Capsulas

Evaluation of medicinal products

Summary of Lluís Alcover's speech at the Course on Pharmaceutical Law of the CEFI Foundation

Introduction

The evaluation of medicinal products is a scientific-technical process with the objective of determining the added value of new medicines compared to existing therapies. It aims to serve as a tool for decision-making in health care, particularly for decisions on the funding and pricing of medicines.

Its rationale derives from the fact that the conclusions of regulatory agencies are essentially individual. To obtain a marketing authorisation, a medicinal product must be safe, effective and of quality, but it does not need to be better than existing alternatives. This is not a requirement for obtaining a marketing authorisation (e.g. efficacy can be demonstrated by a pivotal versus placebo trial). For this reason, further benchmarking is essential to inform decisions on resource allocation and inclusion of medicines in public pharmaceutical provision. This evaluation exercise has different dimensions, including a clinical and an economic one.

The clinical evaluation looks at relative efficacy and safety: is the new medicinal product more effective than existing alternatives? Is it safer? This part of the evaluation concludes with the therapeutic positioning. The economic evaluation answers a different set of questions:
Is investing in the new product the best possible use of resources? How much will the new product cost?

How can the new therapy be included in the public pharmaceutical provision? The first question is answered by efficacy studies (e.g. cost-effectiveness and cost-utility studies). The second by impact on budget analyses.

In Spain, the evaluation of medicines at the national level has been carried out by therapeutic positioning reports ("IPTs" by its Spanish acronym).

IPTs were created in 2013 within the Permanent Pharmacy Commission of the Interterritorial Board of the National Health Service (by its Spanish acronym, "CISNS"). Initially, IPTs were carried out and approved by the Spanish Agency of Medicines ("AEMPS") and included only a clinical evaluation (efficacy and relative safety). Later, in 2020, the Standing Committee on Pharmacy sought to strengthen IPTs with a Consolidation Plan. Among other issues, the Plan created ReValmed (a network involving AEMPS, the Directorate General of Pharmacy at the Ministry of Health and the Autonomous Communities) and foresaw the inclusion of economic evaluation in IPTs. De facto, the Plan brought IPTs "closer" to the Directorate insofar as the economic evaluation was carried out by teams led by the Directorate.

In June 2023, the National High Court (Audiencia Nacional) annulled the Consolidation Plan on formal and substantive grounds. The annulment increased the urgency of enacting a new regulatory framework for the evaluation of medicines in Spain.

In this context, the Ministry of Health held a public consultation in October 2023, regarding

the Draft Royal Decree regulating the evaluation of health technologies.

Prior public consultation on the Draft of Royal Decree

1. Legislative tool

Is it appropriate to regulate with a Royal Decree the issue at hand? Generally, yes. However, two aspects should be noted.

First, the scope of a Royal Decree is limited, e.g., it cannot create an independent medicinal product evaluation body (a proposal that has been much discussed recently and was even included in some political programmes for the last general elections). Consequently, the use of this type of legislative tool inevitably limits the scope and ambition of the reforms to be undertaken.

Secondly, due to the highly technical nature of the subject, it will be necessary to approve guides and other documents under the Royal Decree to guide interested parties on how to carry out the evaluations. These guides will have a major impact on the evaluation exercises insofar as they will determine the methods and procedures to be followed in carrying them out. It is very important that they are developed with broad stakeholder participation and a high degree of consensus.

2. Legal nature of the Reports

The evaluation of medicinal products concludes with a report setting out the outcome of the evaluation. Until now, these reports have been the so-called IPTs; from now on, it unknown what they will be called. We will refer to them by their generic term “Reports”.

Under the Consolidation Plan, the legal nature of the IPTs was unclear, even to the extent of the Administration itself affirming that they were not an administrative act. Their relationship with the funding and pricing procedure was also unclear: Were they a step within the funding and pricing procedure? Were they a stand-alone procedure?

