
# ACCESS AND PRICING OF ORPHAN MEDICINES

JORGE MESTRE-FERRANDIZ

BARCELONA, 18 NOVEMBER

# AGENDA

1. **Setting the context - OMPs**
2. How much do we spend on OMPs?
3. Access to OMPs
4. (Some) final remarks

# WHAT ARE OMPS?

2000R0141 — EN — 07.08.2009 — 001.001 — 1



▶B REGULATION (EC) No 141/2000 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 16 December 1999

on orphan medicinal products

(OJ L 18, 22.1.2000, p. 1)

*Article 3*

**Criteria for designation**

1. A medicinal product shall be designated as an orphan medicinal product if its sponsor can establish:

(a) that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand persons in the Community when the application is made, or

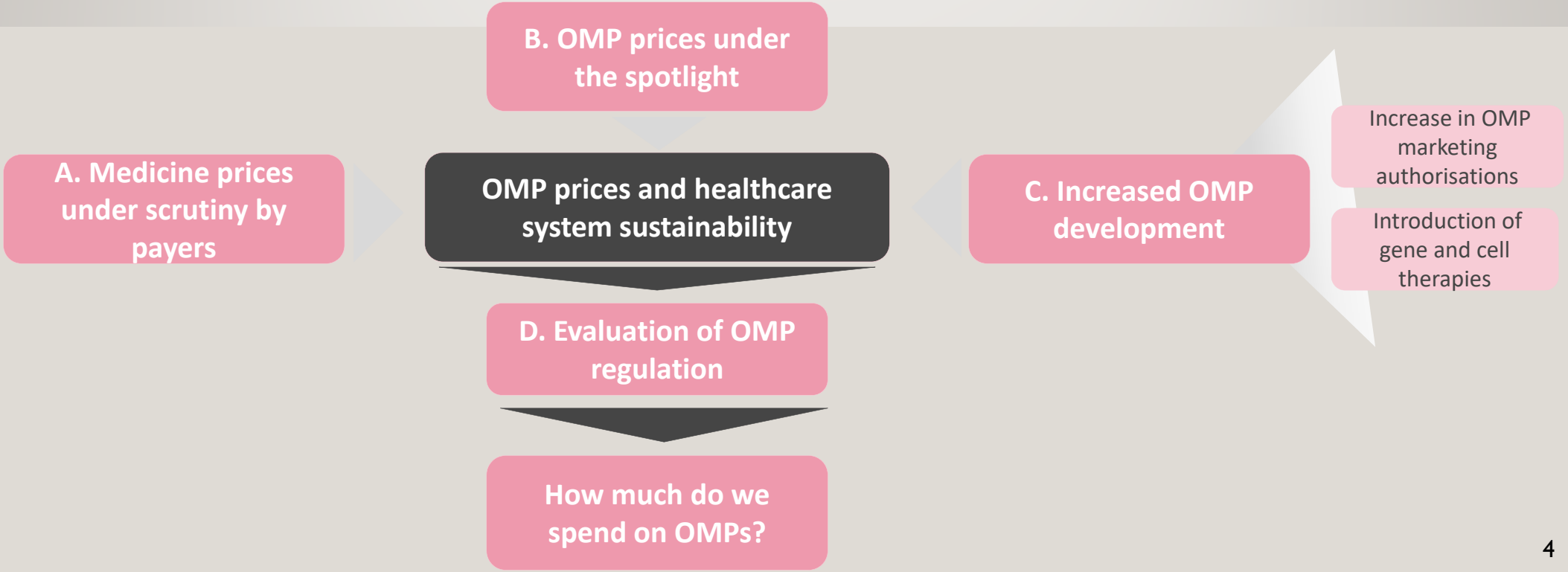
that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the Community and that without incentives it is unlikely that the marketing of the medicinal product in the Community would generate sufficient return to justify the necessary investment;

and

(b) that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorised in the Community or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition.

# SETTING THE CONTEXT

- OMP prices are perceived by some as a challenge to the financial sustainability of healthcare systems



# SITUATION A: Medicine prices are under increasing pressure and scrutiny by payers and are considered by some as a challenge to the healthcare sustainability

Report from the Committee on the Environment, Public Health and Food Safety, EU Parliament[1]

*September 2016*

The **prices of new medicines** have increased during the past few decades to the point of being **unaffordable** for many European citizens and of creating an **unsustainable situation for health care systems**.

Challenges facing policy makers in the pharmaceutical market, OECD Health Policy Study[2]

*November 2018*

The **increasing prices of new medicines** particularly in oncology and orphan drugs are not always justified by commensurate increases in benefits for patients. All these trends have **raised concern** about the value and the **sustainability of pharmaceutical spending**.

