SPAIN
PHARMA MARKET
&
REGULATORY REPORT

Pharmaceuticals Export Promotion Council of India

(Set up by Ministry of Commerce & Industry, Government of India)

CONTENTS

Demography

SL. No	Parameter	Description
1	Region	South Western Europe
2	Country	Spain
3	Capital	Madrid
4	Population	50,015,792 (July 2020 est.)
5	Population growth rate (%)	0.67% (2020est)
6	GDP (purchasing power parity)	$1.778 trillion(2017est.)
7	GDP - real growth rate (%)	3.% (2017est)
8	GDP - per capita (PPP)	$34,800 (2015 est.)
9	Exchange rates	One Euro is equal to a 74.82 INR as on 1st October2016.
10	Population below poverty line	21.1% (2012 est.)(latest figures not available)
11	Age structure (%)	0-14 years: 15.02%
		15-24 years: 9.9%
		25-54 years :43.61%
		55-64 years: 12.99%
		65 year and above: 18.49%
Source: CIA World Fact Book updated to july 2020 on 2nd June 2020		

MARKET REPORT

Introduction

Healthcare expenditure growth is expected to increase in 2020 owing to effects of the Covid-19 pandemic that shook the Spanish healthcare system. However, growth may remain relatively stable thereafter, but will continue to gain momentum over the coming years. Spain's pharmaceutical market may be impacted by the Covid-19 pandemic as healthcare resources shift away from day-to-day operations and towards the treatment of patients with the virus.

The ageing population of Spain, will create significant pressure on government expenditure increasing the off take of generics.

Spain is experiencing falling birth rate and raising death rate which may subsequently bring in decline in population.

Pharma Expenditure:

In 2019 the expenditure on pharma is put at $ 30.19bn with a negative growth of 3% and the forecast for 2020 is put at $ 20.29 bn with a forecasted negative growth of 6.1%. Pharmaceutical per capita expenditure in 2019 is put at $ 646.

Latest Updates

- Spain is among the worst affected countries globally with 235,772 confirmed cases as of May 25 2020 with 28,752 deaths.
- As of May 26, a new R&D pharmaceutical company launched operations in Spain with a Series A round of funding totalling USD8.1mn. The company focuses on R&D in the central nervous system (CNS) field, and is looking to develop a portfolio of new drug candidates to treat CNS diseases.
- In March 2020, Prime Minister Pedro Sánchez announced the creation of a strategic stockpile of personal protective equipment and medication to deal with future pandemics as soon as the country looks to self-sufficiency. It came to light that the Health Ministry has so far spent over ERU1.0bn on medical equipment, which includes 140mn units of products the country is stockpiling.
- On May 14, the Ministry of Health of Spain granted approval to Akcea Therapeutics, a majority-owned affiliate of Ionis Pharmaceuticals for the reimbursement of Tegsedi (inotersen), a once-weekly, at-home subcutaneous injection for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin (hATTR) amyloidosis, a debilitating and progressive disease that is caused by the buildup of TTR proteins that misfold due to inherited genetic mutations characterised by the deposition of amyloid fibrils throughout the body including in nervous tissue and can have a devastating impact on patients' quality of life

Strengths

- The Spanish pharmaceutical market is among the top 20 in the world.
- Spain's regulatory environment, based on EU directives, is more transparent than some of its European peers, notably in Eastern Europe.

- High level of pensionable population, indicating strong potential for chronic and long term treatment. In fact this section of population is one of the drivers of Pharmaceuticals consumption.

Weaknesses

High levels of Unemployment by their own standards slows down the market growth and OTC sector is affected.

Opportunities

- The potential for generic medicines market growth is high, as the generic's penetration is much less among comparable Western Europe's market.

Threats

- Mounting debts owed to the pharmaceuticals sector by the government are a threat to the sustainability of the public health system.

Market Overview

Growth in the Spanish pharmaceutical market may remain sluggish in the coming years, and forecasts has been revised slightly downwards revision due to the effects of the Covid-19 pandemic, even though it was set to return to its 2010 peak value. Post-coronavirus, an ageing population and a high chronic disease burden likely drive demand for patented medicines, which account for the vast majority of the total market. Implementation of further drug price caps across the pharmaceutical sector as the government looks to contain spiralling healthcare costs poses downside risks to analysts forecast.

High preference for branded medicines and investments in R&D has seen the Spanish pharmaceutical market recover from the negative effects of the government's austerity package that focuses heavily on the pharmaceutical and healthcare sectors.

In 2019, pharmaceutical spending in Spain (both pharmacy and hospital spending in consumer price terms) reached a value of USD30.2bn, representing 24.4% of total health expenditure. Medicine consumption per capita was calculated at USD646. In 2020, forecasts say that market growth will fall by 6.3% to USD28.3bn. Up to 2024, it is forecasted that the market will experience a compound annual growth rate (CAGR) of 1.6%, reaching USD32.5bn. Bearish pharmaceutical market forecast for Spain takes into account the country's weak macroeconomics, especially due to the Covid-19 outbreak and the implementation of government cost-containment measures targeting the pharmaceuticals and healthcare industry. Spanish pharmaceutical industry will contribute less towards GDP over the coming years, falling from 2.1% in 2020 to 1.6% by 2029

As the percentage of population over 65 years is rising, Spain being a highly developed country, demand for non-communicable diseases is on the rise (conditions like cancer, Cardio vascular diseases, and central nervous system diseases). This gives an ample opportunities to companies with these product portfolios.

As with other markets in Western Europe, high-value, innovative medicines account for the majority of Spain's pharmaceutical market, with patented drugs comprising 81% of the total in

2019 at a value of USD24.45bn);generic drugs accounted for a low 14.3% of the market and over-the-counter (OTC) medicines accounted for just 4.7% of the market.

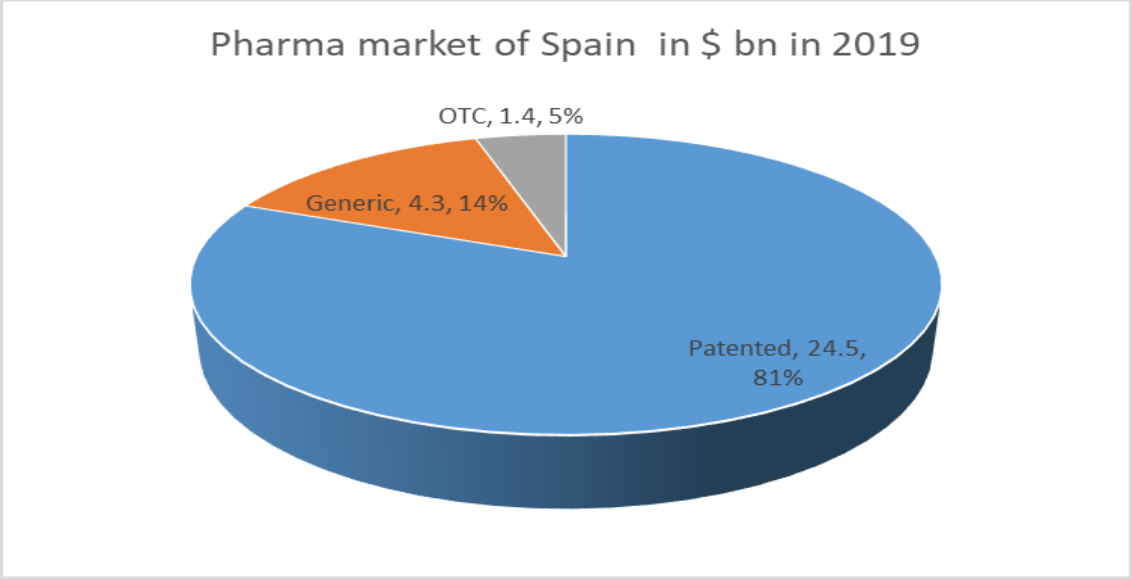
Highlighting the impact of an ageing population on Spain's demands for pharmaceuticals and healthcare, data published by industry association Farmaindustria showed that the correlation between the elderly population (over 65 years old) and the prescription demand per capita is positive and high. While this is positive for innovative drugmakers whose product portfolios contain therapeutics for the treatments of non-communicable diseases - such as cancer, diabetes, cardiovascular and neuropsychiatric conditions - tight budgets for welfare spending will create an increasingly tough environment for these drugmakers.

