

THE LIFE SCIENCES
LAW REVIEW

SEVENTH EDITION

Editor
Richard Kingham

THE LAWREVIEWS

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PREFACE

The seventh edition of *The Life Sciences Law Review* covers a total of 34 jurisdictions, providing an overview of legal requirements of interest to pharmaceutical, biotechnology and medical device companies. The chapters are arranged so as to describe requirements throughout the life cycle of a regulated product, from discovery to clinical trials, the marketing authorisation process and post-approval controls. Certain other legal matters of special interest to manufacturers of medical products – including administrative remedies, pricing and reimbursement, competition law, special liability regimes and commercial transactions – are also covered. Finally, there is a special chapter on international harmonisation, which is of increasing importance in many of the regulatory systems that are described in the national chapters.

The past year has seen a number of significant developments. After many years of negotiations and false starts, the United States and EU have finally begun to implement a programme of mutual recognition of inspections of drug manufacturing establishments, thus simplifying the shipment of drug products between the jurisdictions and freeing resources to carry out more inspections in third countries. In the meantime, the United States continues to debate whether to repeal the comprehensive medical care legislation enacted during the Obama administration, and is now considering measures to improve the transparency of pricing for prescription drugs. The United Kingdom is addressing changes to drug regulatory systems that must accompany the country's planned withdrawal from the EU, and drug and device manufacturers are actively planning for the effects of Brexit on their supply chains. The governments in India and China continue to consider changes in their regulatory systems for drugs and medical devices.

It is vitally important that lawyers who advise companies in the life sciences sector and the business executives whom they serve have a working knowledge of the regulations and policies that govern drugs, biologics and medical devices. It is equally important to keep up to date with developments in the regulatory systems, which govern access to the market, pricing and reimbursement, advertising and promotion, and numerous other matters that are essential to success. It is our hope that this annual publication will be helpful in this respect.

All of the chapters have been written by leading experts within the relevant jurisdiction. They are an impressive group, and it is a pleasure to be associated with them in the preparation of this publication.

Richard Kingham
Covington & Burling LLP
Washington, DC
March 2019

PORTUGAL

*Francisca Paulouro and Inês Caldas de Almeida*¹

I INTRODUCTION

The life sciences sector in Portugal is heavily regulated, with the legal framework applicable both to medicines and medical devices closely following the EU regulatory framework. Nevertheless, in some areas national legislation goes beyond what is provided in the relevant directives; this is particularly noticeable, for example, in matters related to promotion, wholesale distribution and clinical trials. Pricing and reimbursement are exclusively dealt with at national level, as they are outside the scope of EU legislation, with the exception of transparency measures and procedural requirements set out in the Transparency Directive.²

The National Authority of Medicines and Health Products, IP (Infarmed), is the national regulatory agency for medicines and medical devices. In addition to its competence for technical health regulation, Infarmed's powers also cover pricing, reimbursement and market access. Price approval of prescription products, including products for hospital use, is also attributed to this agency. Infarmed plays a significant role in relation to reimbursement and market access of medicines, as it is the entity responsible for conducting the relevant procedures and proposing decisions to the Minister of Health.

II THE REGULATORY REGIME

The Medicines Act³ consolidates in a single legal act the regime applicable to, among other things, the marketing authorisation, manufacture, import, export, marketing, labelling, promotion and pharmacovigilance of medicines; it transposes into Portuguese Law several directives, including Directive 2001/83/EC,⁴ as amended (the Directive).

Medical devices, in turn, are governed by the Medical Devices Act,⁵ which, further to transposing several directives related to the manufacture, marketing and vigilance of medical devices (including Directive 93/42/EEC,⁶ as amended), establishes the regime applicable to promotion. With regard to promotion, the Medical Devices Act closely follows the regime

1 Francisca Paulouro is an of counsel and Inês Caldas de Almeida a senior associate at Vieira de Almeida.

2 Council Directive of 21 December 1988 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems.

3 Decree-Law No. 176/2006 of 30 August 2006, as amended.

4 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.

