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NOTE

Origine:	Secrétariat général du Conseil
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Objet:	Entrée sur le marché des médicaments en Europe: lacunes en matière de données probantes et solutions éventuelles - *Informations communiquées par les délégations autrichienne, belge, irlandaise, luxembourgeoise et néerlandaise*

Les délégations trouveront en annexe une note contenant les informations communiquées par les délégations autrichienne, belge, irlandaise, luxembourgeoise et néerlandaise concernant le point « Divers » qui sera traité lors de la session du Conseil EPSCO (santé) du 14 juin 2022.

ANNEXE

Market entry in Europe for drugs: evidence gaps and potential solutions

Different studies show (1) how important it is to correctly assess the added value of new (cancer) drugs as they often show no (major) added value, and (2) how difficult this is due to the limitations of clinical trials as currently being conducted by the pharmaceutical industry. Today, these trials are sufficient for market entry but do not allow for an informed decision regarding reimbursement.[1][2][3][4][5][6]

To obtain a European market authorisation, manufacturers have to demonstrate the quality, safety and efficacy of their new product to the European regulators (EMA). Conversely, domestic reimbursement decisions remain the responsibility of individual Member States.

However, healthcare payers such as national insurance funds generally consider that the **information that manufacturers provide to the European regulators on which market entry is obtained, is insufficient to allow for a reliable evaluation of a product's therapeutic added value as required for pricing and reimbursement decisions**.

Healthcare payers assess the (potential) added value of the new product by **comparing with the existing alternatives.** This comparative information is used in Health Technology Assessment (HTA) studies, which compare the additional costs of using the product against the additional benefit to the patient. Knowledge of this added value is also necessary to assess the price as demanded by the manufacturers.

[1] https://kce.fgov.be/sites/default/files/atoms/files/KCE_347C_Evidence_gaps_Europe_Synthesis_V2.pdf
[2] https://kce.fgov.be/en/kce-press-release-kce-reports-343-do-innovative-medicines-against-cancer-always-have-a-real-added
[3] France: https://pubmed.ncbi.nlm.nih.gov/33412466/
[4] UK: https://pubmed.ncbi.nlm.nih.gov/28453615/
[5] USA: https://iamanetwork.com/iournals/iamainternalmedicine/article-abstract/2733563
[6] UK, France, USA, Australia: https://www.sciencedirect.com/science/article/pii/S0277953620302616

Currently, clinical trials conducted are generally limited to meet the marketing authorisation requirements of European regulators and do not include such elements. As long as they manage to obtain reimbursement with this approach, the manufactures have **no incentive to conduct comparative clinical trials that include the comparator and patient-relevant outcomes as expected by HTA agencies and healthcare pavers.** Such comparative information is also needed by physicians and patients to make optimal treatment choices.

This creates an untenable situation as it presses healthcare payers to accept reimbursement while lacking the necessary information to evaluate the added value of this product, and hence they also lack the necessary information to negotiate a fair price.

The consequence of this shift away from comparative trials has resulted in delays in access to potentially beneficial drugs for patients in addition to a distortion in fair pricing.

Innovative cancer drugs

This issue is far from hypothetical. The KCE for example, together with the Belgian Cancer Registry, has analysed the extent to which the use of new cancer drugs (used for 12 types of cancer) have contributed towards extending the lives of Belgian patients receiving these since 2004[7]. These results were then compared with the expenditure of Belgian health insurers for these cancer drugs over the same 15-year period.

The results **showed a (very) slight improvement in survival rates for six of the twelve cancers studied, and no improvement for the other six.** On the other hand, expenditure of health insurance increased significantly in all cases. For the oncology drugs included in this report, the health care payer expenditures (excl. confidential discounts) increased from about €50 mln in 2004 to more than €700 mln in 2018.

A new start with the new European HTA regulation?

These findings are most timely as Europe recently approved the new regulation 2021/2282 establishing a structural cooperation on HTA and is currently revising the pharmaceutical legislation on medicines for human use.

[7] https://kce.fgov.be/en/kce-press-release-kce-reports-343-do-innovative-medicines-against-cancer-always- have-a-real-added

However, **Europe can only truly establish a structural cooperation on HTA, if HTA agencies receive the necessary comparative data to conduct their evaluations. Member States have acknowledged the need for a more tailored approach to data in adopting the EU regulation on HTA and its provisions for ensuring that the generation of evidence fulfils the needs of the Joint HTA initiative and the national HTA agencies.** We believe that we need to find ways to encourage and incentivise that clinical trials are designed from the outset so that they generate not only the information needed for market authorisation, but also the comparative data needed for HTA evaluations.

This position is easily to be brought in line with the European Pharmaceutical Strategy that states that *'we need to break silos so that various public authorities responsible for authorization, health technology assessment, healthcare provision, health insurance and financing, work together.'*

We invite the other EU Member States as well as the European Commission to become aware of this issue that is not limited to our countries alone. Accordingly, we draw your attention to the joint statement from the Beneluxa and Nordic Pharmaceutical forum from June 4th 2021. [8]

We value the provisions in the regulation on joint HTA that focus on creating early scientific consultations, potentially addressing both regulatory as well as HTA data requirements. Strengthening early dialogues between companies and HTA agencies are a first way forward to get the set-up of clinical trials right. This dialogue should aim at developing adequate industry guidelines for marketing authorization application dossiers including clear "HTA package" recommendations and requirements.

Further solutions can be discussed both at the level of the Pharmaceutical Committee as well as the EU Member State Coordination Group on Health Technology Assessment. Additionally and importantly, the upcoming negotiations on the revised pharmaceutical legislation on medicines for human use provide a significant opportunity to develop solutions to this challenge.

[8] https://beneluxa.org/statements#toc-04-june-2021-joint-statement-of-the-beneluxa-initiative-and-the-nordic-pharmaceutical-forum