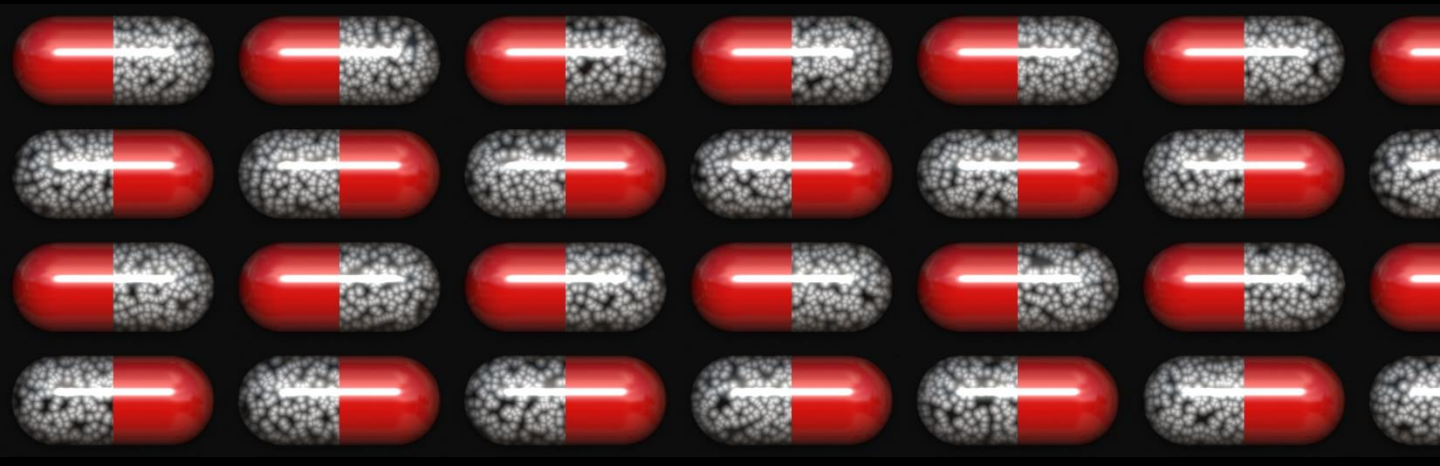
OMAKASE consulting

Annual Omakase Orphan Drugs Report: The impact of the Therapeutic positioning report (TPR) on the pricing and reimbursement process in Spain 2003 – 2021



Annual Omakase Orphan Drugs Report: The impact of the Therapeutic positioning report (TPR) on the pricing and reimbursement process in Spain 2003 – 2021

Authors:

Xavier Badia

Claudia Gómez

John Shepherd

Technical support:

Claudia Gómez, Data compiling, processing and statistical analysis

This report is an update of the previous report: Assessing the criteria that could drive Pricing and Reimbursement approval of orphan drugs authorised in Spain and approved by the European Commission between 2003 & 2020. Analysis of P&R situation in Spain. Available from: https://www.omakaseconsulting.com/publications/

1. Objectives

The objectives of this report are:

1. To understand the Pricing & Reimbursement (P&R) situation in Spain of Orphan drugs (ODs) approved by the European Commission (EC) between 2003 and 2021

2. To identify and describe clinical and regulatory variables for identified ODs

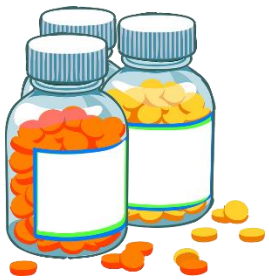
   To analyse the clinical and regulatory variables and establish potential relationships with the reimbursement status

3. To analyse the potential impact of the TPR regulatory process on the P&R of ODs in Spain

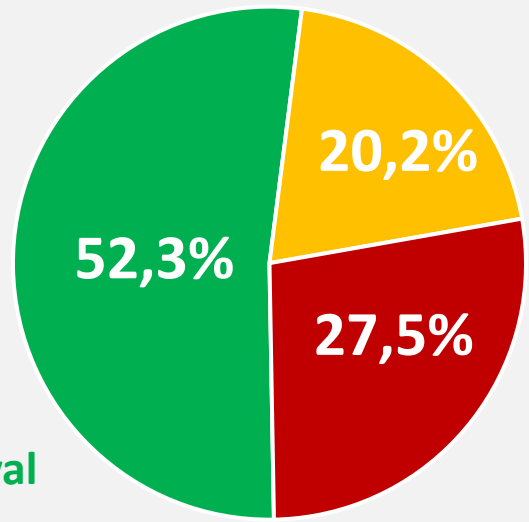
2. Results

Orphan Drugs approved between 2003-2021

A total of **128 ODs approved by the European Commission** (EC) were identified, **of which 109 (85,2%) had been authorised in Spain**.



