

APPROVAL OF ORPHAN DRUGS IN SPAIN?

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BACKGROUND & OBJECTIVES

- P&R decision-making for orphan drugs (ODs) is faced with specific challenges, as the limited knowledge and heterogeneity of rare diseases make it difficult to demonstrate the added clinical benefit of a treatment<sup>1,2</sup>. Achieving approval from the European Commission (EC) does not guarantee access within the Spanish market. In Spain, the Committee on Pricing of Medicines and Healthcare Products (CIPM), responsible for the final pricing and reimbursement (P&R) decision, includes in their P&R resolutions the criteria used to justify such decisions. However, information on how these criteria are neither defined nor measured is not provided<sup>3</sup>. Therefore, the drivers influencing the approval or denial of a drug P&R are not clear<sup>4</sup>.
- The objective of this study was to **identify the clinical and regulatory variables that might be relevant for the P&R decisions of ODs in Spain.**

METHODS

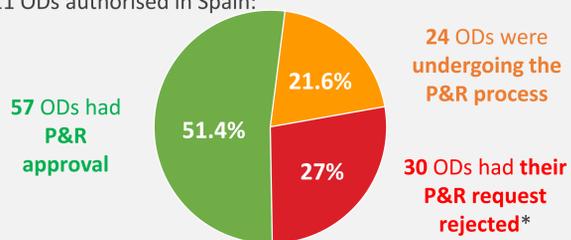
- This study includes ODs approved by the EC between 2006 and 2021 and that subsequently obtained Marketing Authorisation in Spain. ODs were classified according to their P&R status in Spain: approved, undergoing decision and rejected. P&R approval timelines in Spain were analysed.
- The potential variables that might influence reimbursement resulted from the official P&R criteria established by the Royal Decree Law 1/2015 of 24 July to evaluate the reimbursement of new drugs under the Spanish National Healthcare System (NHS) funds<sup>4</sup>, as well as from the variables reported in the mandatory information that Marketing Authorisation Holders (MAHs) must provide to European and Spanish regulatory bodies as part of the Marketing Authorisation Application (MAA) and the national P&R request procedures.
- Variables included in the analysis were: therapeutic area, rarity of the disease, existence of alternative therapies, availability of survival-related outcomes, adequate safety profile, type of population, conditional approval status and a positive Therapeutic Positioning Report (TPR) conclusion. Economic variables have not been assessed due to lack of publicly-available information.

RESULTS

Orphan Drugs P&R status in Spain

A total of **128 ODs approved by the EC** between 2006 and 2021 were identified, of which **111 (86.7%) have obtained marketing authorised in Spain.**

Out of the 111 ODs authorised in Spain:



\*5 ODs were commercialised in the private market without public reimbursement under the NHS: Bronchitol®(mannitol), NexoBrid® (concentrate of proteolytic enzymes enriched in bromelain), Procysbi® (mercaptopamine), Tobi Podhaler® (tobramycin) and Xermelo® (telotristat ethyl)

Regulatory timelines



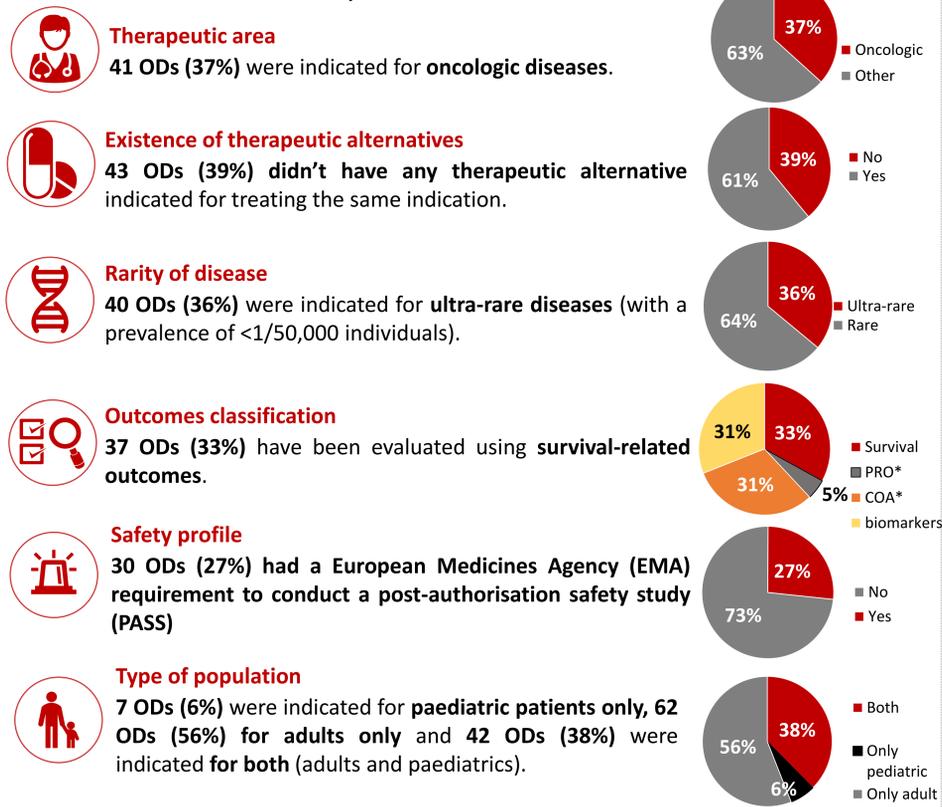
In **May 2013**, the **Therapeutic Positioning Report (TPR)** was introduced as part of the **P&R process** in Spain. The TPR is an **evaluation document** issued by the Spanish Agency of Medicines and Medical Devices (**AEMPS**) that includes a review and summary of **relative (versus Standard of Care) efficacy and safety data** available for the **new product** to determine its **positioning in the treatment pathway**<sup>5</sup>.

