PANORAMIC

# PHARMA & MEDICAL DEVICE REGULATION

Spain

LEXOLOGY

# Pharma & Medical Device Regulation

Contributing Editor

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## Spain


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## REGULATORY FRAMEWORK

### Competent authorities for authorisation

Identify the competent authorities for approval of the marketing of medicinal products and medical devices. What rules apply to deciding whether a product falls into either category or other regulated categories?

The Spanish Agency of Medicines and Medical Devices (AEMPS) is responsible for, among other things, granting marketing authorisations for medicinal products in Spain through national, mutual recognition and decentralised procedures. Additionally, AEMPS is the only notified body in Spain designated by the Ministry of Health for the conformity assessment of medical devices.

**Law stated - 8 octubre 2024**

### Approval framework

Describe the general legislative and regulatory framework for approval of marketing of medicinal products and medical devices.

The current regulatory framework regarding the authorisation of medicinal products includes:

- Royal Legislative Decree 1/2015, approving the revised text of the law on guarantees and the rational use of medicinal products and medical devices (the Law on Medicinal Products); and
- Royal Decree 1345/2007 on the authorisation of industrially manufactured medicinal products (the Decree on the Authorisation of Medicinal Products).

The current regulatory framework regarding conformity of medical devices includes:

- The Law on Medicinal Products.
- Royal Decree 192/2023 on medical devices (the Decree on Medical Devices). The former Royal Decree 1591/2009 on medical devices was partially repealed, except for provisions governing advertising and promotion (articles 39 to 41).
- Royal Decree 1616/2009 on active implantable medical devices (the Decree on Active Implantable Medical Devices).
- Royal Decree 1662/2000 on in vitro diagnostic medical devices (the In Vitro Diagnostic Medical Devices).

A medicinal product can only be placed on the Spanish market upon a marketing authorisation being granted through:

- the AEMPS national procedure, the mutual-recognition procedure or decentralised procedure; or
- the European Medicines Agency the centralised procedure.

The labelling and packaging of medicinal products, including the leaflet and the summary of product characteristics, are regulated by the Decree on the Authorisation of Medicinal Products.

Medical devices are not subject to prior marketing authorisation but to a CE mark granted by a notified body. When placed on the Spanish market, all medical devices (Classes I, IIa, IIb, and III) must bear a CE mark or a declaration of conformity.

The commercialisation of medical devices is subject to notification to the AEMPS, with the exception of custom-made medical devices, which only require that the manufacturer be established in Spain and that the placement of these devices in the Spanish market be registered in the registry of responsible persons for placing custom-made devices on the market.

The labelling, packaging and instructions for the use of medical devices in Spain are regulated by Regulation (EU) 2017/745 on medical devices and the Decree on Medical Devices.

**Law stated - 8 octubre 2024**

## CLINICAL PRACTICE

### Applicable rules

What legislation controls and which rules apply to ethics committee approval and performance of clinical trials in your territory for medicinal products and medical devices?

Clinical trials with medicinal products and medical devices in Spain are mainly regulated by:

- the Law on Medicinal Products;
- the Decree on Medical Devices;
- the Decree on Active Implantable Medical Devices;
- the Decree on In Vitro Diagnostic Medical Devices; and
- Royal Decree 1090/2015 on clinical trials with medicinal products.

Moreover, the Spanish Agency of Medicines and Medical Devices (AEMPS) has issued the Document of Instructions for the conduct of clinical trials in Spain and instructions for the conduct of clinical investigations with medical devices in Spain.

**Law stated - 8 octubre 2024**

### Reporting requirements

What requirements exist for reporting the commencement of a trial and its results to the competent authorities or the public?

To start a clinical trial in Spain, it is necessary to have:

- a favourable opinion from a Spanish ethics committee;
- an authorisation from the AEMPS; and
- a written agreement between the sponsor and the sites where the clinical trials are conducted.

The authorisations must be obtained by the sponsor or the legal entity to which the sponsor has delegated this task. Details of the regulatory approval pathway for clinical trials with medicinal products are set out in the memorandum detailing the procedure for authorising clinical trials in Spain, issued by the AEMPS and the relevant ethics committees. For medical devices, details are set out in European Regulations 2017/745 and 746, on medical devices and in vitro diagnostic medical devices, respectively. The start date of a trial must be notified to the AEMPS and the relevant ethics committee.

One year after the global end date of the trial, the sponsor must submit a report with a summary of the trial or clinical investigation results to the AEMPS and the ethics committee. The sponsor must also publish the trial results, whether positive or negative, preferably in scientific journals, before disclosure to the general public.

Regarding clinical trials with medicinal products, a summary of the results must be published in the Spanish Clinical Studies Registry, which is a free and publicly accessible database managed by the AEMPS. The use or disclosure of participants' data must comply with confidentiality and data privacy regulations. Information identifying trial subjects must not be included.

**Law stated - 8 octubre 2024**

## Consent and insurance

### Are there mandatory rules for obtaining trial subjects' consent to participate? Must sponsors arrange personal injury insurance to a particular limit?

Trial subjects must freely give their written consent before being included in a clinical trial (informed consent) and after the relevant information on all aspects of the trial for the subject to participate has been disclosed. The consent of minors or incapacitated persons must be given by their legal representatives.

