The impact of recent legislative developments on drug reimbursement in the pharma industry

The **legislative framework** (**Law 4512/2018 and FEK 2768-11 Jul 2018**) in **Greece** has been **recently updated** and is expected to **substantially change the reimbursement landscape** for prescribed medicines. **For the first time, Greece** has acquired **an evaluation procedure** of **newly proposed and already existing reimbursable medicines** that relies on **health technology assessment** principles (HTA) for the establishment of **safe and effective health policies** that are **both patient-focused** and **cost-effective**.

The **criteria** that will be used for the evaluation of **inclusion** in or exclusion from the **List of Reimbursable Medicinal Products** include:

- **Unmet medical need,**
- **Therapeutic benefit (including quality-of-life related data),**
- **Safety and risk-benefit balance,**
- **Comparison to existing alternative treatments,**
- **Reliability of submitted clinical data,**
- **Cost-effectiveness, and**
- **Impact on pharmaceutical expenditure.**

Process

The recently published **FEK 2768** clearly defines the goals, scope, context, stakeholders, and methods that will be used for the initial evaluation by the HTA Committee and subsequent referral to the Negotiation Committee. The former will be based in EOF and the latter in the Ministry of Health. These appointed committees will review the applicant's dossier (Added Value Dossier) in a systematic, unbiased, and robust manner within strictly defined timelines that are defined in FEK 2768, while the final decision will lie with the Minister of Health. The Added Value Dossier consolidates information on the target disease (management, treatment, epidemiology globally and locally), the proposed medicinal product and comparator(s), clinical effectiveness, safety and health economic outcomes. The dossier can be developed as an evolving document that may be used for customising submissions to other HTA bodies. For new active substances that are submitted by the MAH for assessment and potential inclusion in the List of Reimbursable Medicinal Products, additional criteria would now have to be fulfilled.

Although assessment criteria may vary among EU countries, **cooperation** among **EU HTA bodies** is anticipated on the basis of **relative effectiveness assessment**. This term can be defined as the extent to which an intervention confers more benefit than harm, compared to one or more intervention alternatives, for achieving the desired results under routine healthcare practice conditions. The new legislation also introduces a web application (EOF webpage) that will provide access on reimbursement data to MAHs. Even more important, **patient involvement** in **pricing and reimbursement** decisions is promoted, as patient organisation representation is encouraged in **HTA meetings**.

For the purpose of the assessment and decision making on reimbursement, **clinical data produced by the MAH** during drug development and **retrieved by the MAH following overview of a wide range of sources (literature, EMA, FDA, other HTA bodies etc.)**, both globally and locally, will be submitted to evaluate the risk-benefit ratio, effectiveness compared with existing

therapies and impact on pharmaceutical expenditure. The submitted economic evidence should include both direct and indirect health cost analysis from sources such as economic models, cost-effectiveness and pharmacoeconomic studies. Nevertheless, the choice of the comparators, as well as, the clinical data, in terms of both quality and quantity, that will be submitted by the MAH may prove quite challenging. In terms of **quality of data**, randomised controlled trials are at the top of the hierarchy of evidence. Adequately justified and detailed meta-analyses are also acceptable. In any case, the submitted clinical data will be scrutinised on aspects relevant but not limited to statistical power, bias, patient compliance, patient disposition (how many patients completed the trial), etc. **Furthermore, the relevance and validity of the submitted global clinical data to routine clinical practice in Greece have to be dully justified by the MAH.** In the course of the assessment, the benefits of introduction or exclusion of already-included medicinal products in the corresponding Reimbursable List will be weighed against the **inevitable uncertainty of evidence**. The uncertainty of evidence can be mitigated by the MAH via the availability and submission of risk management plans and adequate quality **real-world data**. Carefully designed **post-market studies**, **routine pharmacovigilance**, **and disease registries** can significantly contribute to the systematic collection of real-world data. MAHs are also instructed to include a detailed synopsis of future clinical studies that they plan to undertake.

Conclusion

Undoubtedly, HTA is a multidisciplinary process. **The prompt,** without undue delay due to lack of submitted evidence, **HTA and subsequent evaluations** relies solely on the **information that is submitted by the MAH**. In the case of rejection of inclusion, or exclusion of already existing medicinal products from the corresponding Reimbursable List, the MAH may repeat the application procedure within defined timelines as outlined in FEK 2768, but should re-evaluate the submitted data. **Seeking to evaluate and reimburse medicines in relation to the value they confer to society and the Greek healthcare system is considered an approach that will both ensure value in pharmaceutical spending and inevitably affect the pharma industry's R&D and market access strategies.**

Zeincro offers a wide range of medical, clinical, regulatory and pharmacovigilance activities to support this process. **Zeincro's Medical Affairs** can accommodate all aspects of the overall preparation and **selection of data** for the submission of an Added Value Dossier. Zeincro is also able to fully support any missing clinical trial information for this dossier, managing the **design** and **conduct** of **pre-approval interventional trials** and **post-market studies** that will **bridge the research-to-real-world data gap**.

References

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