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Medicinal product regulation and product liability in Portugal: overview

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REGULATORY OVERVIEW

1. What are the main legislation and regulatory authorities for pharmaceuticals in your jurisdiction?

Legislation

The regulatory framework for the authorisation, pricing and reimbursement of medicines, biological and medical devices in Portugal is based on the application at a national level of EU legislation, including:

- Directive 2001/83, on the Community Code relating to medicinal products for human use (Code for Human Medicines Directive).
- Regulation 726/2004, laying down procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency (EMA Regulation).
- Directive 93/42/EEC concerning medical devices.

The relevant legal framework at the national level is contained in the following legislation:

- Statute of the National Health Service (Decree-Law 11/93, 15 January 1993).
- Human Medicines Act (Decree-Law 176/2006, 30 August 2006) (Medicines Act).
- Medical Devices Act (Decree-Law 145/2009, 17 June 2009).
- Medicines and Medical Devices Price and Reimbursement/Funding Act (Decree-Law 97/2015 of 1 June 2015 and Ministry of Health Orders no. 195-A/2015 of 30 June 2015 and no. 195-C/2015 of 30 June 2015).
- Clinical Trials Act (Law 21/2014, 16 April 2014).
- Industrial Property Act (Decree-Law 110/2018, 10 December 2018).

Regulatory authority

The national medicine regulatory authority (INFARMED) (*www.infarmed.pt*) is the authority responsible for the monitoring, supervision and enforcement of the Medicines Act and the Medical Devices Act and related legislation and rulings. It also approves prices and reimbursement of medicines and of medical devices. Members of the respective Board of Directors are appointed for a three-year term by the government.

2. Briefly outline any additional or alternative regulation of large molecule (biological) medicines, and discuss how combination products and gene therapies are classified and regulated in your jurisdiction.

Medicinal products developed using one of the following biotechnological processes are subject to centralised approval by the European Medicines Agency under its centralised procedure:

- Recombinant DNA technology.
- Controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells.
- Hybridoma and monoclonal antibody methods.

In respect of combination products where a medical device is designed to administer a medicinal product:

- The placing on the market of the medical device is generally governed by the Medical Devices Act.
- The placing on the market of the medicinal product is governed by the Medicines Act.

If the medical device is placed on the market in such a way that the device and the medicinal product form a single integral unit that is intended exclusively for use in the given combination and is not reusable, that single-unit product is governed by the Medicines Act.

3. Briefly outline how medical devices and diagnostics are regulated in your jurisdiction. Is there any specific regulation of medical software, health care IT, e-health (such as mobile health apps), or laboratory diagnostic testing kits?

Medical devices and diagnostics (medical devices) are governed by the Medical Devices Act (Decree-Law 145/2009, 17 June 2009).

INFARMED is the national competent authority for medical devices, including:

- Active medical devices.
- Custom-made devices.
- Implantable medical devices.
- Implantable active medical devices.
- *In vitro* diagnostic medical devices.
- Devices intended for clinical investigation.

Medical devices are divided into four different risk classes:

- Class I, low risk.
- Class IIa, medium risk.
- Class IIb, medium risk.
- Class III, high risk.

Each medical device risk class is calculated taking into account the following factors:

- Length of time in contact with the human body (momentary, short-term and long-term).
- Degree of invasion of the human body (invasive, non-invasive).
- Part of the body affected by its use (for example, hands, heart, and lower limbs).
- Potential risks stemming from technical design or manufacture.

Medical devices must have the CE marking, which is a prerequisite for medical devices to be placed on the market.

There is no specific regulation of health IT issues and mobile medical applications, although IT is extensively used in the health sector. For example, electronic prescription of medicines is, as a rule, mandatory for doctors, and INFARMED has a mobile medicine price comparator application, which can be accessed by end users.

PRICING, GOVERNMENT FUNDING AND REIMBURSEMENT

4. What is the structure of the national health care system, and how is it funded? Explain briefly how medicines are introduced into that system.

The public national healthcare system (NHS) comprises all the public services and units that provide healthcare services, including:

- Groups of health centres.
- Hospitals, irrespective of their legal designation.
- Local health units.

The Portuguese Autonomous Regions of Madeira and Azores have a specific Regional Health Service, which is locally supervised and monitored by specific regional entities.

The Statute of the NHS is contained in Decree-Law 11/93, 15 January 1993. The Ministry of Health is responsible for planning, funding, directing, supervising, evaluating and auditing NHS activities.

The NHS is funded through the state annual budget and by moderating fees paid by users. The NHS also includes a centralised procurement system for hospitals addressed to the purchase of medical products, through the Central Purchasing Authority (*Serviços Partilhados do Ministério da Saúde*) (SPMS) (*see* http://spms.min-saude.pt). The procurement for the purchase of medical products in the Portuguese Autonomous Regions is centralised by local designated entities.

The NHS also has arrangements with private providers for the delivery of designated diagnostic and therapeutic services.

5. How are the prices of medicinal products regulated?

Decree Law no. 97/2015 of 1 June 2015 sets out specific price regimes for the different types of medicines, distinguishing the outpatient market from the hospital market (NHS hospitals), as follows.

Outpatient market

The price of medicines subject to medical prescription reimbursed by the state or that are under a reimbursement request, and the price of reimbursed medicines not subject to a medical prescription, is determined in accordance with the maximum price mechanism regulated in Ministry of Health Order no. 195-C/2015 of 30 June 2015. These prices are determined through a comparison with the approved wholesaler prices (PVA) in referenced countries for the same medicine, or for an identical pharmaceutical speciality with the same active substance, pharmaceutical formula and dosage.

The price of generic medicines is obtained by a comparison with a reference medicine with the same dosage, and is to be lower than 50% of the price of the reference medicine, or is to be less than 25% of the price of a medicine with a wholesale price in all its presentations that is equal to or below EUR10.