EU Council Conclusions on Strengthening Balance in EU Pharmaceutical Systems[3]

*March 2017*

New medicinal products may pose new **challenges to public health systems**, in particular … **the financial sustainability of health systems**, their post-market surveillance and patient access and affordability.

Conclusions on Pharmaceutical Expenditure and Policies, OECD Health Working Paper[4]

*April 2016*

The **rise in costs** for specialty drugs suggests that there is a need for a **radical reappraisal of pricing practices** for new products in OECD countries.



1. Committee on the Environment, Public Health and Food Safety. Draft report on EU options for improving access to medicines (2016/2057(NI)). European Parliament 2016. Available from: www.europarl.europa.eu/meetdocs/2014_2019/plmrep/COMMITTEES/ENVI/DV/2017/01-30/1028308EN.pdf; accessed May 2018
2. Pharmaceutical Innovation and Access to Medicines, OECD Health Policy Studies (2018). Available from: https://read.oecd-ilibrary.org/social-issues-migration-health/pharmaceutical-innovation-and-access-to-medicines_9789264305243-en#page1; accessed December 2018
3. Council of the EU. Council conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States. Press Release. 2016. Available from: http://www.consilium.europa.eu/en/publication/pdf/7_publication_7b6e4f07b3e5-11e6-8f69-01aa75ed71a1/language-en
4. Pharmaceutical Expenditure And Policies: Past Trends And Future Challenges. OECD Health Working Papers (2016). Available from: https://www.oecd.org/els/health-systems/DELSA-HEA-WD-HSP(2015)6.en.pdf?expires=1537956878&id=id&accname=guest&checksum=0D9451A0F0B3B1B3A7F4AD7ED0775D80; accessed December 2018

# SITUATION B: Orphan medicines prices have been under the spotlight

## OPINIONS ON OMPS PRICES[1,2]

Viewpoint

### Outrageous prices of orphan drugs: a call for collaboration

*Lucio Luzzatto*, Hanna I Hyry*, Arrigo Schieppati, Enrico Costa, Steven Simoens, Franz Schaefer, Jonathan C P Roos, Giampaolo Merlini, Helena Kääriäinen, Silvio Garattini, Carla E Hollak, Giuseppe Remuzzi, on behalf of the Second Workshop on Orphan Drugs participants*

Few instances of a single act of legislation have shifted industrial policy in the pharmaceutical industry like the Orphan Drugs Act did when it was signed in the USA in 1983. The Act was written to facilitate the development of drugs for rare diseases and health conditions,[1] and the incentives provided by the Act, such as 7 year exclusivity, tax credits of up to 50% of research and development costs, and access to research and development grants, resulted in the US Food and Drug Administration[2] (FDA) approving 575 drugs and biological products for rare diseases between 1983 and 2017—a real success. In 2000, the European Commission passed similar legislation for orphan medicinal products (OMPs). As a matter of fact, the diseases, not the drugs, are the orphans because all drugs are very expensive,[3] having marrying this success story (table).

diseases. So-called orphanisation of common disorders, which is a direct result of the genomics era, enhances the scope for precision medicine and is expected to expand the scope further. At present, 40% of drugs with OMP status are approved for specific types of cancer.[14]

Free market competition is distorted in the case of OMPs. First, often only one drug is available, giving rise to a monopoly situation. Second, in some cases, several OMPs are available for the same disease; for example, three drugs are licensed for treatment of Gaucher's disease (imiglucerase, velaglucerase alfa, and taliglucerase alfa).[15] No evidence favours any one product over the other, and each drug costs about US$200 000 per patient per year. To an outside observer, this might look like a cartel.

*Lancet* 2018; 392: 791–94
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PLOS ONE

RESEARCH ARTICLE

### Profitability and Market Value of Orphan Drug Companies: A Retrospective, Propensity-Matched Case-Control Study

**Dyfrig A. Hughes[1]*, Jannine Poletti-Hughes[2]**

**1** Centre for Health Economics and Medicines Evaluation, Bangor University, Arddwy, Holyhead Road, Bangor, LL57 2PZ, United Kingdom, **2** University of Liverpool Management School, University of Liverpool, Chatham Street, Liverpool, L69 7ZH, United Kingdom

