HOW TO INTERPRET ICERS IN ORPHAN DISEASES? A FRENCH EXAMPLE.

Moutier H, Bourguignon S, Maurel F, Bodaghi C
Real-World Insights, IQVIA, Paris La Défense, France

PSY109

IMS Health & Quintiles are now IQVIA™

BACKGROUND & OBJECTIVES

- In France, pharmacoeconomic evaluations are submitted by manufacturers to the Economic and Public Health Committee (CEESP).
- The CEESP assesses the **methodology** of these evaluations, in order to determine if the efficiency of the drugs can be established.
- Even though there is **no ICER threshold** in France, the CEESP can characterize the level of ICER obtained in the evaluation in order to enlighten public decision making, and to contribute to price negotiations.
- The pharmacoeconomic evaluations of orphan drugs often present **high ICERs** and **important uncertainties**, driven by the high prices requested by manufacturers, and the frequent lack of data used in the evaluation.
- The aim of this analysis was to discuss ICERs of orphan drugs and their characterizations issued by the CEESP.

METHODS

- To conduct this analysis we used an **IQVIA database** that contains all the pharmacoeconomic evaluations issued by the CEESP.
- This database allowed us to analyze the trends of the evaluations made by the CEESP based on structural parameters, cost-effectiveness results, sensitivity analysis, and methodological objections.
- We selected all the opinions published between January 2014 and June 2018 involving **orphan drugs** according to the Transparency Committee opinions and designations. These drugs are typically indicated in conditions that have a prevalence of below **5 in 10,000**.
- For all the eligible drugs, we analyzed several outcomes, including **ICERs** and their **characterization** issued by the CEESP.

RESULTS[1]

- Between January 2014 and June 2018, the CEESP issued 61 “efficiency” opinions on 49 drugs and 3 medical devices. Among the drugs, **11** qualified as **orphans** and their **13 evaluations** are summarized in the table below.
- The 13 orphan drug evaluations pertained to the following therapeutic areas: hematology or oncology (7), cardiology (2), pulmonology (2), endocrinology (1) and the musculoskeletal therapeutic area (1).
- All the orphan drugs targeted **restricted populations**, from 50 to 5,000 patients. Furthermore, they were indicated in both adults or pediatric populations.
- Their ICERs ranged very widely, from **€33,127/QALY** (Imbruvica®) to **€2,661,514/QALY** (Spinraza®). In the case of Venclyxto®’s evaluation, the ICER could not be established, due to the absence of comparative data.

Drug	Opinion date	Therapeutic area	Target population	Population of indication	Comparator	ICER (€ / QALY)	ICER characterization by the CEESP	Methodological validity	Objections		
									Major	Important	Minor
DEFITELIO®	18/02/2014	Hematology	155 - 283	Adult & pediatric	No treatment	33,273	NA	No	4	13	2
OPSUMIT®	24/06/2014	Cardiology	3,000	Adult	Active treatment	85,359	NA	No	3	3	4
ADEMPAS®	14/10/2014	Cardiology	1,133	Adult	No treatment	239,145	*Excessively high*	No	4	4	6
ESBRIET®	03/02/2015	Pulmonology	4,960	Adult	No treatment	70,651	NA	No	0	8	2
NPLATE®	03/02/2015	Hematology	1,887	Adult	Active treatment	Dominant	NA	Yes	0	5	1
IMBRUVICA®	07/04/2015	Oncology	500	Adult	Active treatment	33,127	NA	No	1	1	8
IMBRUVICA®	07/04/2015	Oncology	1,500 - 1,700	Adult	Active treatment	102,483	NA	No	2	3	7
KYPROLIS®	10/05/2016	Hematology	2,350 - 2,500	Adult	Active treatment	287,000 - 293,000	*Extremely high*	Yes	0	2	9
ORKAMBI®	10/05/2016	Pulmonology	1,700	Adult & pediatric	No treatment	574,390	*Extremely high*	Yes	0	4	9
STRENSIQ®	10/05/2016	Endocrinology	50 - 80	Pediatric	No treatment	2,300,000	*Exceptionally high*	No	1	4	2
IMBRUVICA®	14/06/2016	Oncology	1,500 - 1,700	Adult	Active treatment	95,556	NA	No	0	5	3
VENCLYXTO®	13/06/2017	Hematology	1,000	Adult	Active treatment	NA	NA	No	1	0	0
SPINRAZA®	12/12/2017	Musculoskeletal	300	Pediatric	No treatment	2,661,514	*Extremely high*	Yes	0	5	2

- Interestingly, the CEESP has issued a characterization for all the ICERs **above €200,000/QALY**, regardless of the therapeutic area, population of indication, size of the target population, or existence of active comparator.
- Indeed, Adempas®, Kyprolis®, Orkambi®, Strensiq® and Spinraza® presented ICERs that were deemed « **excessively** », « **extremely** », or « **exceptionally** » high by the CEESP. The committee did not comment on the ICER values of the other orphans, but they were almost all below €100,000/QALY.
- The use of the IQVIA database to analyze the characterization of ICERs for **non-orphan** drugs by the CEESP shows that 5 ICERs between €100,000 and €200,000/QALY have been deemed « **very high** ». But since no orphan has presented an ICER in this range, we have no information on the CEESP requirements for orphan drugs.
- Also, for 9 of the 13 evaluations presented in the table, the CEESP determined that the methodology used in the evaluation was **not valid**, mainly due to lack of **clinical data**, **comparative data**, or because of too much **uncertainty**.

Conclusion

- **Today there is no official threshold for ICERs in France, but according to the CEESP evaluations, it seems that orphans ICERs above €200,000/QALY are considered « excessively high ».**
- **However, these ICER characterizations have little impact on a drug’s market access and reimbursement, as only major objections to the methodology of the evaluation can complicate price negotiations, and prevent the achievement of European pricing.**
- **As pharmacoeconomic evaluation is quite a recent addition to the French HTA pathway, the implementation of an official ICER threshold by political decision could heighten its importance, as well as the role of the CEESP.**

1. HAS