The maximum price of parallel imported medicines is to be at least 5% less than the maximum retail price approved for the considered medicine and for the identical and similar medicines that hold a marketing authorisation in Portugal.

Non-reimbursed medicines subject to medical prescription that already have a maximum retail price can be modified under the notification price regime, under which the market holder can notify INFARMED that it intends to market the medicine at a higher retail price. INFARMED can oppose the intended price. If INFARMED fails to oppose it, the market holder notified price is considered as tacitly approved.

Hospital market

Non-reimbursed medicines subject to medical prescription to be purchased by NHS units and services are subject to a specific previous evaluation procedure. As a result, the supply conditions and maximum price of such medicines is regulated in a written contract between the medicine market holder and INFARMED. However, the maximum acquisition price of these medicines cannot exceed the lowest wholesale price in force in designated referenced countries for the same medicines, or the lowest price for identical or essentially similar pharmaceutical medicinal products if these medicines do not exist. The previous evaluation procedure may also apply to other medicines, if the respective sales volume with NHS entities and services is significant.

The maximum acquisition price of generic medicines to be purchased by NHS units and services is determined in accordance with the maximum price mechanism (*see above*).

Reimbursed medicines

The price of both prescription and over-the-counter (OTC) medicines eligible for reimbursement by the NHS is subject to the reference price mechanism, when such medicines are included in homogeneous groups of medicines. The reference price for each homogeneous group of medicines corresponds to the average of the five lowest retail prices, considering the medicines that make up each homogeneous group. The reference countries are subject to a yearly review by the Minister of Health.

In a specific homogeneous group, the maximum retail price of new medicines to be reimbursed should be at least 5% less than the generic medicine that has the lowest price and has at least a 5% market share of generic medicines in the homogeneous group.

The maximum prices of the medicines referenced above are subject to annual revisions, on the basis of a comparison with prices approved in the reference countries. Exceptional reductions may also occur under a specific order issued by the Ministry of Health, due to a need to regularise the relevant market.

The price of OTC medicines that are not subject to reimbursement by the NHS is not regulated by the public authorities.

In relation to medical devices, Decree Law 97/2015 provides that certain medical devices or generic groups of medical devices for NHS users may be subject to a maximum prices special regime, which is to be defined by specific orders issued by the Ministry of Health.

In addition, certain devices may also be subject to a maximum acquisition price by NHS entities, through a previous evaluation contract with the respective market holder or distributor.

6. When is the cost of a medicinal product funded by the government or reimbursed? How is a pharmacist compensated for dispensing services?

The cost of a medicinal product can be funded by the state on the basis of either:

- Its technical-scientific and added therapeutic value.
- Evidence provided in relation to its economic advantage.

(*Decree-Law 97/2015.*)

The scientific and economic assessment for funding by the NHS is carried out by INFARMED. Medicines that receive upfront reimbursement of the pharmacy sale price by the NHS generally fall within one of four rating bands:

- Band A: 90%.
- Band B: 69%.
- Band C: 37%.
- Band D: 15%.

(*Order no. 195-D/2015, 30 June 2015.*)

Decree-Law 97/2015 also establishes that special funding and reimbursement regimes apply.

Special reimbursement for similar biologicals

Similar biological medicines follow the general or special reimbursement regime for biological reference medicines, with adaptations due to market share and prices.

For reimbursement, the retail price of the biological medicine to be reimbursed cannot exceed 80% of the price of the reference biological medicine, when both medicines are to be marketed in the outpatient market. In specific circumstances, the price of a similar biological medicine can be reduced to 70% of the price of the reference biological medicine, notably if the similar biological medicine holds at least a 5% market share in terms of active substance in accordance with the applicable International Common Denomination.

Other special regimes

Special reimbursement regimes can be established for determined pharma therapeutic groups or subgroups, considering users' income, the prevalence of diseases and public health objectives.

Exceptional reimbursement regimes can also be established by specific order of the Ministry of Health, namely for:

- Certain pathologies or special groups of users.
- Certain therapeutic indications.
- Integrated management system of diseases.
- Medicines qualified by a Minister of Health order as indispensable for lifesaving.

A pharmacist in a dispensing pharmacy is remunerated through a maximum legal margin on the reimbursed medicines not subject to medical prescription and on medicines subject to medical prescription (reimbursed or not), based on the approved medicine authorised wholesale price (MAWP). The pharmacist's price margin varies according to the MAWP price, as follows:

- MAWP price equal or up to EUR5: 5.58% over the MAWP (plus EUR0.63).
- MAWP price of EUR5.01 to EUR7: 5.51% (plus EUR1.31).
- MAWP price of EUR7.01 up to EUR10: 5.36% (plus EUR1.79).
- MAWP price of EUR10.01 up to EUR20: 5.05% (plus EUR2.80).
- MAWP price of EUR20.01 up to EUR50: 4.49% (plus EUR5.32).
- MAWP price over EUR50: 2.66% (plus EUR8.28).

(*Order no. 195-C/2015.*)

Pharmacies may also obtain a specific additional remuneration of EUR0.35 per medicine package, provided that they meet the applicable conditions under Order no. 262/2016, 7 October 2016.

CLINICAL TRIALS

7. Outline the regulation of clinical trials.

Legislation and regulatory authorities

Clinical trials are regulated by INFARMED. The Clinical Trials Act (Law 21/2014, 16 April 2014) implements Directive 2001/20/EC on the conduct of clinical trials, which will be repealed by Regulation (EU) 536/2014 on clinical trials on medicinal products for human use when the European Commission publishes a notice of confirmation on a fully functional EU clinical trials portal and database, which is now expected to occur in 2021.

Authorisations

Each clinical trial is subject to prior authorisation by INFARMED. Generally, decisions are made within 30 days of application. Additional requests for information suspend the applicable deadline until the requested information is provided by the sponsor.

Clinical trials must also receive a favourable binding opinion from the competent Ethics Committee (*Comissão de Ética competente*) (CEC).