5 Decree-Law No. 145/2009 of 17 June 2009, as amended.

6 Council Directive 93/42/EEC of 14 June 1993 concerning medical devices.

set out for medicines. In early 2017, Decree-Law No. 5/2017⁷ introduced general principles applicable to the promotion of medicines and medical devices, and further implemented specific rules for scientific, educational and promotional events that take place in National Health Service entities.

i Classification

The definitions of a medicinal product for human use and of a medical device are identical to those arising from EU legislation, with the distinction between them being made on the basis of the intended use and the mechanism through which this is achieved. As is the case under the Directive, where any doubt arises, the classification as a medicinal product prevails.

ii Non-clinical studies

Directive 2010/63/EU⁸ on the protection of animals used for scientific purposes was transposed into Portuguese law in August 2013.⁹ This regime follows closely the one set out in Directive 2010/63/EU, thus establishing several requirements applicable to the use of animals for scientific or educational purposes, namely in what concerns the accommodation, care and use of animals in procedures; the origin, breeding, marking and killing of animals; licensing of breeders, suppliers and users; and the procedures for evaluation and authorisation of scientific or educational projects.

In addition, and similarly to what happens at EU level, the testing of finished cosmetic products and cosmetic ingredients on animals is prohibited, with the same applying to the marketing thereof if animal testing was conducted for cosmetic purposes.

iii Clinical trials

In April 2014, a new legal regime for clinical research was approved,¹⁰ consolidating in one legal act the provisions applicable to clinical studies, whether interventional or not, and covering medicines, medical devices and cosmetics. The regime encompasses the provisions of Directive 2001/20/EC¹¹ regarding the conduct of clinical trials on medicinal products for human use and the provisions of Directive 2007/47/EC¹² on clinical investigation with medical devices.

All clinical studies are subject to a prior favourable opinion from the competent ethics committee. In addition, interventional clinical trials with medicines depend on authorisation from Infarmed, with the same applying to interventional studies with Class III medical devices, implantable medical devices and long-term invasive devices falling within Classes IIa

7 Decree-Law No. 5/2017 of 6 January 2017.

8 Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010.

9 Decree-Law No. 113/2013 of 7 August 2013.

10 Law No. 21/2014 of 16 April 2014.

11 Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

12 Directive 2007/47/EC of the European Parliament and of the Council of 5 September 2007, amending Council Directive 90/385/EEC on the approximation of the laws of the Member States relating to active implantable medical devices, Council Directive 93/42/EEC concerning medical devices and Directive 98/8/EC concerning the placing of biocidal products on the market.

or IIb. For the remaining classes of medical devices, interventional studies depend only on the favourable opinion from the ethics committee and on notification to Infarmed. The conduct of clinical interventional studies with cosmetics should also be notified in advance to Infarmed, with the sponsor being entitled to initiate the study should Infarmed not issue an unfavourable decision within 30 days of the notification.

Both the sponsor and the investigator are jointly and severally liable, regardless of fault, for material and non-material damage suffered by subjects – liability that must be covered by insurance. Should an interventional study be at stake, there is a legal presumption that damage that affects the health of subjects during the study and for a one-year period following its term (which may be extended by the ethics committee) is caused by the study. This reverses the general rule on burden of proof, subject to which whosoever alleges damage should demonstrate the causal relationship between the damage and the act (in this case, the study).

iv Named-patient and compassionate-use procedures

Similar to what happens under EU legislation, the general rule is that medicines can only be marketed following the granting of a marketing authorisation. In exceptional circumstances, however, Infarmed may authorise the use of non-approved medicines, such as when the product is, subject to a clinical assessment, considered indispensable for the treatment of a given pathology and there is no therapeutic alternative among authorised products.

Within the context of interventional clinical studies, following the conclusion of a study, the sponsor is under an obligation to supply the investigational medicinal product or device under clinical investigation for free until its marketing should the investigator consider that continuation of its use by the former participant is indispensable and that there are no therapeutic alternatives with an equivalent degree of safety and efficacy.

v Pre-market clearance

The Medicines Act reflects EU rules in this regard and thus medicines can only be placed on the market following the granting of a marketing authorisation – Infarmed being the competent authority for authorising medicines that follow national procedures.

The marketing in Portugal of medical devices bearing a CE mark does not require any authorisation from Infarmed. Nonetheless, Infarmed must be notified of all medical devices marketed by a given entity prior to its commercialisation.

vi Regulatory incentives

The Medicines Act reflects the regime established in the Directive regarding regulatory data protection and market exclusivity. Generic applications cannot be submitted for a period of eight years following the first authorisation in the European Union. After this eight-year period has elapsed, the generic cannot be launched on the market for an additional two years. This period may be extended for one supplementary year should the innovator, within the data exclusivity period of eight years, obtain a marketing authorisation for one or more indications of significant clinical benefit.

Patent linkage is not permitted. The Medicines Act expressly provides that marketing authorisation applications cannot be dismissed on the grounds of the potential existence of industrial property rights of the reference product. A similar rule exists for pricing and reimbursement decisions.

