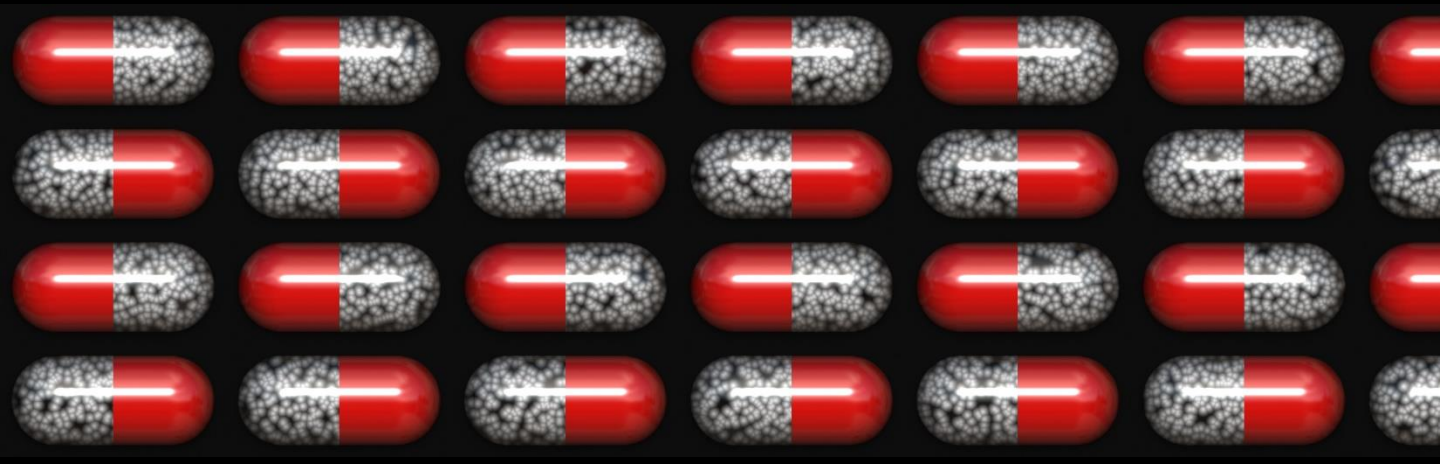
OMAKASE consulting

Updated Annual Report on Orphan Drugs authorised in Spain and approved by the European Commission between 2003 & 2020

Summary of main results



Updated Annual Report on Orphan Drugs authorised in Spain and approved by the European Commission between 2003 & 2020

Authors:

Xavier Badia

Alicia Gil

Adviser:

Jose Luis Poveda. Hospital U. La Fe

Technical support:

Tania Vico and Claudia Gomez, 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 & 2019. 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 2020

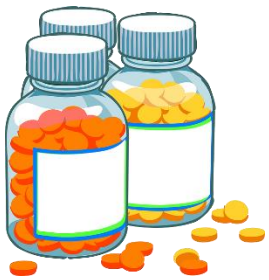
2. To identify and describe clinical and regulatory variables of each ODs identified

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

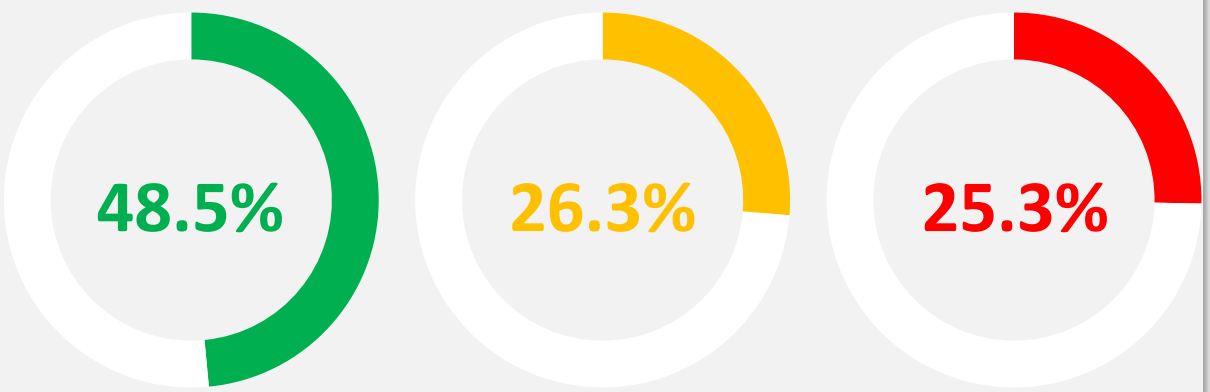
2. Results

Orphan Drugs approved between 2003-2020

A total of **118 ODs approved by the European Commission** (EC) were identified, **of which 99 (83.9%) had been authorised in Spain**.



