European Federation of Pharmaceutical Industries and Associations

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EFPIA Policy Principles for Off-patent Biologic Medicines in Europe

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✱ Policy Principles

Executive Summary

Over the coming years an increasing number of biologic medicines will lose patent protection creating both competition and headroom for governments and payers to further invest in innovation. Biologic medicines have, and continue to play a key role in disease treatment and EFPIA fully supports the creation of competitive, efficient and sustainable off-patent biologic markets as a means to help achieve these goals. However, due to their unique characteristics, it needs to be recognised that policies must be designed specifically for biological medicines.

EFPIA has developed a set of principles to help healthcare systems design and implement policies that can successfully create competitive off-patent biologic markets. The overarching principles that ought to underpin all others are that:

- Patients should have access to the best treatment for their individual needs;
- All biologics, originators and biosimilars approved by the European Medicines Agency (EMA) are safe, effective and of high quality;
- Biologics are not the same as small molecules and policies must be designed specifically for biologic medicines;
- The prescribing physician should always have the option to designate which biological product should be dispensed to the patient;
- To support adverse event reporting, robust pharmacovigilance systems must be in place, including the requirement for prescribing of product brand name and reporting of product brand name and batch number for all biological medicines;
- Competition in off-patent pharmaceutical/biologics markets is key to generate savings, contribute to the sustainability of health systems and foster innovation.

In addition, EFPIA has identified a number of specific principles relating to mechanisms for creating sustainable competition, transparency and information, prescribing framework, purchasing and procurement practices and uptake measures.

EFPIA strongly believes that applying these principles can help healthcare systems to balance patient access to medicine and managing costs through the creation of competitive off-patent biologic markets.

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1. Introduction

Purpose of this paper

For many years European governments have sought to ensure a high degree of competition in off-patent pharmaceutical markets in order to generate price erosion – and hence savings after patent expiry. The pharmaceutical industry supports this as an essential mechanism for ensuring the sustainability of health systems, on the understanding that good access to valuable new treatments is provided for patients that need them.

With biologic medicines becoming increasingly important in pharmaceutical markets, many governments and payers are realising that policies for encouraging competition in small molecule generic markets are not appropriate for off-patent biologics due to the specificities of these medicines.

This has led to the production of a set of industry policy principles that EFPIA believe should guide the development of any policies applicable to European off-patent biologic markets, including the identification of policy measures that EFPIA considers to be appropriate strategies for governments to create sustainable competition and those considered inappropriate when reflecting on the specificities of biological medicines.

Key terminology

- **Biologic medicine:** a medicinal product or a vaccine that consists of, or has been produced by the use of living organisms. Examples include therapeutic proteins such as antibodies, insulins or interleukins; but also vaccines, nucleic acids or tissues and cells.[1]

- **Biosimilar medicine:** a biosimilar is a biological medicinal product that contains a version of the active substance of an already authorised original biological medicinal product (reference medicinal product) in the European Economic Area (EEA). Similarity to the reference medicinal product in terms of quality characteristics, biological activity, safety and efficacy based on a comprehensive comparability exercise needs to be established.[2]

- **Interchangeability:** the medical practice of changing one medicine for another that is expected to achieve the same clinical effect in a given clinical setting and in any patient on the initiative, or with the agreement of the prescriber.[1]

- **Substitution:** practice of dispensing one medicine instead of another equivalent and interchangeable medicine at the pharmacy level without consulting the prescriber.[1]

- **Switching:** decision by the treating physician to exchange one medicine for another medicine with the same therapeutic intent in patients who are undergoing treatment.[1]

Please note: the definitions of the above terms are only applicable to European markets. There are cases, particularly with reference to the US where the use and definition of these terms may differ.

[1] Adapted from the European Commission Consensus Information Paper 2013, What you need to know about biosimilar medicinal products
[2] European Medicines Agency (EMA) (2013), Guideline on similar biological medicinal products

Specific characteristics of biological markets

There are three key characteristics that are specific to European biologic markets that should be taken into consideration when forming policies that relate to biologic medicines.

- Since **traceability requirements** are particularly important for biologics, it is important to maintain product-level traceability throughout the cycle of prescribing, dispensing, recording and reporting of these medicines. To achieve this, measures to identify the product by brand name and batch number are needed in policy and in practice. For routine pharmacovigilance[3], it has been recognized that it is essential that, as a minimum, brand name, active substance, and batch number are captured on the safety database and therefore should be reported in all adverse drug reaction reports. This will allow the case report to be used for signal detection and data quality analyses.