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OPEN ACCESS

**Citation:** Hughes DA, Poletti-Hughes J (2016) Profitability and Market Value of Orphan Drug

## Abstract

**Background**

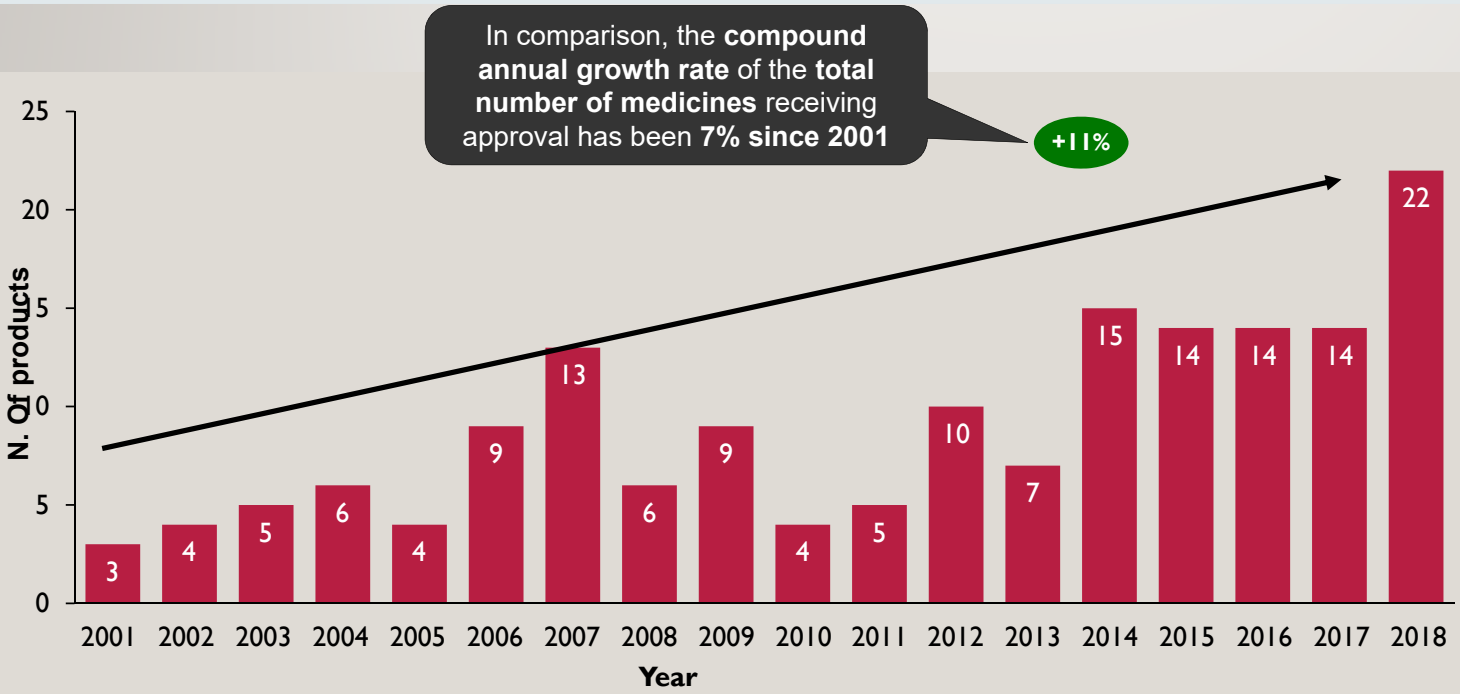
Concerns about the high cost of orphan drugs has led to questions being asked about the generosity of the incentives for development, and associated company profits.

**Drugs** for **rare diseases** are perceived as **high cost** medicines and their **prices** have been **criticised**[1]

1. Luzzatto L. et al. Outrageous prices of orphan drugs: a call for collaboration. Lancet 2018;392:791-4
2. Hughes D. et al. Profitability and Market value of Orphan drug companies: A retrospective, propensity-matched case-control study. PLoS ONE 2016;11(10): e0164681. doi:10.1371/journal.pone.0164681

