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(REVIEW ARTICLE)

The European Union's current regulations for the licensing of generic and hybrid medications

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Abstract

In the European Union, the applicant must specify the legal justification for the application in any Marketing Authorization Application (MAA) for a pharmaceutical product. The dossier's content and the market exclusivity are significantly influenced by this legal foundation, which is outlined in Directive 2001/83/EC as modified. The right legal foundation must be chosen carefully for new development projects involving active chemicals that are already known, including novel strengths, dosage forms, administration methods, and indications. In accordance with Article 10 and the so-called "hybrid" and "generic" applications, this article describes the registration criteria and the procedure for obtaining a marketing authorization for applicants utilizing the Article 8(3) legal foundation.

Keywords: Hybrid medication; Generic medication; License of medications; European union regulations; European Medicine Agency

1. Introduction

The unique regulatory system of medicines has a net of 50 authorities from 28 EU member states along with Iceland, Liechtenstein and Norway (31 EEA countries), EMA and the EC.

The Member state and the European Medicine Agency depend on each other and interchange data of regulating medicines. They both collaborate and bring out information from the assessment of safety and new medications. The EU Member States wants to follows the same method of observation and authorisation of medications, so it is flexible to check on the producers regarding the compliance through good distribution practice (GDP), good clinical practice (GCP), good pharmacovigilance practice (GVP) and good manufacturing practice (GMP). Information Technology system in European Union unite all the parties in the net and simply the transfer of data for observation and authorisation of well-being of trials or compliance with good manufacturing and distribution practices.

2. Committee for Medicinal Products for Human Use (CHMP)

The CHMP plays a vital role in the authorisation of medicines in the European Union (EU). In the centralised procedure, the CHMP is responsible for:

- Conducting the initial assessment of EU-wide marketing authorisation applications;
- Assessing modifications or extensions ('variations') to an existing marketing authorisation;

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- Considering the recommendations of the Agency's Pharmacovigilance Risk Assessment Committee on the safety of medicines on the market and when necessary, recommending to the European Commission changes to a medicine's marketing authorisation, or its suspension or withdrawal from the market.

2.1. Marketing Authorization

Marketing authorisation is given to a medical product based on the decision of skillful expert with complete data of it in a dossier along with SmPC. It is given under three different terminologies under different conditions such as Fig. 1.

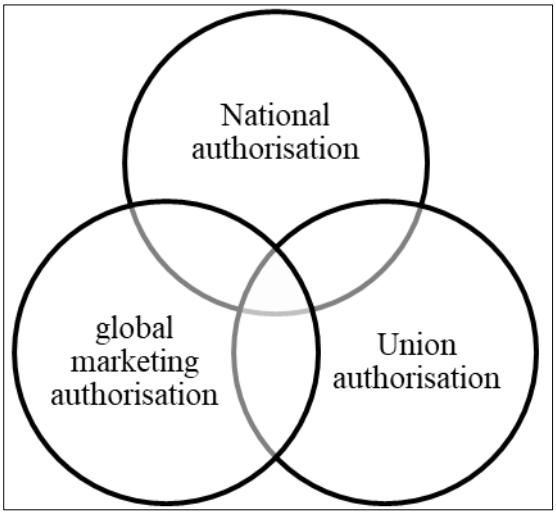

Figure 1 Types of marketing authorisation

Union authorisation is given for new medicinal product via centralised method. National authorisation is given using decentalised and mutual recognition method. The third global marketing authorisation is given under additional dose or dosage form of previously authorised and marketed medical product.

Renewal of MA is done every 5 years provided the application for the same must be submitter before 9 months of the expiry of MA along with the quality, efficacy and safety data of medical product.

Continuous updation of marketing authorisation of an approved medicinal product with the improved technical requirements, or any changes in regulatory guidelines or directives and pharmacovigilance data that must be carried out by the MAH;

Marketing Authorisation is the major step to market a medicinal product in European Member States. Different Marketing authorisation Application is available in EMA where the applicant must chose as per the requirement. There are 6 types of applications available in EMA to obtain marketing authorisation of medicinal products.

Applicant and MAH are considered as one when both are under same company or trade mark. If both are of different member state or company then as per the legal entity they work with an agreement. The legal experts of EMA must make sure that applicant and marketing authorisation holder who function with an agreement for same medicinal product [1].

2.2. Marketing Authorisation Applications

Directive 2001/83/EC give application details for marketing authorisation of medicinal products. Application based on Article 8(3) and Article 10 are discussed as they give data for new medical product, generic and hybrid drug applications

2.2.1. Applications based on Article 8(3) and Article 10

The application under Article 8(3) was previously known as a one application for new medicinal products, but this gives two types of applications. They are Stand-alone and Mixed application with specific document requirements.

The application under Article 10 is not only for generic/hybrid/ bio similar medical products additionally it gives general concepts such as detailed note on contents of Fig 2.