- Unlike the small molecule generics market, **interchangeability and/or substitutability cannot be assumed for biosimilars**. In its scientific evaluation, the European Medicines Agency (EMA) does not make recommendation on the interchangeability and/or substitutability of a biosimilar and its reference product.[4] Furthermore, little is known to date about the potential long-term clinical consequences of repeatedly switching or substituting one biologic to another.

- The '**cost of doing business'** in biologic medicines – (i.e., the cost of development, the cost of setting up and maintaining manufacturing facilities, the cost of fulfilling other regulatory requirements) – is higher than for small molecule medicines. While generic drugs are estimated to cost $1-5 million to develop and take 3-5 years to produce, biosimilars will cost $100-200 million to develop and take 8-10 years to produce.[5] As a result, economic theory suggests a market with a smaller number of entrants and higher market prices compared to markets for generics as a natural outcome for biosimilars markets. In practice, this implies that the level of price erosion seen in small molecule-based medicines would not be realistic or sustainable in competitive off-patent biologics markets.

Such features may limit the applicability in biologic markets of so-called "demand side measures" that have been used to increase competition and generate price erosion in small molecule medicines.

[3] The legal framework of pharmacovigilance for medicines marketed within the EU is provided for in Regulation (EC) No 726/2004 with respect to centrally authorised medicinal products and in Directive 2001/83/EC with respect to nationally authorised medicinal products (including those authorised through the mutual recognition and decentralised systems).

[4] See: EMA (2015), EMA Procedural advice for users of the Centralised Procedure for Similar Biological Medicinal Products applications; EMA/940451/2011; March 2015; p. 35: "The decisions on interchangeability and/or substitution rely on national competent authorities and are outside the remit of EMA/CHMP. Member States have access to the scientific evaluation performed by the CHMP and all submitted data in order to substantiate their decisions."

[5] See e.g. Federal Trade Commission (2009), Emerging health care issues: follow-on biologic drug competition. June 2009; http://www.ftc.gov/os/2009/06/P083901biologicsreport.pdf (accessed: 22/07/2015)

2. Overarching principles for European off-patent biologic markets

There are a number of key principles that underpin all issues outlined in this paper and that EFPIA consider should provide an overarching guide for the formation of all principles relating to off-patent biologic markets in Europe. These are the following:

- All biologics, originators and biosimilars approved by the European Medicines Agency (EMA) are safe, effective and of high quality;
- When designing policies to encourage competition in off patent markets it is essential to distinguish between biologics and small molecules. Biologics, including biosimilars are not the same as small molecules, including generics[6] and policies must be designed specifically for these medicines;
- Patients should have access to the best treatment for their individual needs;
- The prescribing physician should always have the option to designate which biological product should be dispensed to the patient. Treatment decisions, should be made first on the basis of clinical judgment and secondly on the basis of the overall value proposition offered by individual medicines;
- To support adverse event reporting, robust pharmacovigilance systems must be in place, including the requirement for all biological medicines (including biosimilars) to have reporting of brand name and batch number in adverse event reporting. Brand name prescribing is required as outlined by the Commission implementing Directive 2012/52/EU, which needs brand names to be used for the prescription of biological medicines for cross-border prescriptions;
- Competition in off-patent pharmaceutical/biological markets is key to generate savings, contribute to the sustainability of health systems and foster innovation.

[6] Unlike small molecules, for which current analytical methods are adequate to ensure the sameness of a generic product as compared to the innovator product, the size and complexity of the molecular structure of some biologics makes an exact structural comparison of innovator and biosimilar products more challenging. Moreover, given the complexity of biologics and their manufacture (in which living cells produce the core molecule with post-translational modifications), biologic products can have structural changes introduced when made by a different manufacturing process or by a different manufacturer or after manufacturing changes of an originator biologic.

3. Principles for creating sustainable competition

EFPIA supports competitive markets and views the development of competitive and sustainable[7] off-patent medicines markets as an essential mechanism for supporting future innovation.