From November 1 2019, Spain’s Ministry of Health implemented a price reduction across 16,454 medicines. These price cuts will impact prescription (pharmacy and hospital setting) and OTC medicines, which are expected to reduce public expenditure on medicines by USD129mn a year.

Despite hospital dispensed drugs making up just 22% (2,985) of the medicines subject to the price cuts, they make up 67% (USD87mn) of the expected savings. This indicates that manufacturers of high-value medicines will disproportionately bear the brunt of the cuts through reduced revenue. A further third in savings USD43mn is expected across pharmacy dispensed medicines. Within the savings outlined above, there is expected to be a USD6mn direct impact on out of pocket spending.

According to r Disease Database, chronic diseases such as malignant neoplasms and neuropsychiatric conditions place a high burden on Spain's healthcare services and can be partly attributed to the country's high pensionable population. Ischemic heart disease is the leading cause of death in the country, responsible for around 16% of all deaths.

The leading local pharmaceutical companies in terms of market capitalisation include Almirall and Esteve. Most of the leading multinationals have a direct presence in the country including Pfizer, Sanofi-Aventis, Novartis, GlaxoSmithKline and Merck & Co, which are all prominent players in Spain. Other multinationals include AstraZeneca, Johnson & Johnson and Eli Lilly



Generic Drug market

Measures to improve access to generics in Spain, a country that lags behind others in the EU for generic penetration, will lead to an increase in purchasing power at both the individual and state levels. Spanish generic manufacturers will be able to take advantage of the European Commission's proposed supplementary protection certificate waiver, the effect of which will be increased R&D expertise in Spain, potentially improving the economy and reducing the country's drug cost burden. Generic drugs' share of the overall market value will increase significantly over the next 10 years

Generic drug sales accounted for 14.3% of the total drug market in 2019. Generic market was worth USD 4.31bn in 2019 and is expected to negatively grow by 2.5% in 2019, and reach USD4.22bn(Due to price Revisions as explained above). By 2024, forecasts say the market will be worth USD5.51bn, equating to a compound annual growth rate (CAGR) of 5%

The Spanish generic medicines market is small in comparison to other European nations. Government is focused on the generic medicines market to create cost savings. Factors of the price pressure placed on off-patent medicines, as well as the different approach to generic medicines across the country's 17 autonomous regions, some of which offer little incentive for prescribing generic drugs may not help generic forecasts to be met. Other factors include the lack of an accelerated drug registration procedure for generic medicines, insufficient training for pharmacists, negative attitudes towards generic medicines among physicians and anti-competitive practices by patented drug companies. Further price cuts, which is in the offing, on Generic medicines may also be an increased pressure on generic industry.

Pharma Trade Forecast

Spain like many other countries has a negative pharmaceutical trade balance. In 2019, it has imported medicines worth USD14.9bn and exported medicines worth USD11.3bn. Forecasts show that pharmaceutical imports will post a five-year compound annual growth rate (CAGR) of 3.6% to reach USD17.8bn by 2024. while pharmaceutical exports will grow to USD14.0n by 2024 with a CAGR of 4.4%.

According to latest UN Comtrade data, the leading countries of origin for Spanish imports were the US, Germany, Belgium & Switzerland in 2018, with the USA accounting for 21% of the total value. Pharmaceutical products are Spain's fifth largest import group, accounting for 4.6% of total imports.

In 2018, Leading export destinations in the same year included Switzerland, Germany, France, the USA and Italy.

Local Generic Industry

The Spanish Generic Medicine Association (AESEG) is the official generic pharmaceutical industry representative body in Spain. The 27 core members of AESEG represent around 96% of the Spanish generic drug market in value terms. Activity in the underdeveloped generics sector has increased, with strong interest from established local manufacturers. Local companies do not have any international presence.

Indian Companies Dr. Reddy's & Ranbaxy has significant presence. The former has a collaboration with Spanish company Pharma Iberia while the later has acquired some generics earlier marketed by a Spanish company named Efarmes. As mentioned earlier Vivimed labs has wholly owned subsidiary in Uquifa, an API manufacturer.

Statistics:

India's Exports

India Pharma exports to SPAIN by Category $ Million					
Category	2015-16	2016-17	2017-18	2018-19	Change%
Bulk Drugs & Drug Intermediates	76.44	67.70	75.30	95.01	26.18
Drug Formulations & Biologicals	37.41	33.59	39.11	49.10	25.53
Ayush	2.09	1.18	2.31	2.53	9.90
Herbal Products	2.12	2.45	2.61	2.80	7.08
surgicals	16.28	18.94	22.10	21.85	-1.14
Vaccines	0.15	0.24	0.03	0.02	-39.34
Total	134.49	124.08	141.45	171.30	21.10

India's Pharma exports to Spain During April-March $ Million			
Category	Fy-19	Fy-20	Change%
Bulk Drugs & Drug Intermediates	95.13	90.25	-5.14
Drug formulations & Biologicals	48.42	57.19	18.09
Ayush	2.53	2.69	6.30
Herbal Products	2.80	3.28	17.27
surgicals	22.61	18.03	-20.25
Vaccines	0.02	0.00	-99.62
Total	171.51	171.44	-0.04

In spite of Local Generic market has grown only be 1.14% in 2019 India's Generic exports has grown over 18%.

Imports of Spain

Spain's Top ten formulation Importing partners $ Million						
Rank	**Country**	**2016**	**2017**	**2018**	**Gr%**	**Share%**
1	USA	3215.38	2926.42	2941.88	0.53	18.64
2	Germany	2232.03	2161.22	2759.72	27.69	17.49
7	United Kingdom	920.12	880.29	1602.48	82.04	10.15
4	Switzerland	1363.81	1211.62	1388.96	14.64	8.80
5	Netherlands	966.48	1032.01	1358.02	31.59	8.60
6	France	804.17	964.7	1273.48	32.01	8.07
3	Belgium	898.32	1314.29	903.32	-31.27	5.72
8	Italy	524.34	615.97	839.21	36.24	5.32
9	Ireland	692.16	604.37	728.58	20.55	4.62
10	Other Europe, nes	489.28	452.75	720.52	59.14	4.57
16	India	68.12	75.99	102.04	34.28	0.65
	World	13970.51	14001.36	15782.49	12.72	100.00
Source: UN comtrade						

REGISTRATION AND REGULATORY REQUIREMENTS

➢	Regulatory Authority	:	**Spanish Agency for Medicines and Healthcare Products (AEMPS) / European Medicines Agency (EMA)**
➢	Website of regulatory Authority	:	https://www.aemps.gob.es/ https://www.aemps.gob.es/la-aemps/quienes-somos/?lang=en http://www.ema.europa.eu/
➢	Fees for Drug Registration	:	8.603,75 € for Generic Application
➢	Normal time taken for registration	:	12 - 18 Months
➢	Registration Requirement [Dossier Format]	:	e-CTD
➢	Whether plant inspection is mandatory	:	Yes

Regulatory Overview:

The main regulatory authority is the Spanish Medicines and Health Products Agency (Agencia Española de Medicamentos y Productos Sanitarios, or AEMPS). The basis for market regulation is the EU Directives 65/65/EEC, 75/318/EEC and 75/319/EEC. Processing times for marketing authorisation are estimated to range between six and seven months in most instances through EU. However, in Spain it is found to take 14 months for registration and is said to be the longest span in the region.

