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Law & Practice

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Law & Practice

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Faus & Moliner is a modern boutique law firm which specialises in dealing with legal matters associated with the pharmaceutical industry and companies which operate in the life sciences sector. The firm combines legal skills and specialisation with a practical and business-oriented manner of practising law. This allows Faus & Moliner to offer innovative solutions and responses that cater to the specific requirements of the cases that are entrusted to the firm. Since its foundation in 1997, Faus & Moliner has been the market leader in the area of pharmaceutical law in Spain, as recognised in several international publications. The firm advises pharma and healthcare clients, and acts on behalf of large companies and smaller biotech start-ups, and is frequently called upon to advise public authorities on matters such as draft legislation.

Regulatory Framework

1.1 Legislation

Pharmaceutical regulation in Spain currently comprises the following:

- Law 14/1986, the General Health Law.
- Law 29/2006 on guarantees and rational use of medicinal products and medical devices.
- Law 10/2013 on pharmacovigilance and on the prevention of the entry of counterfeit medicinal products into the legal supply chain.
- Royal Decree 824/2010 on pharmaceutical companies, manufacturers of active ingredients, foreign trade of medicines and investigational medicinal products.
- Royal Decree 223/2004, which regulates clinical trials.

- Royal Decree 1345/2007, which regulates the authorisation, registry and dispensation conditions of medicinal products for human use that are prepared industrially.
- Royal Decree 782/2013, which regulates distribution of medicinal products.
- Royal Decree 1416/1994, which regulates advertising of medicinal products.
- Royal Decree 870/2013, which regulates online sales to the public of non-prescription-only medicinal products.
- Royal Decree 577/2013, which regulates pharmacovigilance of medicinal products for human use.
- Royal Decree 1015/2009, which regulates access to medicinal products in special situations.
- Royal Decree 271/1990, which regulates the prices of medicinal products reimbursed by the National Health System.
- Royal Decree 177/2014, which regulates the reference price system and homogeneous groups of medicinal products in the National Health System and information systems on reimbursement and prices of medicinal products and medical devices.
- Royal Decree 618/2007, which regulates the procedure for establishing particular measures for prescription and dispensation of medicinal products.
- Royal Decree 1718/2010 on medical prescription.
- Royal Decree 1785/2000 on intra-community trade of medicinal products.
- Royal Decree 477/2014, which regulates authorisation of medicinal products for advanced therapies that are not prepared industrially.

In addition to these rules, regional authorities may also adopt some rules which may apply at their level, mainly in the context of organising the dispensation of medicines to patients at healthcare centres and hospitals.

1.2 Regulatory Bodies

The Ministry of Health

This is the department of the central Spanish government which is responsible, among others, for drafting and implementing the rules on pricing and reimbursement of medicinal products that are financed through public funds in Spain.

At the Ministry of Health, a specific pricing committee is competent to review and give final approval to applications that companies may file for pricing and reimbursement. The decisions adopted by the Ministry of Health in this regard apply to all of Spain, although they may also be affected by individual positions taken by each region.

The Spanish Medicines Agency

The Spanish Medicines Agency is also part of the central Spanish government and is responsible, among others, for granting marketing authorisations for medicinal products in Spain. With regard to products that have received a marketing authorisation from the European Commission, the Spanish Medicines Agency plays only a secondary role, approving final mock-ups and the contents of the so-called 'blue box' in the packaging of the product. The Spanish Medicines Agency is also competent to prepare a Therapeutic Position Report, the intention of which is to be the only scientific document that is to be considered for the purposes of supporting reimbursement decisions.

The regional authorities

In Spain, the public funds that may be used to finance reimbursement of medicinal products are allocated from the budget of the 17 regions into which the country is divided. Because of this, the regions have an interest in participating in pricing and reimbursement matters.

At present, this participation takes place through two main routes. One is through special meetings at the Ministry of Health where the regions participate in assessing applications and where its representatives may be appointed as rapporteurs. The second route, which is not really a formal one but which is of great practical importance, is through the adoption of regional procedures or guidelines which influence how patients may have access to treatments using certain drugs.

1.3 Challenging Decisions

Decisions taken by regulatory bodies may be challenged through an administrative appeal and through judicial review. In some cases, the administrative appeal is compulsory and has to be filed within a month from the date on which the decision was notified. When the administrative appeal is merely optional, the interested party may go directly to court within two months of the date on which the decision was notified. Pending the court

case, an injunction may be sought. The chances of obtaining an injunction largely depend on whether the applicant is able to show that they would suffer irreparable harm in the event that the injunction is not granted.