The principal investigator is usually in charge of obtaining consent from trial subjects. The ethics committee must approve the process for obtaining consent from trial subjects and the patient information sheet or informed consent form. The AEMPS has issued guidance on the correct preparation of a model patient information sheet and informed consent form.

The sponsor must hold civil liability insurance that covers the sponsor, the principal investigator, the principal investigator's team and the site against any claim brought by trial subjects for damages suffered owing to the trial. The minimum insured amount is €250,000 per trial subject. The maximum insured capital per trial per year is €2.5 million. The AEMPS has issued a template of the insurance certificate to be provided by the sponsor.

**Law stated - 8 octubre 2024**

## MARKETING AUTHORISATION

### Time frame

How long does it take, in general, to obtain an authorisation from application to grant, what fees are payable and what is the normal period of validity of the authorisation?

The answers to this question are restricted to Spanish proceedings for obtaining marketing authorisation. For the proceedings set forth by EU regulations (centralised, decentralised and mutual recognition), please consult the chapter on the European Union.

Medicinal products

Regarding medicinal products, the maximum period for notification of the decision of the medicinal product authorisation procedure is 210 calendar days, starting from the day after the submission of a complete and valid application. This period might easily be longer in cases where the first application does not meet all the requirements. A marketing authorisation has an initial period of five years. Renewals are granted for an indefinite term unless pharmacovigilance reasons justify it being subject to further renewal approvals.

The fees charged by the Spanish Agency of Medicines and Medical Devices (AEMPS) are listed on its website. General marketing authorisations of a complete dossier (other than generics, medicinal gases, traditional herbal medicinal products or homoeopathic medicines) are subject to a fee of €17,073.

Medical devices

Medical devices are not subject to marketing authorisation for commercialisation but to a CE marking and notification for commercialisation to the AEMPS (or a declaration of conformity and registration in the registry of responsible persons for Class I medical devices). The term for obtaining the CE marking depends on the workload of the notified body.

The fees charged by the AEMPS are listed on its website. Notifications for commercialisation are subject to a fee of €99.71 per product. Fees for the evaluation of devices for CE marking certification issuance are not public.

**Law stated - 8 octubre 2024**

### Marketing exclusivity

What protections or exclusivities apply to the marketing period of an approved medicinal product or variation?

There is a marketing exclusivity period of 10 years from the date of the marketing authorisation being granted. This 10-year period can be extended to a maximum of 11 years if, during the first eight years of the 10-year period, the originator obtains authorisation for one or more new therapeutic indications and, during the scientific evaluation prior to its authorisation, it is established that these indications will bring a significant clinical benefit.

**Law stated - 8 octubre 2024**

## Protecting research data

What protections or exclusivities apply to the data submitted by originators to gain initial approval and, on variation or new application, to add indications or pharmaceutical forms?

The data submitted by originators are protected by a data protection period of eight years from the date of the marketing authorisation being granted.

Regarding substances of well-established medical use, new indications based on significant clinical trials or preclinical studies will bring a non-cumulative period of data exclusivity of one extra year. Additionally, in the event that the authorisation of a prescription-only medicinal product has been changed to a non-prescription or vice versa on the basis of clinical or preclinical studies, a period of an extra year of data exclusivity shall be granted.

**Law stated - 8 octubre 2024**

## Freedom of information

To what extent and when can third parties make freedom of information applications for copies of research data submitted by applicants for authorisation to market medicinal products or medical devices?

The Royal Legislative Decree 1/2015 (Law on Medicinal Products) sets out that the marketing authorisation decision must be published by the AEMPS, together with the summary of product characteristics, the leaflet and an assessment report drawn up by the AEMPS, after the deletion of any information of a commercially confidential nature.

**Law stated - 8 octubre 2024**

## Regulation of specific medicinal products

What are the specific requirements and processes for marketing approval of the major categories of regulated products?

Medicinal products

A medicinal product can be placed on the Spanish market if it previously holds a marketing authorisation obtained through one of the following:

- the national procedure, mutual recognition procedure or decentralised procedure at the AEMPS; or
- the centralised procedure at the European Medicines Agency.

The AEMPS is the authority in charge of granting marketing authorisations in Spain, whether they result from a national procedure or a mutual recognition or decentralised procedure. Marketing authorisations granted by the AEMPS are regulated by the Decree on the

Authorisation of Medicinal Products. Some provisions of the Decree on the Authorisation of Medicinal Products also affect medicines authorised by the European Commission pursuant to the centralised procedure.

The AEMPS shall authorise a specific product if such a product:

- fulfils the established quality requirements;
- is safe under normal conditions of use;
- is effective in the therapeutic indications;
- is correctly identified; and
- provides the patient with the necessary information.

The positive therapeutic effects of the medicinal product shall be assessed in relation to any risk for the patient's health or public health, viewed under a risk-benefit perspective.

The key stages of the authorisation procedure are the following:

- submission of the application to the AEMPS;
- validation and acceptance of the submission;
- issuance of the evaluation report; and
- resolution of the application and granting, where appropriate, of the marketing authorisation of the product.

The maximum period to notify the applicant of the resolution of the authorisation procedure is 210 calendar days.