According to AEMPS, approximately 1,800 new authorizations are granted each year

Generic Medicines Regulation

Under EU law, generic drugs cannot be marketed until ten years after the date of the initial authorization of the reference medicinal product, or 11 years if a new indication was approved during the first eight years. It takes a little longer time to get an authorization in case of Spain.

Pricing Regulation:

Industry players, led by the AESEG, have been calling for a change in Spain's reference pricing system and believes that the downward pressure on the cost of medicines has slowed the development of the non-patented drugs market. Generic drug manufacturers are reluctant to market their medicines in the country as they cannot compete with the low prices of the off-patent originator products. The association has also called for an increase in the training provided to physicians in order to overcome stereotypes that prevent the prescription and dispensing of generic medicines.

Additionally, while the new reference pricing scheme will have a negative impact on the Spanish market,critics note that longer term price erosion in the country has the potential to affect market conditions across Europe, especially as Spain is often included in the basket of countries used to determine prices in other European countries, including Greece and Portugal.

EMA Organization:

The European Medicines Agency (EMA) is a decentralised agency of the European Union (EU), located in London and will relocate to Amsterdam. The Agency is responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU.

EMA protects public and animal health in 28 EU Member States, as well as the countries of the European Economic Area, by ensuring that all medicines available on the EU market are safe, effective and of high quality.

EMAs activities:

Facilitate development and access to medicines

EMA is committed to enabling timely patient access to new medicines, and plays a vital role in supporting medicine development for the benefit of patients. The Agency uses a wide range of regulatory mechanisms to achieve these aims, which are continuously reviewed and improved. They are

- Support for early access;
- Scientific advice and protocol assistance;
- Paediatric procedures;
- Scientific support for advanced-therapy medicines;
- Orphan designation of medicines for rare diseases;
- Scientific guidelines on requirements for the quality, safety and efficacy testing of medicines;
- The Innovation Task Force, a forum for early dialogue with applicants.

EMA also plays a role in supporting research and innovation in the pharmaceutical sector, and promotes innovation and development of new medicines by European micro-, small- and medium sized-enterprises.

Evaluate applications for Marketing Authorisation

EMA's scientific committees provide independent recommendations on medicines for human and veterinary use, based on a comprehensive **scientific evaluation of data**.

The Agency's evaluations of marketing-authorisation applications submitted through the **centralised procedure** provide the basis for the authorisation of medicines in Europe.

They also underpin important decisions about medicines marketed in Europe, referred to EMA through referral procedures. EMA coordinates inspections in connection with the assessment of marketing-authorisation applications or matters referred to its committees.

Monitor the safety of medicines across their lifecycle

EMA continuously monitors and supervises the safety of medicines that have been authorised in the EU, to ensure that their benefits outweigh their risks. The Agency works by:

- Developing guidelines and setting standards;
- Coordinating the monitoring of pharmaceutical companies' compliance with their pharmacovigilance obligations;
- Contributing to international pharmacovigilance activities with authorities outside the EU;
- Informing the public on the safety of medicines and cooperating with external parties, in particular representatives of patients and healthcare professionals.

Provide information to healthcare professionals and patients

The Agency publishes clear and impartial information about medicines and their approved uses. This includes public versions of scientific assessment reports and summaries written in lay language.

agencia española de medicamentos y productos sanitarios

Spanish Agency for Medicines and Healthcare Products (AEMPS)

AEMPS, as a state agency attached to the Ministry of Health, Consumer Affairs and Social Welfare, is responsible for guaranteeing to society, from a public service perspective, the quality, safety, efficacy and correct information of medicines and medical devices, from their research to their use, in the interests of the protection and promotion of human health, animal health and the environment.

The activities of AEMPS:

- The evaluation and authorisation of medicinal products for human and veterinary use.
- Authorization of clinical trials with medicines and authorization of clinical research with medical devices.
- Continuous monitoring of the safety and efficacy of medicines once marketed and quality control.
- The authorisation or registration actions as well as the inspection of pharmaceutical laboratories and manufacturers of active substances.
- Monitoring the supply and supply of medicines.
- State inspection and control functions and responsibilities for Narcotics and Psychotropic substances.
- The fight against Illegal and Counterfeit medicines, Medical Devices and Cosmetics.

- Certification, control and monitoring of Medical Devices.
- Monitoring the safety of Cosmetics and Personal care products.
- Information on everything that has to do with these aspects to citizens and healthcare professionals.
- The elaboration of the regulations that facilitate the fulfilment of its functions.

The Agency also has scientific committees and coordination committees specialized in the main areas of intervention.

Scientific committees are advisory bodies that ensure transparency and independence in AEMPS's actions. These are bodies of a mixed nature, with the participation of AEMPS leaders and other renowned experts as well as representatives of consumer associations and users or professional associations of doctors, pharmacists or veterinarians.

There are also AEMPS coordination committees with the authorities of the autonomous communities and with peripheral pharmaceutical inspection services.

One of the strengths of AEMPS is undoubtedly the interaction with the excellent professionals of the National Health System and Spanish universities, through the AEMPS Expert Network, which provides scientific and clinical advice in specific areas of knowledge.

Mission

Provide guarantees to society on medicines, sanitary products, cosmetics and personal care products, promoting scientific-technical knowledge and putting it at the service of society for its benefit and progress.

Vision

To be the reference health authority for citizens and health professionals in terms of quality assurances, safety, efficacy, information and accessibility of medicines, sanitary products, cosmetics, and personal care products.

REGISTRATION OF MEDICINES IN SPAIN

Medications are regulated throughout their life cycle. All medicines used in Spain must have a marketing authorisation granted by AEMPS once it has positively assessed its quality, safety and efficacy, and any variation that occurs must also be authorised or notified to AEMPS. These evaluations ensure that a positive relationship between the benefit and risk of the drug is maintained throughout its life cycle in the market.

AEMPS-regulated medicines include products as diverse as chemical or biotech-related drugs, blood products, vaccines, plant-based medicines, homeopathic medicines, radiopharmaceuticals or cell therapies.

To find out whether a drug is authorized, you can consult the AEMPS Online Drug Information Centre (CIMA), available on the Internet www.aemps.gob.es, which provides a permanently up-to-date information on all medicines authorized by AEMPS.

Marketing Authorization

o medicine may be placed on the market in Spain without the prior authorisation of AeMPS or the European Commission.

