White Paper

Launch Activities

2022

BlueReg

A ➤ PHARMALEX COMPANY

10 key requirements to launch your medicinal product in the EU

Introduction

BlueReg is well known for supporting companies through product registration and the launch phase. Not only are there specific steps required to turn the regulatory filing into a tangible product for supply and distribution but also this is happening usually when the client is transitioning from Research and Development to a commercial organization.

The EU defines an EU marketing authorization as one pan-European Marketing Authorization for the EU (30 countries) for which EU guidelines are applicable.

Nevertheless, the reality is not so straightforward as there are:

- **30 local variations due to mandatory local law/guidelines**
- **30 different local Health Agencies in addition to EMA**
- **30 different National Health Systems (NHS)**
- **25 languages**

For the UK:

The UK left formally the EU on 31st January 2020

- **In Practice:**
  - **Great Britain (GB) which represents England, Wales and Scotland**
    - **EU rules are no longer applicable**
    - **Medicines and Healthcare products Regulatory Agency (MHRA) guidelines/ recommendations must be followed**
  - **Northern Ireland (NI)**
    - **EU rules are applicable**
    - **NI can be considered as a European Member State**

Summary

01

Local Representatives

For regulatory affairs, local representatives can be mandatory in some countries. They are responsible for regulatory actions at the local level, such as the completion of local databases, obtaining the national code, blue box validation, etc... Many forms/databases must be completed in the local language. The qualification of the regulatory representative varies by country (specific qualifications e.g. a pharmacist in France). Finally, a notification to the local competent authority must be completed when required (Germany, France, Spain, Italy, etc).

Then for Pharmacovigilance, the Local pharmacovigilance officer works in conjunction with the EU Qualified Person Responsible For Pharmacovigilance (QPPV). He/She is Responsible for all national PV requirements / actions e.g. adverse event reporting, contact point for local approval of educational material etc. The officer will have to be fluent in local language. This qualification required varies by country, but generally must be able to demonstrate valid experience. Finally, a notification to the local competent authority must be undertaken when required.

Finally, for Scientific advices, responsibilities vary per market, but commonly may include responsibility for : review, approval and submission (when required) for promotional and non promotional materials (in-line with the approved MA); legal responsibility for some local activities and verification that sales representatives have been adequately trained. He/She will be required to be fluent in local language. A notification to the local competent authority must be undertaken when required.

02

National Codes

There are varying rules across Europe for national codes. They can be obtained after the CHMP positive opinion or after the EC decision (sometimes with the blue box validation). They will need to be requested at local level, using different forms / websites all in local language. The Timelines vary significantly between markets. The number of digits is defined by individual countries which enable identification of the product by the packaging. National codes can be linked to the National Health System. There are different local names (PZN, CIP code, PL number etc). Finally, they must be printed in the blue box when defined in the local regulations / laws.

Example in Germany:

- The **MAH** must first obtain the national numbers:

PNR ("Pharmazeutischer Unternehmernummer" – Pharmaceutical company number)

ENR ("Eingangsnummer beim BfArM" – BfArM submission number)

The **PNR** and **ENR** are obtained in less than 1 week

- Then the **PZN** (Pharmazentralnummer) forms must be completed in German (PNR and ENR are included in the forms)

The **PZN** is obtained in few days. Just before the commercialization, the **PZN** must be activated, a new local submission has to be completed by the local representative in a defined time frame.

03

Blue Box

The information specific to a Member State should be accommodated on the **label in a single blue boxed area** (the so-called 'blue box') to appear on one side of the pack. The Blue Box must be in compliance with "Guideline On The Packaging Information Of Medicinal Products For Human Use Authorised By The Union", version 14.4 dated December 2016. It should be presented in the local language/languages of each country.

Finally, with 1 box specific per country with different information stipulated (as example: at a minimum country + local national code for Nordics, Germany, Austria, and Northern Ireland and Acronyms, legal status, and symbols can also be required for France and Spain).

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Serialization

The Falsified Medicines Directive (FMD) 2011/62/EU came into force in February 2019. For all medicinal products subject to prescription which are not included in the list set out in Annex I to the directive. This is characterized by a Unique Identifier (UI) and an Anti-Tampering Device (ATD). All EU countries except Greece and Italy have until 2025 to implement the directive (for Italy: Bollino is already in place in line with local regulation and for Greece: EOF code is in place in line with local regulation).

The Unique Identifier (UI) is defined through four data lines and is also represented using the data matrix. For the product code, in countries where the national code is mandatory (AT, DE, ES, FR, and Nordics), the NTIN (National Trade Item Number) can be used. The national code is embedded in the product code. In countries where the national code is not mandatory, the GTIN is used. This number is assigned by (Global Standards 1) GS1. The serial number is assigned by the finished product manufacturer, a batch number, and expiry date.