The following medicinal products are subject to specific regulations:

- For blood-derived medicinal products and vaccines, each batch of the finished product is subject to prior authorisation or certification, which implies the review of the production and control protocols and, if necessary, the performance of the analytical tests.
- For radiopharmaceutical medicinal products, marketing authorisation applications must include a full and detailed explanation of the internal radiation dosimetry. For radionuclide generators, a general description of the system must also be included, together with a detailed description of the components that may affect the composition or quality of the derived radionuclide, as well as the qualitative and quantitative characteristics of the eluate or sublimate. For radiopharmaceuticals requiring extemporaneous preparation, additional detailed instructions for extemporaneous preparation and quality control of this preparation should be included, together with maximum storage time, if applicable.
- Medicinal gases must comply with the technical quality characteristics required by the Spanish Pharmacopoeia, the European Pharmacopoeia or other pharmacopoeias to which the Ministry of Health recognises its equivalence, or otherwise subject to evaluation of their quality, safety and efficacy.
- For advanced therapy medicinal products, those that are industrially manufactured are subject to general legal requirements on the authorisation of medicinal products with particularities set out in Annex I, Part IV of the Decree on the Authorisation of

Medicinal Products, setting out specific technical requirements for the marketing authorisation application (chemical, pharmaceutical and biological information; non-clinical reports; and clinical studies). Those non-industrially manufactured are regulated by Royal Decree 477/2014 on the authorisation of non-industrially manufactured advanced therapy medicinal products, which sets out that their individual use and manufacture must be authorised on a case-by-case basis.

- Traditional herbal medicinal products must be registered in the register of traditional herbal medicinal products created by the AEMPS and are subject to a simplified procedure for authorisation, provided that, among other requirements, they have indications exclusively appropriate for traditional herbal medicines, which are not subject to be monitored by a healthcare professional or the period of traditional use has elapsed, consisting of a minimum period of 30 years, at least 15 of which have been used in the European Union.
- Homeopathic medicines approved with a specific therapeutic indication are subject to the ordinary procedure of authorisation. A simplified procedure is applicable for medicinal products with no indications approved, in which case the medicinal product must only have an oral or external route of administration, or the degree of dilution guarantees the innocuousness of the product.

Medical devices

Medical devices are divided into four classes (III, IIb, IIa and I), ranked mainly considering the level of invasiveness of the device, the part of the body it is in contact with and the duration of such contact. Except for custom-made devices, all medical devices must bear a CE marking of conformity when they are placed on the market in Spain. The CE marking provides evidence of conformity of the device with the requirements of the applicable laws. For Class I and custom-made devices, such conformity must generally be evaluated and declared under the exclusive responsibility of the manufacturer. For Class IIa, IIb and III devices, the declaration of conformity requires an evaluation of the device by a notified body (the AEMPS in Spain or any other notified body of another EU member state). Additionally, for Class IIa, IIb and III devices, the AEMPS must be informed the first time that a person places a medical device for distribution or use on the Spanish market.

Finally, the company responsible for placing on the market any food supplement must notify the Spanish authorities at the start of its commercialisation, submitting an example of the labelling of the product, prior to or simultaneously with the first placing on the market of the product. The companies responsible for the production, transformation, packaging, storage, distribution, import and commercialisation of food supplements must be registered with the General Registry of Food Companies and Food Products. All food supplements must meet the purity and composition requirements laid down in Royal Decree 1487/2009 on food supplements.

**Law stated - 8 octubre 2024**

## Rewards and incentives

## What rewards or incentives for approval are applicable to the major product categories, including orphan drugs, drugs for paediatric use, generic drugs and biosimilars?

The authorisation process for the marketing of generic versions of medicinal products is simpler than that for brand-name medicinal products because the applicant shall not be required to provide the results of preclinical and clinical trials if they can demonstrate that the medicinal product is a generic medicinal product of a reference medicinal product that is or has been authorised for not less than eight years in an EU member state.

The applicant may also replace the preclinical and clinical trial results with appropriate scientific literature if they can demonstrate that the active substances of the medicinal product have been in well-established medical use within the European Union for at least 10 years with recognised efficacy and an acceptable level of safety.

Finally, where the medicinal product possesses the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form as another medicinal product that has already been authorised, the applicant may rely on the preclinical and clinical documentation of the authorised medicinal product with the permission of the holder thereof.

In the case of biological medicinal products that are similar to a reference biological medicinal product but do not meet the conditions in the definition of generic medicinal products, the results of appropriate preclinical tests or clinical trials relating to these conditions must be provided.

As regards orphan medicinal products, there is a market exclusivity period conferred by Regulation (EC) 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, which is directly applicable in Spain. Pursuant to the provisions contained in article 8 of this regulation, when there is a marketing authorisation granted in Europe for an orphan drug, the authorities in Europe and in all EU member states must refrain during a 10-year period from accepting another marketing authorisation application or from granting another marketing authorisation when there is an existing marketing authorisation for a similar medicinal product that has the same therapeutic indication. Such a 10-year market exclusivity period may be shortened to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria laid down for granting the orphan designation in the first place and it is proven that such a product is sufficiently profitable not to justify the maintenance of market exclusivity. However, the market exclusivity period for orphan drugs will not apply and therefore another marketing authorisation may be granted for a similar medicinal product that has the same therapeutic indication if:

- the marketing authorisation holder (MAH) for the original orphan medicinal product has given their consent to the second applicant;
- the MAH for the original orphan medicinal product is unable to supply sufficient quantities of the medicinal product; or
- the second applicant can establish in the application that the second medicinal product, although similar to the orphan medicinal product already authorised, is safer, more effective or otherwise clinically superior.