Consent

Clinical trial participants must provide written informed consent (*see below, Trial pre-conditions*).

Trial pre-conditions

The conditions that must be met before the trial can begin include:

- A satisfactory evaluation to be performed by INFARMED and by the CEC of the anticipated benefits and risks, concluding that the potential benefits overcome the foreseeable risks.
- The existence of a protocol.
- Complete details of the clinical trial sponsor, investigator, principal investigator or investigator-co-ordinator.
- Details of the qualifications of all the team members involved in the clinical trial.
- The existence of an investigator's brochure.
- Details of the clinical trial centre(s) and validation of the adequacy of the facilities.
- The provisions for indemnity or compensation in the event of injury or death attributable to the clinical trial.
- The existence of an insurance or indemnity to cover the liability of the investigator and sponsor.

- In the case of multicentre trials involving trial centres of other EU member states, the identification of the competent authorities and, if available, the opinions adopted by the respective ethics committees, translated into Portuguese.
- Details of the amounts and, where appropriate, the arrangements for rewarding or compensating investigators and trial subjects, and the relevant aspects of any agreement between the sponsor and the site.

In respect of trial participants, certain minimum conditions must be met:

- A prior interview with the investigator, in which the participant must be informed of the:
  - clinical trial objectives;
  - risks and inconveniences;
  - associated conditions of performance; and
  - the participant's right to withdraw from the clinical trial at any time.
- The right of the patient's moral and physical integrity is to be secured.
- The protection of data privacy rights.
- The existence of an insurance or indemnity to cover the liability of the investigator and sponsor.
- Written informed consent, referring to the nature, scope, consequences and risks of the clinical trial.
- Details of the associated medical care must be provided during the clinical trial.
- Designation of a contact person to disclose detailed information to participants.
- Pecuniary benefits or incentives cannot be granted to patients, except for the reimbursement of expenses and the compensation of damages incurred by the participant that arise from participation in the clinical trial.

Procedural requirements

A clinical trial must be conducted in accordance with:

- Good clinical practices.
- The approved protocol.
- INFARMED's clinical trial authorisation.
- The decision of the CEC.

Amendments to the protocol can be made provided they:

- Do not affect the safety of participants.
- Do not alter the scientific evidence on which the conduct of the trial is based.

During the course of the trial, the investigator must report any adverse events to the sponsor, except those identified in the investigator's brochure or in the protocol as not requiring immediate (within a 24-hour period) notification. The sponsor must keep detailed records of all adverse events.

Serious unexpected adverse events that have caused or may cause the death of a participant must be registered and notified to:

- INFARMED.
- All the competent public authorities of all the participating EU member states involved in the trial.
- The CEC.

Transparency and reporting requirements

The National Registry for Clinical Studies (RNEC) (*www.rnec.pt*) is the mechanism for registration and publication of all clinical studies undergoing in Portugal and that comprise human beings, namely, clinical trials and other studies of clinical nature involving, among others, investigational products, medicines, medical devices and studies that use human biological samples.

The objectives of the RNEC are set out in its regulation (Order 65/2015, 5 March 2015) and include the creation of an information database of clinical studies to facilitate:

- The transmission and monitoring of information.
- The authorisation and notification procedures presented to INFARMED and ethics committees.
- Access and knowledge to the research community, healthcare professionals and by the general public to all clinical studies undergoing in Portugal.

(*See above, Procedural requirements*).

MANUFACTURING AND DISTRIBUTION

8. What is the authorisation process for manufacturing and distributing medicinal products?

The national manufacturing authorisation process closely follows EU law (*Medicines Act*).

Application

The application must be submitted to INFARMED.

Conditions

The application can be made by a natural or legal person and must contain the following information:

- The specification and pharmaceutical form of the medicine.
- Details of where the manufacture of the medicine will be carried out.
- Evidence of compliance with the applicable technical requirements in relation to:
  - technical director;
  - premises;
  - equipment;
  - monitoring; and
  - identity of the technical director and respective qualifications.

Restrictions on foreign applicants

There are no specific restrictions on foreign applicants. The manufacturing facilities must, however, be located in Portugal.

Key stages and timing

The application for authorisation must be decided within a maximum period of 90 days from the date the request is submitted.

Fee

INFARMED applies a standard fee of EUR588.23 for each medicine manufacturing request (*Order 377/2005, 4 April 2005*). INFARMED's fees are published online at: *www.infarmed.pt/documents/15786/17838/Payment_form.pdf/c317884e-1682-4c8e-bc62-11fb06427786*.

Authorisations, variations, and renewals

The manufacturing authorisation remains valid until INFARMED cancels it or the holder of the licence withdraws it.

Monitoring compliance and imposing penalties

A manufacturer's facilities are subject to ad hoc inspections by INFARMED. INFARMED can also request access to reports regarding each manufactured medicine lot.

In cases of non-compliance with the applicable manufacturing obligations, INFARMED can suspend or revoke the manufacturing licence (for example, if the manufactured medicine does not meet its declared qualities or quantities).

Without prejudice to potential criminal liability, breach of the relevant obligations is a misdemeanour under the Medicines Act, punishable with a fine for each infringement:

- From EUR2,000 up to 15% of the annual turnover of the infringer or EUR180,000 (whichever is the lower amount) for breaches of manufacturing obligations.
- From EUR2,000 up to 10% of the annual turnover of the infringer or EUR120,000 (whichever is the lower) for breaches of the requirements related to technical directors.

MARKETING

Authorisation and abridged procedure

9. What is the authorisation process for marketing medicinal products?

Application

The application for authorisation to market a medicinal product in Portugal must be submitted to INFARMED. The Medicines Act follows EU law (*Code for Human Medicines Directive*).