The marketing authorisation is granted on the basis of scientific criteria on the quality, safety and efficacy of the medicinal product concerned. These three criteria allow to assess the relationship between the benefits and risks of the drug for diseases and situations for which it is approved.

For years, there have been common technical criteria in the European Union for the evaluation and authorisation of medicines.

This allows for European-wide authorisation procedures and for medicines to be eligible for a national authorisation valid for a single country or to an authorisation valid for more countries within the European Union by increasing the effectiveness and efficiency of the network of European medicines agencies.

After authorisation, the medicinal product is subject to constant monitoring of developments in risks and new uses, so that such authorisation can be reviewed at any time. Any changes that you want to introduce into a medicine once authorised must be evaluated following the same procedure as your original authorisation.

Authorization Procedures

National Procedure: The applicant submits to AEMPS the dossier with all the information for the marketing authorisation of the medicinal product in Spain.

Decentralized Procedure. The applicant submits his application for authorisation simultaneously in several countries of the European Union. The different agencies evaluate the medicine in a coordinated manner, acting as a coordinating or reference agency and, at the end of the process, all agencies issue an identical and valid authorization for their territory of competence.

Mutual Recognition procedure: It is used when a medicinal product already has a Community marketing authorisation. The holder of that authorisation may submit an application for recognition of it in other Member States of the EUC and to communicate that particular both to the Member State which granted the authorisation (Member State of reference) and to the European Medicines Agency. The Member State of reference forwards the evaluation report of the medicinal product to the States concerned who recognise, where appropriate, the initial marketing authorisation.

Centralized Procedure: The applicant opts for an authorisation for all Member States of the European Union at the same time. In this case, the administrative process rests with the European Medicines Agency and scientific assessments are undertaken by two Member States (rapporteur and co-rapporteur), which send their reports to the other Member States. a scientific committee, which is up to the European Medicines Agency, is responsible for preparing the European Medicines Agency's opinions on any issues relating to the evaluation of medicinal

products. once a positive technical opinion has been issued, it is the European Commission which grants the applicant the marketing authorisation valid for the whole European Union.

Of the 1,800 new annual drug authorisations in Spain, 55% follow decentralised or mutual recognition procedures, 33% follow the national procedure, and around 12% the centralized procedure.

In all procedures the same evaluation equipment acts and the same technical criteria are used.

Authorization Dossier:

Once the research stages of the medicinal product have been successfully completed, in order to market a medicinal product, it is necessary to apply for an authorisation by providing in a dossier all the results of the investigation on the drug, the data on its manufacture, a risk management plan and, in general, all documentation demonstrating compliance with all the requirements necessary for its authorisation.

During the evaluation process, AEMPS reviews the available data from both the preclinical phase and clinical trials and information on its manufacture and chemical and pharmaceutical controls, and may test the medicinal product, its raw materials or intermediate product in the official control laboratories of the agency itself or to inspect the facilities where the medicinal product concerned or its active ingredients are manufactured.

When the evaluation of a medicinal product is concluded favourably, a marketing authorisation is issued which includes the conditions laid down by AEMPS for proper use (dose, precautions, contraindications,). These conditions are contained in the information on the use of the medicinal product for healthcare professionals (available in the data sheet) and patients (in the package leaflet for each medicinal product).

The Data Sheet, the Package Leaflet and the Public Evaluation Report:

From the evaluation of all the information that exists on the medicine, the AEMPS develop three documents intended to inform on its use: the data sheet, the package leaflet and the public evaluation report.

The data sheet is the document authorized by AEMPS which reflects the conditions of use authorized for the medicinal product (indications, posology, precautions, contraindications, adverse reactions, use under special conditions) and collects the scientific information essential for doctors and other healthcare professionals (summary clinical data, pharmacological properties or preclinical safety data).

The package leaflet is the written information that accompanies the medicine, addressed to the patient or user. It includes its complete composition and contains instructions for administration, employment and conservation; the package leaflet also specifies the adverse effects of the medicinal product, its interactions and contraindications, all in order to achieve its correct use

and compliance with the prescribed treatment. It is clearly and understandably worded to enable patients and users to act appropriately, when necessary with the help of healthcare professionals.

AEMPS also publishes the public assessment report for each medicinal product for human use that it has authorised since March 2013. These reports have all the scientific information that has been assessed by AEMPS to give a marketing authorisation including, for example, the clinical or bioequivalence studies that have been submitted by the holder. This information is displayed at the AEMPS Online Drug Information Centre, CIMA next to the package leaflet and the smpc.

Texts and other characteristics of the labelling and the package leaflet require authorization from AEMPS.

Any modifications to the data sheet and the package leaflet are also evaluated and authorized by AEMPS and all are available, with their latest updates, on their website within the AEMPS Online Drug Information Centre, CIMA.

Centralised Authorisation Procedure/Community Procedure

Under the centralised authorisation procedure, pharmaceutical companies submit a single marketing authorisation application to EMA.

This allows the marketing-authorisation holder to market the medicine and make it available to patients and healthcare professionals throughout the EU on the basis of a single marketing authorisation.

EMA's Committee for Medicinal products for Human Use (CHMP) or Committee for Medicinal products for Veterinary Use (CVMP) carry out a scientific assessment of the application and give a recommendation on whether the medicine should be marketed or not.

Each European Member State has a representative in the CHMP and an alternate. The members of the CHMP are acting in their personal capacity. They act as intermediaries between European and national systems. The CHMP, two rapporteurs, following the product during its entire life cycle, are appointed for each drug. If new request, the CHMP maximum of 210 days to reach a final evaluation. This period can be interrupted to allow the firm to answer questions. There is also the possibility for a firm to give oral explanations on the submitted file. The CHMP final evaluation, the "Opinion", is sent to the European Commission for final decision-making. In case of positive evaluation, the Summary of Product Characteristics (SPC) and the package leaflet are established. A European Public Assessment Report (EPAR: European Public Assessment Report) is made in which any positive or negative opinion is justified. The EPAR (link is external) is published on the EMA website.

After a positive decision, the applicant receives European authorization on the market (AMM), which carries a number that is valid in every Member State of the EU and EEA.

Scope of the centralised authorisation procedure

The centralized procedure is **compulsory** for:

- Human medicines containing a new active substance to treat:
  - HIV or AIDS; Cancer; Diabetes; Neurodegenerative diseases; Auto-immune and other immune dysfunctions &Viral diseases.
- Medicines derived from biotechnology processes, such as genetic engineering.
- Advanced therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines;
- Orphan medicines (medicines for rare diseases);
- Veterinary medicines for use as growth or yield enhancers.

It is **optional** for other medicines:

- Containing new active substances for indications other than those stated above;
- That are a significant therapeutic, scientific or technical innovation;
- Whose authorization would be in the interest of public or animal health at EU level.

Steps involved in obtaining an EU Marketing Authorisation

Submission of eligibility request

18 to 7 months before submission of marketing authorisation application(MAA)
To find out whether a product can be evaluated under the centralized procedure, applicants should always submit an **eligibility request** using the specific form and accompanied by a justification

Notification of intention to submit an application

7 months before submission of MAA
Applicants should consider the date of submission carefully, referring to the published submission dates and the guidance below: Best practice guide on measures improving predictability of submissions/responses and adherence to communicated submission/responses deadlines To notify the Agency of the intended submission date, they should email the pre-submission request form (intent to submit MA) to pa-bus@ema.europa.eu. The selected scope of request should be: 'Centralized Procedure – Intent to submit a MAA'

Appointment of rapporteurs

7 months before submission of MAA
The Committee for Medicinal Products for Human Use (CHMP) and the Pharmacovigilance Risk Assessment Committee (PRAC) appoints (co-)rapporteurs to conduct the scientific assessment.

