

# COST-EFFECTIVENESS ASSESSMENT OF ORPHAN DRUGS IN FRANCE: KEY INSIGHTS FROM CEESP REVIEWS (2021-2024)

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## INTRODUCTION

In France, the Commission for Economic and Public Health Evaluation (CEESP) assesses the methodological robustness of cost-effectiveness analysis, based on guidelines issued by the French National Authority for Health (HAS)<sup>1</sup>.

It identifies methodological reservations and, since 2021, also characterizes the level of uncertainty.

Orphan drugs, often developed in contexts of high unmet need and limited evidence, present specific challenges for economic evaluation. This study focuses on CEESP evaluations of orphan drugs since 2021, to explore how these challenges are reflected in recent appraisals.

## OBJECTIVE & METHODS

The objective is to analyze CEESP evaluations of orphan drugs published between 2021 and 2024, with a focus on the reported incremental cost-effectiveness ratios (ICERs), their methodological validity, and the nature and frequency of major methodological reservations leading to invalidation.

All CEESP health economic opinions on orphan drugs published between this period were reviewed using the **Vyoo Agency database**<sup>2</sup> which collects all the opinions published by the CEESP since 2014.

Descriptive statistics were used to summarize the results and to identify common methodological issues reported by CEESP.

## RESULTS

— Between 2021 and 2024, 31 CEESP health economic evaluations on orphan drugs have been published.

Six ICERs €/QALY could not be included in the analysis: three were dominant cases, one was dominated, one lacked a reported ICER in €/QALY and one was deemed “non evaluable” by CEESP.

Consequently, cost-per-QALY analyses were conducted on 25 ICERs.

The average published ICER was €1,041,448 per QALY with values ranging from €7,392 to €4,753,788 per QALY.

### Validity of health economic dossier

More than half cases were invalidated due to methodological issues or high uncertainty. Among the 31 cases reviewed, 29% were validated (N=9), while 71% were invalidated (N=22). Invalidated cases were classified under two types of qualification<sup>3</sup>:

- **Major methodological reservations 52% (N=16):** element deemed non-compliant with current recommendations, invalidating all or part of the economic assessment.

- **Major overall uncertainty 19% (N=6):** A major overall uncertainty occurs when multiple strong assumptions or weak evidence create instability in model results, even without a specific major methodological reservation.

Three dominant cases and one dominated were identified, but all were invalidated by CEESP.

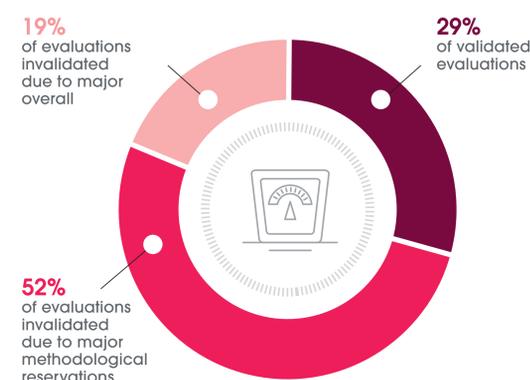


FIGURE 1. DISTRIBUTION OF VALIDATED AND INVALIDATED ECONOMICS DOSSIER IN RARE DISEASES (N=31)

### ICER €/QALY distribution

ICER values were highly variable across evaluations. Among the 25 available ICERs, one third exceeded €1 million per QALY, while 8% were below €100,000 per QALY. The remaining evaluations were distributed between these two ranges, showing substantial dispersion of results. The average validated ICER was €954,174 per QALY, and the overall mean ICER reached €1,041,448 per QALY.

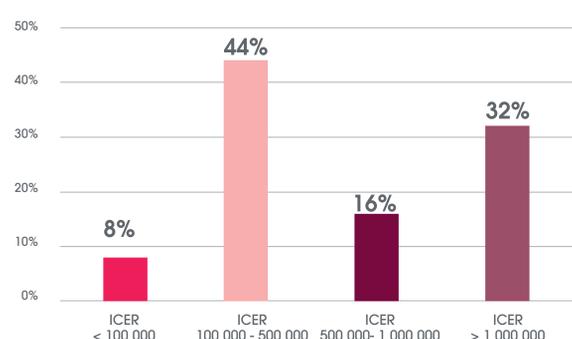


FIGURE 2. PROPORTION OF CEESP EVALUATIONS IN RARE DISEASES BY ICER LEVEL (N=25)

### Major Methodological Reservations

Among the 16 cases invalidated due to major methodological reservations, four evaluations included two major reservations, and one evaluation reported up to three, for a total of 22 reservations.

The 22 major reservations were mainly related to utility estimation (n=9), lack of data or robustness (n=8), sensitivity analyses (n=2), model structure (n=1), economic analysis (n=1) and objective (n=1).

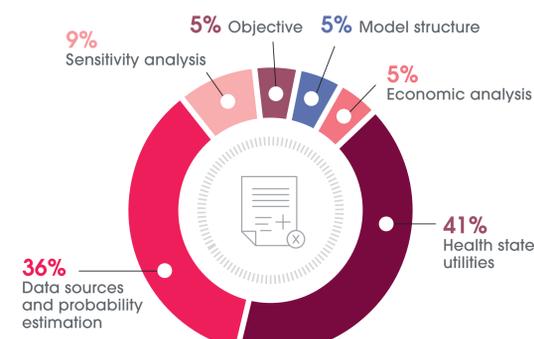


FIGURE 3. DISTRIBUTION OF MAJOR METHODOLOGICAL RESERVATIONS IN RARE DISEASES (N=22)

## CONCLUSION

The overall mean ICER of the economic evaluations of orphan drugs between 2021 and 2024 is greater than €1 million per QALY. The average validated ICER was €954,174 per QALY. Most economic dossier for orphan drugs were invalidated.

These results reflect the recurring methodological challenges in generating robust cost-effectiveness evidence in the context of rare diseases, where limited data, small populations, and uncertain long-term outcomes. Considering the low number of validated evaluations of orphan drugs, it seems important to consider how to improve the ability of these evaluations to produce relevant economic information.

### References

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