Clinical Trials

2.1 Regulation

At present, clinical trials are regulated by Royal Decree 223/2004. However, this regulation is in the process of being replaced by a new one. In May 2013, the Ministry of Health released the draft for the new regulation. The new legislation has not yet been approved, and it may be that approval will be delayed, because the government will probably review the draft in the light of Regulation No 536/2014 which was adopted on 16 April 2014. The most important aspects of the projected Spanish legislation are the following:

- The procedure for obtaining approvals to carry out a clinical trial in Spain is to be simplified, which is intended to improve the co-ordination between the Spanish Medicines Agency and the new Evaluation Committees for Research into medicinal products.
- A 'single ruling' system is finally to be implemented. The opinions issued by any of the Evaluation Committees for Research into medicinal products must be accepted by all the other committees involved in the trial.

Other measures aiming to make the process easier for applicants include the introduction of the concept of 'low-risk clinical trials', for which there will be less burdensome requirements, the introduction of a single point of contact between the sponsor and the authorities, the generalisation of the use of electronic media in the communications between the two, and the approval of a template for clinical trial agreements that will be used by all public hospitals.

More and better information on clinical trials carried out in Spain will be put at the disposal of the public, through the creation of a national registry of clinical trials.

Marketing Authorisations

3.1 Types of Marketing Authorisation

Supply of medicines prior to obtaining a marketing authorisation

Under Spanish law, early-access programmes which allow a product to be marketed prior to its having obtained marketing authorisation are possible, although they are subject to strict regulatory controls. The use of a product which has not yet obtained a marketing authorisation in Spain but which has obtained a marketing authorisation in another country requires prior administrative approval from the Spanish Medicines Agency. All requests of this nature are examined on a case-by-case basis.

Off-label use of medicinal products

Under Royal Decree 1015/2009, the use of a licensed medicinal product under conditions different from those of the marketing authorisation is subject to the following requirements:

- Off-label use is only possible if there is no other medicinal product licensed in Spain which is already authorised to be used in the specific indication according to its Summary of Product Characteristics (SmPC).
- The doctor responsible for the treatment must justify in writing the reasons why the patient should use a specific medicinal product under off-label conditions.
- The patient must consent in writing to off-label prescription, after having been informed about the benefits and risks of the treatment.

Off-label use must be authorised by the health authority of the region where the healthcare centre is located. In practice, the healthcare centre is required to send an application to the authority for an authorisation, accompanied by a report by the physician. Once the authorisation has been issued, the healthcare centres of that region no longer need to request subsequent authorisations to use the medicinal product under these off-label conditions on other patients.

The Spanish Medicines Agency may approve guidelines on off-label use. The Agency may issue these guidelines when: (i) off-label use of a given medicinal product may generate a risk for patients; (ii) the medicinal product may be prescribed only

by a hospital specialist; or (iii) when it expects that the impact of the use of the medicinal product off-label may be significant. This last situation would include cases where the economic impact may be significant as well as cases where the impact may be of any other nature (eg public health interest concerns).

So far, the Spanish Medicines Agency has approved three guidelines on off-label use: a guideline on the use of boceprevir and telaprevir for treatment of Hepatitis C in HIV patients, in patients who have undergone a liver transplant and on the paediatric population (26 July 2012); a guideline on the use of pegylated liposomal doxorubicin (Caelyx) during a shortage situation (14 February 2012); and a guideline recommending that growth hormone should not be used for treating brain and peripheral nerve disorders (18 May 2012).

Compounding of medicinal products at hospital pharmacies

Under Article 7 of Royal Decree-law 16/2012, regional authorities may approve hospital pharmacies for the purposes of carrying out activities involving fractioning, dosage personalisation and also "other operations of manipulation and transformation of medicines." The approval process shall be monitored to ensure that the general quality standards to be set up by the Ministry of Health are respected. Thus, hospital pharmacies may manipulate drugs in the interests of improving the efficiency of their usage and, ultimately, cutting costs, and this may involve the use of a product under conditions different from those of its marketing authorisation. The rules on general quality standards have been recently approved by the Ministry of Health.

3.2 Validity of Marketing Authorisations

Keeping the market supplied

Royal Decree 1345/2007 provides, in line with EU Directive 2001/83, that a marketing authorisation is to be revoked if the product is not marketed for three consecutive years.

In addition, Article 62 of Royal Decree 1345/2007 imposes an obligation to keep the market supplied and to maintain continuity of service, so each year, during the month of October, authorisation holders have to declare whether or not they intend to market the product during the following year. If they do not, they will be deemed to be requesting a suspension of the validity of the marketing authorisation.