There are no special provisions to encourage the development or market launch of innovative products. On the other hand, special provisions to encourage the sale of generics exist in a variety of areas; for example, generics benefit from a simplified regime regarding pricing and reimbursement, and prescription is mandatorily made by active substance once a generic is launched in the market, the rule being that of generic substitution, save in very limited circumstances expressly provided for by law.

vii Post-approval controls

Pharmacovigilance rules applicable to medicinal products were modified in 2013 with the transposition into Portuguese law of Directive 2010/84/EU and Directive 2012/26/EU.¹³ In the same year, the provisions of Directive 2011/62/EU¹⁴ regarding prevention of entry into the supply chain of falsified medicinal products were also transposed, with the Medicines Act currently closely following EU legislation on these matters, such as the placing of safety devices on the packaging of certain medicinal products, to identify and authenticate them. Detailed rules for these safety devices were to be adopted through Delegated Regulation 2016/161,¹⁵ including a repository system containing information on the safety features. These rules were to be implemented by marketing authorisation holders up until 9 February 2019. In 2018, the Medicines Act was amended, to adapt local legislation to Delegated Regulation 2016/161.

A similar regime applies regarding medical devices, with the vigilance requirements stemming from the relevant directives. In addition, a pharmacovigilance system has been implemented that is similar to the system applicable to medicines.

viii Manufacturing controls

In line with the Directive, the manufacture of medicinal products is subject to prior authorisation by Infarmed, even if products are intended for export. An authorisation will only be granted if the applicant has adequate premises that comply with the applicable legislation and with the European Commission Guidelines on Good Manufacturing Practice (in 2018, the Medicines Act was amended to transpose Directive 2017/1572)¹⁶ and has a qualified person permanently and continuously at its disposal. The qualified person, who is responsible for all manufacturing activities performed, must be a pharmacist registered with the Portuguese Order of Pharmacists.

Any change to the manufacturing authorisation requires prior authorisation by Infarmed.

In 2013, the Medicines Act was amended, transposing Directive 2011/62/EU and thus requiring that the manufacturers of active substances established in Portugal register their activity with Infarmed.

The manufacture of medical devices, as well as the assembling, packaging, processing, fully refurbishing, labelling or assigning to them a purpose different from that of its original intended use, among others, is subject to prior notification to Infarmed. The engagement

13 Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 and Directive 2012/26/EU of the European Parliament and of the Council of 25 October 2012.

14 Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011.

15 Commission Delegated Regulation 2016/161 of the European Commission, of 2 October 2015.

16 Directive 2017/1572 of the European Commission of 15 September 2017.

in these activities is dependent on the applicant having adequate premises and equipment with capacity to ensure the manufacture, storage and conservation of medical devices and a technician responsible to ensure the quality of the activities performed.

In addition, and in line with what is set out in EU directives, manufacturers or their authorised representatives placing medical devices on the Portuguese market should notify Infarmed, providing in the notification the required level of information depending on the classification or nature of the device concerned.

ix Advertising and promotion

The regime applicable to the advertising of medicines closely follows the regime set out in the Directive. The major differences relate to the definition of advertising, to the scope of the prohibition on granting benefits to healthcare professionals and to the prohibition on granting any kind of benefit to patients, matters in respect of which the Medicines Act goes beyond what is established in the Directive.

The definition of advertising is broader than that set out in the Directive, advertising being considered, under the Medicines Act, as any kind of information, canvassing activity or inducement that has as its object or effect the promotion of the prescription, dispensation, sale, purchase or consumption of medicines. Contrary to what is foreseen in the Directive, Portuguese law does not require that the conduct be designed to promote a given product for it to qualify as advertising. It suffices that the conduct at issue has that effect.

Second, the Medicines Act extends the scope of the prohibition on pharmaceutical companies granting gifts, pecuniary advantages or benefits in kind to healthcare professionals to also include bonuses – a notion that is associated with the granting of discounts in kind, such as free products. The broadening of this prohibition is particularly relevant to the relationship between pharmaceutical companies and pharmacies, being hardly in line with the EU legal framework and with the principle that promotion rules do not apply to measures or trade practices related to prices, margins and discounts – provided for in both the Directive and the Medicines Act.

Finally, pharmaceutical companies are prevented from granting any kind of benefit to patients. Similarly to what happens in relation to healthcare professionals, companies cannot grant or promise to grant, directly or indirectly, gifts, prizes, bonuses, pecuniary advantages or benefits in kind to patients.

Although companies are under an obligation to provide Infarmed with a summary description of all advertising materials, no prior-approval requirement exists. In addition, companies must notify Infarmed in advance of the sponsorship of any congress, symposium or event of an educational or promotional nature.