Regarding the EU MAH to be registered in the EU Hub (EMVS European Medicines Verification System), the contract and fees must be paid only at the time of registration. **For the EU MAH to be registered in each EU country** where a local launch is planned (NMVS National Medicines Verification System), the contract and fees at a local level must be paid (fee due initially at registration then annually based on turnover). Finally, for **the EMVS and NMVS**, all submissions must be performed by someone from the MAH (with an email address linked to the MAH) the timelines are variable and careful planning required

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Local Databases

There are accessible to healthcare professionals (HCPs) and sometimes also to patients. There are some key points to consider. First, all the databases are in the local language. But there are different routes of registration :

1. **Automatic – Without MAH action**
   France : Public database at ANSM level
   UK : Public database at MHRA level

2. **Mandatory – With MAH action**
   Spain : Raefar
   Sweden : Liiv

3. **Recommended – With MAH action and fees**
   Germany : Rote Liste & FachinfoService
   France : Vidal
   Sweden : Fass

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Local launch Date Notification

The European marketing status must be submitted to the EMA and in addition, local actions may be required. There are two types of mandatory actions :

1. **Mandatory: Simple notification in the database (in local language) :**
   Sweden : to be completed 1 working day before the launch date
   Spain : to be undertaken a minimum of 15 days before the product commercialization

2. **Mandatory: Declaration to be submitted (in local language) :**
   France : form to be completed and submitted to the local Agency
   Germany : form to be completed and submitted to the local Agency approximately 3 weeks before the expected launch date

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Promotional Materials

EU countries have Local code/laws applicable per country for promotional materials. For instance, there are two main federations in the EU:

- **International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)**
  Global standards for the ethical promotion of pharmaceutical products to HCPs

- **European Federation of Pharmaceutical Industries and Associations (EFPIA)**
  European ethics rules for the promotion of medicinal products to HCPs
  Advertising of prescription-only medicines is limited to healthcare professionals
  Materials must be compliant with the approved Summary of Product Characteristics
  Information must be accurate, up to date and verifiable
  Product must be presented objectively and without exaggerating its properties

Local code/laws applicable per country

	Local law	Signatory	Submission to the Authority
Germany	Law on Advertising in the Health Sector (Heilmittelwerbegesetz - HWG), Law on the Trade in Medicinal Products (Arzneimittelgesetz - AMG) Act against Unfair Competition (Gesetz gegen den unlauteren Wettbewerb - UWG) which contains more general advertising rules	Information officer	Not applicable
France	Consumer Code (Code de la Consommation) Public Health Code (Code de la Sante Publique - CSP)	Responsible Pharmacist / Chief Pharmaceutical Officer	A «Visa» must be obtained from French Agency before any use. Careful planning required as only four submission slots per year
UK (GB and NI)	Blue Guide «Advertising and Promotion of Medicines in the UK» For prescription medicines: Code of Practice of the Association of the British Pharmaceutical Industry» (ABPI)	Qualified signatories to certify advertising material	Not required unless requested by MHRA («Vetting») for an agreed period / until notified no longer required

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Educational Materials

Educational materials can be requested by the EMA (as part of the RMP) during the assessment. The EMA approves the English version.

All the national competent authorities must approve the local version prior to dissemination. The local version must be translated into local language. Also, some additional local requirements must be added (such as blue hands for Germany). The Submissions are managed locally (and must be submitted by local PV representatives in some countries such as CZ and SK). Finally, the timelines are country-dependent (approval timelines vary from 1 month to 1 year, with an average approval received in approximately 4 to 6 months).

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Local Wholesale Distribution Authorization (WDA)

European WDA is required to distribute the product within the EU. A local WDA may also be required in some EU countries: France – under the "Exploitant" responsibility, Hungary, Sweden if there is a local warehouse, and UK

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Shared Pack and Stock Keeping Unit

Shared packs permitted to rationalize European SKUs. There is no specific guideline/law regarding the shared packs and SKUs. But there are things to be aware of, first, the layout of the outer packaging is validated by EMA during the registration procedure. Then, all the required information in local language (including the blue box) must be printed on the outer packaging. Also, All the serialization requirements must be followed. Finally, consideration needs to be given to the outer packaging size for readability for the patients / HCPs.

Typically, the main shared packs in Europe are often:

- BeNeLux
- Austria and Germany
- Iberia (Spain and Portugal)
- Baltics (Estonia, Lithuania, and Latvia)
- Nordics (Sweden, Finland, and Denmark or Sweden, Finland, and Norway)

Conclusion

Here you've learned what the key requirements for launching a medicinal product in the EU were. To support launch activity there must be a robust and comprehensive launch plan, involvement of stakeholders, and the manpower to support the varying tasks. BlueReg has templates to help with this, best practice from years of support, and inherent expertise. We are constantly referred by clients to their peers in the industry.

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Any questions? Contact-us!

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