Furthermore, the Royal Decree empowers the Spanish Medicines Agency to require actual marketing of the medicine and to keep the marketing authorisation in force where there are reasons of health or public health interest for so doing; such reasons include the creation of a pharmaceutical gap, either in the market in general or in the pharmaceutical provision of the National Health Service. Some companies have argued that this is contrary to EU law provisions which allow the authorisation holder to cease placing a product in the market by giving two months' prior notice to the authorities.

3.3 Obtaining a Marketing Authorisation

The main regulation on marketing authorisations for medicinal products in Spain is Royal Decree 1345/2007, which has been in force since December 2007. The most relevant aspects of this regulation are the following:

Marketing authorisations covered by the Royal Decree

For an applicant to become the holder of a marketing authorisation, whether they are an individual or a legal entity, it will be sufficient that they are established in the European Union. The applicant needs only to prove that they have adequately qualified persons available, in addition to the infrastructure necessary to provide information about any adverse reactions suspected or arising in Spain or in another country.

Spanish law does not require the appointment of a local representative of the marketing authorisation holder, and there is no legal obstacle preventing an authorisation holder who is located in any other EU Member State from supplying their products directly to wholesalers, pharmacy offices or hospitals located in Spain. However, as a matter of practice, appointing a local representative has become the rule, and it is now very common to appoint a local representative who is given the task of handling communications with Spanish regulatory authorities, providing a scientific service (including review of marketing materials for compliance with Spanish law) and also carrying out local pharmacovigilance reporting.

The designation of this local representative will be stated in the marketing authorisation, and will be registered as such at the Medicines Registry. Such a designation does not alter the administrative responsibility of the holder. The agreements between the holder and their local representative may make provision for transferring to the latter the responsibility required by the authorities if legal obligations are not complied with, but the effects of such agreements are limited to the parties and do not extend to the authorities.

Transferring a marketing authorisation
A change of holder of a marketing authorisation is possible and is subject to authorisation by the Spanish Medicines Agency. Any modifications of the marketing authorisation that result from the change must be processed as variations.

Unlike the approach used under the preceding regulations, Royal Decree 1345/2007 does not anticipate the change of marketing authorisation holder until the approval procedure has been completed.

Applications based on informed consent
Royal Decree 1345/2007 contains some especially interesting provisions on applications based on the informed consent of the applicant or the holder of another marketing authorisation, allowing for these applications to refer to a dossier that is still being assessed by the Spanish Medicines Agency. The medicine for which an approval is sought under this procedure must be of identical qualitative and quantitative composition in terms of active substances and of the same pharmaceutical form as the original medicine, and both parties must certify that the pharmaceutical, pre-clinical and clinical documentation of the two dossiers is identical, except the information relating to the medicine identification data and the design of the labelling.

3.4 Pharmacovigilance

Pharmacovigilance rules are mainly contained in Royal Decree 577/2013. In line with the provisions of EU regulations and directives, this legislation aims to improve the efficiency of the system and also to allow patients to have a more active role. In this sense, the obligations of the industry regarding information and collaboration with the authorities have been reinforced, and public participation is promoted by allowing patients to notify adverse effects directly. The most important features of this Royal Decree are the following:

- The definition of 'adverse reaction' is widened and includes any response to a medicinal product which is harmful and was not intended. Therefore, responses produced as a result of abuses, medication errors or off-label use shall be considered as 'adverse reactions' for the purposes of these rules.
- The Spanish Medicines Agency is to advertise the measures that need to be adopted in this field. This aims to increase the trust of the general public in the system.
- Patients will be able to notify adverse effects directly through the website of the Spanish Medicines Agency.
- Apart from having to comply with the guidelines on pharmacovigilance best practices, approved by the European Medicines Agency in co-operation with Member States, some obligations intended to identify potential safety problems are imposed on the industry. These measures may require companies to carry out post-authorisation studies. For these purposes, a favourable ruling from an Ethics Committee will still be necessary, but such a ruling will be unique and must be recognised by all regional authorities.

In the area of post-approval controls, reference may also be made to measures adopted against counterfeiting. Law 10/2013 includes some provisions in this area, enabling the creation of a registry of manufacturers, importers and distributors of active ingredients, as well as another registry in which intermediaries who participate in the marketing of medicinal products must be listed, even if they do not physically handle any product. The obligations concerning traceability of medicinal products are also extended to pharmacies.

3.5 Third Party Access to Pending Applications

The position of third parties in connection with marketing authorisation procedures
Can third parties access any information about pending applications for marketing authorisations for pharmaceuticals and can they challenge such approvals once granted? This is a complex area of law in Spain.