The regime applicable to advertising and promotion of medical devices is very similar to that applicable to medicines. There is, however, no prohibition on granting gifts or benefits to the public. The advertising of medical devices, the use of which requires the intervention of healthcare professionals, such as implantable medical devices, cannot be promoted to the public.

Medical device companies are also required to notify Infarmed in advance of the sponsorship of any congress, symposium or event of an educational or promotional nature.

x Distributors and wholesalers

Wholesale distribution of medicines is subject to prior authorisation from Infarmed, the only exception being for holders of manufacturing authorisations in relation to the products covered by those authorisations (similarly to what happens under the Directive).

The granting of such an authorisation is dependent on the applicant having adequate equipment and premises, located in Portugal, to ensure proper conservation and distribution of medicines and a technical director, who must ensure, effectively and permanently, the quality of the activities carried out in the distribution premises. The technical director must be a pharmacist registered with the Portuguese Order of Pharmacists and personally fulfil his or her responsibilities in the wholesale premises. Until 2013, the technical director had to exercise the functions of this role exclusively and could not perform those functions for more than one company, even if the wholesale distribution premises were the same. Currently a technical director may cumulate functions within the same wholesale premises, up to a limit of five wholesale distribution authorisations. In 2015, a new regulation on good distribution practices applicable to the wholesale distribution of medicines¹⁷ was approved, closely following Commission Guideline 2013/C 343/01.¹⁸

In addition, wholesalers are under a legal obligation to have medicines permanently available in sufficient quantity and variety to ensure the appropriate and continued supply of medicinal products with a view to guaranteeing the satisfaction of patients' needs. The minimum quantities of products that wholesalers must keep at all times to comply with this public service obligation were set out in a regulation issued by Infarmed.

In 2013, to address shortages of medicinal products on the Portuguese market, mainly resulting from parallel exports to other EU Member States, the Medicines Act was amended, granting Infarmed powers to list the medicines of which it requires notification prior to exportation (within and outside the European Union). In 2015, Infarmed published a regulation setting out the terms applicable to the notification and to the medicines covered (a list that has been regularly updated), and wholesalers are currently under an obligation to notify in advance all sales of medicines included on this list made to countries outside Portugal. In addition, marketing authorisation holders, wholesalers and pharmacies must notify Infarmed, once a month, of the quantities of certain listed medicinal products that are sold, dispensed, exported or subject to intra-community commerce. The compatibility of this regime with principles of EU law has always been far from clear. In 2016, the European Commission initiated a procedure against Portugal, determining, in its reasoned opinion, that Portugal should suppress unjustified and disproportionate notification obligations because they constitute an obstacle to the free movement of goods within the European Union. To comply with the terms of the reasoned opinion, Infarmed revised its rules in 2017.¹⁹ Although the regime of prior notification was maintained, clear and transparent criteria for the inclusion of medicines on the list in question, and for the list's revision, were implemented. Finally, Infarmed has the power to prevent the exportation of medicines – be it inside or outside the European Union – on the grounds of protection of public health or to ensure patient access to a given medicinal product.

17 Infarmed Resolution No. 047/CD/2015 of 19 March 2015.

18 Commission Guideline 2013/C 343 of 5 November 2013.

19 Infarmed Resolution No. 524/2017 of 14 June 2017.

The regime governing the brokering of medicinal products under the Medicines Act follows closely that of Directive 2011/62/EU,²⁰ thus engagement in the activity of brokering does not require prior authorisation from Infarmed; neither is it dependent on the existence of premises or a permanent address in Portugal. Persons brokering medicines with a permanent address in Portugal must register their activity with Infarmed.

The engagement in the activity of wholesale distribution of medical devices, although not subject to express authorisation from Infarmed, must be notified in advance to that authority, and is only permitted if (as is the case for medicines) the applicant has adequate premises and equipment with capacity to ensure good storage, conservation and distribution of medical devices and a responsible technical director is appointed to the wholesale premises to ensure the quality of the activities performed. In contrast to the regime applicable to medicines, the technical director does not have to be a pharmacist but must have an adequate technical qualification to ensure the quality of the distribution activity, as well as adequate knowledge of the legislation and regulations applicable to medical devices. Also, differently from the regime applicable to medicines, the wholesale premises do not have to be located in Portugal. Nonetheless, should the premises be located abroad, the applicant must comply with the Portuguese legal provisions applicable to the wholesale distribution of medical devices. In 2016, good distribution practices applicable to the wholesale distribution of medical devices were approved (although initially legally set out in 2009).²¹ This regime is extremely demanding and, in many aspects, follows the good distribution practices for medicines.

xi Classification of products

The criteria laid down in the Medicines Act for classifying a medicine for medical prescription are very similar to those set out in the Directive.