Out of the 109 ODs that were authorised in Spain…



22 were **undergoing the P&R process**

30 had **P&R request rejected***

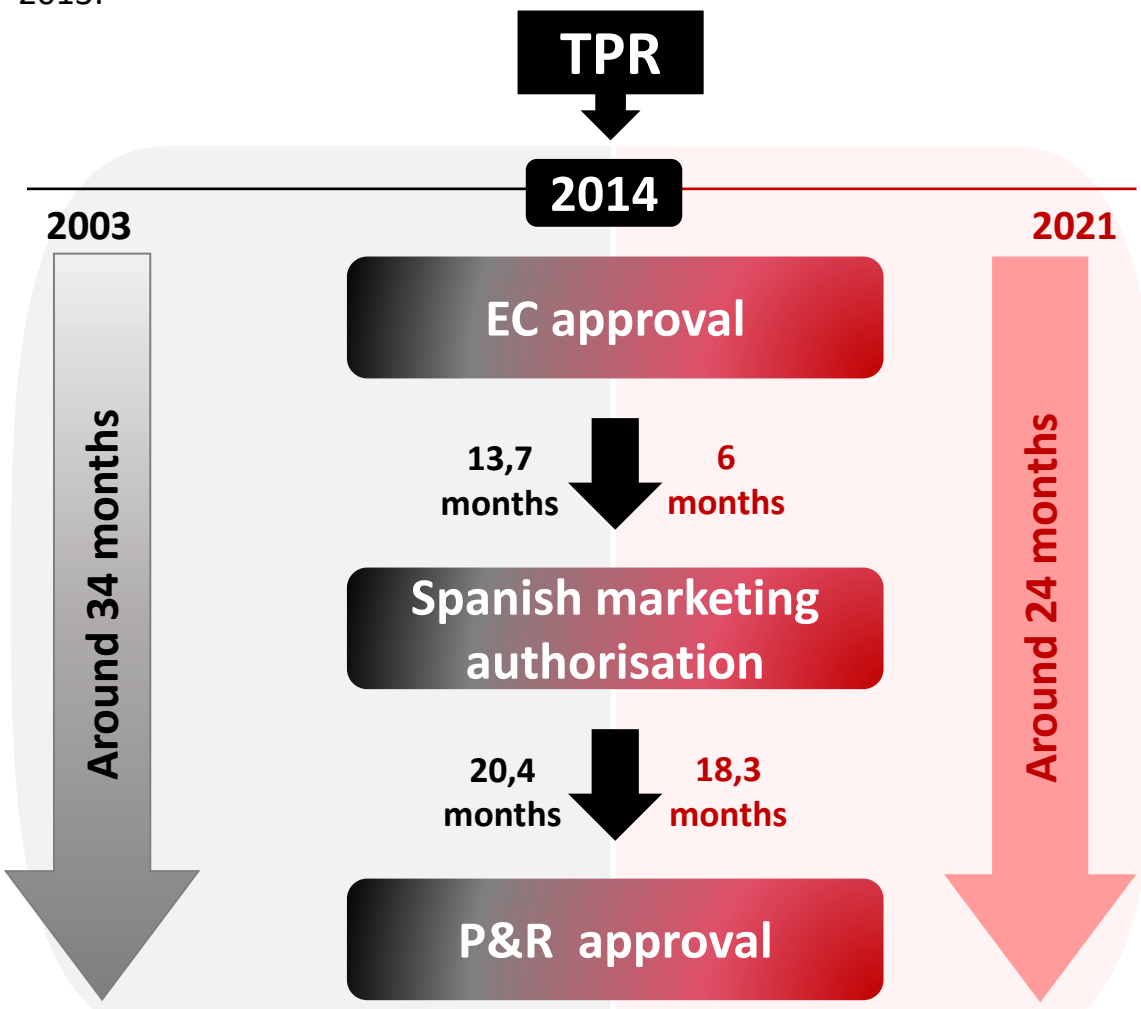
57 had **P&R approval**

***5 ODs were commercialised in the private market:** Bronchitol®, NexoBrid®, Procysbi®, Tobi Podhaler® and Xermelo®.

2. Results

P&R timelines have been reduced after the inclusion of the TPR by an average of 10 months

The **mean regulatory times** of approved EC ODs from 2003 to 2021 from EC approval to P&R approval