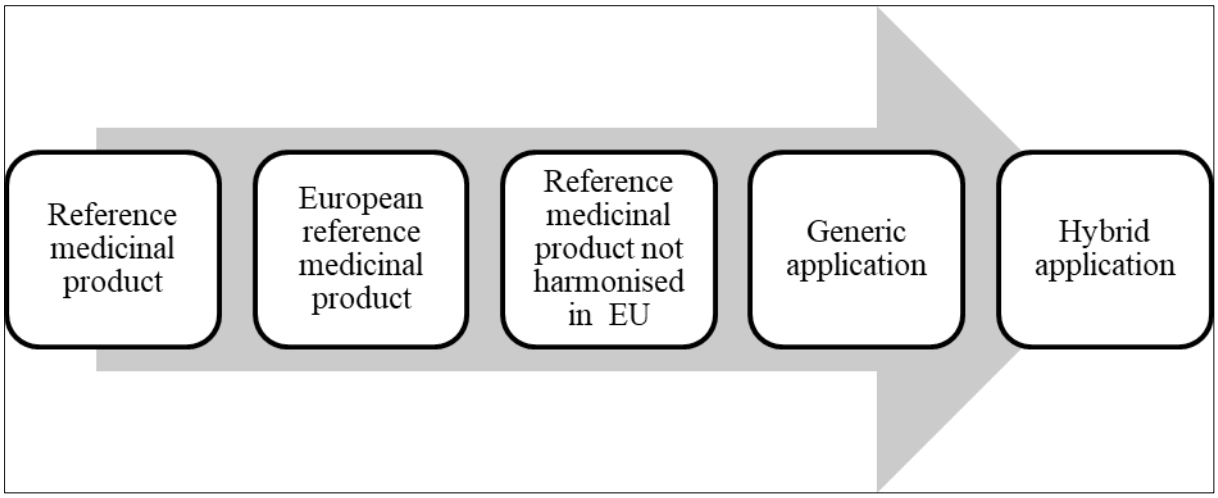

Figure 2 Article 10 based on Directive 2001/83/EC

2.3. Marketing Authorisation Procedures

There are 5 procedures for marketing authorisation such as Fig. 3.

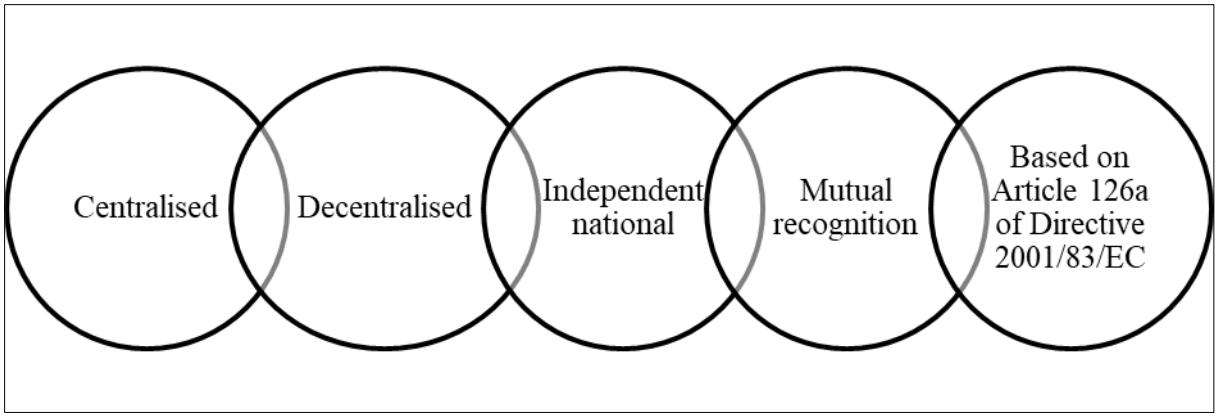

Figure 3 Marketing Authorisation Procedures

For generic and hybrid medicines centralised, decentralised or mutual recognition procedures are generally used; only under specific conditions the other two procedures are used to obtain a marketing approval. These 5 procedures have its positive and negative effect on the European Member States which is negligible because the positive results are higher than the negatives effects [2,3,4].

2.4. Generic and Hybrid Medicine

Generic and hybrid medicines are provided authorisation for marketing the product in EU Member States only using Centralised Procedure, even though the reference medical product is approved via any other procedure. This is possible by submitting the required condition satisfying documents to skillful experts in EMA.

Article 3 of 726/2004 Regulation and Article 6 of 2001/83/EC Directive gives the legal basis for both the hybrid and generic medicines.

For generic medicines rapporteur and co-rapporteur are employed 3-7 months prior to the Marketing Authorisation Application in the meeting of the CHMP team but the actual team is hired 2-6 months prior to the MAA.