As a matter of law and practice, the only information which is available in Spain about pending applications for marketing authorisations is the publication of the positive opinion given by the Committee for Human Medicines of the Spanish Medicines Agency. Typically, after the positive opinion has been given, no more than four to six weeks will elapse until the marketing authorisation is granted, but it is important to note that the opinion of the Committee is not binding. When companies have tried to access other information about applications, the Spanish Medicines Agency has refused to disclose any on the grounds that Article 15 of Royal Decree 1345/2007 states that the documentation of the application and the expert reports is confidential.

After the marketing authorisation has been granted, third parties cannot gain access to documents from the dossier pursuant also to Article 15 of Royal Decree 1345/2007. The only documents to which a third party may have access are the assessment report and the SmPC. Access is possible via the website of the Agency. For generic drugs, the Agency does not publish an assessment report.

After 10 December 2014, the situation may change in this area as a result of the entry into force of the new general rules on transparency. These rules separate the right to obtain information from the right to locus standi. This is important because, until now, the Spanish Medicines Agency has always feared that any relaxation of its position regarding requests for information would imply recognition of the right to locus standi for third parties with respect to the approval process. However, the new rules provide for an appeal mechanism at a Transparency Board, which may then facilitate access.

It is also important to note that Spanish courts have repeatedly denied locus standi to companies wishing to challenge the grant of marketing authorisations to competitors. In the most recent case (26 December 2012), the Spanish Audiencia Nacional denied locus standi to Italfarmaco and, obiter, stated that by denying locus standi the court was avoiding any attack against the confidentiality of the dossier.

Pharmaceutical Pricing and Reimbursement

4.1 Extent of Price Control

Pricing and reimbursement

In Spain, the general rule is that pricing of medicinal products which are reimbursed by the National Health System is not free and requires prior approval. Under Royal Decree-law 16/2012, however, the Ministry of Health is also entitled to control the prices of medicines which are not reimbursed. This is intended to ensure that if the government decides to delist a product whose retail price is rather low (in many cases under EUR3), companies are not permitted to raise their prices sharply in an attempt to compensate for the situation regarding reimbursed products. The law is not explicit as to how the government may exercise this power to control the prices of delisted products; it simply states that it may oppose price increases for reasons of public interest.

Under Law 29/2006, the criteria which must be taken into account in order to decide whether or not a product is to be reimbursed are the following:

(a) the seriousness, duration and sequelae of the pathologies for which the product is approved;
(b) the needs of special groups of persons;
(c) the therapeutic and social utility of the product;
(d) the need to limit public pharmaceutical expenditure;
(e) the existence of medicines already available and the existence of other alternatives for the same illnesses; and
(f) the degree of innovation of the product.

On the other hand, Royal Decree-law 16/2012 introduced new rules stating that, when deciding whether or not a product must be accepted for reimbursement, the Ministry of Health shall also specifically consider the impact that financing such product may have on the public budget and the cost-efficiency ratio of the product, based on the Therapeutic Position Report that the Spanish Medicines Agency may prepare. The pricing authorities are also entitled to consider how the product helps sustain the National Health System, taking into account its contribution to GDP. Public officials in charge of the system are showing, in day-to-day practice, a clear inclination not to favour compa-

nies that do not carry out any industrial operations in Spain or that do not perform R&D activities (including clinical trials). Finally, the law also allows the Ministry of Health to take into account the return mechanisms which may be proposed by the company (discounts, price reviews). This is the result of the increasing relevance that risk-sharing schemes are having in Spanish practice nowadays.

With regard to setting the price, Spain has always been said to follow a cost-plus system under which the maximum ex-factory price should be based upon the cost of the product plus a given profit margin. This is what Royal Decree 271/1990 establishes, in accordance with the provisions of Directive 89/105/EEC.

The cost of the product is to be decided through the analytical determination of the 'Complete Cost', including R&D, manufacturing costs, and allocations corresponding to commercial and administration costs. As regards the profit component, the rule is that the target profit of each company is to be within a range of 12% to 18% on capitals allocated to exploitation, including their own resources and external resources with financial cost.

As a matter of practice, however, the process requires negotiation with the authorities. Within this negotiation, the decision on reimbursement and price takes into account the aforementioned criteria and also the existence of alternative products and the price at which the same or equivalent products are marketed in other EU Member States. At present, Spain looks at prices in all EU Member States, and it is very common for the Ministry of Health to press the company to offer them a price no higher than the lowest price found in Europe.