in Spain are shown below, stratified by before (n=15) or after (n=94) the inclusion of the TPR during P&R process in Spain in 2013:



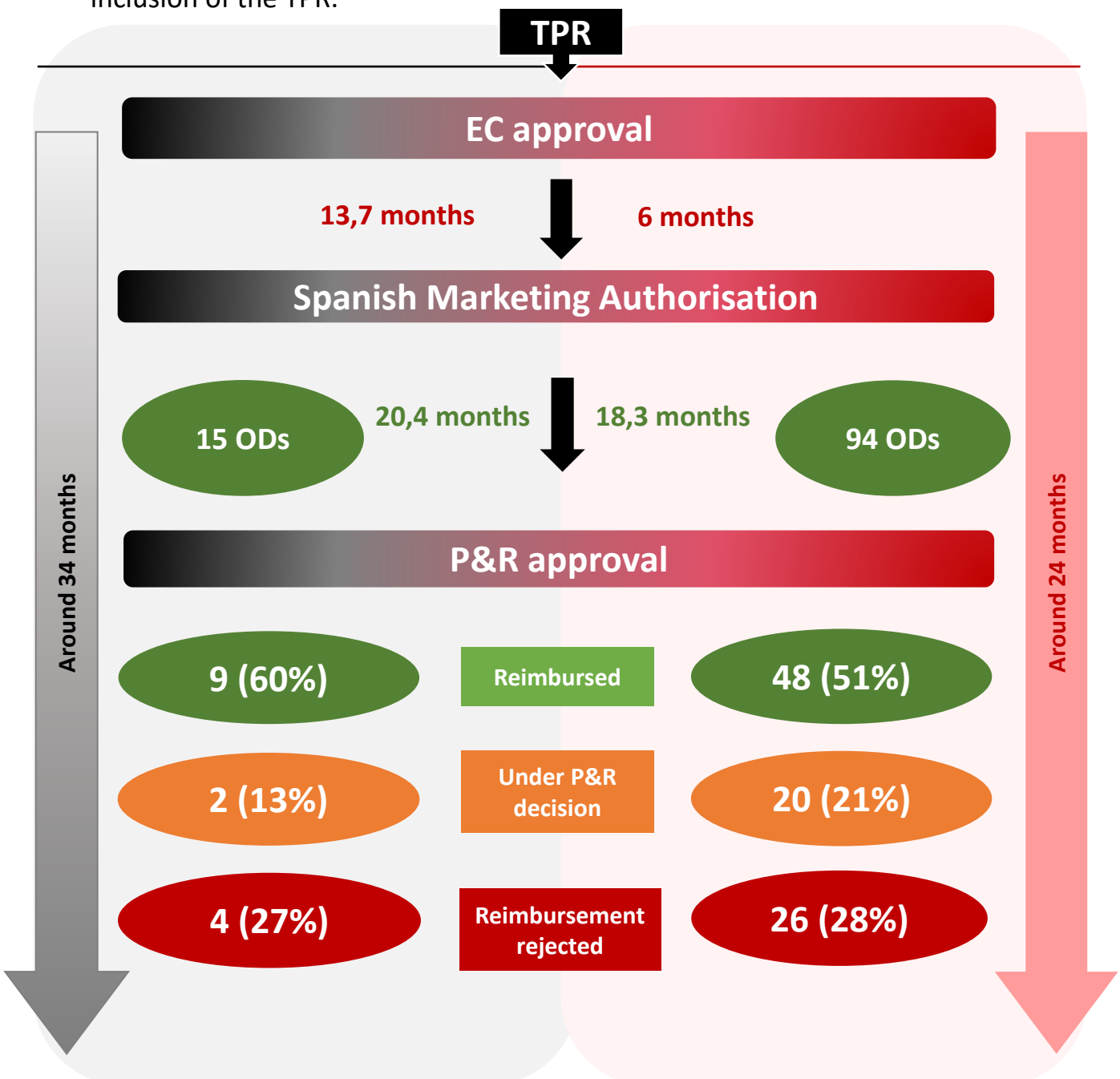
The mean time from EC approval to Spanish marketing authorisation has decreased by an average of 7,7 months (from 13,7 months to 6 months) and from **the Spanish marketing authorisation to P&R approval it has decreased by an average of 2,1 months (**from 20,4 months to 18.3 months) **after the inclusion of TPRs during P&R process**

