts based on the principles of equal treatment, transparency and free competition and the performance of same pursuantto ad hoc public procurement rules.

Contracting authorities award the relevant supply contract either on the basis of the lower price criteria (option more frequently used for low/medium-technology products) or the most economically advantageous offer (option more frequently used for medical devices characterized by a higher technological level). Exceptions to said rules may apply with respect to medical devices that can only be supplied by one economic operator due to technical reasons or IP rights protection, for which contracting authorities can allow one-to-one negotiated procedures (e.g. in case of urgency).

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

I. Medicinal products

In Italy the development and testing of medicinal products is mainly governed by Legislative Decree No. 211/2003 and Legislative Decree No. 200/2007 on clinical trials on medicinal products for human use according to which trials are subject to the prior authorization issued by the AIFA and the positive opinion of the Ethics Committee(s) relating to the clinical site(s) where same trials are conducted. The above-mentioned Legislative Decrees also set forth specific rules on good clinical practice, informed consent, responsibilities of sponsors and investigators and other entities involved in the clinical trial (e.g., contract research organizations). Less stringent rules apply to observational studies, according to the AIFA's Resolution dated 20 March 2008.

As to the authorization to market products, under Italian law the approval pathway for new drug applications does not differ from that ordinarily envisaged for all medicines, according to the Pharma Code. That said, simplified procedure for the authorization of generic drugs[1] as well as schemes for expedited approval and programs to encourage the development of new drugs are available.

Under Italian law, there are two main routes for authorizing medicines: a centralized route, governed by Regulation (EC) No. 726/2004 (i.e. the centralized authorization procedure), and a national route, regulated by the Pharma

1 Pursuant to the Pharma Code, a generic medicinal product is a medicinal product which has the same qualitative and quantitative composition in active principles and the same pharmaceutical form of the reference medicinal product, and whose bioequivalence with the latter has been demonstrated by appropriate bioavailability tests. In other words, generic drugs are those medicinal products that, on the basis of predetermined, objective and measurable scientific and methodological criteria, can be regarded as equivalent, in terms of quality, safety and efficacy, to reference originator drugs developed and authorized following clinical studies which confirmed the relevant prerogatives.

Code, which in turn comprises three different authorization procedures, namely the national procedure, the mutual recognition procedure and the decentralized procedure.

Pursuant to the centralized authorization procedure, pharmaceutical companies submit a single marketing-authorization application to the European Medicines Agency (the "EMA")[2]. The advantage of this procedure is to allow the marketing-authorization holder to market the medicine and make it available to patients and healthcare professionals throughout the EU on the basis of a single marketing authorization. Today, the great majority of new, innovative medicines pass through the centralized authorization procedure in order to be marketed in the EU[3] .

In the EU, marketing authorization applications for biotechnology-derived medicinal products, including biosimilars[4] , are by law reviewed centrally by the EMA. The European Commission issues the decisions concerning the authorization of these medicinal products on the basis of the scientific opinions from the EMA. The resulting marketing authorization is valid in all EU Member States. Other biological medicinal products can also be authorized through the national, mutual recognition or decentralized procedure on the basis of the same scientific and regulatory standards required under the centralized procedure before the EMA.

With specific regard to biosimilars, developers are required to demonstrate through comprehensive comparability studies with the reference biological medicine that:

- their biological medicine is highly similar to the reference medicine, notwithstanding natural variability inherent to all biological medicines;
- there are no clinically meaningful differences between the biosimilar and the reference medicine in terms of safety, quality, and efficacy.

2 The centralised procedure is compulsory, amongst others, for:
• Human medicines containing a new active substance to treat HIV, AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions, and viral diseases;
• Medicines derived from biotechnology processes, such as genetic engineering;
• Advanced-therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines;
• Orphan drugs (medicines for rare diseases).
It is optional for other medicinal products:
• Containing new active substances for indications other than those stated above;
• That are a significant therapeutic, scientific or technical innovation;
• Whose authorisation would be in the interest of public health at the EU level.

3 Pursuant to the centralized procedure, the EMA's Committee for Medicinal products for Human Use carries out a scientific assessment of the application and gives a recommendation on whether the medicine should be marketed or not. It should be noted, however, that the EMA has no authority to actually authorize marketing in the different EU countries since, under EU law, the authorizing body for all centrally authorized product is the European Commission, who takes a legally binding decision based on the EMA's recommendation. Once granted by the European Commission, the centralized marketing authorization is valid in all EU Member States as well as in the European Economic Area countries Iceland, Liechtenstein and Norway. Commission decisions are published in the Community Register of medicinal products for human use.

4 A biosimilar is biological medicine highly similar to another already approved biological medicine in the EU, for which marketing exclusivity rights have expired.