The **inclusion of the TPR** during the P&R process **has not shown a significant impact on P&R evaluation timelines of ODs in Spain.**

**P&R evaluation timelines** have been **slightly reduced** with the inclusion of TPRs by an **average of less than 1 month**. The mean time from Spanish marketing authorisation to P&R decision after introduction of TPR is **18.2 months** (with a minimum of 3 months and a maximum of 50 months).

Clinical variables results

Out of the 111 ODs authorised in Spain:



Relationship of the clinical and regulatory variables with the reimbursement status

Out of the 111 ODs authorised in Spain:

CLINICAL

Variables that seem to influence P&R decision:

- Therapeutic area:** For ODs indicated for oncology diseases, **21 (51%)** were reimbursed and **7 (17%)** had their P&R request rejected.
- Rarity of disease:** For ODs indicated for ultra-rare diseases, **25 (63%)** were reimbursed and **10 (25%)** had their P&R request rejected.
- Outcomes classification:** For ODs evaluated with survival-related outcomes, **21 (57%)** were reimbursed and **7 (19%)** had their P&R request rejected.

Variables that seem not to influence P&R decision:

- Existence of therapeutic alternatives:** For ODs that did not have any therapeutic alternative, **18 (42%)** were reimbursed and **14 (32%)** had their P&R request rejected.
- Safety profile:** For ODs that did not require a PASS study, **41 (51%)** were reimbursed. For ODs that required a PASS study, **16 (53%)** were reimbursed.
- Type of population:** For ODs indicated for paediatric population, **23 (47%)** were reimbursed and, for ODs indicated for adults, **55 (53%)** were reimbursed.

REGULATORY

Variables that seem to influence P&R decisions:

- TPR conclusion:** For ODs with a positive TPR conclusion, **43 (80%)** were reimbursed and **11 (20%)** had their P&R request rejected.
- Conditional approval:** For ODs without conditional approval granted by the EMA, **51 (55%)** were reimbursed and **24 (26%)** had their P&R request rejected.

CONCLUSIONS

- From all ODs approved by the EC between 2006 – 2021 and which have obtained MAA in Spain, **57 (51.4%)** were reimbursed, **30 (27%)** were rejected and **24 (21.6%)** were undergoing decision with the **potential to be reimbursed in the future.**
- Before the inclusion of the TPR in 2013**, the mean time from Spanish marketing authorisation to P&R decision was **19,1 months** and **after the TPR inclusion**, the mean time decreased to **18,2 months**. **P&R evaluation timelines** have been **slightly reduced** since the inclusion of TPRs by an **average of less than 1 month.**
- ODs **might be more likely to be reimbursed** in Spain if they have a **positive TPR conclusion** (80% were reimbursed), if indicated for an **ultra-rare disease indication** (63% were reimbursed), if their clinical programme is based on **survival-related outcomes** (57% were reimbursed), if they are approved **without conditional approval** (55% were reimbursed) and if directed to an **oncology indication** (51% were reimbursed).
- Economic variables could not be assessed in this study because of lack of transparency in public sources.** Spain operates a **dual pricing system** for hospital medicines and the **official listed prices** in the available databases **do not reflect the real reimbursed prices**, since **these are confidentially agreed between the Ministry of Health and the MAH.**

REFERENCES

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