PRICE DIFFERENCES FOR ORPHAN DRUGS ACROSS THE EU-5 COUNTRIES: A COMPARATIVE ASSESSMENT

PSY165

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INTRODUCTION

- Pricing and reimbursement decisions after the European marketing authorization are the responsibility of each country, which can lead to inequalities and differences in access and prices for drugs[1].
- **The aim of this study was to assess market access and price differences in the five European Union countries (EU5) for orphan drugs approved by the European Commission (EC).**

METHODS

- Countries included in the analysis were: **France, Germany, Italy, Spain and the United Kingdom** (UK).
- **Orphan drugs for which a marketing authorization was granted by the EC centralized procedure between January 2016 and September 2017** were extracted for the analysis from the European Medicines Agency (EMA) website[2].
  - Only initial authorizations were considered.
- **Commercialization status** was confirmed via country-specific health authorities' official websites (Table 1).
  - Orphan drugs that followed an early access pathway (commercialized before receiving the marketing authorization) in France and those that were approved with C-nn class (commercialized even if not yet reimbursed) in Italy were also considered as commercialized.
- The **official ex-factory list prices** were extracted through country-specific official sources (Table 1).
  - National statutory discounts to drug prices were considered in Spain (*Royal Decree-Law 8/2010*[3]) and Italy (*Determinations of July 2006 and September 2006*).
  - In Germany, prices after the early benefit assessment were included.
- **Market access** was analyzed considering the percentage of drugs commercialized at a national level with respect to all orphan drugs approved at EU level.
- In order to have an **anchor price for the comparison**, the country with the lowest expected price, i.e. UK, was chosen to be compared with.

Table 1. Market access and price data sources in each country

Country	Market Access*	Price*
Germany	G-BA[4]	LauerTaxe[5]
UK	NICE[6]	MIMS[7]
France	French Official Journal[8] ANSM[9]	French Official Journal[8]
Italy	Italian Official Journal GURI[10]	AIFA[11]
Spain	BotPlus[12]	BotPlus[12]

*Accessed June 2018.

ANSM: Agence Nationale de Sécurité du Médicament et des Produits de Santé; G-BA: Gemeinsamer Bundesausschuss; AIFA: Agenzia Italiana del Farmaco; UK: United Kingdom; NICE: National Institute for Health and Care Excellence; MIMS: Monhly Index of Medical Specialities

RESULTS

- **28 orphan drugs** were authorized by the EC between January 2016 and September 2017 (Table 2).

Table 2. Orphan drugs approved by the EC between January 2016 and September 2017

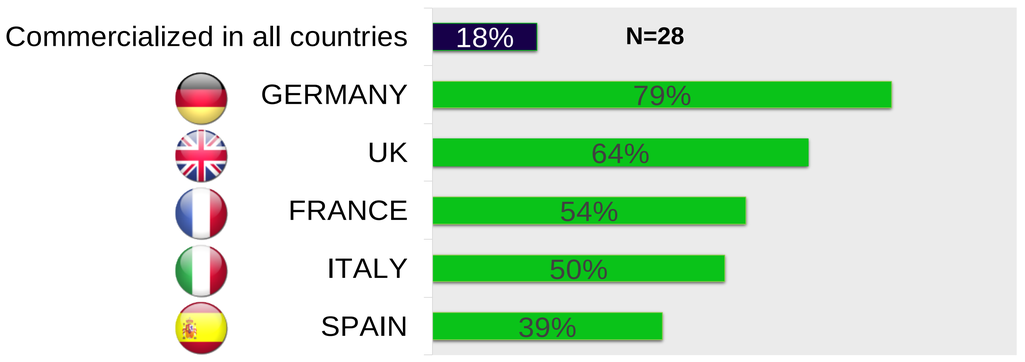
Brand name	Active substance	European Marketing Authorization date
Coagadex®	human coagulation factor X	16/03/2016
Idelvion®	albutrepenonacog alfa	11/05/2016
Alprolix®	eftrenonacog alfa	12/05/2016
Darzalex®	daratumumab	20/05/2016
Galafold®	migalastat cloridrato	26/05/2016
Strimvelis®	autologous CD34+ enriched cell fraction	26/05/2016
Zalmoxis®	allogeneic T cells genetically modified	18/08/2016
Onivyde®	irinotecan hydrochloride trihydrate	14/10/2016
Lartruvo®	olaratumab	09/11/2016
Ninlaro®	ixazomib	21/11/2016
Venclyxto®	venetoclax	05/12/2016
SomaKit TOC®	edotreotide	08/12/2016
Ocaliva®	obeticholic acid	12/12/2016
Cystadrops®	mercaptamine	19/01/2017
Ledaga®	chlormetine	03/03/2017
Chenodeoxycholic acid leadiant	chenodeoxycholic acid	10/04/2017
Natpar®	parathyroid hormone	24/04/2017
Qarziba®	dinutuximab beta	08/05/2017
Brineura®	cerliponase alfa	30/05/2017
Spinraza®	nusinersen	30/05/2017
Besponsa®	inotuzumab ozogamicin	29/06/2017
Oxervate®	cenegermin	06/07/2017
Cuprior®	trientine	05/09/2017
Bavencio®	avelumab	18/09/2017
Rydapt®	midostaurin	18/09/2017
Xermelo®	telotristat	18/09/2017
Lutathera®	lutetium (^{177}Lu) oxodotreotide	26/09/2017
Zejula®	niraparib	16/11/2017