Out of the 99 ODs that were authorised in Spain…



48 had **P&R approval**

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

25 had **P&R request rejected***

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

2. Results

Regulatory timelines of approved ODs between 2003-2020

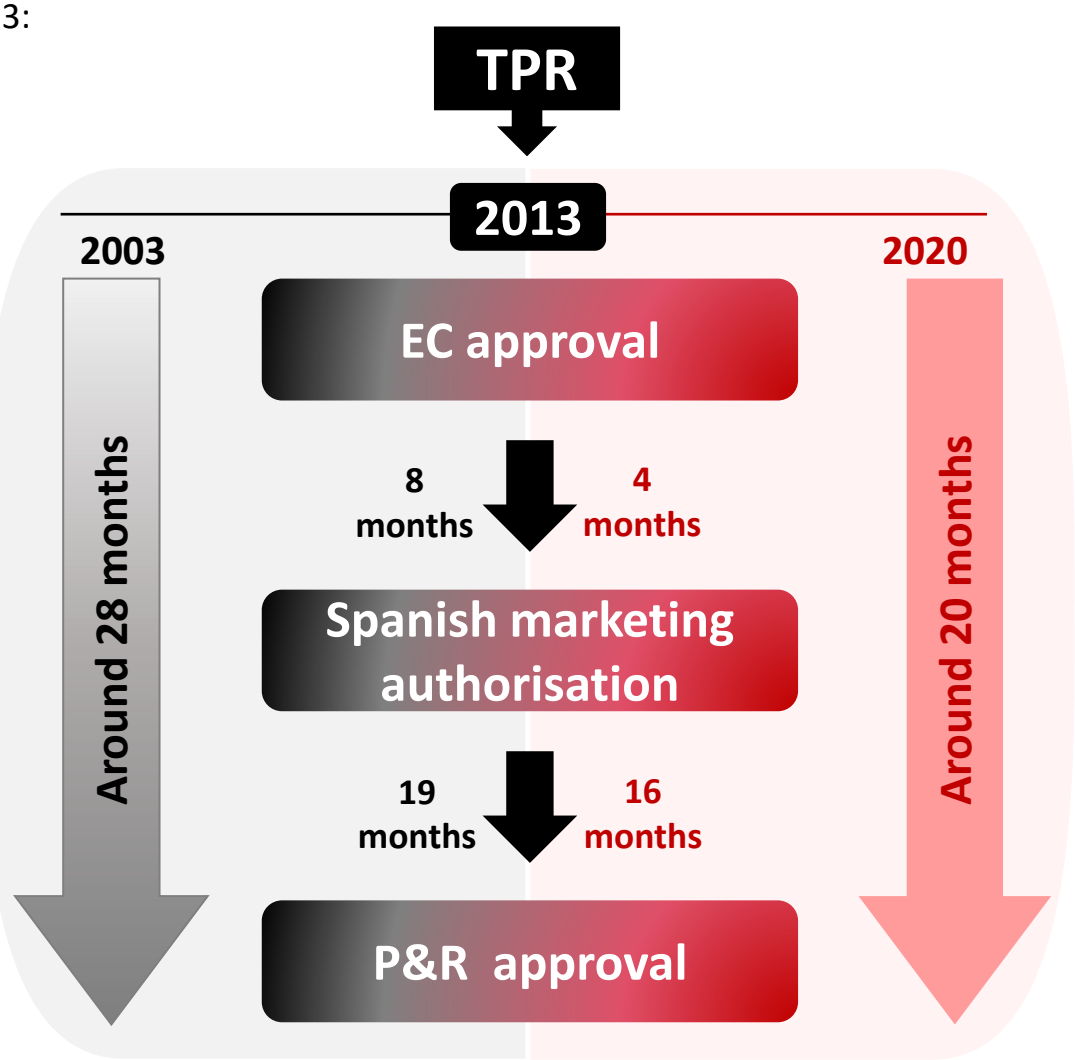
The mean regulatory times from EC approval to P&R approval date in Spain are shown below (n=48):

- The **mean time from EC approval to P&R approval in Spain was 23.4 ± 14.2 months**, with a minimum of 4 months (Kymriah®) and a maximum of 61 months (Revestive®).