A medicinal product must hold a marketing authorisation obtained through one of the following:

- The national procedure.
- The EU member states (including Portugal) procedure, which includes the decentralised procedure and the mutual recognition procedure.
- The centralised procedure of the European Medicines Agency. This is usually used for medicinal products for human use containing a new active substance for which the therapeutic indication is the treatment of any of the following diseases:
  - acquired immune deficiency syndrome;
  - cancer;
  - neurodegenerative disorder;
  - diabetes;
  - auto-immune diseases and other immune dysfunctions; and
  - viral diseases.
- (*EMA Regulation.*)

Exceptions

Subject to prior authorisation by INFARMED and reasoned on exceptional public health reasons products can be marketed without a valid marketing authorisation in Portugal. One of the following conditions must be met:

- Upon clinical justification, they are considered essential to the prevention, diagnosis or treatment of certain pathologies, if it is demonstrated that there is no alternative in the set of medicines with marketing authorisation.
- They are necessary to prevent or limit the spread, current or potential, of pathogens, toxins, chemical agents or nuclear radiation, that are likely to cause harmful effects

Authorisation conditions

An application for a marketing authorisation must include:

- The name or corporate name and permanent address of the applicant and, where applicable, of the manufacturer.
- The name of the medicinal product.
- Detailed qualitative and quantitative particulars of the constituents of the medicinal product in standard scientific terminology.
- A description of the medicinal product's manufacturing method.
- The medicinal product's:
  - therapeutic indications;
  - contra-indications;
  - adverse reactions;
  - posology;
  - pharmaceutical form;
  - method and route of administration; and
  - expected shelf life.
- If applicable, reasons for any precautionary and safety measures to be taken for the storage of the medicinal product, its administration to patients and for the disposal of waste products, together with an indication of any potential risks presented by the medicinal product for the environment.
- A description of the control methods used by the manufacturer.
- The results of physico-chemical, biological or microbiological tests, toxicological and pharmacological tests and clinical trials.
- A summary of the product's characteristics.
- One or more specimens or mock-ups of the product's outer packaging, immediate packaging and package leaflet.

Key stages and timing

INFARMED must make a final decision on a complete marketing authorisation application within a period of 210 days, without prejudice to potential time suspensions (for example, requests for information from the applicant due to detected deficiencies in the submitted file).

Fee

The applicable marketing authorisation application base fees are as follows:

- Under the national procedure (per dosage and pharmaceutical form): EUR2,915.55.
- From a member state with Portugal as the reference member state (per dosage and pharmaceutical form): EUR7,672.50.
- For the parallel import of a medicine (per dosage and pharmaceutical form): EUR1,759.56.

(*Order 377/2005, 4 April 2005.*)

INFARMED's applicable fees are published online at: *www.infarmed.pt/documents/15786/17838/Payment_form.pdf/c317884e-1682-4c8e-bc62-11fb06427786.*

Effect of authorisation and related protections

The marketing authorisation is initially granted and valid for a period of five years. After the first renewal, following a formal request by the market authorisation holder, the subsequent

authorisation is valid for an indefinite period. In exceptional cases, the renewal of the marketing authorisation may be subject to a limited five-year period.

Authorisations, variations, and renewals

See above, *Effect of authorisation and related protections.*

Monitoring compliance and imposing penalties

INFARMED has the following powers to monitor compliance with marketing authorisations:

- Conduct inspections at the premises of manufacturers, wholesalers, pharmacies and entities responsible for laboratorial controls or a specific medicinal product's manufacturing stages, as well as any other facilities used for such purposes.
- Conduct unannounced inspections of the manufacturers of active substances used in the production of medicines, as well as at the premises of holders of marketing authorisations, when there are grounds to suspect non-compliance with good manufacturing practices.
- Verify the facilities, records, documents and pharmacovigilance system of the marketing authorisation holder.
- Collect samples to carry out tests in a laboratory.

INFARMED can also decide to:

- Suspend, forfeit or alter the content of a marketing authorisation.
- Impose fines between EUR2,000 and 15% of the annual turnover of the infringer or EUR180,000 (whichever is the lower) for each infringement, subject to judicial review.

INFARMED can also report criminal liability to the Public Prosecutor.

Protection of confidential information

Access by third parties to documents and information disclosed in a marketing authorisation application must be assessed on a case-by-case basis. For guidance purposes, detailed information on the synthesis or manufacture of the active substance, including details on the by-products and degradation products of active ingredients and validation of the manufacturing or synthesis process, can be deemed confidential information. The final qualitative formulation (composition) of the authorised product cannot be deemed as confidential information.

Release requirements

The marketing authorisation is initially granted and valid for a period of five years. The authorisation is not dependent on the fulfilment of advertising requirements by the holder, or on the prior inspection of the respective facilities by INFARMED.

10. What pharmacovigilance obligations and other commitments apply after a company has obtained marketing authorisation? Are there further conditions on how the medicinal product is distributed and made accessible to patients?

Commitments and pharmacovigilance obligations

The market authorisation holder must have a qualified person responsible for:

- Pharmacovigilance.
- Maintaining a pharmacovigilance master file.
- Operating a risk management system (*see Question 20*).

INFARMED, in collaboration with the European Medicines Agency and other member states, must have a list of medicinal products that are subject to additional monitoring under the EMA Regulation (which sets out EU procedures for the authorisation and supervision of medicinal products for human use). The list contains the names and active substances of both:

- Medicinal products authorised in the EU that contain a new active substance which, on 1 January 2011, was not contained in any medicinal product authorised in the EU.
- Any biological medicinal product not covered in the bullet point above that was authorised after 1 January 2011.

The medicinal products listed must include:

- A summary of product characteristics.
- The following statement on the package leaflet: "This medicinal product is subject to additional monitoring", preceded by a black symbol.

Other conditions

INFARMED can attach supplementary obligations to the marketing authorisation, for example, the execution of post-authorisation safety studies. In addition, failure to effectively commercialise the medicine for a period of three consecutive years, regardless of the reasons, generally leads to forfeiture of the authorisation. Loss of the marketing authorisation is published on INFARMED's website.

