Are orphan drugs in France priced according to international prices, and which factors could influence the negotiated prices?

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Objectives:

As orphan drugs aim to **treat a limited number of patients** (in Europe less than 5 persons out of 10 000[1]), offering incentives is needed to **compensate development costs**. Regulatory help is given in the EU, but it is generally understood that **higher prices or shorter access delays** can further encourage the development of such products. This analysis was conducted to determine whether France offered the same level of incentives as **its reference countries** – Germany, Italy, Spain, and the United-Kingdom. Another objective was to identify factors likely to influence prices of orphan drugs in France.

Methods:

Drugs with orphan drug designation and with an initial list price publication in France between 2016 and 2021 were included in the analysis. Daily treatment costs, first price publication date, and the price evolution in each country were collected. All the analysis were conducted on publicly available prices and does not account for potential confidential rebates

A **one-to-one analysis was conducted to account for drugs not available in a country. Daily treatment cost** was our main means of comparison between countries.

Results:

1. Price incentives

The research yielded 17 products, out of which 11 (65%) had their lowest price in France. France also had the **lowest mean price** of the five countries (*figure 1*).

Costs were significantly lower in France compared to the UK, **Italy and Spain.** This suggests **low pricing incentives**.

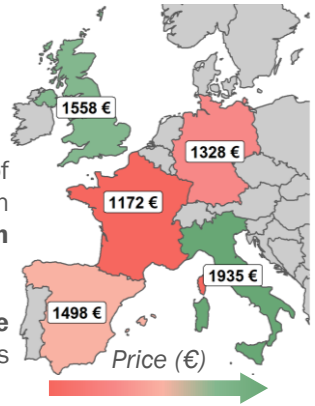

Figure 1 . *Mean price at launch*

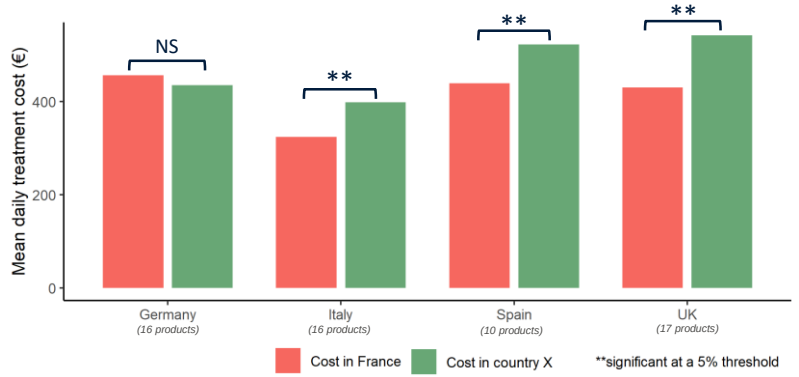

Figure 2. *Mean daily costs in France versus its four reference countries*

2. Market-access delays

Delays were assessed by averaging scores between one and five (one being the first country to list the negotiated price of a product). France was usually the **fourth country to publish** a listed price, a consequence of long negotiations and lower incentives.

Figure 3. *Expected timeline for market access of an orphan drug*

3. Cost drivers for orphan medicines

Linear regression models were used to identify price determinants in France. **Population size and level of Added Medical Value** ("ASMR") **were the two major factors that drove the treatment cost** (*adjusted R^2 = 0,7305; P-value < 0.001*). While Added Medical Value is a major criterion for setting prices within the French framework-agreement, this is not the case for the size of the targeted population. This could be specific to orphan medicines due to lower budget impacts.

Discussion :

The statistical significance of some tests was limited since only 17 products fulfilled all of the criteria mentioned.

Moreover, the analysis was restricted to **list prices.** Net prices and regional market access discrepancies were not considered. Due to international reference pricing, the listed price can act as a strong financial incentives for the manufacturer.

Finally, this study had a **French scope** whereby authorized orphan drugs that were not available in France were not considered. This does not impact the results of the one-to-one analysis presented here.

1 : EMA definition of the orphan statut *(https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview)*
****January 2016 and May 2021*** *: This timeframe was chosen as it was the period of application of the previous framework agreement (LEEM-CEPS), used for price negotiations in France.*

Conclusion

These findings suggest that **France granted lower listed price** to orphan drugs than its reference countries. Consequently, incentives are lower, which reflects on the time needed to market new drugs. Products with fewer patients obtained higher prices, acting as a compensation for lower sales. A new framework agreement in 2021 could change the lower prices observed as orphan drugs will access European prices with an AMV level of IV (instead of III before), guaranteeing a list price at least equal to the lowest price in the four countries considered. A mean price higher by at least 6% would have been observed if applied to the sample used.

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