The classification has related consequences for the regime applicable to advertising, pricing, reimbursement and point of sale or dispensing. Only non-prescription products may be promoted to the general public, which is the same under the Directive. In addition, while there is no price control for non-prescription drugs (unless these are reimbursed – the general rule, however, is that non-prescription products are not subject to reimbursement), prescription products have their maximum sale prices approved, regardless of whether they are reimbursed or not. Finally, whereas the dispensing of prescription drugs is restricted to pharmacies – unless subject to restricted medical prescription, in which case they can only be dispensed or administered in hospitals – over-the-counter products (OTCs) may be sold at points of sale duly authorised by Infarmed.

xii Imports and exports

In line with the regime laid down in the Directive, the importation of medicines is subject to prior authorisation from Infarmed, with requirements very similar to those applicable to the manufacture of medicines (see Section II.viii). The importation of active substances is also subject to registration with Infarmed. The export of medicinal products does not require any authorisation from Infarmed, nor does it require registration with Infarmed.

20 Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011.

21 Ministerial Order No. 256/2016 of 28 September 2016.

As regards medical devices, there are no additional requirements related to imports and exports other than those applicable to the manufacture, placing on the market and wholesale distribution, analysed above.

xiii Controlled substances

The manufacture, use, marketing, distribution, importation, exportation and possession of narcotics and psychotropic substances are subject to a specific regime. Narcotics and psychotropic substances are divided into several categories, each identifying the relevant substances. Infarmed is the entity responsible for authorising engagement in these activities in relation to certain categories of substances. Specific requirements also exist for prescribing, dispensing and keeping records when such substances are included in medicinal products.

Further to constituting a misdemeanour punishable with a fine, engagement in any of the above-mentioned activities without the relevant authorisation may be considered a criminal offence.

In addition, the use of cannabis-based medicines, preparations and substances for medicinal purposes, was authorised under Law No. 33/2018,²² which came into force on 1 August 2018. ‘Cannabis-based medicines, preparations and substances’ are defined as the leaves, flowers and fruits of the cannabis plant, as well as oil and other standard extracts or preparations obtained from the plant.

Physicians are only allowed to prescribe cannabis-based products if conventional treatments with authorised medicines are not having the expected effects or they are generating relevant adverse effects; also, cannabis-based products can only be prescribed for use in indications authorised by Infarmed.

Law No. 33/2018 further indicates that these products must be prescribed by a physician, pursuant to a special medical prescription, which must be approved by the Ministry of Health. The prescription must mention the names of the physician and the patient, and it must identify the cannabis-based medicine, preparation or substance, as well as the relevant quantity, dosage and form of administration.

Since they are considered medicinal products, they will, generally, require a marketing authorisation from Infarmed before being placed on the market.

Cannabis-based products can only be sold in pharmacies. The buyer is required to provide identification, or evidence of being the legal guardian of the patient, together with the prescription. Each prescription can only be used once (i.e., the law does not provide for a renewable prescription, or for a prescription that can be used several times).

xiv Enforcement

Infarmed is entrusted with the supervision and enforcement of regulatory provisions applicable to medicines and medical devices.

A breach of these provisions is considered a misdemeanour punishable with a fine calculated according to the infringer’s annual turnover, or a fine of a predetermined fixed amount (whichever is lower). In addition to this penalty, a breach of the provisions of the Medicines Act, including advertising, may also give rise to ancillary sanctions to be applied

22 Law No. 33/2018 of July 18.

by Infarmed, such as a prohibition on exercising the activity, exclusion from participation in public tenders and the suspension of any authorisations and permits – all up to a maximum of two years.

Should the infringement of promotion rules be at stake, both regarding medicines and medical devices, Infarmed may order that the condemnatory decision be published in the media as well as the suspension of advertising of the product concerned for a period of up to two years. Medicinal products may further be delisted as a result of infringement of promotion rules.

III PRICING AND REIMBURSEMENT

On 1 June 2015, Decree-Law No. 97/2015 was published, creating the System of Assessment of Health Technologies (SiNATS). In creating SiNATS, this single Decree-Law consolidated the provisions applicable to pricing, reimbursement and prior evaluation procedures, and introduced three main changes:

- a* clear reinforcement of the powers of public authorities – with the state being granted the capacity to unilaterally and in an almost unlimited manner amend and terminate contractual agreements executed with the pharmaceutical industry;
- b* an unprecedented concentration of powers within Infarmed; and
- c* flexibility on applicable rules, considering that several matters are referred to governmental and Infarmed regulations, thus facilitating the swift change of provisions.