However, prices of medicines are subject to additional pressure and companies cannot expect that they will always be able to sell the product at such maximum ex-factory prices. In a hospital environment, for instance, companies are legally obliged to grant a discount at a general rate of 7.5%. A reduced rate of 4% applies for orphan drugs, and an increased rate of 15% for products that have been in the market for more than ten years and for which a generic or biosimilar version does not yet exist (unless this is due to product patent issues). In addition to this, companies may need to lower their prices at tenders, and in some market sectors such as those subject to generic competition, discounts are commonly offered to pharmacies at the maximum permitted rate of 10%.

4.2 Prescribing and Dispensing Regulation

Rules on prescription, reference pricing and substitution

The rules on how to write prescriptions, reference pricing and substitution are nowadays consolidated in Law 29/2006, as amended.

The system works around the concept of 'homogeneous groups'. Each of these comprises products having the same characteristics and which are basically interchangeable when dispatched. The Ministry of Health publishes a list of the groups with the actual prices for each product on a monthly basis, and companies whose product is priced above the lowest in the group have a period of two to three days to reduce their price and thus match the lowest price in the group.

The general rule is that doctors should write prescriptions by making reference to the International Non-proprietary Name (INN) of the active ingredient. However, they may prescribe using the trade mark for follow-on prescriptions in chronic treatments, provided that the price of the branded product is not higher than the lowest within the homogeneous group where the product is included, or provided that the product is subject to reference pricing. In all cases, pharmacists must dispense the product which has the lowest price within its homogeneous group, and if a branded product and a generic share the same lowest price, the pharmacist must dispense the generic version.

The homogeneous groups system mentioned above relies on the idea that products included in each group are substitutable when dispatched. The prices of other products, such as biological ones facing competition from biosimilars, could therefore not be tackled through this system. The same could happen with products that have no generic competition. In this situation, the rule is that any product for which a generic or a biosimilar exists, even if it is not substitutable, and products which have no generic competition and have been in the market for more than ten years, may be subject to reference pricing, which essentially means that their price

shall be lowered to the level of the lowest comparable product. Reference prices are to be revised annually.

Pharmaceutical Distribution, Promotion and Marketing

5.1 Legal Governance

Distribution

Distribution of medicines is governed mainly by Royal Decree 782/2013. This regulation provides that the main activity of wholesalers is to distribute medicines to pharmacies located in Spain, and that wholesalers must ensure a timely and continuous distribution service to pharmacies. However, the regulation does not include any provision forcing pharmaceutical companies to supply products to wholesalers on a general basis. This has been a critical issue in Spain in view of the level of parallel exports that have originated from Spain as a result of its low pricing policy. Instead, the Royal Decree allows the Spanish Medicines Agency to restrict exports in cases of shortage of supply that creates therapeutic gaps or that affects products for which no alternative is available.

The rules on distribution also provide that healthcare professionals who may need to acquire medicinal products for treating patients are to buy them from pharmacies, but these rules also allow for the possibility that the Spanish Medicines Agency may approve the direct supply of some products by companies or wholesalers.

Royal Decree 870/2013 deals with internet sales through websites to the general public of medicinal products for human use which are not subject to prescription. Such internet sales are permitted provided that the products are supplied by a pharmacy, with the intervention of a pharmacist, after that pharmacist has provided personalised advice to the purchaser, and in accordance with the rules applicable to the products to be sold. Under this Royal Decree, only approved websites may offer these products, and prior to using the internet as a sales channel the pharmacy must first communicate its intention to the regional authority. In order to ensure that the internet channel is properly used, the regulation obliges the pharmacist to make an individual assessment of each order to make sure that even these over-the-counter (OTC) drugs are used properly. However, no gifts, discounts or similar offers connected with the promotion or sale to the public of medicinal products through websites can be made, except for legally admitted discounts.

Promotion and advertising

Advertising of medicinal products in Spain is governed by a combination of legislation and codes of practice. The provisions contained in EU Directives regarding advertising of medicinal products have been implemented through Royal Decree 1416/1994. The Ministry of Health issued an instruction in 1995 (Circular 6/1995) reflecting the position of the authorities with regard to the interpretation of Royal Decree 1416/1994 on certain matters. Some regions which are competent to implement these rules have also issued guidelines. Certain provisions contained in Law 29/2006 on medicinal products and medical devices may also be relevant, especially with regard to sanctions for breach of the rules.

In addition to this set of rules, in 2002 Farmaindustria, the Spanish pharmaceutical industry association, published a Code of Conduct for the pharmaceutical industry which has been amended and updated several times. The last version of the Code came into force on 1 January 2014. The Code updates and consolidates into a single text the rules on the interaction of the pharmaceutical industry with healthcare organisations and patient organisations.