Sources: The EMA's website. www.ema.europa.eu/en; AEMPS. CIMA. cima.aemps.es/cima/publico/home.html; MoH. BIFIMED: www.mscbs.gob.es/profesionales/medicamentos.do

2. Results

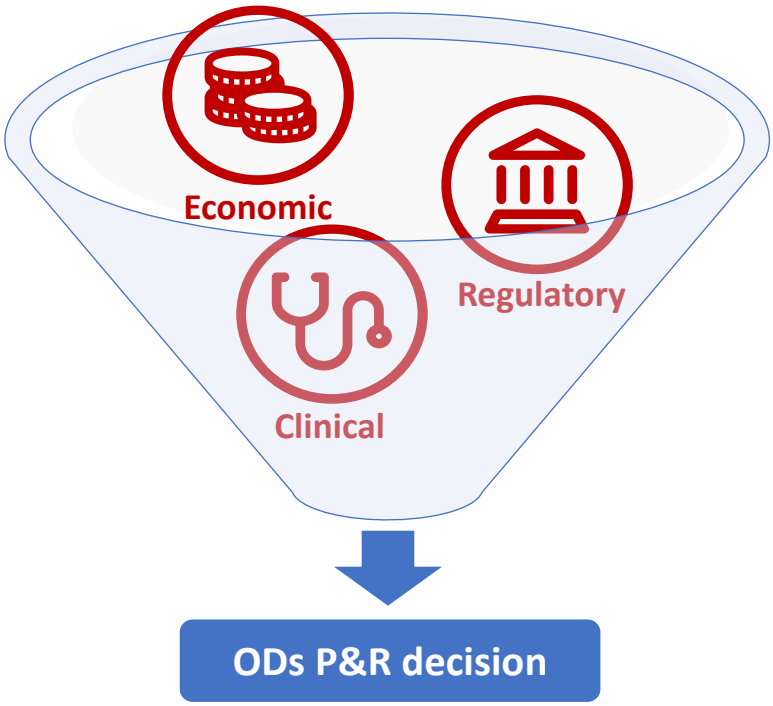
P&R timelines have been reduced after the inclusion of the TPR by an average of 10 months

The **number (percentage) of P&R approval ODs, the ODs under P&R decision process, and P&R rejected ODs** after obtaining the **Spanish Marketing Authorisation** are shown below, stratified by before and after the inclusion of the TPR.



2. Results

Clinical and regulatory variables were identified to be relevant for the P&R process in Spain



CLINICAL VARIABLES

Therapeutic area, rarity of disease, existence of therapeutic alternatives, outcomes classification, efficacy profile, safety profile and type of population.

REGULATORY VARIABLES

Conditional approval by the European Medicines Agency (EMA) and Therapeutic Positioning Report (TPR) conclusion in Spain.

ECONOMIC VARIABLES were not included in this report because the lack of validity. . Spain operates a dual pricing system for hospital medicines. Official listed prices in the available databases do not reflect reimbursed price agreed with the Ministry of Health. The reimbursed price is usually 40% lower in relationship with the list price.

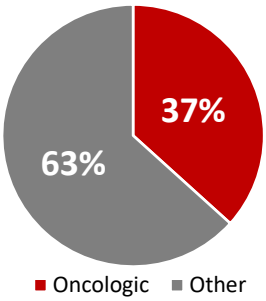
2. Results

Clinical variables results (cont.)