Several decrees have been approved since the entry into force of SiNATS, establishing the regime regarding specific matters, such as the procedure for reimbursement and prior evaluation,²³ and the rules and procedures applicable to the setting and revision of prices of medicines subject to medical prescription and reimbursed OTCs, as well as corresponding marketing margins.²⁴

Notwithstanding the importance of SiNATS, the essential features of the previous regimes remain untouched. For example, the rules on pricing and reimbursement of medicines continue to differ, essentially depending on the classification of the product for dispensing purposes.

Medicines subject to medical prescription but not a restricted medical prescription, and generally sold in street pharmacies, have to undergo a price approval procedure before Infarmed prior to being launched on the market. In this context, a maximum sale price is approved, which, in the case of branded products, is determined by reference to the price applied in three reference countries. This price is subject to annual revision in accordance with the same criteria.

Approval of reimbursement is within the competence of the Minister of Health and will only be granted should the therapeutic added value and economic advantage of the product be demonstrated.

Another striking feature of SiNATS lies in the increased importance of the execution of agreements between Infarmed and the marketing authorisation holders, although the execution of such agreements is still not legally mandatory – save in the case of hospital products. These agreements typically set a maximum sale value for the product, which, once

23 Decree No. 195-A/2015 of 30 July 2015 as amended.

24 Decree No. 195-C/2015 of 30 July 2015 as amended.

exceeded, will determine a payback by the marketing authorisation holder to the National Health Service equivalent to the amount of public expenditure in excess of the limit. Other types of agreements are now expressly provided for under SiNATS, such as risk-sharing arrangements. SiNATS also approved specific rules for the reimbursement of similar biological medicines conditioning the approval thereto to its price not exceeding 80 per cent of the price of the reference biological medicine.

A 'reference price' system exists in the context of reimbursement. Until a generic is launched on the market, the percentage of state reimbursement, ranging from 15 per cent to 90 per cent, save in exceptional circumstances provided for in specific regulations, applies to the sale price of the product. The placing on the market of a generic, however, gives rise to the creation of a 'homogenous group', composed of branded or innovative medicines and generics with the same active substance, dosage, method of administration and pharmaceutical form, and to the approval of the corresponding reference price – equivalent to the average of the retail sale price of the five lowest-priced products included in the group. Following approval of the reference price, the maximum amount of state reimbursement for products included in the relevant group will be determined by applying the applicable reimbursement percentage to the price.

Similarly, before they can be sold to National Health Service hospitals, medicines subject to medical prescription have to undergo an evaluation procedure, in the context of which the applicable maximum sale prices are approved by the Ministry of Health, or Infarmed, should this competence be delegated. Until the approval of SiNATS, this regime only existed for medicines subject to restricted medical prescription. Note, however, that if the medicine is already subject to reimbursement, it is exempt from this procedure – unless otherwise decided by the Ministry of Health, or Infarmed, should this competence be delegated.

As with reimbursement, the therapeutic added value and economic advantage of the product under evaluation must be demonstrated within this procedure for a favourable decision to be issued. That decision further implies the execution of an agreement between Infarmed and the marketing authorisation holder. Just as we have seen in the context of reimbursement, these agreements also usually establish a maximum sale value for the product and, if this amount is exceeded, the difference should be refunded by the marketing authorisation holder.

Prior to the approval of SiNATS in 2015, the applicable rule regarding medical devices was that the relevant sales price was either free or arose from public procurement procedures, whenever applicable, with the exception of test strips, needles, syringes and lancets destined for persons with diabetes that were subject to a price control and reimbursement regime.

Since then, reimbursement regimes have been set for pressurised inhalers,²⁵ medical devices for ostomates²⁶ and medical devices for patients with urinary incontinence and urinary retention.²⁷

As a result of SiNATS, the medical devices sector may evolve from a state of relative commercial freedom, in which only the prices of these products were controlled, to one of high regulation. In fact, SiNATS sets out the possibility of administratively determining the sale prices of medical devices and of approving their reimbursement, as well as requiring these products to undergo a prior evaluation procedure, similar to the existing procedure

25 Ministerial Order No. 246/2015 of 14 August.

26 Ministerial Order No. 284/2016 of 4 November.

27 Ministerial Order No. 92-E/2017, of 3 March.

for medicines being considered for use or purchase by National Health Service hospitals. In practice, this general legal framework has rarely been enforced and the medical devices sector continues to be poorly regulated. In September 2017, significant changes were made to SiNATS.²⁸ Homogeneous groups were created for similar biological medicinal products and a maximum price was enacted for the sale of these products to National Health Service hospitals.