Paediatric medicinal products are subject to specific incentives as set forth by Regulation (EC) 1901/2006 of the European Parliament and of the Council on medicinal products for paediatric use directly applicable in Spain. This regulation eases the authorisation process for paediatric products, contemplating the possibility of specific investigation plans for such products, waivers regarding the obligation to submit certain studies and information, and deferrals. For more information, please refer to the chapter on the European Union.

Additionally, medicinal product presentations indicated for paediatric treatments have a specific regime within the Spanish reference pricing system, which entails that such presentations shall not be included in reference groups with other medicinal products but form their own independent reference group, meaning that they will not be subject to the same price reductions and price competence.

**Law stated - 8 octubre 2024**

## Post-marketing surveillance of safety

### What pharmacovigilance or device vigilance obligations apply to the holder of a relevant authorisation once the product is placed on the market?

Medicinal products

Royal Decree 577/2013 on pharmacovigilance of medicinal products imposes, among other things, the following pharmacovigilance obligations on MAHs:

- respect the good practices on pharmacovigilance published by the AEMPS;
- have an adequate pharmacovigilance system;
- have a suitably qualified person responsible for pharmacovigilance in both the European Union and Spain;
- submit periodic safety reports to the European Medicines Agency;
- have a risk management system for each medicinal product;
- notify and record suspected adverse reactions;
- monitor scientific literature worldwide;
- carry out post-authorisation studies of efficacy and safety; and
- perform a continuous evaluation of the risk-benefit parameters of the medicinal product.

Medical devices

Post-market surveillance and vigilance activities and obligations are set out at the European level in Regulations 2017/745 and 746 on medical devices and in vitro diagnostic medical devices, respectively.

**Law stated - 8 octubre 2024**

## Other authorisations

What authorisations are required to manufacture, import, export or conduct wholesale distribution and storage of medicinal products and medical devices? What type of information needs to be provided to the authorities with an application, what are the fees, and what is the normal period of validity?

Medicinal products

Industrial manufacturing of medicinal products in Spain requires authorisation from the AEMPS (except for non-industrial compounded medicinal products in hospitals and community pharmacies). This authorisation is required for both total and partial manufacture, and also for the various processes of dividing up, packaging and presentation. Import of medicinal products and their associated tests, controls and analysis are also subject to the same authorisation regime.

The manufacturing and importing application to the AEMPS must include:

- a description of and a technical report on the relevant medicinal products, together with a description of the premises where the quality control of the medicinal products will be performed;
- evidence that the applicant has sufficient and adequate premises and technical and control equipment; and
- evidence that the applicant has a duly qualified technical director (qualified person) and sufficient and adequate personnel for the activity.

Manufacturing authorisations are granted for an indefinite period (except in the event of suspension or revocation) and the fees charged by the AEMPS, according to the current list price, amount to €9,418.

Companies operating with controlled medicinal products and drug precursors are subject to additional controls and regulations.

Distribution of medicinal products is subject to prior authorisation from the competent authorities of the autonomous region where the distributor is based. Exceptionally, for warehouses under customs supervision, authorisation is granted by the AEMPS. This authorisation is not required of entities authorised for the manufacturing of medicinal products that distribute their own products, as such distribution activities would be covered by the manufacturing authorisation.

Conditions to get authorisation for the distribution of medicinal products are laid down in Royal Decree 782/2013 on the distribution of medicinal products and include:

- the need to have a qualified person (or technical director), competent personnel, and suitable and sufficient premises, equipment and facilities to ensure adequate conservation and distribution of the products; and
- an adequate quality system and an emergency plan to ensure the effective implementation of any recalls ordered by the competent authorities.

These authorisations are granted for an indefinite period (except in the event of suspension or revocation) and the fees vary depending on the autonomous region in which the application is submitted.

Medical devices

Manufacturing, importing, refurnishing and sterilisation of medical devices are subject to prior authorisation from the AEMPS covering the premises where the activities are performed.

Any economic agent that markets medicinal products in Spanish territory, other than custom-made products, must be included in the Commercialization Registry of the AEMPS. Regarding custom-made medical devices, only manufacturers established in Spain and placing such devices in the Spanish market need to be included in the Commercialization Registry.

**Law stated - 8 octubre 2024**

## Sanctions

### What civil, administrative or criminal sanctions can authorities impose on entities or their directors and officers for breach of the requirements concerning controlled activities?

Apart from civil liability, which will depend on the case at hand, a breach of the requirements concerning controlled activities may lead to administrative sanctions or criminal liability.

Administrative sanctions are mainly set out in the Law on Medicinal Products and are divided into minor, serious and very serious infringements. These infringements are sanctioned with fines ranging from €6,000 to €30,000 for minor infringements, €30,001 to €90,000 for serious infringements, and €90,001 to €600,000 for very serious infringements.

