

Authors: Attoumani 1*, Law-Koune 2*, Plessala 3, Breau-Brunel 3, Genestier 1, Gauthier 4

Affiliations: 1. Amaris Consulting, Toronto, ON, Canada, 2. Amaris Consulting, Montreal, QC, Canada, 3.Amaris Consulting, Paris, France, 4. Amaris Consulting Barcelona, Spain

* These authors contributed equally to this publication

INTRODUCTION

When the French National Health Authority (Haute Autorité de Santé or HAS) evaluates medications in France, it assesses their effectiveness, particularly if they have a significant economic impact. The process begins with an optional meeting called a "pre-submission discussion," which allows alignment between the industry and the health agency on initial terms. Subsequently, after an initial evaluation, a list of questions and clarifications could be provided by the Department for the Evaluation of Access to Innovation (DEAI), the manufacturer has the opportunity to provide additional information during the technical exchange phase, which represents the final chance for the industry to submit supplementary data for evaluation. It should be noted that this phase is not mandatory and does not occur with every evaluation.

Following this, the DEAI undertakes a second phase of expertise and drafts a preliminary opinion. The latter is then submitted to the Commission for Economic Evaluation and Public Health (CEESP) for approval. Once approved, the opinion is transmitted to the manufacturer for a potential contradictory phase, which may or may not take place, and for the drafting of a final opinion.

During the drafting of the economic opinion, the CEESP can issue three types of reservations: minor, important, and major. These reservations play a role in negotiations regarding the price of the medication with the Economic Committee for Health Products (CEPS).

OBJECTIVES

This research aimed to analyze the impact of questions raised during TE on the reservations in the final opinions.

METHODS

We conducted an analysis of final opinions published throughout the year 2022 with the aim of comparing the technical exchange questions and reservations obtained in the publicly released final opinion reports. For each opinion, we tallied the number of minor, significant and major reservations. We meticulously examined the questions profiles, categorizing them into six modalities: structuring assessment choices; modeling; identification, measurement, and valuation of utilities and costs; validation; and results of the analysis, as well as sensitivity analyses. Ultimately, we compared the question profiles with the reservation profiles and derived an analysis based on our observations.

RESULTS

Out of a total of 28 opinions published by the CEESP in 2022 were examined and analyzed, 27 included an efficiency assessment. There was no assessment for the nirmatrelvir/ritonavir combination (Paxlovid®). Twenty-seven opinions had at least one reservation, with eleven featured major reservations regarding the analysis. Within this dataset, 19 opinions pertained to oncology, while the remaining 9 covered various other therapeutic areas.

The number of reservations in the final opinions is presented in Figure 1 and is notably lower than the count of questions posed during the technical exchanges. Modeling accounted for most of the questions raised during technical exchanges (N=298), followed by sensitivity analyses and structural choices. Conversely, fewer inquiries were directed towards validation and costs. A distinct contrast emerges between the number of questions raised and the number of reservations encountered in the final opinion reports.

This emphasizes the crucial importance of addressing questions during these exchanges for a comprehensive evaluation of healthcare products. Figure 1 also illustrates the distribution of reservations, categorized as minor, significant, and major, according to their respective domains. Major reservations were primarily associated with the modeling category, whereas no choices led to major reservations in the cost domain.

Category	Minor	Substantial	Major	Total
Results of sensitivity analysis	10	10	0	138
Validation	5	5	0	46
Identify, measure and valorize costs	10	10	0	87
Identify, measure and valorize utilities	10	10	10	99
Modeling	55	75	10	298
Structured choice of assessment	10	10	0	138

Figure 1. Distribution of Reservations According to Technical Exchange Questions

Figure 2. Correlation between the Number of Technical Exchange Questions and the Number of Reservations for Medications

Overall, there is an increase in the number of reservations in correlation with the growing number of questions asked. Interestingly, some final opinions received only a limited number of reservations but had a considerable number of questions, as exemplified by Wegovy® (semaglutinib). Additionally, three medications did not undergo any technical exchanges.

CONCLUSIONS

Upon analysis of CEESP opinions, it becomes evident that the effort invested during Technical Exchanges (TE) is crucial. This is underscored by the fact that a significant portion of questions asked during TE do not lead to reservations, particularly in the realm of parametric choices. Most importantly, proactively justifying assumptions, rigorously validating models, and addressing issues of transposability during the dossier development phase, well before submission, can potentially avert reservations that might not even arise as questions during TE. This proactive approach to avoiding reservations holds the promise of optimizing price negotiation strategies. This work also shows the importance of anticipating submissions, especially if the manufacturers want to avoid questions and reservations by incorporating real-world evidence results in their dossiers (SNDS studies for example). Proactive steps in preparing for such submissions, including addressing potential issues related to data quality and adequacy, can significantly enhance the evaluation process and further contribute to the optimization of price negotiation strategies.

REFERENCES

- All CEESP opinions were comprehensively analyzed and utilized in this study, and they are accessible on the Haute Autorité de Santé (HAS) website https://www.has-sante.fr/jcms/p_3149875/fr/avis-economiques-rendus-par-la-commission-d-evaluation-economique-et-de-sante-publique-ceesp

- CEESP doctrine
- Deposit form
- The HAS 2022 Activity Report
- The CEPS 2021 Activity Report