Descriptive results of clinical variables are shown below. Out of the 109 authorised ODs in Spain:

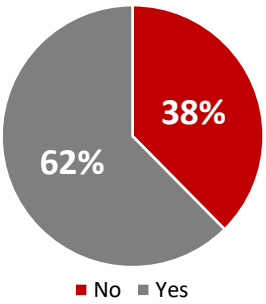
Therapeutic area

40 ODs (37%) were indicated for **oncologic diseases**.



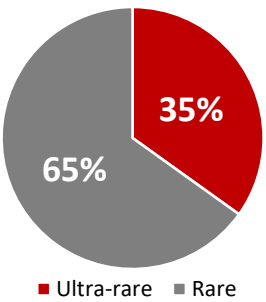
Existence of therapeutic alternatives

41 ODs (38%) didn't have any therapeutic alternative indicated for treating the same indication.



Rarity of disease

38 ODs (35%) were indicated for **ultra-rare diseases** (with a prevalence of <1/50,000 individuals).



Continues on next page

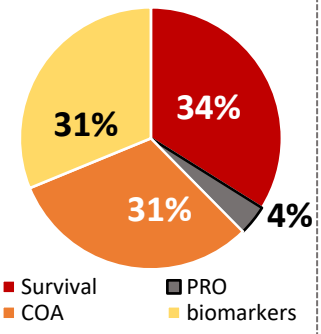
2. Results

Clinical variables results (cont.)

Out of the 109 authorised ODs in Spain :

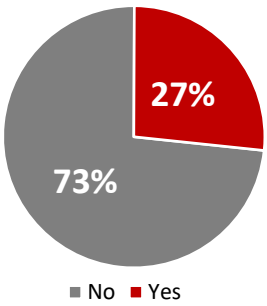
Outcomes classification

37 ODs (34%) have been evaluated with survival-related outcomes.



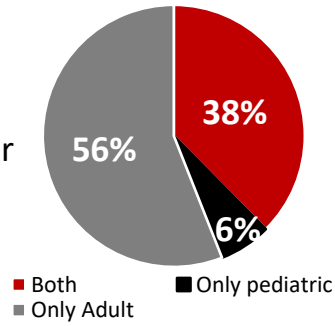
Safety profile

29 ODs (27%) had to conduct a Post-authorisation safety study (PASS) according to EMA.



Type of population

48 ODs (44%) were indicated for **paediatric patients.**



* Clinical outcomes assessment

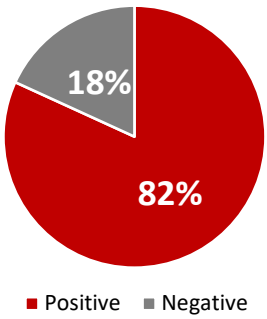
2. Results

Regulatory variables results

Descriptive results of regulatory variables are shown below. Out of the 109 authorised ODs in Spain:

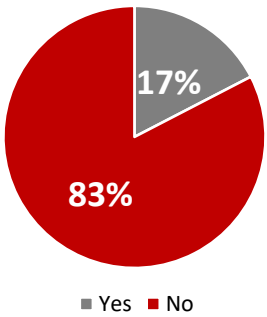
*TPR conclusion**

Out of the 66 published TPR, **54 ODs (82%)** had a **positive conclusion**.



Conditional approval

19 ODs (17%) were granted conditional approval marketing authorisation by the EMA.



* The TPR conclusion refers to the final efficacy and safety conclusion of the ODs according to the TPR. This variable was based on a subjective interpretation by the authors of this report (without considering the final P&R approval decision indicated in the TPR).

2. Results

Clinical variables by reimbursement status

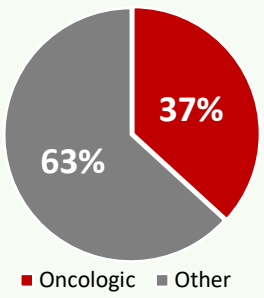
The defined clinical variables have been related with the reimbursement status of the ODs approved by the EC between 2003 and 2021.