Criminal penalties are set out in the Criminal Code and the specific criminal liability depends on the penalty. Distribution or manufacture of non-authorised medicinal products, drug dealing and the drafting of false documents regarding medicinal products or medical devices are considered crimes against public health, which are sanctioned with terms of imprisonment of between six months and four years, and occupational prohibition of up to 10 years.

These sanctions and penalties are usually imposed on the entities, except in the event of a breach of professional obligations imposed on a particular individual, or in the case of intentionality or gross negligence of an individual.

**Law stated - 8 octubre 2024**

## Exemptions

### What, if any, manufacture and supply of medicinal products is exempt from the requirement to obtain an approval to market?

Magistral formulas and official formulas, which are medicinal products prepared in a pharmacy in accordance with a medical prescription for an individual patient and in line with the prescriptions of a pharmacopoeia, are not subject to prior marketing or manufacturing authorisation.

**Law stated - 8 octubre 2024**

### Parallel trade

**Are imports allowed into your jurisdiction of finished products already authorised in another jurisdiction, without the importer having to provide the full particulars normally required to obtain an authorisation to market? What are the requirements?**

According to Royal Decree 1785/2000 on the intracommunity movement of medicinal products for human use, parallel imports are allowed in Spain, provided that:

- the medicinal product has marketing authorisation both in Spain and the country of origin;
- the product's labelling and leaflet comply with Spanish regulations;
- the product's importer is a licensed manufacturer if the parallel importer performs repackaging or relabelling activities in Spain;
- the product's parallel importer notifies the MAH of the activity; and
- the AEMPS authorises the parallel commercialisation of the relevant medicinal product in Spain.

AEMPS must analyse whether the parallel importer has appropriate human and material resources to guarantee, among other things, the quality of the product in connection with the conditioning, packaging and relabelling, and the correct conservation and distribution of the medicinal products.

**Law stated - 8 octubre 2024**

## AMENDING AUTHORISATIONS

### Variation

**What are the main requirements relating to variation of authorisations for medicinal products and medical devices?**

The main requirements for the different types of variations of marketing authorisations of medicinal products are regulated in the Decree on the Authorisation of Medicinal Products, which refers to Annex IV of Regulation (EC) 1234/2008 in respect of the elements to be submitted by the MAH for each type of variation (ie, Types IA, IB and II, and extensions).

Applications for variations must be submitted to the Spanish Agency of Medicines and Medical Devices (AEMPS). The AEMPS has 30 days to approve or deny Type IA and Type IB variations, and 60 days for Type II variations. The extension of a marketing authorisation is subject to the same procedure as the original marketing authorisation.

The variation of authorisations is not applicable to medical devices.

**Law stated - 8 octubre 2024**

## Renewal

### What are the main requirements relating to renewal of authorisations for medicinal products and medical devices?

The marketing authorisation of a medicinal product is valid for an initial period of five years, as provided for in the Decree on the Authorisation of Medicinal Products. At least nine months before the expiration of the initial period, the MAH may apply for an authorisation renewal. Together with the renewal application, the applicant must pay the relevant fees and provide a consolidated version of the registration dossier, including evaluation data contained in suspected adverse reactions reports and periodic safety update reports, as well as all the variations introduced since the marketing authorisation was granted.

Once renewed, the marketing authorisation will be valid for an unlimited period, unless the AEMPS requires an additional five-year renewal based on duly justified pharmacovigilance-related reasons.

CE marking certificates are valid for periods of five years and can be renewed for successive periods of the same duration at the request of the company six months before the expiry of the validity period.

**Law stated - 8 octubre 2024**

## Transfer

### How easy is it to transfer the existing approvals or rights to market medicines and medical devices? How long does this take in general?

Transfer of a marketing authorisation may be formalised through relatively easy and straightforward proceedings before the AEMPS. These proceedings are regulated in the Decree on the Authorisation of Medicinal Products. The AEMPS usually takes between one and three months to make a decision on a transfer request.

CE marking certificates do not confer rights (such as the right to commercialise under a marketing authorisation for medicinal products) and are transferable. Only the manufacturer of the medical device (or its authorised representative) can affix a CE marking to medical devices, therefore only the manufacturer (or its authorised representative) can be granted a CE marking certificate.

**Law stated - 8 octubre 2024**

# RECALL

## Defective and unsafe products

### What are the normal requirements for handling cases of defective or possibly unsafe products, including approvals required for recall and communication with health professionals?

The Royal Legislative Decree 1/2015 (Law on Medicinal Products) obliges distributors and marketing authorisation holders (MAHs) that directly commercialise their products to have an emergency plan in place in case the products placed on the market need to be recalled (either because it is ordered by competent authorities or decided by the relevant operators). This emergency plan must ensure that products are recalled in an orderly and rapid manner.

The competent authorities may order products to be recalled if there is an imminent and serious risk to health or if there is a reasonable suspicion of such a risk.

Manufacturers, MAHs and importers of products commercialised in Spain must immediately notify the AEMPS of any deficiency that could lead to the recall of the product and provide all possible information in connection with the affected batch. The AEMPS may agree on the recall and inform the competent authorities of the autonomous region about the recall. Both the AEMPS and the authorities of the autonomous region will jointly analyse the deficiency and quality problems of the products recalled.