ANEFP, the industry association which is responsible for OTC medicines, has also approved its own Code of Conduct on the promotion of OTC medicinal products. In April 2011, the Ministry of Health published in April 2011 a guide on the advertising of OTC medicinal products (which includes a Code of Conduct on the promotion of medicinal products to the general public). In addition to medicinal product-specific rules, other general legislation may be relevant, such as the 1988 Law on Advertising and the 1991 Law on Unfair Competition (both of which were modified by Law 3/2013).

Failure to comply with the rules governing the advertising of medicines may result in administrative sanctions. The general rule is that a breach of the law on this matter may result in a fine being imposed. The amount will depend on various factors, includ-

ing negligence, whether it was intentional, whether there was fraud or connivance, whether there was a failure to comply with previous requests made by the authorities, the company's turnover, the number of persons affected, the harm caused, and the profits obtained from the infringement.

The responsibility for enforcing these rules lies with the regions. The authorities are rather strict in scrutinising advertising materials which companies notify to them and they may suspend an advertisement if it is considered to be in breach of the rules. Furthermore, if an advertisement is considered to constitute a risk to the health or security of consumers, the authorities may order the publication of the decision and a corrective statement where the advertisement was published.

Under the Code of Conduct of Farmaindustria, companies have agreed not to file complaints against each other directly before the courts or the health authorities without first raising the issue with the Code of Conduct Commission. The procedure at the Commission may conclude with a fine, the amount of which shall be determined according to a variety of factors. The damage that a breach of the rules may cause to the image of the industry is one of the criteria to which the Code of Conduct refers. The competent body to impose these sanctions is the Jury of Advertising, a specialised body within the Association for Self-regulation of Advertising. The resolutions of the Jury are made public through its website.

The issues which have been discussed most frequently under these procedures involve the distinction between advertising and information on products, the conformity of advertising materials to the contents of the SmPC, and the conditions under which comparative advertising is fair. It is important to stress that comparative advertising is acceptable if the products or characteristics compared are comparable, essential and relevant, and if the comparison is objective, scientifically proven and verifiable through sources immediately accessible to the competitor. The competitor's brand name or trade mark can be used as part of the comparison, provided that such use is proportionate and is not made with the objective of taking unlawful advantage of the reputation of such trade mark.

In another area in which various rulings have been adopted, referring to the limits on hospitality that may be offered to healthcare professionals, any disputes have been overcome.

A very important novelty since 2013 refers to transparency obligations. Effective from 1 January 2014, the Code of Conduct has implemented the rules contained in the EFPIA Code on disclosure of transfers of value from pharmaceutical companies to healthcare professionals and healthcare organisations and patient organisations. The new obligations are consistently similar to the rules contained in the EFPIA Code. Consequently, from 2015, companies will be obliged to document and disclose all transfers of value made during the previous year, such as any direct or indirect payment or grant, either cash or benefits in kind, and regardless of its purpose, made to recipients who are healthcare professionals or a healthcare organisation. The only payments excluded from this obligation are those associated with (i) commercial transactions with distributors, pharmacy offices, including certain transactions with healthcare organisations, (ii) activities relating to products or medicines that are not prescription-only medicines, and (iii) activities not detailed in Appendix I of the Code of Conduct, such as the provision of educational materials or materials of medical utility, samples, dinners or luncheons. Disclosure is to be made on an individual basis or in the aggregate under terms and conditions similar to those set out in the EFPIA Code.

Finally, it is important to emphasise that, since 2013, it is no longer necessary to obtain prior administrative approval for the advertising of OTC products. These products may now be promoted without the need for a prior authorisation. This is of course without prejudice, given the fact that any advertising is subject to review by the authorities and to sanctions if it does not comply with the rules.

Marketing research

Market research studies may be different from advertising and promotion, and the general rule is that involving healthcare professionals in them may be acceptable. However, according to the Code of Conduct, market research studies (including social and opinion research) must meet some specific requirements:

- The conduct of the study must not constitute an inducement to recommend, prescribe, purchase, supply, sell or administer a given product.
- Studies must be approved by the scientific service or by the compliance officer, and sales personnel cannot play any role in the conduct and implementation of the study.
- Written agreements must be signed with the professionals and/or the entities with which the studies will be carried out, specifying the nature of the services to be provided, the professionals' participation and payment conditions.
- The company cannot have access (before, during or after the study) to the identity of those health professionals who participate in the study, and cannot participate in their selection, other than by defining the type of healthcare professional who is eligible to participate.
- Payments to participating professionals must be based on market criteria and be proportionate to the time expended, the work carried out and the responsibilities assumed, and must be adequately documented. Payments cannot be made in kind.
- The results of the study must not be advertised or used in promotional material.