For hybrid medicines rapporteur and co-rapporteur are employed 7 months prior to the Marketing Authorisation Application in the meeting of the CHMP team but the actual team is hired 6 months prior to the MAA.

The dossier is submitted in CTD format for both the generic and hybrid medicine.

Commonly generic and hybrid medicines are approved via centralised procedure so the cost of MAA via centralised procedure starts from €297,400.

Safety variation in generic or hybrid medicines must be informed to the competent authority within 30 days to 2 months of time period. After valuation by DHPC the batch will be further released into the market.

USR is a regulatory action taken by the authority under risk condition of a centrally approved product to avoid public under risk. To avoid unavoidable circumstances CHMP valuates the generic and hybrid drug and submits the report within 24 hours. If the generic/hybrid drug is risk for public then the applicant submits a letter to CHMP and DHPC regarding the recall of the product. Time period for recall will be determined based on the case [5].

3. Labelling Requirements

There are sure obligatory prerequisites as per EU guidelines. That incorporates name and address of the responsible individual, country, ostensible substance, DOMD (date of minimum durability) and PAO (period of opening), specific protection of purpose and alerts, batch number, item capability, ingredients list. The most notable European consistence mark is CE. Similarity with wellbeing, security, and end ecological assurance principles are shown by CE mark for items sold inside the European Economic Area. Medical products should be joined by external and/or quick packaging data (marking) and a package leaflet as per article 54, 55 and article 59 of investigator 2001/83/EC of the European parliament, CHMP. Article 58 0f analyst 2001/83/EC considers the exclusion of a package leaflet where all the expected data can be straightforwardly passed on the packaging The specifics on to be remembered for the marking all be effectively decipherable, obviously conceivable and permanent as expected by the article 56 of order 2001/83/EC. According to the article 57 of mandate 2001/83/EC it is expressed that an extra labeling prerequisite might be expected while applying specifically states as for cost, lawful status for supply, ID and validity.

Labeling should contain all the important data as expected by article 54 of mandate 2001/83/EC or a lesser arrangement of parts where the arrangements of article 55 of a similar mandate apply. By the by, of the data things recorded in article 54 of analyst 2001/83/EC, certain things are considered basic for the protected utilization of medication.

Table 1 Labeling requirements in European Union medical products

Directive	**The labelling and the package leaflet as indicated by Articles 54, 55, 59 and 63 of 2001/83/EC**
Regulation	For hazardous substances are characterized in 67/548/EEC and its corrections, and the guidelines for perilous arrangements are characterized in 1999/45/EC, as last changed by 2006/8/EC.
Section/Part	Characterization, Labelling and Packaging (CLP Regulation) Services GHS (Global Harmonized System) Synthetic Classification and Labelling Services for Consumer Products
Dialectal	As per the requirement of member country
Order of Label presentation	It incorporates address and name of the producer. Additionally incorporates batch number, lot number, sign, handling and storage.
Name and Strength of the product	Laid out name and International non-proprietary name of medication.
Initial approval method	Proclamation of starting endorsement interaction ought to be shown with year
Number of the Barcode	Universal product code (UPC number)
Expiration date and Batch number	It ought to be incorporated
Administration and Dosage	Inclusive of dose and strength of dose. For the administration route Ph. Eur. Rundown of standard terms ought to be utilized.

Precautions and Warning	Other extraordinary admonition if required
Adverse reaction	It ought to be remembered for the label.
Drug interaction	The succinct data ought to be given
CE mark	CE mark is mandatory
Prescription grade	Prescription-only-medicines (POM)[6]

4. Discussion

The overall goal is to make sure the availability of generic and hybrid medicines including innovator products to reduce disease burden in the EU Member States. To improve sustainable availability and access to affordable, quality, safe and effective essential medicines to the European citizens;

Harmonizing standard assessment guidelines and essential check list to market the generic and hybrid medicine;

Future Aspects

Strengthening regulatory capacity, supply and distribution of generic and hybrid medicine products by ensuring fully functioning regulatory authorities;

Procuring joint authorization of generic and hybrid medicine as the procedure are changed under submission of required documents.

Rationalizing and maximizing research and production capacity of hybrid medicines.

5. Conclusion

The aim of this review is about Marketing Authorization, registration procedures and process for generic and hybrid medicine and Labeling in European Union as an a drive, pondering its long stretches of activity, what actually should be accomplished. Proposition are introduced to address the moves related to a few extra proposals to additionally fortify the drive. The drive is meeting its goals to have a product information on selling authorization, fabricate the limit of the member states, share restricted assets for most extreme result, and construct trust among controllers through EMA directives and Regulations. The drive has proactively made rules for assessors, layouts and standard working methods for appraisals and GMP, GCP examinations to fit the nature of the work delivered.

Compliance with ethical standards

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Disclosure of conflict of interest

Authors declares no conflicts of interest between them.

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