Capsulas

The proposed revision of the European pharmaceutical legislation in detail (I): changes to the regulatory protection periods, goodbye to the one-size-fits-all model?

About regulatory protection in the revision of the pharmaceutical legislation of the EU

1. Introduction

One of the objectives of pharmaceutical regulations is to manage the coexistence of innovative medicines and generics or biosimilars. Regulatory protection, including data and market protection periods, plays a key role in maintaining this balance.

Despite having been in place for a long time, we are facing a new round in the debate on how much time should elapse between the marketing authorisation of an innovative medicinal product and the admission of applications for authorisation and marketing of generics and biosimilars. Historically, the model has not been a watertight one. In fact, the current system with different intensities of protection, known as "8+2+1", is heir to a model where the term of protection was one.

In the coming months we are likely to see a new configuration of this system. A new perspective is now introduced in the debate as regulatory protection can be partly shaped as an incentive system. This again questions the essence of such protection. To facilitate a thorough debate, let's take a brief historical journey through the evolution and purpose of this protection. We will focus on three pivotal moments: its incorporation in 1987, its first revision in 2004 and the proposal currently undergoing consideration in the European Parliament and the European Council.

2. The beginning of regulatory protection in the EU and Directive 87/21/EEC

The genesis of regulatory protection in the European Union (EU) can be traced back in Directive 87/21/EEC, adopted in 1986. Back then, not only Spain, but also Greece and Portugal did not allow the patenting of pharmaceutical products. Regulatory protection was introduced to partially fill this gap.

At that time, a single six-year protection period was established, i.e. without differentiation between data and market protection periods. From a practical standpoint, this meant that the protection period was longer: generic or biosimilar did not enter the market immediately after the expiry of the protection period, but could only apply for a marketing authorisation. This led to a delay in their actual commercialisation until regulatory approvals were obtained.

The period of protection could be increased to ten years in two circumstances: firstly, in the case of high-technology medicinal products; secondly, if a Member State decided to extend the period for all products marketed on its territory.

Directive 87/21/EEC was in the pipeline for more than two years (from September 1984 to December 1986) with differing positions. An example of this is that the Parliament argued

that Member States should be able to adopt a licensing system instead of a regulatory protection period.

The adoption of this regime led to some heterogeneity in the regulatory protection periods among the EU, as Member States had the option to choose between six- or ten-years periods. This meant that an applicant for a marketing authorisation for a generic or biosimilar might apply in one Member State and have to wait up to an extra four years before submitting the same application in another Member State.

3. Directive 2004/27/EC and Regulation (EC) 726/2004

The current system was introduced in 2004 by Directive 2004/27/EC and Regulation (EC) 726/2004. In particular, Article 14(11) of Regulation (EC) 726/2004 and Article 10(1) of the revised Directive 2001/83/EC provide for a dual system, with differentiated periods:

(i) The applicant shall not be required to provide the results of pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product authorised for at least eight years in at least one Member State or in the Union;

(ii) Generic medicinal products shall not be placed on the market until ten years have elapsed from the date of the initial authorisation of the reference medicinal product;

(iii) Protection shall be extended to eleven years if, during the first eight years of the protection period, the marketing authorisation holder obtains an authorisation for one or more new therapeutic indications and, during the scientific evaluation prior to authorisation, it is established that these indications will bring a significant clinical benefit compared to existing therapies.

The 8+2+1 system represented an upward harmonisation of the regulatory protection regime and a change in its configuration: the data protection period increased to eight years, and two more years of market protection were added. During this second period, the submission of a marketing authorisation application for a generic or biosimilar is possible, but not its commercialisation. This meant that those who were to market the generic or biosimilar could apply for marketing authorisation during this two-year period and market immediately upon expiry of regulatory protection period.

As with any system of a certain complexity, the process was long and not without its challenges. In November 2001, the European Commission initially proposed a single (data) protection of ten years (a model similar to that of 1986), in order to overcome the existing disparity between Member States. It was the Parliament that explicitly incorporated into the text the idea of an initial period of stricter protection followed by a second two-year period where the only limitation was that the generic or biosimilar could not be commercialised.

4. The proposed revision of EU pharmaceutical legislation

The path travelled so far illustrates that adjustments to the regulatory protection system for medicinal products are the subject of intense debate and sometimes conflicting opinions. Therefore, while it is important to recognise and analyse the proposal put forth by the European Commission's in April 2023, it is equally important to bear in mind that similar proposals have, on other occasions, undergone significant modifications by the Parliament and the Council.

The Commission proposes to reduce the data protection period from eight to six years. The objective is to incentivise the early availability of generics and biosimilars. However, companies would be able to increase their initial data protection period from six to ten years under certain conditions. These include that the medicinal product (i) addresses an unmet medical need (six months); (ii) obtains authorisation for a new therapeutic indication by demonstrating significant clinical benefit over existing therapies (one year); (iii) is marketed in all Member States within up to two years of obtaining marketing authorisation (two years); or (iv) comparative clinical trials are conducted (six months).

In light of the proposal, the innovative industry has highlighted that meeting these targets or incentives would not be possible in practice, mainly because they depended on external factors beyond their control, such as administrative action (e.g. the need to obtain price and reimbursement to market). There is a strong indication that the Commission's proposal will be amended, at least by the Parliament.

The draft report by rapporteur Pernille Weiss in the Parliament's Committee on the Environment, Public Health and Food Safety (ENVI) increases the initial data protection from six to nine years. In addition, it removes some of the milestones enabling the increase of this protection period, such as marketing in all Member States. This incentive is replaced by an obligation to submit a bona fide application for price and reimbursement outside the regulatory protection regime. All other incentives are maintained, and even the extension for meeting an unmet medical need is increased from six to twelve months.

These draft amendments must be discussed within the ENVI Committee itself and the plenary of the Parliament. The plenary is expected to adopt its negotiating position in April next year, in the penultimate plenary session before the European elections in 2024.

On the other hand, the two-year period of market protection is maintained. Therefore, the total period of regulatory protection will be between eight and twelve years. The Commission considers it is a "competitive" period compared to other regions. To give context to this statement, it should be noted that the U.S. Food and Drug Administration (FDA) grants five years of exclusivity for new molecules, three years for new indications and a twelve-year exclusivity regime for biologics.

As for the Council's position, an intense and nuanced debate also lies ahead. The first sign of this was seen on June 13th at the Employment, Social Policy, Health and Consumer Affairs Council (EPSCO Council), where some Member States expressed differing opinions. For instance, smaller Member States view the measure positively because they understand that the incentive to market throughout the EU territory could lead to greater availability of medicines. Other Member States have mixed opinions, with concerns about the possibility that the proposal will reduce the incentive to develop and market medicines, and doubts about the real scope of this measure, given that in most cases patent protection is the last to expire. The Spanish Minister of Health avoided making an explicit statement on the matter and focused his speech on the priorities of the Spanish Presidency of the Council.

These dynamics show, on a small scale, the interesting debate that will take place over the next two years. Undoubtedly, an exciting moment to shape pharmaceutical legislation that can endure for another twenty years.