11. Is there an abridged procedure for marketing authorisation? Which medicinal products can benefit from it and what conditions and procedure apply? What information can the applicant access and rely on?

The abridged procedure is set out in the Medicines Act. If the market authorisation applicant can provide evidence that the medicine's active substance has had an established clinical use in the EU for a period of ten years with acceptable safety and recognised efficacy, the applicant is not required to provide pre-clinical and clinical trials data. It is sufficient if the applicant provides an adequate scientific bibliography.

INFARMED has 210 days to make a decision on the applicant's request. Requests for more information by INFARMED suspend this period.

12. Are foreign marketing authorisations recognised in your jurisdiction?

Marketing authorisations granted under the centralised procedure by the European Medicines Agency are recognised in Portugal.

Marketing authorisations granted by the equivalent authorities of other EU member states are also, generally, recognised in Portugal. INFARMED usually makes its decision on marketing authorisations within 30 days of access to the assessment report of the equivalent regulatory authority of the other EU member state.

If INFARMED considers that there is a potential serious risk for public health, it can adopt an unfavourable opinion on the request for approval of the marketing authorisation. In the absence of any subsequent agreement between the relevant EU national agencies, an arbitration procedure can be initiated before the European Committee for Medicinal Products for Human Use (CMPH).

In the mutual recognition and decentralised procedures, the CHMP arbitrates in cases where there is a disagreement between member states concerning the marketing authorisation of a particular medicine. The CMPH consists of one member appointed by each EU member state.

Parallel imports and cross-border trade in medicines

13. Are parallel imports of medicinal products into your jurisdiction allowed? What are the general requirements for imports of medicinal products into your jurisdiction? Are particular foreign markets or products favoured?

Parallel imports of medicinal products are allowed into Portugal, provided the following conditions are met:

- The medicine must have a valid marketing authorisation in the EU member state of origin.
- The medicine is commercialised in compliance with the conditions established in the Medicines Act.
- The medicine must have the same:
  - quantitative and qualitative composition in terms of active substances;
  - pharmaceutical form; and
  - therapeutic indications (different excipients can be used or different quantities of the same excipients if they have no therapeutic impact).
- The authorisation does not pose a risk to public health.

The conditions set out in the second and fourth bullet points above are presumed to be verified if:

- The medicine to be imported is manufactured in another EU member state by a company contractually linked to the marketing authorisation holder in Portugal, or by a company that is part of the same corporate group.
- The company that holds the marketing authorisation of the medicine in Portugal manufactures or markets in Portugal the medicine under an agreement with a company contractually linked to the market holder in the member state of origin.

The parallel import is subject to a previous authorisation procedure that requires the submission of a specific form and documents. The authorisation must be granted by INFARMED within 45 days, if this time period is not suspended due to pending clarification requests or additional submission of documents.

Generally, the holder of intellectual property rights in a medicinal product that has been placed on the market in the European Economic Area (EEA) is not legally able to impede further marketing of that product in another EEA country.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, see *Pharmaceutical IP and competition law in Portugal: overview*.

RESTRICTIONS ON DEALINGS WITH HEALTH CARE PROFESSIONALS

14. What are the restrictions on marketing practices such as gifts, sponsoring, consultancy agreements or incentive schemes for health care establishments or individual medical practitioners?

Marketing authorisation holders or companies responsible for the promotion of medicines and distributors cannot offer or promise to offer, directly or indirectly, to health professionals or to the respective patients any gifts, bonuses, pecuniary or non-pecuniary benefits, unless the offer relates to an object relevant to the practice of medicine and is of insignificant economic value (*Medicines Act*).

Both the sponsoring of scientific promotions addressed to health professionals and consultancy agreements engaging health professionals are allowed, provided payments are not conditional on the prescription or dispensing of medicines. Health professionals can also be remunerated for their participation in scientific and promotion events, as speakers or consultants, for the respective travel and hosting costs of such participants supported by the event promoter, subject to certain requirements

However the granting of pecuniary or non-pecuniary benefits (assessable in cash) by pharma companies to any individual, private or public entity, including NHS hospitals and healthcare professionals or to any employee of the Ministry of Health bodies and services, patients associations or to medical societies of clinical studies or of scientific nature must be reported by the pharma company on INFARMED's transparency platform, 30 days after their effectiveness.

Decree Law 5/2017, 6 January 2017, established a new set of rules on publicity and transparency. One of the most relevant restrictions is the prohibition on NHS hospitals or Ministry of Health bodies and services to receive benefits from pharma or medical devices companies unless previously authorised by the Ministry of Health. In addition, scientific or similar actions of pharma companies cannot be conducted at NHS hospitals or services premises. Further, scientific actions in NHS facilities cannot:

- Have a promotional nature.
- Be sponsored by companies that manufacture, distribute or market medicines or medical devices.

An infringement by market holders or distributors of the rules in the Medicines Act (*Decree Law 176/2006*) concerning the prohibition of concessions to health professionals of certain pecuniary or non-pecuniary benefits can lead to the imposition of fines of between EUR2,000 and 15% of the annual turnover of the infringer or EUR180,000 (whichever is the lower) for each infringement, subject to judicial review.

Anti-bribery legislation also applies to the life sciences sector, notably when dealing with public officials and state institutions.

The following provisions may apply:

- Receiving improper payment (*Article 372, Criminal Code*).
- Passive corruption (*Article 373, Criminal Code*).
- Active corruption (*Article 374, Criminal Code*).

Penalties can include imprisonment and fines for representatives of the company, public officials and other third parties for committing certain offences.

Portuguese anti-bribery provisions can apply to offences occurring outside Portugal, but exceptions may apply.

SELLING RESTRICTIONS

15. What are the restrictions on selling medicinal products? Are there specific regulations for the sale of medicinal products on the internet, by e-mail and by mail order?