2. Results

P&R timelines have been reduced after the inclusion of the TPR by an average of 8 months

The **mean regulatory times** of approved EC ODs from 2003 to 2020 from EC approval to P&R approval in Spain are shown below, stratified by before (n=17) or after (n=31) the inclusion of the TPR during P&R process in Spain in 2013:

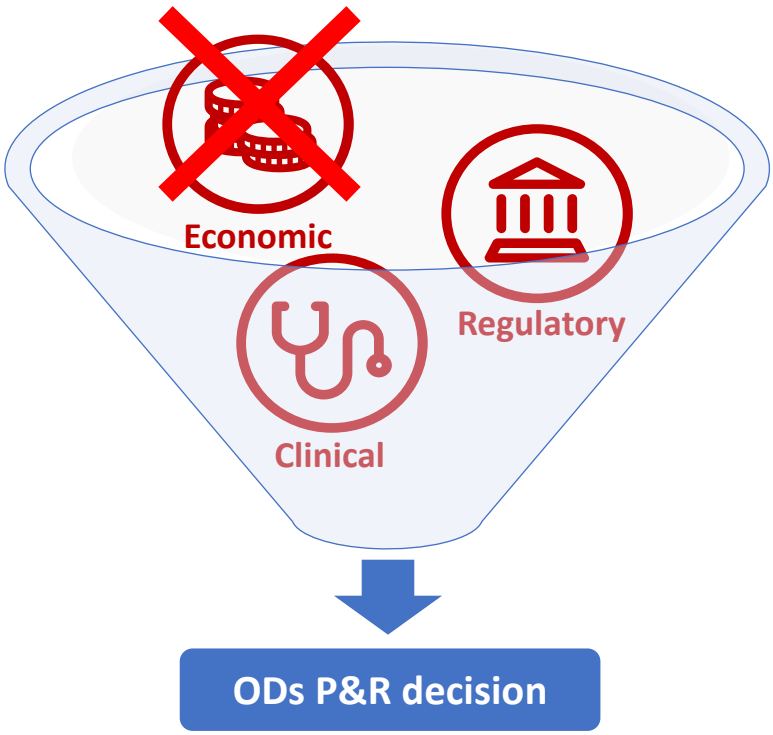


The mean time from EC approval to Spanish marketing authorisation has decreased by an average of 4 months (from 8.1 ± 11.3 months in years 2003-2013 to 4 ± 7.3 months in years 2014-2020) and from **the Spanish marketing authorisation to P&R approval it has decreased by an average of 3 months (**from 19.4 ± 13.5 months in years 2003-2013 to 16.3 ± 11.35 months in years 2014-2020) **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

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 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 reimbursement price agreed with the MAH. The real price can be reduced between 20-45%.

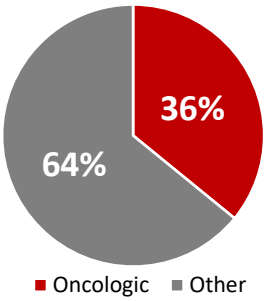
2. Results

Clinical variables results

Descriptive results of clinical variables are shown below. Out of the 99 studied ODs:

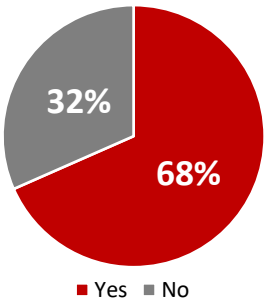
Therapeutic area

36 ODs (36.4%) were indicated for **oncologic diseases**.



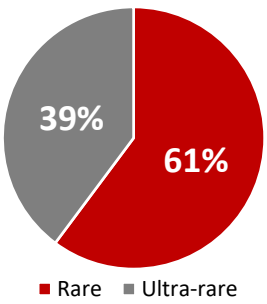
Existence of therapeutic alternatives

67 ODs (67.7%) had a therapeutic alternative indicated for treating the same condition.



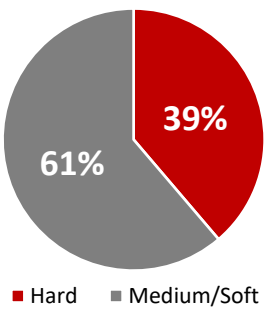
Rarity of disease

60 ODs (60.6%) were indicated for **rare diseases** (with a prevalence of <5/10,000 to >1/50,000 individuals).



Outcomes classification

39 ODs (39,4%) had **hard clinical trial outcomes** (survival and patient reported outcomes, PRO).



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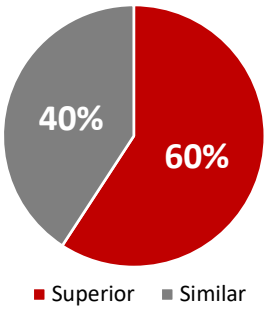
2. Results

Clinical variables results (cont.)

Out of the 99 studied ODs:

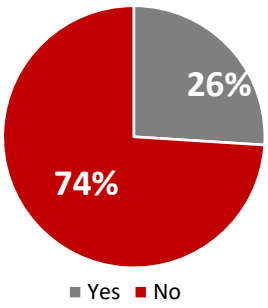
Efficacy profile

59 ODs (59.6%) had a **superior efficacy profile**.



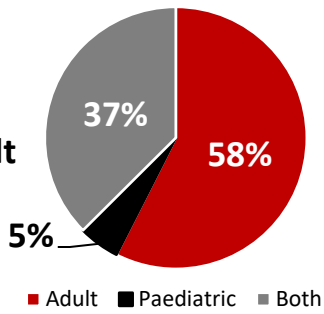
Safety profile

73 ODs (73,7%) did not have the obligation by the EMA to conduct a Post-authorisation safety study (PASS).



Type of population

57 ODs (57.6%) were indicated for **adult patients**.



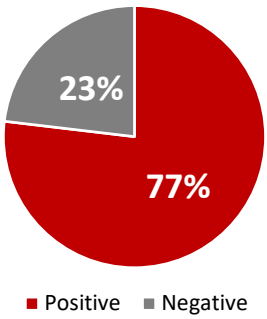
2. Results

Regulatory variables results

Descriptive results of regulatory variables are shown below. Out of the 99 studied ODs:

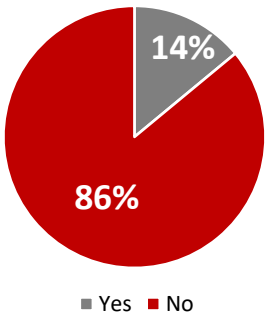
TPR conclusion

Out of the 56 published TPR, **43 ODs (76.8%)** had a **positive conclusion**.



Conditional approval

85 ODs (85.9%) were not granted conditional approval marketing authorisation by the EMA.



2. Results

Clinical variables by reimbursement status

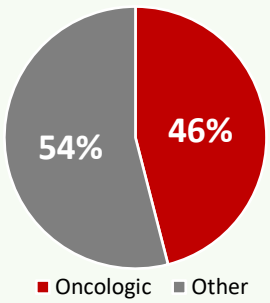
The defined clinical variables have been related with the reimbursement status of the ODs approved by the EC between 2003 and 2020.