In my opinion, the new regulatory framework should make it clear that the Reports are administrative acts that conclude an autonomous administrative procedure that is different from the funding and pricing procedure. First, because there is no doubt that, conceptually, the evaluation has its own entity, separate from the financing and pricing procedure. The evaluator “evaluates” and the decision-maker “decides”, both being distinct procedures with different methods and criteria. Secondly, because in view of what has happened in recent years, the Reports are much more than a simple input to the funding and pricing procedure. They are documents that go beyond the internal sphere of the Administration and that have real effects to third parties, which means that they must necessarily be considered as administrative acts finalising a procedure. Reports, when published, have an impact on the positioning of the medicinal product and on its value and use in clinical practice. They also contribute to the drafting of regional and hospital guidelines.

Considering the Reports as the decisive acts of an autonomous administrative procedure would allow the interested parties, including the developer, to exercise the rights that they have in the framework of any administrative procedure. These include the right to have access to the complete file, to know the status of the file, to make allegations, to file appeals, etc.

Regarding the possibility of making allegations, two further proposals can be made in view of the dynamics under the Consolidation Plan.

Firstly, it would be desirable for the evaluator to reply more precisely to each of the allegations received and to indicate for each allegation, whether it is being considered and the specific justification for the conclusion. Not infrequently the allegations to the IPTs were not explicitly answered. The more dialogue there is between the assessor and stakeholders, the more robust and legitimate the final report will be.

Secondly, it would be desirable for companies to be able to make allegations, in addition to the initial draft of the Report, to the final Report sent to the Directorate (with the contributions of the other stakeholders incorporated). This would avoid situations in which the final report includes additions on which the company has not had the opportunity to comment.

3. Non-prescriptive reports

Reports should be "non-prescriptive", i.e. not be mandatory for the initiation and/or continuation of funding and pricing procedures.

Reporting may not be necessary for all medicinal products and new indications in the first place. It is therefore advisable to be flexible and not require a formal obligation. Additionally, delays in reporting not attributable to the development company should not affect the timing of the financing and pricing procedures.

Lastly, it would be desirable for the new system to provide for the possibility of replacing the information plans with "evidence generation plans" if the Commission were to be able to identify and assess the impact of the new system. The report would not be made available until there is sufficient data to make the report (e.g. after a positive opinion of the CHMP). In the "meantime", real-life data would be collected to allow for a robust report; after some time, a funding and pricing procedure with interim conclusions would be followed; and, very importantly, access to patients would be allowed.

4. Non-binding reports

The conclusions of the reports should be "non-binding", i.e., the evaluator's conclusion does not necessarily have to coincide with that of the decision-maker. The criteria to be considered by each are different, and so are the conclusions they may reach. In this sense, proposals such as the one put forward by Airef to provide for binding cost-effectiveness criteria are not, in my opinion, desirable.

5. Relationship with Regulation 2001/2282

The fit between the new Royal Decree and Regulation (EU) 2001/2282 on health technology assessment will be a very relevant aspect. The crux of the matter will the extent to which the National Reports respect the Joint Clinical Assessment Reports published from January 2025 for antineoplastics and advanced therapies.

The new regulatory framework, in my opinion, should recognise the existence of different levels of assessment (European, national, regional and hospital); strengthen coordination between them; and provide for the impossibility for a lower level to reassess the same as a higher level except in exceptional and duly justified cases (e.g. absence of the comparator used at the higher level in the lower level, clearly differentiated epidemiological situation between levels, etc.).

6. Technical evaluation criteria

The technical criteria of the evaluation should be outlined by the Royal Decree. The Royal Decree could indicate the direction to be followed and the general lines. In this respect, there are two

aspects that deserve particular attention. Firstly, the choice of comparators. The new regulatory framework should be sensitive to the level of evidence available for each product and its regulatory status (e.g. master formulations vs. industrially manufactured drugs with marketing authorisation, advanced therapies with different regulatory profile, etc.).

Secondly, the perspective of the analyses. Traditionally, IPTs have been conducted from the perspective of the national health system. It would be desirable for the new regime to focus on broader perspectives that would allow the full value of the medicinal product to be captured.

°°°°°