RESULTS

MARKET ACCESS OF ORPHAN DRUGS IN THE EU5

- Figure 1 shows the percentage of orphan drugs commercialized at the national level.
  - **Germany was the country with the highest number of orphan drugs commercialized, while the least access was in Spain**.
  - **Five orphan drugs** have been commercialized in **all EU5 countries**.
  - **Three orphan drugs** have yet not been commercialized in **any of the EU5 countries**.
  - 36% and 73% of drugs commercialized were introduced through **early access to medicines scheme in Italy and France**, respectively.

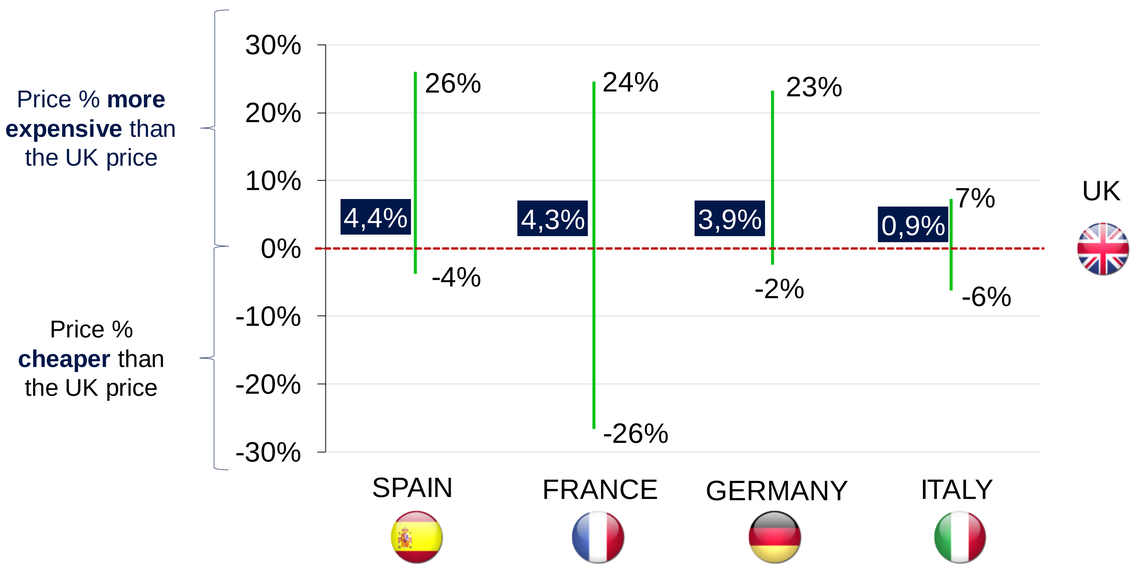
Figure 1. Orphan drugs commercialized in the EU5



PRICE DIFFERENCES OF ORPHAN DRUGS IN THE EU5

- Germany and the UK have publicly-available list prices for all commercialized drugs, while Spain, Italy and France have 91%, 71% and 67% of drugs with a list price, respectively.
- The UK is the country with the lowest prices for orphan drugs, followed by Italy. Spain, France and Germany have similar median prices between each other (Figure 2).

Figure 2. Price differences across the EU5 (median [IQR])



UK: United Kingdom; IQR: Interquartile Range.

DISCUSSION

- **Hidden discounts, performance agreement and budget cap** that are increasingly common in Europe are unrevealed[13].
  - The frequency and complexity of confidential negotiations suggests that the **official list prices may not represent the reimbursed price** paid by many institutional payers[13].
- The **joint analysis of EU5 countries** is important in order to understand differences in market access and pricing processes across countries and to implement strategies accordingly.
  - The **transparency** of negotiated prices would allow to perform **better and more realistic price comparisons** across these countries.
- **National/regional budgets and negotiations** in other countries play an important role in **achieving price agreements** at a national level, which delays the availability of new drugs to patients.
- A potential reason for **unknown list prices** of commercialized medicines might be that some orphan drugs were introduced with an **early access to medicines scheme**, in which price and reimbursement are still not negotiated.

CONCLUSIONS

- **Wide disparity exists in the number of approved drugs available** in each of the European countries since the proportion of orphan drugs commercialized varies from 39% to 79%.
  - Access to new orphan drugs is limited in the Southern European countries.
  - These disparities could be attributed to the different policies of each country.
- Notably, **more than three quarters of the orphan drugs are still not commercialized** in all the countries.
- **Substantial differences in price exist across countries**.

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