Results are shown **by reimbursement category**:

Therapeutic area

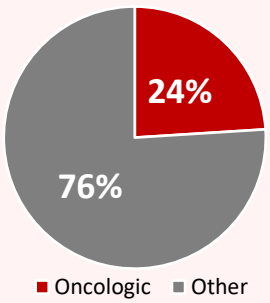
From the **P&R approved ODs**:

- **22** (45.8%) were indicated for **oncologic diseases**



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

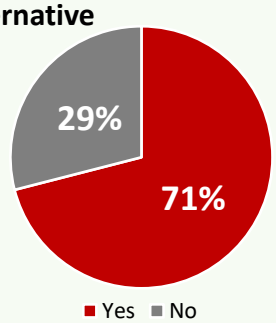
- **6** (24%) were indicated for **oncologic diseases**



Existence of therapeutic alternatives

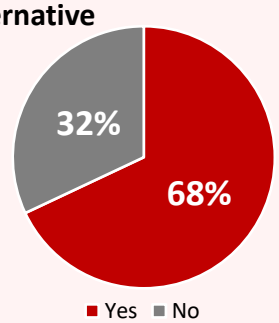
From the **P&R approved ODs**:

- **34** (70.8%) had a **therapeutic alternative**



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

- **17** (68.0%) had a **therapeutic alternative**



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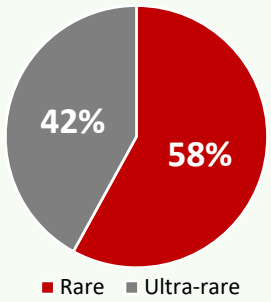
2. Results

Clinical variables by reimbursement status (cont.)

Rarity of disease

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

- **28** (58.3%) were indicated for **rare diseases**



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

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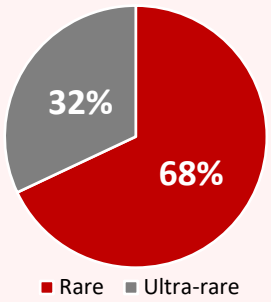
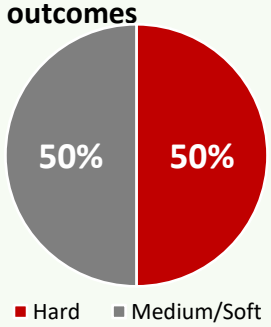


Outcomes classification

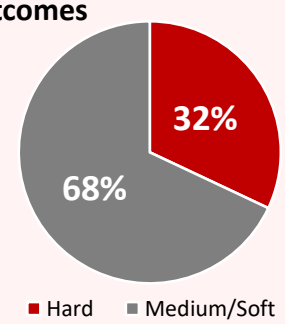
From the **P&R approved ODs**:

- **24** (50.0%%) had **hard clinical trial outcomes**



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

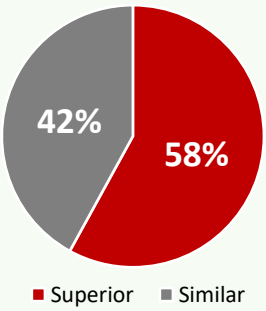
- **8** (32%) had **hard clinical trial outcomes**



Efficacy profile

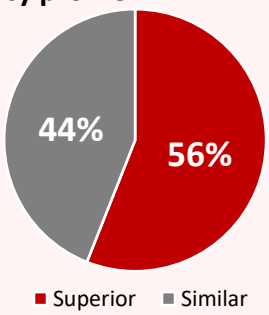
From the **P&R approved ODs**:

- **28** (58.3%) had a **superior efficacy profile**



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

- **14** (56.0%) had a **superior efficacy profile**



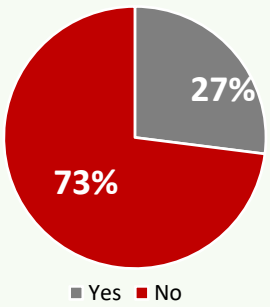
2. Results

Clinical variables by reimbursement status (cont.)

Safety profile

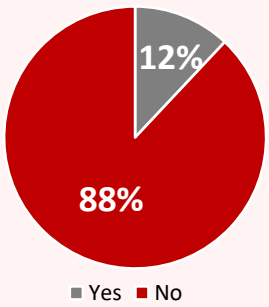
From the **P&R approved ODs**:

- **35** (72.9%) **did not have the obligation to conduct a PASS**



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

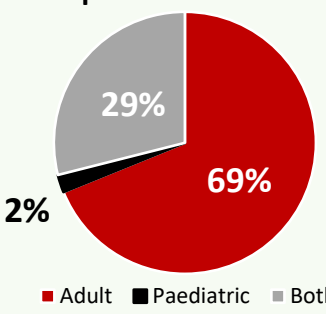
- **22** (88%) **did not have the obligation to conduct a PASS**