For advanced therapy medicinal products, (co-)rapporteurs are also appointed from members of the Committee for Advanced Therapies (CAT), who will lead the assessment.

Pre-submission meetings

6 to 7 months before submission of MAA

Pre-submission meetings are the best opportunity for applicants to obtain procedural and regulatory advice from the Agency:

Marketing authorisation application pre-submission meeting request form

Successful pre-submission meetings along with the information in the guidance should enable applicants to submit applications in line with legal and regulatory requirements. This speeds up the validation process.

Re-confirmation of communicated submission date

2-3 months before submission of MAA

Applicants should re-confirm the submission date initially communicated to EMA, or inform EMA of any delays or cancellations, following the guidance below:

Best practice guide on measures improving predictability of submissions/responses and adherence to communicated submission/responses deadlines

If the planned submission date is changed, applicants must inform EMA by re-sending the completed pre-submission request form to pa-bus@ema.europa.eu, selecting 'notification of change' as the scope of the request and stating the new intended submission date in the corresponding field.

Holding successful pre-submission meetings and following this guidance should enable applicants to submit applications in line with legal and regulatory requirements, speeding up the validation process.

Submission and validation of the application

Applicants should use the electronic common technical document (eCTD) format and submit the application through the eSubmission gateway or web client.

If the Agency needs additional information to complete its validation of the application, it will ask the applicant to supply this by a deadline. For more information: check What is eSubmission?

Scientific evaluation

Up to 210 active days of assessment

The CHMP evaluates MAA submitted through the centralised procedure. The PRAC provides input on aspects related to risk management and the CAT on advanced therapy medicines.

CHMP Scientific Opinion

After the evaluation, the CHMP must issue a scientific opinion on whether the medicine may be authorized or not.

EMA sends this opinion to the European Commission, which issues the marketing authorization. The Agency then publishes a summary of the committee's opinion.

European Commission decision

Within 67 days of receipt of CHMP opinion
Commission decisions are published in the Community Register of medicinal products for human use and EMA publishes a European public assessment report (EPAR). When a new marketing authorisation application is refused, the Agency publishes a refusal EPAR, including a question and answer document and an assessment report.

Please check the pre-authorisation guidance for detailed guidance for submission of applications.

Mutual Recognition procedure & Decentralized Procedure

Today, **the great majority of new, innovative medicines** pass through the centralized authorization procedure in order to be marketed in the EU.

If a company wishes to request marketing authorisation in several EU Member States for a medicine that is outside the scope of the centralised procedure, it may use one of the following routes:

- **The Mutual-Recognition Procedure (MRP)**: Whereby a marketing authorisation granted in one Member State can be recognised in other EU countries;

- **The Decentralised Procedure (DCP)**: whereby a medicine that has not yet been authorised in the EU can be simultaneously authorised in several EU Member States.

Please refer Best Practice Guide for the Decentralised and Mutual Recognition Procedures *(February 2020)*

Mutual-Recognition Procedure (MRP):

- Under MRP, the assessment and marketing authorisation of one Member State ("Reference Member State (RMS)") should be "mutually recognised" by other "Concerned Member States (CMS)". Since the introduction of the DCP, the MRP is mainly used for extending the existing marketing authorisation to other countries in what is known as the "repeat use" procedure.

- The pharmaceutical company submits their application to the country chosen to carry out the assessment work, which then approves or rejects the application. The other countries have to decide within 90 days whether they approve or reject the decision made by the original country (RMS).

- Two groups are working for the facilitation of the Mutual Recognition Procedure:

  - ✓ **CMD(h)** (Coordination Group for Mutual recognition and Decentralised procedures (human)) - For human medicinal products.

- ✓ **CMD(v)** (Coordination Group for mutual recognition and Decentralised procedures
  (veterinary))- For veterinary medicinal products.

- If a member state cannot approve the assessment report, the summary of product characteristics, the labelling and the package leaflet on grounds of potential serious risk to human and animal health or to the environment, a pre referral procedure should be issued by the relevant Co-ordination Group.

- If the Member State(s) fail to reach an agreement during the 60-day procedure of the pre-referral, a referral to the CHMP/CVMP for arbitration may be made through its secretariat at the EMEA

Repeat Use Procedure (RUP)

One can use the mutual recognition procedure more than once to add more member states to a mutually-recognized license – this is known as a repeat-use procedure. The process for repeat use is identical to the first mutual recognition procedure.

Decentralized Procedure (DCP):

- It is applicable in cases where an authorisation does not yet exist in any of the EU Member States.

- Identical dossiers are submitted in all Member States where a marketing authorisation is sought. A Reference Member State, selected by the applicant, will prepare draft assessment documents and send them to the Concerned Member States.

- They, in turn, will either approve the assessment or the application will continue into arbitration procedures.

- The new Decentralised Procedure involves Concerned Member States at an earlier stage of the evaluation than under the MRP in an effort to minimise disagreements and to facilitate the application for marketing authorisation in as many markets as possible.

- The applicant may request one or more concerned Member State(s) to approve a draft assessment report, summary of product characteristics, labelling and package leaflet as proposed by the chosen reference Member State in 210 days.

Common Technical Document:

An application for authorization to place a medicinal product for human use on the market must be submitted in CTD format. This is described in Annex I of the Royal Decree of 14/12/2006 on medicinal products for human and veterinary use and in the Annex to the European Directive 2001/83 /EC http: //ec.europa .eu / enterprise / pharmaceuticals / eudralex / vol1_ en.htm

The CTD format includes 5 modules that are identical for all EU Member States. The exact structure of the format is described in part 2B of the Eudralex collection, published by the European Commission http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol2_en.htm .

In this volume, you will find references to European and international guidelines on the scientific content of a dossier and a question and answer document on the practical use of this format in the European Union.

Modules 2 to 5 are identical for the European Union, the United States and Japan. More information can be found on the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceutical Human Use (ICH) website: http://www.ich.org

Technical Validation:

Your file is validated to check if all the documents required by the law are in conformity and present. Some points of attention:

- Further information on the legal basis and the guidelines for medicinal products for human use: http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm
- The CMDh has published guidelines related to validation: http://www.hma.eu/91.html
- You can also find the requirements regarding the number of copies, the format, the language used, the samples on the CMDh website; http://www.hma.eu/91.html

Parallel Import and Deployment

Parallel imported medicines are drugs, registered and regularly on the market in a State of the European Union or the European Economic Area, for which AIFA, at the request of the importer, if there is a similar medicine on the market Italian, authorizes the import into our country.

The parallel import medicine has the same therapeutic effects and the same safety of use as the medicine authorized in Italy. The Summary of Product Features and the Parallel Import Medicine Illustration Sheet correspond to those of the medicine already authorized in Italy. Information about the owner and number of the AIC, the manufacturer, as well as, in some cases, the name and information on "How to store the medicine" and "Contents of the package and other information" may be different, including for the composition of the excipients. Parallel imported medicines have the instructions of the product and the importer on the outer packaging and in the Illustrative Sheet.