Competition Law

6.1 Infringing Activities and Agreements

Spanish competition law, which incorporates the same principles laid down by European legislation in this area, applies to pharmaceuticals in the same manner that it affects other industries. However, the characteristics of the pharmaceutical market, in particular the way the demand and supply for products are structured, has resulted in a special focus on certain areas.

Pricing and other commercial strategies in connection with parallel trade

As previously mentioned, Spanish pricing rules operate on the premise that only the maximum ex-factory and retail prices set by the government will apply to units of products which are financed by the public health system. As a result, this system allowed companies to invoice their products at a higher price and then offer discounts to pharmacies or wholesalers who were able to provide evidence that the item for which they claimed the discount was indeed financed by the public health system. In the past, the Spanish Association of Pharmaceutical Wholesalers and the Spanish Federation of Pharmacists considered that this legal framework could be contrary to EU rules on free movement and on free competition, but the Spanish Supreme Court dismissed these actions in two judgments issued on 21 June 2005 and 21 February 2006. At a European level, the system was the subject of a complaint filed by the European Association of Euro Pharmaceutical Companies with the EU Commission. This complaint did not result in any action by the Commission against the Government of Spain for breach of the EU Treaties.

In recent years, various companies have implemented systems under this principle, thus supplying products at a list price, and allowing chargebacks for items which in effect are financed by the public system. Some wholesalers and associations of pharmacies have initiated various legal actions against the implementation of such systems before the Spanish competition authorities. In three leading cases, dated 21 May 2009, 14 September 2009 and 17 February 2010, several of these claims were dismissed. Spanish competition authorities considered that the principle of free pricing (laid down in the Constitution) would be unjustifiably limited if the maximum authorised ex-factory price were applied to products that are not financed by the National Health System. The position of the competition authorities was, however, called into question by the judgment of the Spanish Audiencia Nacional of 5 December 2012, under which these pricing mechanisms were considered to fall under the concept of prohibited agreements which could nevertheless merit an individual exemption. Given that Spanish competition law does not provide for the grant of individual exemptions since the approval of Law 15/2007, the issue has become moot because companies may keep the system without the need of any individual decision by the competition authorities.

The aforementioned rulings adopted by the competition authorities also established that the mechanisms laid down by the manufacturers to obtain data from wholesalers in order to verify which items were eligible for the discount were also legal because the manufacturer received only codified data, precluding identification of the clients of wholesalers. The position of the competition authorities on this issue has been confirmed by a recent judgment

of the Spanish Audiencia Nacional dated 19 March 2014, under which the court has confirmed that the Spanish Data Protection Agency acted correctly by not initiating a case against a company operating under such a system.

6.2 Pay-for-Delay Agreements

Generic competition

We are not aware of Spanish cases dealing with pay-for-delay agreements nor of any cases addressing life-cycle strategies of originators versus generic drug companies in a thorough manner. In a recent ruling by the Spanish competition authorities, dated 13 February 2014, the behaviour of Pfizer in connection with patent protection for latanoprost was examined in the light of the case that had been initiated in Italy. The Spanish competition authorities did not initiate any procedures against Pfizer. This ruling indicates that Pfizer did not oppose generic competition even while discussions were taking place at European level regarding the validity of its patent rights.

Spanish competition authorities have also investigated commercial practices by various generic companies who were accused of granting illegal discounts to pharmacies, thereby blocking the entry into the market of smaller companies who were not able to offer such discounts. The complaint in this case is in connection with Article 3 of Law 29/2006, under which discounts exceeding 10% are not allowed because they are deemed to be an illegal inducement for the pharmacist to dispense a particular product. The prohibition is based on the principle that decisions on dispensation should not be based on economic grounds. The case was dismissed at a ruling adopted on 23 January 2014, where the Spanish competition authorities stated that the claimant had not been able to provide evidence of any illegal behaviour by the defendant companies.

Product Liability

7.1 Regime for Pharmaceuticals

The general regime on liability for defective products or services is established in Royal Legislative Decree (RLD) 1/2007, of 16 November, approving the consolidated text of the General Law on the Protection of Consumers and Users and other complementary regulations. Such regime is found in Articles 128 to 146 of RLD 1/2007.

Article 136 of RLD 1/2007 defines which types of products are subject to the regime on product liability, namely any movable asset, even when this is combined or incorporated into another movable or immovable asset, as well as gas and electricity. The concept of 'any movable asset' is very broad and comprises practically all consumer goods.

The regime for product liability established in RLD 1/2007 is of a strict nature and does not provide for any scheme of compensation for particular products.

7.2 Liability

General prerequisites for a potential liability for pharmaceuticals

As detailed in the EU Directive, product liability may appear when a product does not provide the safety which a person is entitled to expect, taking all circumstances into account, including its presentation, its prospective use, and the time when the product was put into circulation.