Type of population

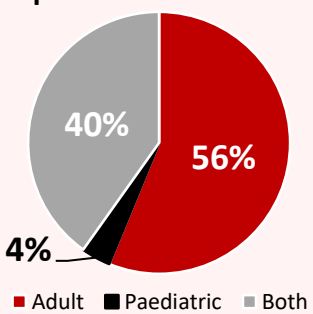
From the **P&R approved ODs**:

- **33** (68.8%) were indicated for **adult patients**



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

- **14** (56%) were indicated for **adult patients**



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2. Results

Regulatory variables by reimbursement status

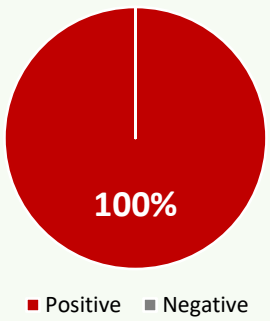
The defined regulatory variables have been related with the reimbursement status of the ODs approved by the EC between 2003 and 2020.

Results are shown **by reimbursement category**:

TPR conclusion (ODs with published TPR)

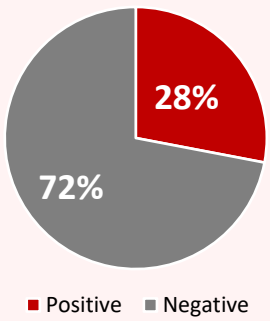
From the **P&R approved ODs**:

- **38** (100%) had a **positive conclusion**



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

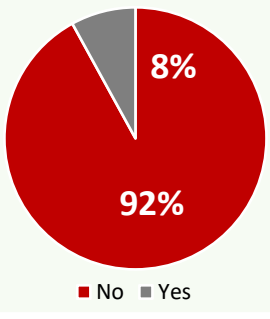
- **5** (28%) had a **positive conclusion**



Conditional approval

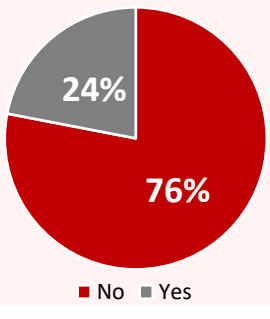
From the **P&R approved ODs**:

- **44** (91.7%) **were not granted conditional approval**



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

- **19** (76%) **were not granted conditional approval**



3. Conclusions

01 From all ODs approved by the EC and which had obtained Marketing Authorisation in Spain, **48 (48.5%)** were **reimbursed**, **26 (26.3%)** were **undergoing decision** and **25 (25.3%)** were **rejected**.

02 In 2020, it continues to be verified that the inclusion of the TPR has been a key element in making P&R decisions in Spain. The average Spanish regulatory timeline from EC approval to P&R decisions before TPR inclusion is 28 months, and the average regulatory timeline after TPR inclusion is 20 months. The Spanish **regulatory timelines for ODs have been reduced after the inclusion of the TPR during P&R process by an average of 8 months**.

03 Out of the reimbursed ODs, **the majority are oncology drugs (45.8%)**, which may reflect further research in oncology area. In contrast, only four reimbursed ODs in Spain treat nervous system diseases.

One in three reimbursed ODs does not have a therapeutic alternative. In addition, 50% reimbursed ODs generate **important** patient reported **outcomes** (PRO), such as quality of life.

The type of rarity of the disease is not relevant for the P&R approval of OD in Spain; nor the efficacy profile of the drug because its previously approved by the EMA for their effectiveness.

Furthermore, **73%** reimbursed ODs **did not** have the request by the EMA to **conduct a PASS**.

The type of population that ODs are indicated does not influence a lot in the P&R decisions.

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3. Conclusions

04

Out of the 48 reimbursed ODs, **38 had a published TPR, and 100% of ODs with published TPR (n=38) had a positive TPR conclusion.**

14% ODs have received **conditional marketing authorization by the EMA**, and in Spain there is 8% reimbursed ODs with conditional authorization; this ODs could be hardly reimbursed in Spain. This may be a consequence that, despite allowing early access to ODs for patients with an unmet need, this also generate uncertainty of efficacy and sustainability to the National Health System.

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