Parallel import of authorised drugs by national procedure, mutual recognition and decentralized Medicines of parallel import must have a valid AIC issued by the competent authority of the country of origin and be identical or similar to a product that has already received the AIC in Italy. The AIFA issues the Parallel Import Authorization (AIP), in a "simplified" procedure, by assigning a specific AIC code for the individual package to be imported, following the verification of the requirements of the legislation. To submit an AIP request, you must have a SIS code (identification code within the Healthcare Information System assigned by AIFA at the request of the company) and not be the AIC owner of the Italian reference product or company affiliated with it.

Parallel import applications (AIPs, changes to IPPs, renewals) are subject to a fee. Importers must also pay an annual right for each medicine with AIC in the process of being valid.

Parallel distribution of authorized drugs with centralized procedure

For authorized drugs with a centralized procedure, the evaluation of a parallel distribution application is conducted by the EMA. If successful, the EMA issues the importer with a Notice for Parallel Distribution indicating the country of origin and the country of origin (which can be more than one).

AIFA, at the request of the importer, verifies the EMA's authorization and assigns national identification data (description of the medicine to be imported, identification number, classification for reimbursement and supply).

Additional regulatory approvals

The Parallel Import Authorization is issued on the basis of the dossier submitted, except for the possession of additional regulatory authorizations:

- Authorization for the wholesale distribution of medicines issued by the autonomous regions and provinces, or by the relevant authorities identified by them;
- Authorizations issued by the relevant offices of the Ministry of Health, as in the case of drugs based on drugs or psychotropic substances.

Renewal:

In accordance with Article 9 of the Royal Decree of 3 July 1969 on the registration of medicinal products, the registration of a medicinal product was valid for 5 years and was renewable for a period of five years.

Any request for renewal of a national MA, granted either by the national procedure or by the MRP procedure, must be introduced at least 9 months before its expiry date The file should no longer include a periodic safety report, but should contain all the documents as described in Annex 3 of the "Best Practice Guide for Mutual Recognition and Decentralized Procedures"

Since 1 st January 2016 , the use of the electronic application form for the introduction of a renewal package of authorization on the market is required . This form is available at the following address: http://esubmission.ema.europa.eu/eaf/index.html.

EU Pharmaceutical legislation - Hierarchy

Regulation – Binding to all Member States (MS), no national changes allowed (e.g. Paediatric Regulation)

Directive – Results binding but method up to MS, local interpretation (e.g. Clinical Trials Directive)

Guidelines – Interpretation of requirements, recommended but not binding (e.g. "Guideline on the readability of the labelling and package leaflet of medicinal products for human use")

Current Pharmaceutical Legislation

Directive 2001/83/EC - the core legislation governing the regulation of drugs in EU, provides the framework for regulation of medicines at national level

Regulation (EC) No 726/2004 – Sets out the centralised procedure

Legal basis for applications in the EU:

The following Articles of Directive 2001/83/EC gives the legal basis for various types of applications.

- Article 8(3) Full application i.e New Drug Application
- Generic, hybrid or similar biological applications - Article 10
  - Article 10a Well-established use application
  - Article 10b Fixed dose combination application
  - Article 10c Informed consent application
  - Article 10(1) Generic application
  - Article 10(3) Hybrid application
  - Article 10(4) Similar biological application

Article 8(3) - Full application:

For full applications according to Article 8(3) of Directive 2001/83/EC, the results of pharmaceutical tests (physico-chemical, biological or microbiological), pre-clinical tests (pharmacological and toxicological), and clinical trials need to be submitted.

Article 10 - Generic, hybrid or similar biological applications:

Generic applications: Article 10(1)

According to Article 10(1) of Directive 2001/83/EC, the applicant is not required to provide the results of pre-clinical tests and clinical trials if he can demonstrate that the medicinal product is a generic medicinal product of a reference medicinal product which is or has been authorised under Article 6 of Directive 2001/83/EC for not less than 8 years in a Member State or in the Community.

A generic medicinal product is defined as a medicinal product that has:

- Same qualitative and quantitative composition in active substances as the reference product,
- Same pharmaceutical form as the reference medicinal product and
- Whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

It should be noted that the period of **8 years** from initial authorisation of the reference medicinal product, providing a period of so-called "**data exclusivity**", only applies to those reference medicinal products for which the initial application for authorisation was submitted through the centralised procedure after 20 November 2005.

Hybrid applications: Article 10(3)

Hybrid applications under Article 10(3) of Directive 2001/83/EC differ from generic applications in that the results of appropriate pre-clinical tests and clinical trials will be necessary in the following three circumstances:

- Where the strict definition of a 'generic medicinal product' is not met;
- Where the bioavailability studies cannot be used to demonstrate bioequivalence;
- Where there are changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration of the generic product compared to the reference medicinal product.

These applications will thus rely in part on the results of pre-clinical tests and clinical trials for a reference product and in part on new data.

Similar biological application: Article 10(4)

In Article 10(4) of Directive 2001/83/EC it is stated that where a biological medicinal product which is similar to a reference biological product, does not meet the conditions in the definition of generic medicinal products, owing to, in particular, differences relating to raw materials or differences in manufacturing processes of the similar biological medicinal product and the reference biological medicinal product, the results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided.

Well-established use application: Article 10a

According to Article 10a of Directive 2001/83/EC, it is possible to replace results of preclinical and clinical trials by detailed references to published scientific literature (information available in the public domain) if it can be demonstrated that the active substances of a medicinal product havebeen in well-established medicinal use within the Community for at least 10 years, with recognised efficacy and an acceptable level of safety.

Applicants should submit Modules 1, 2 and 3. For Modules 4 and 5, a detailed scientific bibliography shall address all required pre-clinical and clinical characteristics, and should be summarised in Module 2.

It should be noted that, if well-known substances are used for entirely new therapeutic indications, it is not possible to solely refer to a well-established use and additional data on the new therapeutic indication together with appropriate pre-clinical and human safety data should be provided. In such case, Article 8(3) of Directive 2001/83/EC should be used as legal basis.

Fixed combination application- Article 10b

According to Article 10b of Directive 2001/83/EC, in the case of medicinal products containing active substances used in the composition of authorised medicinal products but not hitherto used in combination for therapeutic purposes, the results of new pre-clinical tests or new clinical trials relating to that combination shall be provided in accordance with Article 8(3)(i) of the same Directive, but it shall not be necessary to provide scientific references relating to each individual active substance.

The combination of active substances within a single pharmaceutical form of administration according to this provision is a so-called 'fixed combination'.

Applications for fixed combination medicinal products can be accepted and validated under Article 10b on condition that the individual substances have been authorised as a medicinal product in the EEA via a Community or national procedure.

A full dossier, comprising all the information of modules 1 to 5, has to be provided in relation to the fixed combination. Any absence of specific fixed combination data should be duly justified in the Non-clinical and/or clinical Overviews.

Informed consent application- Article 10c

According to Article 10c of Directive 2001/83/EC, following the granting of a marketing authorisation, the authorisation holder may allow use to be made of the pharmaceutical, non-clinical and clinical documentation contained in the dossier of the medicinal product for the purpose of examining subsequent applications relating to other medicinal products possessing the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form.

It is a prerequisite for the use of Article 10c as legal basis that consent has been obtained from the marketing authorisation holder of the reference product for all three modules containing the pharmaceutical, pre-clinical and clinical data (modules 3, 4 and 5), and the applicant of the informed consent application should have permanently access to this documentation or should be in possession of the information.