In accordance with Spanish doctrine and case law, there are three groups of defects that products may suffer from: (i) manufacturing defects; (ii) design defects; and (iii) information defects.

The absence of the necessary warnings or instructions for use, or the inappropriateness of such information, may give rise to an information defect. As a consequence, when the information that accompanies a product is inappropriate or insufficient, that product may be considered to be defective and may give rise to liability in the event that the product causes harm.

In principle, the information and the warnings that are to be taken into account in order to determine whether a product suffers from an information defect is the information provided directly to the user of the product.

However, for certain types of product for which the intervention of an intermediary is required, the courts may take into consideration the information provided to the intermediary, in order to determine whether the information provided to the consumer

is sufficient and appropriate. Specifically, in the case of medicinal products, Law 41/2002, of 14 November, governing patient autonomy and rights and obligations with regard to clinical information and documentation, establishes that it is the doctor's duty to guarantee that the patient has the necessary information to decide freely on the therapeutic strategy prescribed by the doctor. As a consequence, the information provided by the manufacturer to the doctor may be taken into consideration in order to assess the set of information provided to the patient.

The responsibility for the defect is borne by the manufacturer or by the importer that introduces the product into the EU.

In the event that the manufacturer cannot be identified, the supplier of the product (the distributor or the 'retail' supplier) is to be considered as such, unless they inform the injured party of the identity of the manufacturer or of the person who supplied the product to them, within a period of three months. This same rule applies in the case of imported products, if the product does not indicate the name of the importer, even if the name of the manufacturer is shown.

However, the supplier of the defective product will be liable to the injured party as if they were the manufacturer, if they supplied the product knowing that the defect existed. In such a case, the supplier may enforce their right of recovery against the manufacturer.

7.3 Standard of Proof

The burden of proving the defect, the harm and the causal link rests on the injured party. In order to establish the causal link, the claimant must provide solid and substantial evidence that supports causation, and the harm caused must be the result of the defect.

In some cases, Spanish courts have accepted that the causal relation is proven by means of presumptions or circumstantial evidence, but the principle of generic causation, ie that in order to prove the causal link it would be sufficient to demonstrate that a product is capable of causing the alleged injury, is not applied. The Spanish courts have established that the mere fact that a product is capable of causing damage is not sufficient to establish the defective nature of such a product.

In the event that it cannot be established which of several manufacturers is responsible for the defective product, all of the manufacturers shall be jointly and severally liable to the injured parties. The manufacturer that compensated the injured party shall have the right to claim recovery from the other manufacturers, depending on their involvement in causing the harm or damage.

7.4 Specific Defences

The only defence that the manufacturer or importer of a medicine may raise in order to avoid liability are the general ones:

- That they did not put the product into circulation.
- That, given the circumstances of the case, it may be presumed that the defect did not exist when the product was put into circulation.
- That the product had not been manufactured for sale or for any other form of distribution with an economic purpose, nor that was it manufactured, imported, supplied or distributed within the context of a professional or entrepreneurial activity.
- That the defect is due to the fact that the product was developed in accordance with existing mandatory rules. This does not mean, however, that liability is excluded under a 'regulatory compliance defence'. Liability cannot be excluded by proving that all regulatory requirements have been complied with.
- The so-called 'development risks defence' cannot be raised for medicinal products. Therefore, a manufacturer cannot escape liability by arguing that the state of scientific and technical knowledge existing at the time the product was put into circulation did not allow for the discovery of the existence of the defect.
- On the other hand, claims under RDL 1/2007 are barred by limitation if filed later than three years, starting from the date the damages were incurred by the injured party, provided that, at the time, the identity of the party liable for the damages was known to the injured party.

7.5 Damages

Remedies

Under RDL 1/2007, a party who has suffered damage caused by a defective product may claim mon-

etary compensation for physical and moral damage. Under Spanish law, the concept of punitive damages does not exist. However, the courts have some discretionary powers in awarding compensatory damages and the conduct of the defendant may be expected to have some impact on the amount of damages awarded.

The overall civil liability of one manufacturer for damages caused by identical products with the same defect is limited to the maximum amount of EUR63,106,270.96.

7.6 Trial Structure

In the case of court proceedings, the case is to be resolved by a judge and not by a jury, relying on the materials and evidence presented by the parties, including expert reports. Class actions are possible under the Code of Civil Procedure but they are not common in Spain.

Cases are heard by civil courts and the process may normally last between 12 and 18 months in the first instance; mediation and arbitration are possible as alternative dispute resolution mechanisms.

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