Manufacturers are also requested to implement a complaints registration and complaints review system.

**Law stated - 8 octubre 2024**

## ADVERTISING AND PROMOTION

### Regulation
### Summarise the rules relating to advertising and promotion of medicinal products and medical devices, explaining when the provision of information will be treated as promotional. Do special rules apply to online advertising?

The advertising and promotion of medicinal products and medical devices are subject to the general rules on advertising in General Law 34/1988 on advertising and Law 3/1991 on unfair competition. Specific requirements on promotion of Medicinal Products are set out in Royal Decree 1416/1994. Advertising of medical devices is regulated under Royal Decree 1591/2009 and Royal Decree 1662/2000.

The Law on Medicinal Products sets forth the sanctions for breach of the rules on advertising medicinal products and medical devices.

Some autonomous regions have adopted guidelines reflecting the position of the regional authorities on this matter (the most notable of which are those issued in the regions of Madrid and Catalonia). The Ministry of Health has issued a guide on the advertising of over-the-counter medicinal products (last updated in 2019). There are also codes of conduct adopted on a voluntary basis by the pharmaceutical and medical devices industry, such as:

- FarmaIndustria's Code of Practice for the Pharmaceutical Industry;
- Spanish Association of Generic Medicines (AESEG)'s Code, which applies to generic medicinal products; and

- Spanish Association of the Self-Care Industry (ANEFP)'s Code, which applies to over-the-counter, cosmetic and self-care products; and
- Spanish Federation of Health Technology Companies (Fenin)'s Code, which applies to medical devices.

Regarding when the provision of information will be treated as promotional, this is something that must be assessed on a case-by-case basis, considering whether the relevant activity fits the legal definition thereof. Spanish authorities are rather strict when interpreting these definitions.

On the one hand, the advertising of medicinal products is defined as any form of informative offer, commercial research or inducement designed to promote the prescription, dispensation, sale or consumption of medicinal products. There are certain activities included in this definition, such as visits by medical sales representatives to persons qualified to prescribe or dispense medicinal products, supply of samples of medicinal products, sponsorship of promotional or scientific meetings and, in particular, payment of travel and accommodation expenses in connection therewith.

There are activities expressly excluded from this definition, such as:

- the labelling and the leaflet of the medicinal product;
- the correspondence, together with any non-promotional documents needed to respond to a specific question about a particular medicinal product;
- information and documents specifically related to changes in packaging and adverse reaction warnings in the framework of pharmacovigilance;
- sales catalogues and price lists; and
- information regarding human health or diseases, provided that there is no reference to the medicinal product.

The FarmaIndustria Code further provides certain activities that are not considered advertising of medicinal products (eg,texts written and produced by journalists in their professional remit, and literal translations of scientific articles and abstracts published in recognised scientific sources).

Online advertising of medicinal products and medical devices is subject to the same rules as those applicable to advertising through any other means.

**Law stated - 8 octubre 2024**

## Inducement

### What regulations exist to discourage the provision of inducements to healthcare professionals to prescribe, sell, supply or recommend use of a particular medicinal product or medical device?

Under the Law on Medicinal Products, it is expressly prohibited to offer any sort of improper inducement to healthcare professionals involved in the cycle of prescribing, dispensing and administering medicinal products and medical devices. Violation of this prohibition is considered a serious breach and is sanctioned with fines of up to €90,000.

Notwithstanding the above, it is permitted to provide certain gifts to healthcare professionals when the cost of the gift is insignificant, and the gift is relevant to the practice of medicine or pharmacy. The FarmaIndustria Code further provides that offering gifts to healthcare professionals is only allowed if the items have stationary or professional use, the items are not related to prescription-only medicinal products and their market price does not exceed €10, among further exceptions.

**Law stated - 8 octubre 2024**

## Reporting transfers of value

### What requirements apply to recording and publishing details of transfers of value to healthcare professionals and organisations by companies marketing medicinal products or medical devices?

According to the FarmaIndustria Code, companies are obliged to document and publish on their website (the first publication was made in 2016) all transfers of value made during the previous year – meaning any direct or indirect payment or grant, either cash or benefits in kind, and regardless of their purpose – whose recipients were healthcare professionals or organisations. The only payments excluded from this obligation are:

- activities associated with commercial transactions with distributors and retail pharmacies, as well as certain transactions with healthcare organisations;
- activities related to non-prescription medicinal products; and
- activities not detailed in Appendix I of the FarmaIndustria Code (provision of gifts, samples, dinners or luncheons).

Disclosures must be made on an individual basis, except for transfers of value related to research and development, with no need for the healthcare professional to consent to the disclosure of their personal data (but they must be informed by the company about such disclosure).

In addition, companies adhering to Fenin's code must also document, and publish on their website, all transfers of value made during the previous year to healthcare professionals and organisations, following the model in article 15 of the Code.

**Law stated - 8 octubre 2024**

## Enforcers

### Describe the bodies involved in monitoring and ensuring compliance with advertising controls for medicinal products and medical devices, distinguishing between any self-regulatory framework and control by the authorities.

The responsibility for enforcing the rules on advertising and inducements lies with the health authorities of the Spanish autonomous regions and courts. With regard to the enforcement of rules resulting from industry codes of conduct, the codes of FarmaIndustria, AESEG,

ANEFP and Fenin are enforced by self-regulatory bodies in agreement with AUTOCONTROL, an association for self-regulation in advertising.