Prescription medicines and over-the-counter (OTC) medicines reimbursed by the NHS are exclusively sold in pharmacies. OTC medicines not subject to reimbursement by the NHS can be sold by OTC retailers (*parafarmácias*).

The home delivery of medicinal products is allowed by:

- Pharmacies in relation to prescription medicines.
- Pharmacies and OTC retailers in respect of OTC medicines.

(*Order 1427/2007, 2 December 2007.*)

Home delivery must be provided in the geographic municipality where the pharmacy or OTC retailer is located and in the surrounding geographic municipalities.

Orders by patients can be placed through any of the following methods:

- Telephone.
- Fax.
- Online pharmacy.
- OTC retailer website.
- Email.

Pharmacies are governed by the rules of Decree Law 307/2007, 31 August 2007, as amended. OTC medicine retailers are governed by Decree Law 134/2005, 16 August 2005, as amended.

ADVERTISING AND PROMOTION

16. What restrictions apply to the advertising and promotion of medicinal products and the provision of samples, and how are adverts and promotional activity regulated?

Legislation and regulatory authority

The advertising of medicinal products is governed by the Medicines Act. INFARMED is responsible for the supervision and enforcement of the provisions on advertising to healthcare professionals and the general public.

INFARMED will open an inquiry where non-compliance is suspected, either on its own initiative or based on a complaint. This can lead to penalties including fines and loss of licences, authorisations or permits. Decisions are subject to judicial review.

Restrictions

Certain medicines cannot be promoted or advertised to the general public, only to healthcare professionals (for example, doctors, pharmacists and nurses). They must be advertised in scientific publications or other forms of communication with restricted use by health professionals. These medicines include:

- Prescription medicines.
- Medicinal products that contain psychotropic or narcotic substances.
- Medicines subject to reimbursement by the NHS.

Over-the-counter (OTC) medicines can be advertised to the general public.

The advertising of any of the above categories of medicinal products must:

- Comply with the particulars listed in the summary of product characteristics.
- Encourage the rational use of the medicinal product by presenting it objectively, without exaggerating its properties.
- Not be misleading.

Any advertisement to the general public of an OTC medicine must:

- Clearly indicate that it is an advertisement.
- Clearly identify the product as a medicinal product.
- Include the following minimum information:
  - the name of the medicinal product;
  - its common name if the medicinal product contains only one active substance;
  - the information necessary for correct use of the medicinal product; and
  - a legible invitation to read the instructions on the package leaflet or the outer packaging (as the case may be) carefully.

The advertising of a medicinal product to the general public must not contain any material that:

- Gives the impression that a medical consultation or surgical operation is unnecessary, in particular by offering a diagnosis or by suggesting treatment by mail.
- Suggests that the effects of taking the medicine are guaranteed, are unaccompanied by adverse reactions or are better than, or equivalent to, those of another treatment or medicinal product.
- Suggests that the health of the subject can be enhanced by taking the medicine.
- Suggests that the health of the subject could be affected by not taking the medicine.
- Is directed exclusively or principally at children.
- Refers to a recommendation by scientists, health professionals or persons who are neither of the foregoing but who, because of their celebrity, could encourage the consumption of medicinal products.
- Suggests that the medicinal product is a foodstuff, cosmetic or other consumer product.
- Suggests that the safety or efficacy of the medicinal product is due to the fact that it is natural.
- Could, by a description or detailed representation of a case history, lead to erroneous self-diagnosis.
- Refers, in improper, alarming or misleading terms, to claims of recovery.
- Uses, in improper, alarming or misleading terms, pictorial representations of changes in the human body caused by disease or injury, or of the action of a medicinal product on the human body or parts of it.

Advertising to persons qualified to prescribe or supply medicinal products must include the following:

- Essential information compatible with the summary of product characteristics.
- The supply classification of the medicinal product.
- The conditions for reimbursement by the NHS.

Measures or commercial practices related to margins, prices and discounts are not subject to the advertising rules of the Medicines Act.

The Portuguese Association of the Pharmaceutical Industry (*Associação Portuguesa da Indústria Farmacêutica*) (Apifarma) has produced a Code of conduct for promotional practices by the pharmaceutical industry with healthcare professionals. The Code reflects the rules and principles of the Medicines Act and the European Federation of Pharmaceutical Industries Code on the Promotion of Prescription-Only Medicines to and Interactions with Healthcare Professionals.

Infringements by market holders or distributors of the Advertisement Chapter of the Medicines Act (*Decree Law 176/2006*) can lead to a fine of between EUR2,000 and 15% of the annual turnover of the infringer or EUR180,000 (whichever is the lower) for each infringement, subject to judicial review.

Internet advertising

Advertising on the internet is subject to the same rules (*see above, Restrictions*).

DATA PRIVACY

17. Do privacy and data protection laws impact on pharmaceutical regulation in your jurisdiction?

The national data protection legislation (*Law 67/98, 26 October 1998*), enforced by the Portuguese Data Protection Agency (*Comissão Nacional Nacional de Proteção de Dados*) (CNPD), applies to personal health data, including within clinical trials, pharmacovigilance, adverse event reporting and patient data processing. Since 25 May 2018, Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (GDPR) is also directly applicable in Portugal.

There is also a specific legal regime that regulates the processing of personal genetic information and health information (*Law 12/2005, 26 January 2005 as executed by Decree Law 131/2014, 29 August 2014*). Under this regime, the collection of human biological samples or related derivatives, with the aim of establishing a database of biological products with personal information, is subject to prior authorisation by CNPD.

PACKAGING, LABELLING AND TRACKING

18. Outline the regulation of the packaging and labelling of medicinal products.

Legislation and regulatory authority

The Medicines Act governs the packaging and labelling of medicinal products. INFARMED is responsible for the supervision and enforcement of the provisions applicable to the packaging and labelling of medicinal products.