Results are shown **by reimbursement category**:

Therapeutic area

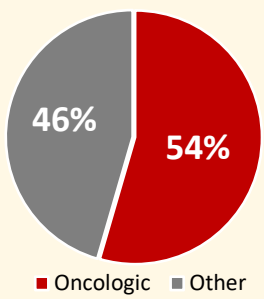
From the **P&R approved ODs**:

- **21** (37%) were indicated for for **oncologic diseases**



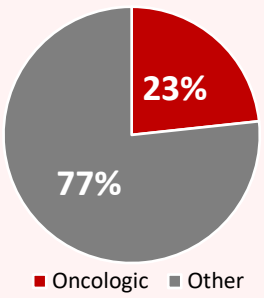
From the **under P&R decision ODs**:

- **12** (54%) were indicated for **oncologic diseases**



From the **P&R rejected ODs**:

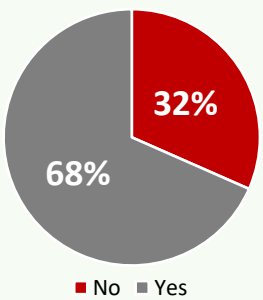
- **7** (23%) were indicated for **oncologic diseases**



Existence of therapeutic alternatives

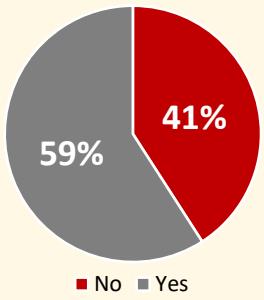
From the **P&R approved ODs**:

- **18** (32%) didn't have a **therapeutic alternative**



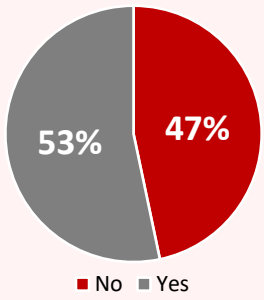
From the under **P&R decision ODs**:

- **9** (41%) didn't have a **therapeutic alternative**



From the **P&R rejected ODs**:

- **14** (47%) didn't have a **therapeutic alternative**



Continues on next page

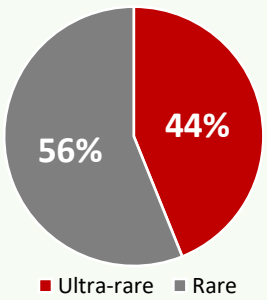
2. Results

Clinical variables by reimbursement status (cont.)

Rarity of disease

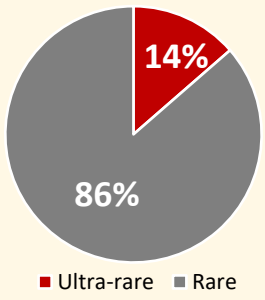
From the **P&R approved ODs**:

- **25** (44%) were indicated for **ultra-rare diseases**



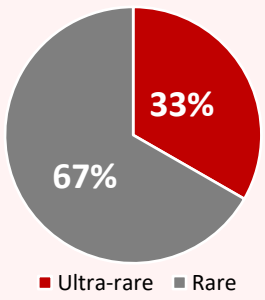
From the **ODs under P&R decision**:

- **3** (14%) were indicated for **ultra-rare diseases**



From the **P&R rejected ODs**:

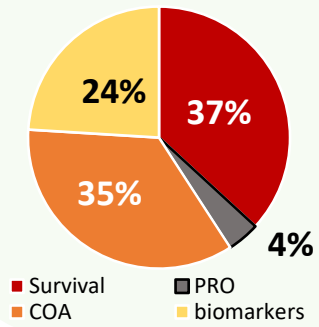
- **10** (33%) were indicated for **ultra-rare diseases**



Outcomes classification

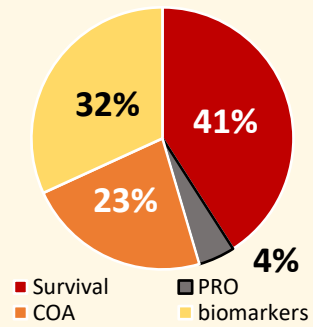
From the **P&R approved ODs**:

- **21** (37%) **have been evaluated with survival-related outcomes and 20 (35%) with COAs***



