

# Assessing the influence of the orphan drug status on medicine prices in the EU4 + UK

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## Objectives

Orphan drug status offers incentives for :

- Drug development : protocol assistance
- Central procedure, reduced registration fees
- 10 years of market exclusivity

**Research question** : does the orphan status also offer price incentives in the EU4 markets + United-Kingdom (UK) ? If yes, is the level of incentive the same between these 5 countries ?

## Methods

Scope of the analysis

- Commercialized orphan drugs and their clinical comparators
- 5 European countries : France, Germany (before price negotiations), Italy, Spain, UK
- From January 2015 to December 2021

Data collected

- Prices : from launch until end of study period
- Posology
- Added medical value and population size (assessed by the HAS<sup>1</sup> in France)

Statistical analysis conducted

Comparing the absolute price difference between orphan drugs and their non-orphan clinical comparators : student t-test and multiple linear regression on annual treatment cost (weighted on treatment duration)

Comparing relative prices between countries : price index comparison.

## Results

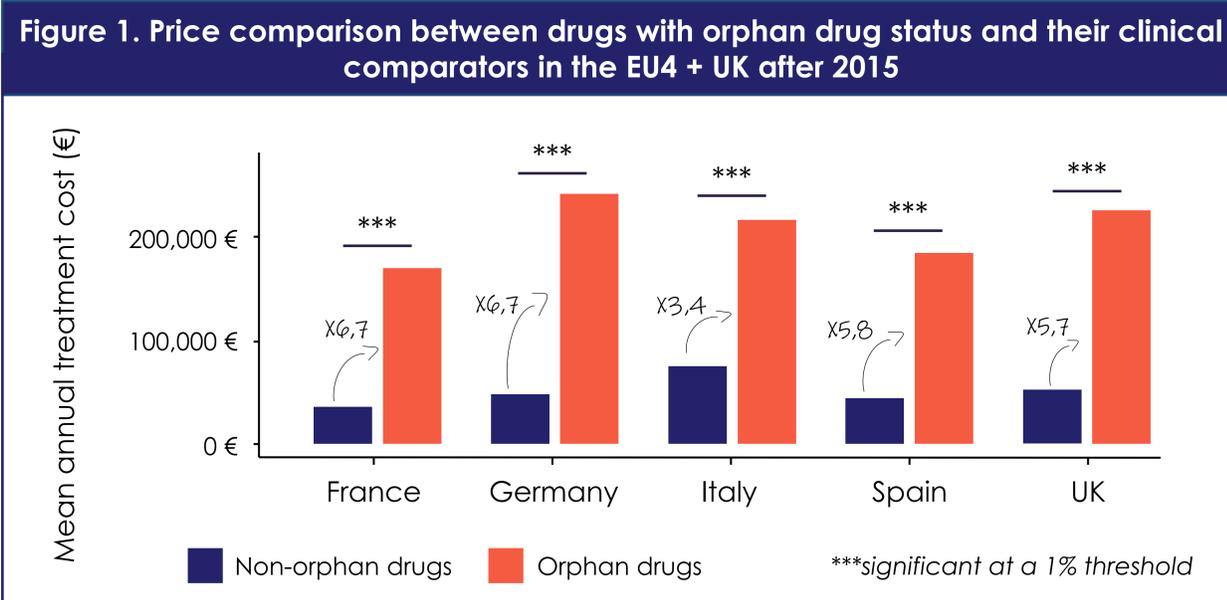
Products characteristics

47 orphan drugs and 9 clinical comparators were identified and analyzed.

The most represented drugs were antineoplastic and immunomodulating agents (ATC class L) representing 49% and 41% respectively.

40 other clinical comparators were commercialized before 2015. They were also added to the database as a supplementary analysis.

Absolute price difference between orphan and non-orphan drugs



Orphan drugs benefited from significantly (p-value < 0.001) **higher annual treatment costs** than their clinical comparators in **all the countries** studied (Figure 1.) : France (179,878€ vs 26,801€), Germany (247,110€ vs 37,035€), Italy (218,173€ vs 64,767€), Spain (188,593€ vs 33,213€) and UK (238,173€ vs 41,067€).

When including products launched before 2015 our conclusions did not change. A linear regression was conducted on this larger sample (96 products) to adjust for level of innovation (added medical value), target population (both based on French assessment by HAS) and launch date. Even after adjusting for these parameters, orphan drugs seemed to benefit from higher prices (Table 1.).

**Interpretation** : The orphan status is **correlated with higher prices in the 5 markets** studied. This could be an incentive to develop products in rare diseases.

Incentive comparison between European markets

Germany (before price negotiations) offered the highest prices for orphan drugs with an average index of 1.5, followed by the UK (2.3), Italy (2.6), Spain (3.5) and France (4.1).

While France offered high price incentives for orphan drugs compared to their clinical comparators, these prices remain lower than other European countries.

How did we build the price index ?

For country comparison, a country pricing index was developed: for each product, a score was given to a country according to its price positioning at launch vs. other markets with 1 for the highest price down to 5 for the lowest price. A mean rank was then calculated (Figure 2.)

**Interpretation** : a **price disparity** is observed between the 5 markets, with some giving relatively high prices (Germany, UK) compared to others (France, Spain).

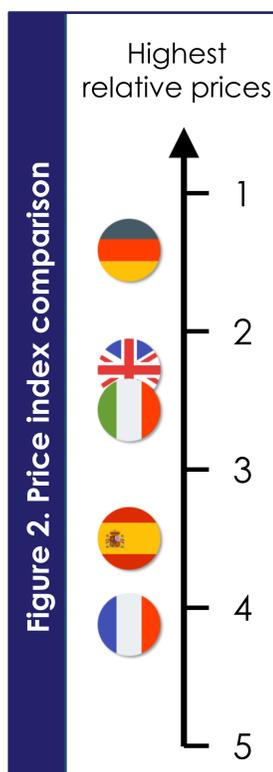


Table 1. Results of the linear regression

	France	Germany	Italy	Spain	UK
p-value	0.001	0.02	< 0.001	0.004	0.002
R <sup>2</sup>	0.29	0.27	0.34	0.34	0.32
<b>Orphan-status</b>	<b>+1.1x10<sup>4</sup></b>	<b>+19x10<sup>4</sup></b>	<b>+2.5x10<sup>4</sup></b>	<b>+1.8x10<sup>4</sup></b>	<b>+4.8x10<sup>4</sup></b>
Population size	-2.4	-4.4	-1.8	+0.4	-2.3
Launch Date (days)	+42.4	+6.8	+8.0	+69.4	+76.8
Level of innovation	Ref				
No added value	Ref				
Minor added value	+0.3x10 <sup>5</sup>	-1.2x10 <sup>5</sup>	+1.5x10 <sup>5</sup>	-0.02x10 <sup>5</sup>	+1.0x10 <sup>5</sup>
Important added value	+1.5x10 <sup>5</sup>	+2.9x10 <sup>5</sup>	+2.9x10 <sup>5</sup>	+1.2x10 <sup>5</sup>	+1.7x10 <sup>5</sup>
Major added value	+3.4x10 <sup>5</sup>	/	+4.6x10 <sup>5</sup>	+2.5x10 <sup>5</sup>	+2.9x10 <sup>5</sup>

\* Haute Autorité de Santé : French HTA agency

## Conclusion

All five EU4+UK markets grant higher prices to orphan drugs versus their comparators. This incentive is not uniform as Germany and UK, having the highest prices at launch also have the highest absolute difference in cost between orphan and non-orphan products.