For such informed consent applications, only a complete module 1 should be submitted, including the Application Form with relevant Annexes (e.g. copy of correspondence with the European Commission for multiple applications, if applicable, and the letter of consent from the MAH of the authorised medicinal product allowing access to modules 2, 3, 4, 5 of the initial dossier and any subsequent documentation submitted)

If the dossier of the authorised medicinal product includes an ASMF, a new letter of access should be included in module 1 of the informed consent application.

Data Exclusivity, Market Protection and Paediatric Rewards

Data exclusivity: 08 Yrs

Period of time during which a Company cannot cross-refer to the data in support of another marketing authorisation, i.e.: generics, hybrids, biosimilars cannot be validated by the Agency

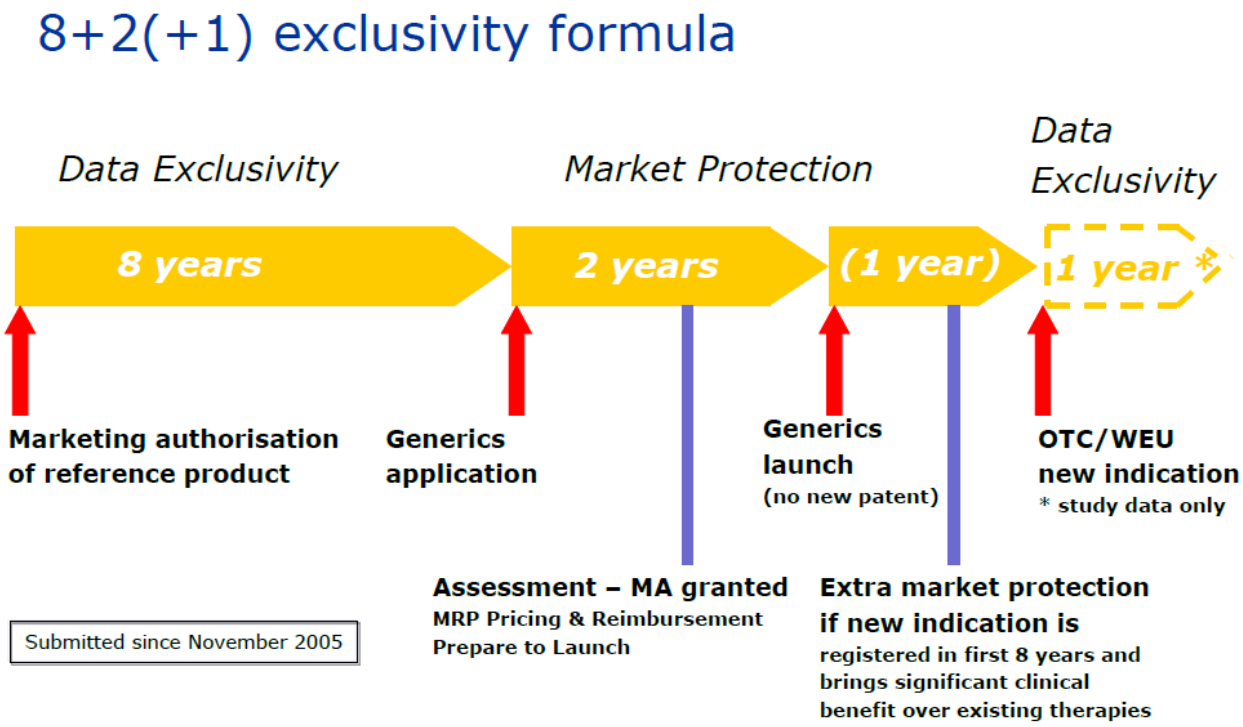
Market protection: 02 Yrs

Period of time during which a generic, hybrid or biosimilar cannot be placed on the market, even if the medicinal product has already received a marketing authorisation.

+1 year market protection for a new therapeutic indication which brings significant benefit in comparison with existing therapies (Art. 14(11) Reg. (EC) No 726/2004) - *For initial MAA and authorisation of new indication within 8 years*

+ 1 year data exclusivity for a new therapeutic indication for a well-established substance, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication *(Art. 10(5) Dir. 2001/83/EC) (=+1 WEU)*

+1 year data exclusivity for a change in classification of a medicinal product on the basis of significant pre-clinical tests or clinical trials *(Art. 74(a) Dir. 2001/83/EC) (=+1 OTC switch)*



Orphan Drugs: 10 Yrs Market Exclusivity

Orphan designation criteria

- Rarity of condition (< 5 in 10,000) or insufficient return on investment
- Seriousness of condition (Life threatening/chronically debilitating)
- Existence of satisfactory methods

Paediatric Exclusivity: **Six-month extension** to the product's SPC (Supplementary protection certificate)

Paediatric orphan Drugs: **12 Yrs Market Exclusivity**.

Paediatric Use Marketing Authorization (PUMA):

For products developed exclusively for use in the paediatric population

8 Yrs - Data Exclusivity and

10 Yrs - Marketing Exclusivity

VARIATIONS TO MARKET AUTHORIZATIONS:

A variation to the terms of a marketing authorization is an amendment to the contents of the documents of the approved dossier.

Variations are broadly categorized into Minor & Major.

- Minor Variations : Type IA
  Type IB
- Major Variation : Type II

Type IA variations:

Type IA variations are the minor variations which have **only a minimal impact or no impact at all**, on the quality, safety or efficacy of the medicinal product, and **do not require prior approval before implementation ("Do and Tell" procedure).** Such a minor variations are "classified" two subcategories, which impact on their submission:

A) Type lA variations requiring immediate notification ('IA IN'):

Type IA variations must be notified (submitted) immediately to the National Competent Authorities/European Medicines Agency ('the Agency') following implementation, in order to ensure the continuous supervision of the medicinal product.

Examples of Type IAIN variation:

- Change in the name and/or address of the marketing authorization holder
- Change in the name and/or address of a manufacturer/importer of the finished product (including batch release or quality control testing sites)
- Changes in imprints, bossing or other markings
- Change in the shape or dimensions of the pharmaceutical form particularly Immediate release tablets, capsules, suppositories and pessaries.

B) Type lA variations NOT requiring immediate notification ('IA'):

Variations which do not require immediate notification may be submitted by the marketing authorisation holder (MAH) within 12 months after implementation, or may be submitted earlier should this facilitate dossier life-cycle maintenance or when necessary.

Examples of Type IA variation:

- Addition of physico-chemical test in specification.
- Deletion of non-significant test (ex: Identification test in Stability study).
- Tightening of specification limits (ex: Tightening of test limit for water content, Residual solvents and Related substances..etc.
- CEP updates/renewal.
- API and FP Batch size increase/decrease within 10 fold.

For the national procedure, in the absence of opposition within 10 working days of receipt of a validated notification, the change may be applied. For the mutual recognition procedure, the approval period is set by the reference Member State (RMS).

The following national administrative variations are treated as variations of type IA (Article 34 §1 of the Royal Decree of 14.12.2006): a modification of the marketing authorization holder, a modification of the linguistic role and a modification of the wholesale distributor.