Information requirements

The following information must appear on the outer packaging of medicinal products or, where there is no outer packaging, on the immediate packaging:

- The name of the medicinal product followed by its strength and pharmaceutical form, and, when applicable, whether it is intended for babies, children or adults.
- Where the product contains up to three active substances, the international non-proprietary name must be included, or, if one does not exist, the common name.
- A statement of the active substances expressed qualitatively and quantitatively per dosage unit or according to the form of administration for a given volume or weight, using their common names when available.
- The contents by weight, volume or number of doses of the product.
- A list of those excipients known to have a recognised action or effect. If the product is injectable or a topical or eye preparation, all excipients must be stated.
- The method of administration and, if necessary, the route of administration.
- A space must be left for the prescribed dose to be indicated by the healthcare professional.
- A special warning that the medicinal product "must be stored out of the reach and sight of children" (*manter fora do alcance e da vista das crianças*).
- The expiry date in clear terms (month/year).
- Special storage precautions, if any.
- The name and address of the marketing authorisation holder and, where applicable, the name of the representative appointed by the holder to represent him/her.
- The number of the authorisation for placing the medicinal product on the market.
- The manufacturer's batch number.
- The sale price, through printing, label or stamp.
- Elements that guarantee the identity and authenticity of the medicine.
- When applicable, "free sample" (*amostra gratuita*) or "sale to the public not authorised" (*proibida a venda ao público*).

Serialisation

Safety features enabling wholesale distributors and persons authorised or entitled to supply medicinal products to the public to verify the authenticity of the medicinal product, and identify individual packs, must appear on the outer packaging of medicinal products or (if there is no outer packaging) on the immediate packaging.

Other conditions

The packaging and labelling information referred to above must be:

- In Portuguese.
- Indelible.
- Easily readable and comprehensible.

The marketing authorisation applicant must conduct tests on target users in relation to the packaging and leaflet, and the results must be taken into account. The labelling and the package leaflet can also be provided in other languages in addition to Portuguese.

PRODUCT SAFETY, QUALITY AND LIABILITY

19. Outline the key regulators and their powers in relation to medicinal product safety.

INFARMED is the key regulator of medicinal product liability and its powers in this context are extensive. Under the Medicines Act, there is also a National Pharmacovigilance System of Medicines.

In this context, marketing authorisation holders, wholesalers, distributors and pharmacies must make their premises, installations, products and documents (including sensitive information and proprietary data) accessible at all times to INFARMED. In addition, market authorisation holder/wholesalers must have an emergency plan, which ensures effective implementation of any recall from the market ordered by INFARMED for the medicinal product concerned.

Non-compliance with the relevant provisions of the Medicines Act or with INFARMED's decisions is subject to a misdemeanour fine of between EUR2,000 up to 15% of the annual turnover of the infringer or EUR180,000 (whichever is the lower) per infringement imposed by INFARMED, without prejudice to potential criminal, tort and disciplinary liability.

INFARMED can also revoke, suspend or modify a marketing authorisation based, among other things, on a medicine being unsafe. As a rule, when the medicine is marketed in other EU member states, any such decision is co-ordinated with the European Medicines Agency and the competent national authorities of the other EU jurisdictions where the product is marketed.

20. Are there any mandatory requirements relating to medicinal product safety?

Under the Medicines Act, market authorisation holders must have a pharmacovigilance system that:

- Registers information on medicine risks for patients or public health, mainly relating to adverse reactions in human beings, arising from:
  - use of the medicinal product within the terms of the marketing authorisation;
  - use outside the terms of the marketing authorisation; and
  - occupational exposure.
- Evaluates all information scientifically, and considers options for risk minimisation and prevention, and adopts appropriate measures as necessary.
- Is subject to regular audits, including a note concerning the main findings of the audit on the pharmacovigilance system master file.

Marketing authorisation holders must:

- Submit information electronically to the EudraVigilance database and data processing network referred to in the EMA Regulation on all serious suspected adverse reactions occurring in the EU and third countries, within 15 days following the day on which the marketing authorisation holder concerned gained knowledge of the event.
- Submit electronically to the EudraVigilance database information on all non-serious suspected adverse reactions that occur in the EU, within 90 days following the day on which the marketing authorisation holder concerned gained knowledge of the event.
- Notify INFARMED immediately of any urgent safety decision or action to suspend or recall a medicinal product, when the medicine's efficacy or public health is at stake.

Public disclosure of a medicinal product warning directly by a marketing authorisation holder is, as a rule, subject to prior approval from INFARMED. The information contained in such notice must be objective and not misleading.

When applicable, INFARMED's public warning identifies the relevant medicinal product batch number.

In this context, non-compliance with the relevant rules of the Medicines Act is subject to penalties (*see Question 19*).

21. Outline the key areas of law applicable to medicinal product liability, including key legislation and recent case law.

Legal provisions

Medicinal product liability can arise under criminal law, contract and tort law.

Portugal has a specific legal regime for product liability set out in Decree-Law 383/89 of 6 November 1989, as amended (Product Liability Act) based on Directives 85/374/EEC and 1999/34/CE on liability for defective products.

Substantive test

The injured person must prove:

- Damage.
- The defect.
- A causal relationship between the defect and the damage.

(*Product Liability Act.*)

The Civil Code also recognises tort liability based on:

- The infringement of legal provisions (*Article 483*).
- Joint and several liability (*Articles 490 and 497*).
- Indemnity limitation in cases of negligence (*Article 494*).
- A general limitation period of three years (*Article 498*).

Under the Civil Code, liability depends on the fulfilment of five cumulative requirements:

- Conduct (act or omission) controllable by human resolution.
- The unlawfulness of the conduct.
- Imputation of the conduct to a natural or legal person.
- The existence of damages.
- A causal link between the conduct and the damage.

A damage claim can also be brought under contractual liability, where there is a contract between the wrongdoer and the natural or legal person suffering the damage.