Infarmed's powers regarding reimbursement have been strengthened. Not only can it modify the terms of reimbursement, but it can also now promote, on its own initiative and at any time, the evaluation or re-evaluation of reimbursement when public health reasons require it.

The rule that medicines covered by the prior evaluation procedure can only be purchased by National Health Service hospitals on an exceptional basis (namely when the patient suffers from a life-threatening disease or risks severe complications and there is no therapeutic alternative), following a specific request from the hospital concerned and prior authorisation from Infarmed, was reiterated and reinforced. This matter was further developed in a regulation approved by Infarmed regarding early access programmes.²⁹ Subject to this regulation, and in line with what is set out in the law, prior to obtaining a favourable decision within the context of a prior evaluation procedure, medicines should be supplied to National Health Service hospitals free of charge. Supply free of charge is subject to a maximum period, determined by reference to the legal deadline for the procedure.

IV ADMINISTRATIVE AND JUDICIAL REMEDIES

Final decisions from Infarmed in the context of regulatory, pricing and reimbursement matters are subject to judicial review by administrative courts. The decisions are immediately effective, with the initiation of legal action *per se* not suspending the effects thereto. Matters of a technical nature are not reviewed by administrative courts, except in cases of manifest error, and administrative courts do not issue technical judgments.

In addition, decisions issued by Infarmed within the context of misdemeanour proceedings initiated for a breach of regulatory provisions are subject to appeal before the judicial courts.

V FINANCIAL RELATIONSHIPS WITH PRESCRIBERS AND PAYERS

The Medicines Act transposed into Portuguese law the provisions of the Directive on the promotion of medicinal products, including interactions with healthcare professionals. The rule is, therefore, that pharmaceutical companies cannot offer or promise to offer, directly or indirectly, gifts, pecuniary advantages or benefits in kind to healthcare professionals, unless they are inexpensive and relevant to the practice of medicine or pharmacy. For several years there was no legal indication as to what should be considered inexpensive. This state of affairs changed in 2013 when for the first time a decree was published that set the inexpensive limit – as had been foreseen in the Pharmaceutical Industry Association Code of Ethics. Since then, this amount has been increased and is currently set at €60.³⁰

28 Decree-Law No. 115/2017 of 7 September 2017.

29 Infarmed Resolution No. 80/CD/2017 of 24 October 2017.

30 Order No. 1542/2017 of 31 January 2017.

In addition, transparency obligations were enacted in 2013, requiring pharmaceutical companies to notify Infarmed of any payment or offer in excess of €60 made to any individual or legal entity, such as healthcare professionals, medical or scientific associations, patient associations and healthcare institutions. The recipient is also required to validate this notification and the absence of a validation, or a rejection, will be taken to indicate that the notification is correct. This information is publicly available on Infarmed's website.

Similar rules exist in the context of medical devices. The principle that no offer can be made to healthcare professionals unless of insignificant value and relevant to the healthcare professional's practice dates back to 2009 and, as from 2017, is subject to the exact same limit as that provided in relation to the promotion of medicinal products: €60.³¹ Also in 2017, the transparency obligations that apply in the medicines sector were implemented for medical devices. Currently, pharmaceutical companies and medical device companies are subject to the exact same transparency rules.

In early 2014, a specific conflict-of-interest regime for the health sector was approved. The regime prevents, among other things, members of commissions, working groups, juries and National Health Service consultants whose role involves the market access of products (e.g., involvement in pricing and reimbursement procedures, in pharmacoeconomic assessments, in the approval of therapeutic guidelines and purchase procedures) from performing functions, either regularly or occasionally, for payment by pharmaceutical companies. A breach of these rules constitutes a misdemeanour punishable with a fine. In addition, in the event of such a breach, the opinions issued or decisions adopted by the commissions, working groups, juries and consultants do not produce any legal effects and any decisions adopted by decision-making bodies based on the same are considered null and void.

In addition, as from 2017,³² National Health Service establishments and services are prohibited from receiving direct or indirect financial benefits or benefits in kind from pharmaceutical and medical device companies, unless it can be demonstrated that receiving these benefits does not compromise the establishment or service's exemption or impartiality, and prior authorisation from the Ministry of Health is obtained. Furthermore, educational or scientific events with promotional purposes or sponsored by pharmaceutical or medical device companies cannot take place in National Health Service establishments and services.