Type IB variations:

- Commission Regulation (EC) No 1234/2008 ('the Variations Regulation') defines a minor variation or Type 1B as a variation which is neither a Type lA variation nor Type II variation nor an Extension.
- Such minor variations must be notified to the National Competent Authority/European Medicines Agency by the Marketing Authorisation Holder (MAH) before implementation, but do not require a formal approval.
- However, the MAH must wait a period of 30 days to ensure that the
- Post-Authorisation procedural advice for users of the centralised procedure notification is acceptable by the Agency before implementing the change **(Tell, Wait and Do procedure).**

Examples of Type IB Variations

- Major change the approved Analytical method
- FP Mfg. site changes
- Shelf-life extension
- Change in storage condition
- Minor changes to approved manufacturing process
- Change in batch size beyond 10 fold category
- SmPC /PIL changes in-line with innovator product

For the national procedure, in the absence of opposition within 30 days of receipt of a validated notification, the change may be applied. For the mutual recognition procedure, the approval period is set by the reference Member State.

Type II variations:

Commission Regulation (EC) No 1234/2008 ('the Variations Regulation') defines a major variation of Type II as a variation which is not an extension of the Marketing Authorisation (line extension) and that may have a significant impact on the quality, safety or efficacy of a medicinal product.

Examples of Type II Variations

- Addition of alternate/new API DMF supplier
- Relaxation of approved specification
- Major change in approved manufacturing process
- Major change in approved composition

For the national procedure, a period of 60 days is provided for the examination of these applications. It can be extended to 90 days for changes regarding the change or addition of therapeutic indications. These deadlines may also be extended by 30 days if the Commission for Medicinal Products for Human Use (CMH) deems it necessary.

For the mutual recognition procedure, the approval period is set by the reference Member State.

National Modifications Type II of Module 3: Clarification of the evaluation strategy

Type II changes involving revision of sections 4.6, 5.3 and 6.6 of the SPC: Guidance (23/12/2011)

Clinical variations of type II in the national procedure "Out of scope comments" - v.2.2 (10/05/2012)

Readability User Testing

Since May 26, 2006, applications for a MA for medicinal products for human use must include the evidence and the result of the consultation of groups of patients with regard to the readability of the package leaflet (Article 6 (1d), fourth paragraph of the Law on medication). This consultation of patient groups can take place in any Member State and therefore also in any language. The report on the results of this consultation must be in one of the three national languages or in English.

For MA applications and MAs introduced or granted before 26 May 2006, the Royal Decree of 14 December 2006 (part 1 - part 2) provides for a transitional period of 5 years to comply with these provisions.

To help MAHs comply with these legal requirements, the FAMHP has drafted a Q & A document .

Extension of Market Authorizations:

Certain changes to a marketing authorization, however, have to be considered to fundamentally alter the terms of this authorization and therefore cannot be granted following a variation procedure. These changes are to be submitted as 'Extensions of marketing authorizations.
Three main categories of 'changes requiring an extension of marketing authorization:

- Changes to the active substance;
- Changes to the strength, pharmaceutical form and route of administration;
- Other changes specific to veterinary medicinal products to be administered to food-producing animals or change or addition of target species.

Detailed guidelines on variations/Extensions (European Medicines Agency post-authorisation procedural advice for users of the centralised procedure) can be identified @ http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500003981.pdf

Sunset Clause:

The so-called "sunset clause" is a provision leading to the cessation of the validity of the marketing authorization if:

- The medicinal product is not placed on the market within three years of the authorization being granted or,
- Where a medicinal product previously placed on the market is no longer actually present on the market for three consecutive years.

The European Commission may grant exemptions on public health grounds and in exceptional circumstances if duly justified.

Fees payable to the EMA for Marketing Authorizations through CP

Fee type	Human medicines	Veterinary medicines
Marketing-authorisation application (single strength, one pharmaceutical form, one presentation)	From €291,800	From €146,100
Extension of marketing authorisation (level I)	€87,600	€36,500
Type-II variation (major variation)	€87,600	€43,700
Scientific advice	From €43,700 to €87,600	From €14,400 to 43,700
Annual fee (level I)	€104,600	€35,000
Establishment of MRLs	-	€72,600

Full details on all fees and fee reductions are available in: Explanatory note on general fees payable to the EMA as of 1 April 2019.

Fees payable to the AEMPS

Fee for Medicines for Human Use

Type	Description	Euros
1.01	Fee for the evaluation, authorisation and registration of a new medicine for human use (application in accordance with article 17, with the exception of the provision in 17.3)	21.151,22
1.02	Fee for the evaluation, authorisation and registration of a new generic medicine for human use (application in accordance with article 17.3)	8.603,75
1.03	Fee for the evaluation, authorisation and registration of a new medicinal gas	8.603,75
1.04	Fee for changing the ownership of a marketing authorisation for a medicine for human use, or for changing the owner's representative	718,72
1.05	Fee for the variation of a marketing authorisation for medicines for human use, classified as of «major importance» Type II	7.265,4
1.06	Fee for the variation of a marketing authorisation for medicines for human use, classified as Type IB	1.274,33
1.07	Fee for the variation of a marketing authorisation for medicines for human use, classified as type IA (including those of type IA with immediate notification)	738,98
1.08	Fee for the renewal application for a medicine for human use	2.389,8
1.09	Annual fee for the maintenance of an already-authorised medicine for human use	381,21
1.10	Fee for the authorisation procedure for a parallel imported medicine for human use	923,65
1.11	Fee for the variation for a parallel imported medicine for human use	373,85
1.12	Fee for the renewal for a parallel imported medicine for human use	373,85
1.13	Fee for the notification of an imported medicine for human use	366,26
1.14	Fee for issuing an European certification for the batch release of vaccines and blood products for human use when the batch-analysis of a medicine is required	1.236,36
1.15a	Fee for the batch release of blood products and vaccines in accordance with articles 41.4 and 43.3 of Royal Decree 1345/2007, of 11th October: (a) each individual application	103,03

1.15b	Fee for the batch release of blood products and vaccines in accordance with articles 41.4 and 43.3 of Royal Decree 1345/2007, of 11th October: (b) between 6 and 10 applications/year (per year)	515,15
1.15c	Fee for the batch release of blood products and vaccines in accordance with articles 41.4 and 43.3 of Royal Decree 1345/2007, of 11th October: (c) between 11 and 40 applications/year (per year)	1.545,45
1.15d	Fee for the batch release of blood products and vaccines in accordance with articles 41.4 and 43.3 of Royal Decree 1345/2007, of 11th October: (d) between 41 and 160 applications/year (per year)	3.606,05
1.15e	Fee for the batch release of blood products and vaccines in accordance with articles 41.4 and 43.3 of Royal Decree 1345/2007, of 11th October: (e) for more than 160 applications/year (per year)	5.151,51
1.16	Fee for issuing an European certification for the batch release of vaccines and blood products for human use when a bulk-analysis is required (by bulk)	346,18
1.17	Fee for the evaluation of an application for a galenic innovation	1.003,82
1.18	Authorisation to export narcotic and psychotropic medicines to EU countries and third countries	175,15
1.19	Fee for the activities outlined in section 6 of article 11	373,85
1.20	Fee for reserving a slot to act as the Reference Member State in a Decentralised or Mutual Recognition Procedure	772,73

****

- **Details of importing country embassy in India:** http://www.exteriores.gob.es/
- **Contact details of Indian Embassy abroad:** https://www.eoimadrid.gov.in/

List of Local Pharma Associations:

- Farmaindustria (National Trade Association of the Spanish based pharmaceutical industry) https://www.farmaindustria.es/web_en/