22. Who is potentially liable for defective medicinal products?

The producer is liable for any damage, independently of fault, caused by a defect in his/her product. The producer is defined as one of the following:

- Manufacturer of a finished product.
- Producer of any raw material.
- Manufacturer of a component part.
- Any person who, by putting his/her name, trade mark or other distinguishing feature on the product presents himself/herself as its producer.

(*Product Liability Act.*)

In addition, without prejudice to the liability of the producer, any person who imports into the EU a product for sale or any form of distribution in the course of his/her business is also considered to be a producer and is responsible as a producer. If the producer cannot be identified, each supplier of the product is treated as its producer unless he/she informs the injured person, within a reasonable time, of the identity of the producer or of the person who supplied him/her with the product.

23. What defences are available to product liability claims? Is it possible to limit liability for defective medicinal products?

Standard defences in a product liability claim include that:

- The defendant did not put the product into circulation.
- The defect that caused the damage did not exist at the time the product was put into circulation and came into being afterwards.
- The product was either not:
  - manufactured by the defendant for sale or any form of distribution for economic purpose; or

- manufactured or distributed by the defendant in the course of his/her business.

- The defect is due to compliance of the product with mandatory regulations issued by the public authorities.
- The state of scientific and technical knowledge at the time the defendant put the product into circulation was not such as to enable the defect to be discovered.
- In the case of a manufacturer of a component, the defect is attributable to the design of the product in which the component has been fitted or to the instructions given by the manufacturer of the product.

24. How can a product liability claim be brought?

Limitation periods

The limitation periods for bringing a product liability claim are:

- Three years from the day on which the claimant became aware, or should reasonably have become aware, of the damage, the defect and the identity of the producer.
- Ten years from the date on which the producer put into circulation the actual product which caused the damage, unless the injured person has since started proceedings against the producer.

(*Product Liability Act.*)

Class actions

Law 83/95 of 31 August 1995 establishes the legal framework applicable to a representative action. The aim of this type of action is to represent collective or diffuse interests either for prevention (injunction) or for redress (claims for damages). A representative action for a product liability claim in the Portuguese courts can be brought by:

- A natural person.
- An association or foundation (in cases that are directly connected with their purpose).

(*Law 83/95, 31 August 1995.*)

Companies cannot use the representative action procedure.

The Portuguese procedure is an opt-out system. The claimant automatically represents all the holders of similar rights or interests at stake who do not opt out following, among others, a public notice of submission of the representative action before the court. The claimant can seek redress for damages suffered, but compensation cannot be individually identified and will be determined globally. Representative actions in the context of product liability claims are rare in Portugal.

25. What remedies are available to the claimant? Are punitive or exemplary damages allowed for product liability claims?

The claimant (or his/her estate) can claim damages for:

- Death.
- Personal injury.
- Non-patrimonial damages.
- Damage to, or the destruction of, property (other than the defective product itself), provided the property:
  - is of a type ordinarily intended for private use or consumption; and
  - was mainly used by the injured person for his/her own private use or consumption.

Punitive damages are not available in Portugal for product liability claims.

LOCAL ESTABLISHMENT, REPRESENTATION AND RESIDENCY REQUIREMENTS

26. What local requirements apply to businesses and individuals (such as the person responsible for releasing a product onto the market) acting within or in relation to the jurisdiction?

Businesses and individuals established in Portugal are responsible (for example, when releasing the product on the Portuguese market), in the event of fault or negligence, and can be subject to criminal, misdemeanour, contractual and tort liability.

REFORM

27. Are there proposals for reform and when are they likely to come into force?

The current Government has set the following goals for the National Health Policy:

- Creation of a National Programme of Education for Health, Literacy and Self-care, preparing and supporting informal care providers, preventing diabetes, obesity, promoting mental health and healthy ageing and the rational and safe use of medicinal products.
- Implementing Local Health Plans in compliance with the National Plan of Health (PNS).
- Strengthening epidemiological surveillance, health promotion, primary prevention and secondary prevention.
- Revitalising the Communicable Disease Control Programme to address new epidemics, the recurrence of known infections and multiple resistance to antibiotics.
- Promoting measures to prevent smoking (by increasing access to smoking cessation), healthy eating (in schools and work environments) and prevention of alcohol consumption and other dependency-generating products.
- Increase the importance, in the context of the NHS, of the National Mental Health Network.
- Evaluate and update the National Vaccination Programme.
- Expansion and enhancement of the capacity of the primary health care network.
- Improved management of NHS hospitals, circulation of clinical information and co-ordination with other levels of care and other agents in the health sector.
- Expansion and improvement of the integration of the Network of Continuous Care and of other support services in relation to persons in a dependent situation.
- Promote a sustainable policy in the field of medicinal products so as to reconcile budgetary rigour with access to therapeutic innovation, through review of mechanisms for dispensing and reimbursing medicines of chronic outpatients, promoting the increase of the market share of generic medicines (in value) to 30%, and encouraging research and national production in the medicine sector.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of

dominance and parallel imports, see *Pharmaceutical IP and competition law in Portugal: overview.*

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Recent transactions

- Practises mainly in the health sector as a life sciences lawyer.
- Advising several pharmaceutical companies.
- Co-ordinates the firm's Life Sciences Practice Area, including legal teams representing companies in the pharmaceutical sector, in areas such as regulation (prices and reimbursement regulation, medicine legal framework, marketing authorisation procedures, promotion activities and clinical trials), commercial policies, litigation and arbitration.

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- *Distribution and Marketing of Drugs Global Guide, Thomson Reuters, General Editors: Eric Stupp and Markus Schott, Bar & Karrer AG and Alison Dennis, Fieldfisher, First Edition.*
- *Medicinal product regulation and product liability in Portugal: overview, Practical Law Life Sciences Global Guide, Thomson Reuters.*
- *Pharmaceutical IP and competition law in Portugal: overview, Practical Law Life Sciences Global Guide, Thomson Reuters.*
- *Healthcare Enforcement and Litigation, Getting the Deal Through.*

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