Mechanisms for creating competition

- Industry supports increased competition in the off-patent sector, provided it creates a level-playing field and generates genuine competition. Effective mechanisms should ensure that potential cost-savings from increased competition are not retained in the distribution channel but are passed on to payers and patients.
- Competition should be non-discriminatory and not create any bias towards either originator or biosimilar medicines.
- Competition also requires early and sustained access to innovative medicines, the opportunity for swift market entry of competitors on the innovator's loss of exclusivity and incentives for sustainable medical innovation and biosimilars development.

Transparency and information

- Information and education play an important role to increase the knowledge of biosimilars, particularly among prescribing physicians, other healthcare professionals and patients. Information should not create any bias towards either originator or biosimilar medicines and should focus on the most appropriate and cost effective treatment option(s). EFPIA supports policies aiming at disseminating information on, where applicable, publicly available list prices of off-patent medicines, including information on differences in costs of therapies and any clinical differences (e.g. indications approved) between originator products and biosimilars, as well as on savings achieved since new entrants increased competition. At the country level, medicines databases, electronic prescribing systems and prescribing guidelines can easily include comprehensive and up-to-date pricing information. Companies should be able to validate and, if necessary correct information about prices held in such databases, although, confidentiality of net prices must be preserved. Transparent information should be provided on the safety, efficacy and cost effectiveness of all medicines. Transparency and information should lead physicians and patients to act rationally by integrating economic and medical factors into their behaviour: doctors can adopt an 'economic' prescribing behaviour without being forced to write prescriptions for biosimilars.

4. Principles for prescribing framework

The prescribing physician should always have the option to designate which biological product should be dispensed to the patient. It is essential that physicians are fully informed and actively involved in advance of any decision to change a patient's biological medicine, so they can appropriately manage their patients. To ensure this the following must occur:

[7] By 'sustainable' we refer to markets which exhibit dynamic rather than static allocative efficiency. In plain English this means that price competition should result in a level of price erosion that, whilst delivering savings, still ensures the ongoing availability of treatment and ongoing competition into the future.

- **physicians should have access to accurate, transparent and up to date information** about the availability, cost, safety and efficacy profile of biologic medicines, including biosimilars to guide prescribing choices;

- **prescribing guidelines and electronic prescribing systems should not undermine doctors' freedom to prescribe** what in their professional clinical judgment they consider to be the most appropriate medicine for their patients and must also avoid discriminating against originator products;

- **brand name prescribing is imperative and INN prescribing is not an appropriate policy for biological medicines** as it may lead to unintended switching of patients on treatment and may also undermine the traceability of the medicine dispensed as INN alone is not enough to appropriately identify any biological medicine;

- **the decision to switch patients from one biological product to another can only be made by the treating physician** to allow a decision to be made that is in the clinical interest of the patient. If switching does occur it must be accompanied by adequate clinical monitoring and the patient must be properly informed at all times;

- **pharmacy level substitution is not an acceptable practice for biologic medicines** as long as the biological medicines are not designated as being substitutable by the competent regulatory authority.

5. Principles for specific market mechanisms

Purchasing and procurement practices

Purchasing and procurement practices must always involve a medical committee, i.e. physicians in the decision making process and be sufficiently flexible to enable physicians to make treatment choices that are in the best clinical interest of the patient. Design of tenders should not contravene any of the principles found in this document and in addition must always:

- contain a variety of selection criteria and not only focus on price, e.g. ability to supply;
- guarantee security of supply and continuation of treatment by providing a sufficiently broad choice of products and avoiding a winner takes all" scenario;
- lead to conditions that create both sustainable and competitive markets;
- be restricted to molecule level, (ATC 5).

Uptake measures

There are a number of biosimilar uptake measures that have been implemented in Europe, such as quotas and financial incentives/sanctions, where EFPIA strongly opposes the way in which they have been implemented as they undermine two key principles outlined in this document. Firstly, they can significantly restrict the physician's role in determining which patient gets which medicine and secondly they do not foster sustainable competition in a non-discriminatory manner. If implemented, biosimilar

uptake measures should:

- explicitly retains doctors' freedom to prescribe;
- create a clear level playing field between off-patent originators and biosimilars;
- propose a level of volume shift in the market that is, at a maximum, in line with a policy of naïve patient initiation;
- ensure that treatment decisions are always made first on the basis of clinical judgment and secondly on the basis of an overall value proposition offered by the individual medicine.

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