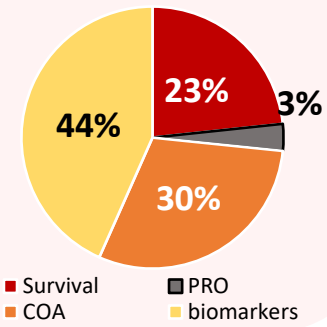
From the **ODs under P&R decision**:

- **9** (41%) **have been evaluated with survival-related outcomes and 7 (32%) with biomarkers**



From the **P&R rejected ODs**:

- **13** (44%) **have been evaluated with biomarker outcomes and 9 (30%) with COA***



* Clinical outcomes assessment

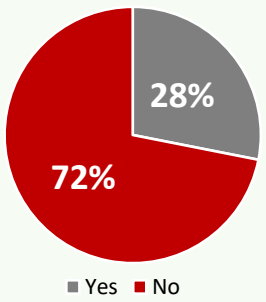
2. Results

Clinical variables by reimbursement status (cont.)

Safety profile

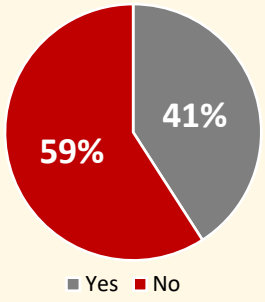
From the **P&R approved ODs**:

- **41** (72%) **did not have the obligation to conduct a PASS**



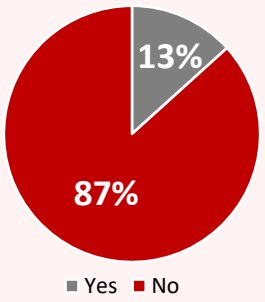
From the **ODs under P&R decision**:

- **13** (59%) **did not have the obligation to conduct a PASS**



From the **P&R rejected ODs**:

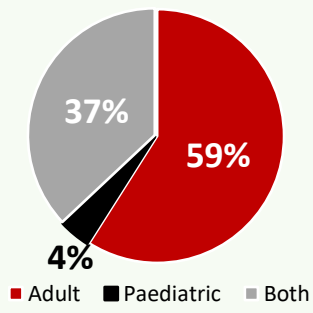
- **26** (87%) **did not have the obligation to conduct a PASS**



Type of population

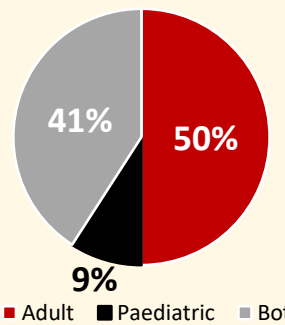
From the **P&R approved ODs**:

- **23** (41%) were indicated for **paediatric patients**



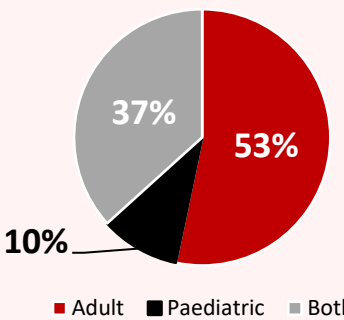
From the **ODs under P&R decision**:

- **11** (59%) were indicated for **paediatric patients**



From the **P&R rejected ODs**:

- **14** (47%) were indicated for **paediatric patients**



Continues on next page

2. Results

Regulatory variables by reimbursement status

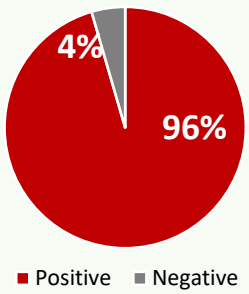
The defined regulatory variables have been related with the reimbursement status of the ODs approved by the EC between 2003 and 2021.