**Law stated - 8 octubre 2024**

### Sanctions

What are the possible financial or other sanctions for breach of advertising and promotional controls for medicinal products or medical devices?

The Law on Medicinal Products regulates the sanctions for breach of the rules on the advertising of medicinal products and medical devices. Breaches are classified as minor, serious or very serious.

Promoting, or informing about, unauthorised medicinal products or without complying with applicable provisions on advertising are considered very serious breaches, which can be subject to fines of up to €1 million.

Advertising medical devices to the public when not allowed is considered a serious breach, which can be sanctioned with fines up to €90,000, except for the promotion of medical devices for genetic diagnosis, in which case the breach will be considered very serious and fined up to €1 million. Other sanctions may be applied, such as publication of the infringement in the Official Gazette or cessation of the infringing activity.

**Law stated - 8 octubre 2024**

## OFF-LABEL USE AND UNLICENSED PRODUCTS

### Off-label use

May health professionals prescribe or use products for 'off-label' indications? May pharmaceutical companies draw health professionals' attention to potential off-label uses?

Off-label use of medicinal products is permitted in Spain under the Law on Medicinal Products and Royal Decree 1015/2009 on the availability of medicinal products in special situations (the Decree on Medicinal Products in Special Situations). However, this is limited to cases in which there are no authorised therapeutic alternatives for a given patient. Healthcare professionals must adequately justify the need for the off-label use of the medicinal product in the medical record and must also inform the patient of the possible benefits and the potential risks, obtaining the patient's informed consent.

Contrary to the compassionate use of medicinal products, off-label use does not require notification to or authorisation by the Spanish Agency of Medicines and Medical Devices (AEMPS).

Regarding medical devices, off-label use is also permitted in Spain under Circular 7/2004 on clinical investigations with medical devices (the Circular on Clinical Investigations). This requires a clinical report justifying the need for such treatment, the patient's informed

consent and express agreement of the medical site. In this case, authorisation from the AEMPS is needed.

The promotion of off-label uses is strictly prohibited under Spanish regulations. Therefore, information from companies to healthcare professionals on the off-label alternatives of their portfolio might easily be regarded as a promotion.

**Law stated - 8 octubre 2024**

## Unlicensed products

### What rules apply to the manufacture and importation and supply to healthcare providers of unlicensed medicines or medical devices?

The manufacturing and importation of investigational medicinal products are regulated by the Decree on Medicinal Products in Special Situations and Royal Decree 824/2010 on the regulation of pharmaceutical companies and manufacturers of active ingredients. These activities require a prior authorisation granted by the AEMPS – the same as in the case of the manufacture and import of approved medicinal products.

Manufacture and import of investigational medical devices (devices without a CE mark) are regulated by the Circular on Clinical Investigations, according to which these activities require the specific prior authorisation of the AEMPS. This authorisation will be in force during the period of the investigation of the medical device. These activities will also be subject to a prior licence from the AEMPS for the operation of facilities under the Decree on Medicinal Products in Special Circumstances – the same as in the case of medical devices with a CE mark.

**Law stated - 8 octubre 2024**

## Compassionate use

### What rules apply to the establishment of compassionate use programmes for unlicensed products?

Compassionate use of medicinal products is regulated by the Law on Medicinal Products and the Decree on Medicinal Products in Special Situations, and it is only permitted for patients or groups of patients with chronic or severe conditions in cases where there are no available therapeutic alternatives authorised in Spain. The patient's informed consent and authorisation from the AEMPS are required to implement a compassionate use programme.

The authorisation request for the compassionate use programme must be filed before the AEMPS by the medical site where the patient is to be treated and must include a medical record justifying the need for the programme.

**Law stated - 8 octubre 2024**

# SALE AND SUPPLY

## Regulation

### Are there special rules governing the dispensing or sale of particular types of medicinal products or medical devices?

General rules on the sale and dispensing of medicinal products and medical devices are set out in the Law on Medicinal Products. This Law provides specific rules depending on the type of product. For example, the dispensation of narcotic medicinal products requires a specific prescription note, and its dispensation must be notified annually to the AEMPS for control purposes. Other medicinal products, such as medicinal gasses, can only be supplied to medical premises or hospitals.

**Law stated - 8 octubre 2024**

## Online supply

### What laws and guidelines govern online dispensing, sale and supply of medicinal products and medical devices?

The online sale of medicinal products is governed by Royal Decree 870/2013 on the distance selling of medicinal products for human use not subject to medical prescription to the public through websites. Further, Aragonese and Catalan authorities issued specific guidelines governing the online sale of medicinal products in December 2018 and October 2021, respectively. The AEMPS has also provided a Q&A document on the online sale of medicinal products. The online sale of medicinal products subject to medical prescription is prohibited under the Law on Medicinal Products. Due to the emergence of several business ideas involving online or telematic sales, dispensation and/or shipment of medicinal products, including those subject to medical prescription, there has been a lot of discussion, at the judicial level, on what is considered to be an 'online sale'. Spain is a conservative country in this regard and most of these businesses have not succeeded due to this prohibition.