VI SPECIAL LIABILITY OR COMPENSATION SYSTEMS

With the exception of damages arising from harm suffered by subjects in clinical studies (see Section II.iii), there is no specific compensation or liability regime applicable to damages arising from harm caused by the use of medicines or medical devices. Product liability claims are therefore subject to the general legal regime concerning liability for defective products.

VII TRANSACTIONAL AND COMPETITION ISSUES

The Portuguese Competition Law³³ prohibits agreements, concerted practices and decisions by associations of undertakings, as well as abuses of a dominant position, capable of preventing,

31 id.

32 Decree-Law No. 5/2017 of 6 January 2017.

33 Law No. 19/2012 of 8 May 2012.

distorting or restricting competition in the Portuguese market. Competition rules apply to pharmaceutical companies whenever possible, despite these companies being subject to strict regulation in matters such as market access, distribution and pricing.

On June 2017, the Lisbon Court of Appeal confirmed the decision by the Portuguese Competition Authority (PCA) fining the National Association of Pharmacies (ANF) and three undertakings of the same group for an abuse of dominant position in the form of a margin squeeze in the market for the sale of studies based on pharmacies' commercial data; however, the Court of Appeal reduced the amounts of the fines significantly.

The case dates from 2015, when the PCA concluded an investigation into the market for the sale of pharmacies' commercial data, a market in which the ANF group is dominant. The PCA decided that, between 2010 and 2013, the prices charged by the ANF group for the sale of pharmacies' commercial data (the upstream market), when compared to the prices charged by the same group for the sale of market studies based on those data (the downstream market), did not allow an equally efficient competitor active in the downstream market to achieve an adequate margin to cover its production costs. The PCA found that this behaviour had affected not only ANF's competitors, which were unable to enter or compete in the downstream market, but also consumers purchasing such studies, namely pharmaceutical laboratories.

When the decision was first challenged, the Competition, Regulation and Supervision Court (TCRS) upheld the PCA decision but reduced the fines to a total of €6.89 million on the understanding that only the turnover related to the markets in which the abuse of dominance took place should be considered for the purpose of calculating fines. On 14 June 2017, the Lisbon Court of Appeal rendered a final judgment in this case, confirming the existence of an abuse, but dismissing the finding that the holding company (Farminveste SGPS) was also liable for the infringement. Since that company had the highest turnover, the fine initially imposed by the PCA was substantially reduced, to a mere €815,000 (a reduction of 92 per cent of the fine imposed by the PCA).

In September 2017, the TCRS confirmed a PCA decision to close an investigation into pharmaceutical companies that had unilaterally decided to refuse to supply a new wholesaler. The TCRS decision established that:

- a* a distinction could be established between the relevant market for the medicine and the relevant market for the wholesale distribution of the medicine;
- b* if a company holds a dominant position, a refusal to deal may be justified by objective reasons related to legitimate commercial interests of the supplier;
- c* a refusal to supply a (potentially) new counterparty to ensure the stability of the existing distribution network may be treated differently from a termination of an existing commercial relationship;
- d* a refusal to deal may also be considered a discrimination; and
- e* the effects of the refusal to deal on consumer welfare may be disregarded as long as the wholesale distribution market remains competitive.

During 2018, the PCA continued to engage in a nationwide awareness campaign on the need to fight bid rigging, with a focus on awarding authorities. As a result, an increased number of investigations launched by the PCA may be expected, namely regarding the conditions under which public hospitals are supplied.

VIII CURRENT DEVELOPMENTS

Public policy continues to be driven by a desire to contain public expenditure on pharmaceuticals. The National Strategy for Medicines and Health Products, approved by the government in October 2016 for the period 2016–2020, is consistent with this purpose. The stated priorities for this period include the systematic re-evaluation of reimbursed medicines, the issuance of therapeutic recommendations, the introduction of changes to the price-referencing system when generics or biosimilars exist, and an increase in the quota of generics and biosimilars. The recently approved Major Planning Options for 2019³⁴ establish as priorities the continuity of the policies on price revision of medicines, re-evaluation of reimbursed medicines and the increase in the quota of biosimilars and generics. As regards the quota of biosimilars and generics, the State Budget Law for 2019 provides that the government should take further measures to encourage the use of generics with a view to increasing their market share to the level of 30 per cent.

Finally, the approval in 2018 of the use of cannabis for medicinal purposes has the potential to be a game changer in certain therapeutic areas. The full extent of the changes that this will produce is unknown as yet and will very much depend on the upcoming implementing regulation.

34 Law No. 70/2018, of 31 December 2018.

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