Results are shown **by reimbursement category**:

TPR conclusion (ODs with published TPR)*

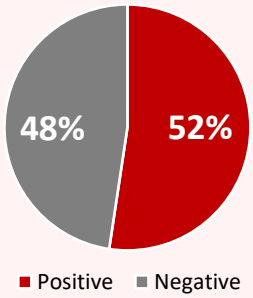
From the **P&R approved ODs**:

- **43** (96%) had a **positive conclusion**



From the **P&R rejected ODs**:

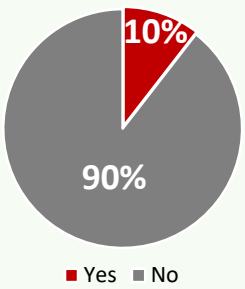
- **11** (52%) had a **positive conclusion**



Conditional approval

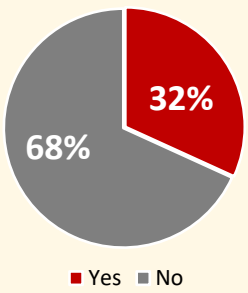
From the **P&R approved ODs**:

- **6** (10%) **were granted conditional approval** and **51** (90%) **were not granted conditional approval**



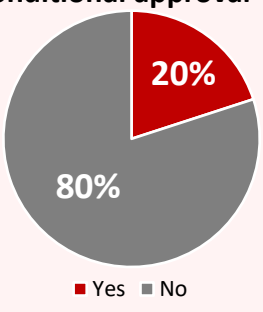
From the **ODs under P&R decision**:

- **7** (32%) **were granted conditional approval** and **15** (68%) **were not granted conditional approval**



From the **P&R rejected ODs**:

- **6** (20%) **were granted conditional approval** and **24** (80%) **were not granted conditional approval**



* The TPR conclusion refers to the final efficacy and safety conclusion of the ODs according to the TPR. This variable was based on a subjective interpretation by the authors of this report (without considering the final P&R approval decision indicated in the TPR).

3. Conclusions

01

Out of the **128 ODs approved by the European Commission, 109** (85,2%) **ODs were authorised in Spain.**

Out of the **109 ODs that obtained Spanish Marketing Authorisation**, **57 (52,3%)** were **reimbursed**, **22 (20.2%)** were **undergoing P&R negotiations** and **30 (27,5%)** were **rejected**.

02

The **mean Spanish regulatory timeline from EC approval to P&R approval decision before TPR inclusion** was **34 months**, and the **mean regulatory timeline after TPR inclusion is 24 months**. The Spanish regulatory timelines for ODs have been reduced after the inclusion of the TPR during P&R process by an **average of 10 months.**

03

Out of the 57 reimbursed ODs, 21 (36.8%) **are oncology ODs**, which might reflect increasing research in oncology area. In contrast, only 2 reimbursed ODs in Spain treat cardiovascular system diseases.

A **higher percentage of reimbursed ODs** (44%) **are indicated for ultra-rare disease compared to reimbursement rejected ODs** (33%), so the indication for ultra-rare diseases (prevalence <1 per 50.000 inhabitants) **could influence the P&R decision.**

Regarding the clinical trial outcomes, **most of the ODs that were evaluated with survival-related endpoints have been reimbursed**, and this could be in line with the fact that a **high percentage** (44%) **of reimbursement rejected ODs were assessed with biomarkers.**

Continues on next page

3. Conclusions

The other clinical variables would not be influenced by the inclusion of TPR in the P&R decision. These variables are the **existence of therapeutic alternatives, the type of population** for which ODs are indicated, and the **obligation to conduct a PASS.**

04

Out of the **reimbursed ODs with published TPR, 96% had a positive TPR conclusion***. Moreover, **52% of the reimbursement rejected ODs also had a positive TPR conclusion and nonetheless the reimbursement were denied**.

A **lower percentage of reimbursed ODs** (10%) **were granted conditional approval compared to reimbursement rejected ODs** (20%)**.** This could be due to, despite allowing early access to ODs for patients with an unmet need, a conditional approval could also generate uncertainty of efficacy and sustainability to the Spanish National Health System.

05

Economic variables were not included in this report because the **lack of validity**. Spain operates a dual pricing system for hospital medicines and the official listed prices in the available databases do not reflect reimbursed price agreed with the Ministry of Health. **The reimbursed prices are confidentially agreed between the Ministry of Health and the company**.

* The TPR conclusion refers to the final efficacy and safety conclusion of the ODs according to the TPR. This variable was based on a subjective interpretation by the authors of this report (without considering the final P&R approval decision indicated in the TPR).

OMAKASE
consulting