Regarding medical devices, the Decree on Medical Devices sets out the prohibition of online sale of medical devices subject to medical prescription.

**Law stated - 8 octubre 2024**

## Pricing and reimbursement

### What are the controls imposed on pricing of medicines and medical devices and reimbursement by national social security systems that are applicable to manufacturers, distributors and pharmacists?

With regard to setting the price of reimbursed medicinal products (including both hospital use and retail products), it is important to distinguish between theory and practice.

In theory, Spain follows a cost-plus system, under which the maximum ex-factory price should be the cost of the product plus a given profit margin. This is what Royal Decree 271/1990 on the reorganisation of price intervention for medicinal products for human use contemplates in accordance with the provisions of Council Directive 89/105/EEC.

The cost of the product is to be determined through the analytical application of the complete cost, including research and development, manufacturing costs and allocations

corresponding to commercial and administration costs. With regard to the profit component, the rule is that the target profit of each company shall be within a range of 12 per cent to 18 per cent of the capital allocated to exploitation, including own resources (share capital, update and revaluation accounts, reserves, etc) and external resources with financial costs.

As a matter of practice, it has always been known that the price-approval process entails negotiation with the authorities where the cost and the profit margin are not the variables that are considered. Companies should be prepared for prices to be determined by the following two points:

- comparative pharmacoeconomic evaluation of the medicine in which the advantages of the new product should be quantified; and
- the price of the product in other EU member states.

Health technology assessments also play an important role in the reimbursement and pricing process. Since 2013, the health technology assessment has been made through the therapeutic position reports (TPRs). TPRs were coordinated and prepared by a network called REvalMED, which comprised therapeutic evaluation groups (led by the AEMPS), economic evaluation groups (led by the Ministry of Health) and therapeutic area specialists.

TPRs included an analysis of how the new product or new indication compares with the existing alternatives from both a therapeutic and economic standpoint. This is expected to change in the near future because, in June 2023, the National High Court declared the plan that created REvalMED null and void. This judgment expressly stated that under the current laws on medicinal products, TPRs could not contain an economic assessment. As a result, of this judgment, the Spanish government is working on a new Royal Decree on Health technology assessment. The draft of this Royal Decree was published in August 2024 and it is expected to be in force by the end of 2024.

Spanish regulations do not set special rules for generics or biosimilar medicinal products. As a matter of practice, generics and biosimilars are at least expected to offer a 30 per cent cut on the price authorised for the reference product.

Finally, in July 2022, the Ministry of Health opened a public consultation on the first draft of the law that will amend the current Law on Medicinal Products. The new law (which still has a long legislative proceeding ahead) may introduce important modifications to the current rules governing the pricing and reimbursement of medicinal products.

**Law stated - 8 octubre 2024**

## UPDATE AND TRENDS

### Forthcoming legislation and regulation

**Is there any current or foreseeable draft legislation or other rules that will affect the regulation of pharmaceuticals and medical devices? What is likely to change, and what steps need to be taken in preparation?**

According to Law 50/1997 on the government, the government must annually approve a regulatory plan containing the legislative or regulatory initiatives to be submitted for approval during the following year.

The Regulatory Plan for 2024 foresees the following legislative initiatives.

Law amending the Law on Medicinal Products

According to the Regulatory Plan, an amendment of the Law on Medicinal Products is foreseen for 2024 with the aim of clarifying certain aspects that are considered necessary given the experience accumulated during its validity. The purposes of this amendment include:

- improving the co-payment pharmaceutical system for a better redistribution of its economic burden;
- improving the reference price system to incorporate elements that increase competition and value incremental benefits of medicinal products;
- amending the system for calculating the four-monthly contribution to the Spanish National Health Service (NHS) by manufacturers, importers and marketers of funded medicinal products;
- clarifying competencies in the control of advertising of medicinal products;
- incorporating the definitions and modifications arising out of EU regulations for medical devices;
- updating the regime for advertising medical devices, including a new regime on guarantees of use and commercialisation; and
- modifying and updating the sanctioning procedure and breaches.

The public consultation for this amendment was issued in July 2022.

Health technology assessment

According to the Regulatory Plan, the aim of this Royal Decree is to regulate an independent, transparent and participatory system for the evaluation of health technologies through an evidence-based scientific process to determine the relative efficacy and effectiveness of existing or new health technologies in comparison with others.

Advertising

Currently, new regulations on the promotion of medicinal products and medical devices, which would repeal Royal Decree 1416/1994 and Decree 1591/2009 provisions, are progressing through the legislative process. At the moment, it is difficult to estimate when these new regulations will be passed.

Additionally, so far in 2024, the Ministry of Health has begun public consultations regarding the Royal Decree regulating the procedure for the selective financing of reimbursed medical devices for non-hospitalised patients. This new Royal Decree aims to replace the 1994 one. The objective of this Royal Decree is to develop the procedure for reimbursement and to set the prices of medical devices for non-hospitalised patients, as well as their selection, acquisition, supply and dispensing regime. It also intends to regulate the procedure for the modification or, where appropriate, exclusion from the reimbursement of the NHS.

Finally, this Royal Decree will determine the margins corresponding to the distribution and dispensing of these products within the NHS.

**Law stated - 8 octubre 2024**