# SITUATION C: THE NUMBER OF OMPS RECEIVING MA HAS INCREASED EACH YEAR SINCE 2001

**NUMBER OF OMP MA PER YEAR**[1]




***164 OMPs approved since the introduction of EU regulation***

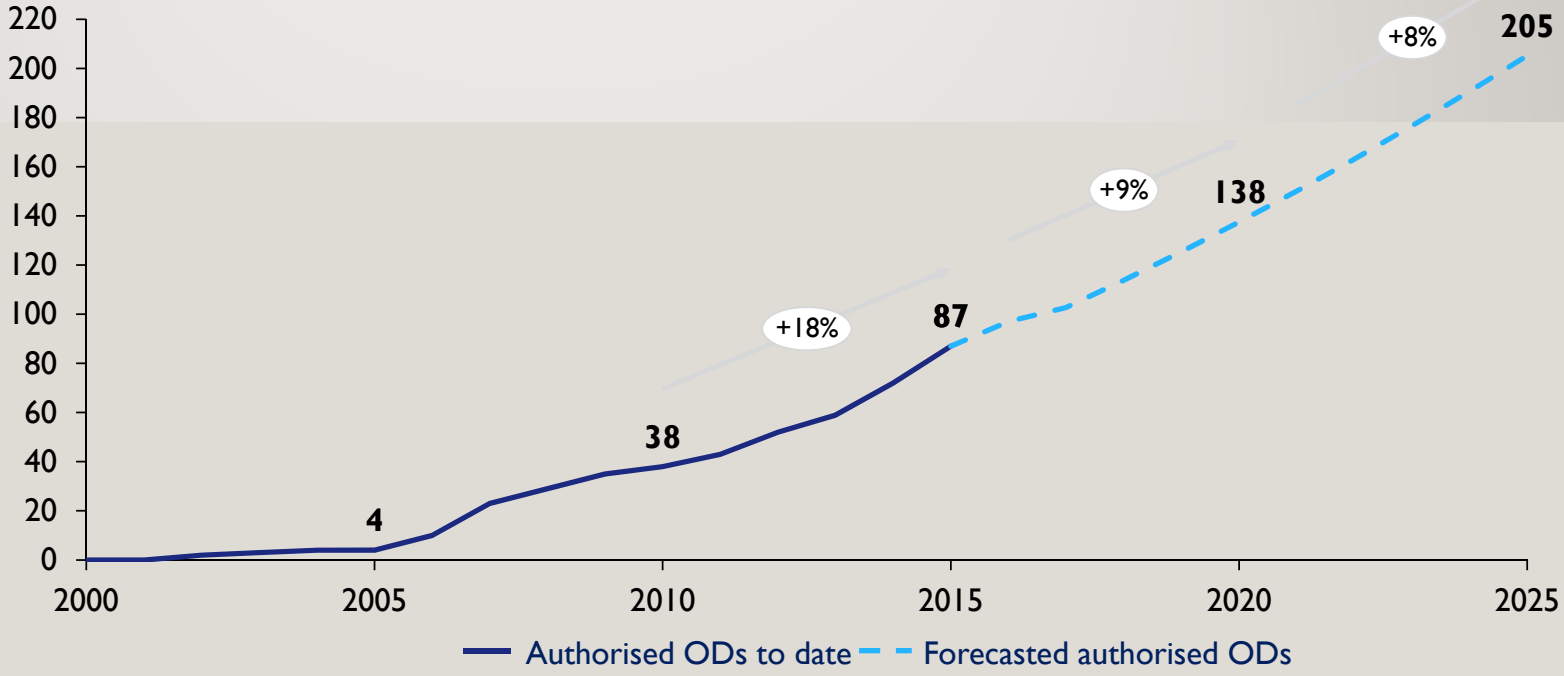
1. European Medicines Agency. Orphan medicines figures 2000-2018. 2018. Available at: https://www.ema.europa.eu/en/documents/other/orphan-medicines-figures-2000-2018_en.pdf Accessed May 2019

The **number of OMPs** receiving MA each year has experienced a **compound annual growth rate of 11% since 2001**, but with **high variability between years**

# WITH SOME PROJECTIONS REFLECTING FUTURE AUTHORISATIONS…

> *"Although we are dealing with rare diseases, the* ***increasing number of new OMPs*** *introduced each year is beginning* ***to threaten the sustainability of healthcare systems***"[2]

**ACTUAL & FORECASTED NUMBER OF OMPS RECEIVING MA PERYEAR[1]**




- Between 2011–2016, the **number of OMPs** obtaining marketing authorisation **increased by 18%** per year across the EU-5[1]


1. Flostrand S. et al. Is the Orphanage Filling Up? Projecting the Growth and Budget Impact of Orphan Drugs in Europe. Value in Health 2016;19:A347-766. Available at: https://www.valueinhealthjournal.com/article/S1098-3015(16)32820-0/pdf
2. Luzzatto L. et al. Outrageous prices of orphan drugs: a call for collaboration. Lancet 2018;392:791-4

# SITUATION D: Affordability concerns (among others) prompted the European Council to advise the European Commission to evaluate its OMP regulation

## BACKGROUND ON OMP EU REGULATION[1-2]

| | |
|---|---|
| **Context** | The EU adopted the Regulation (EC) 141/2000 on Orphan Medicinal Products in December 1999[1] |
| **Objectives** | • To meet the needs of rare disease patients<br>• To enhance the development of orphan medicines |
| **Number of OMPs at time** | In the period before the regulation came into force, only eight OMPs were developed in Europe[2] |

## CALL FOR PUBLIC CONSULTATION[3]

**PUBLIC CONSULTATION**

European Commission

Evaluation of the legislation on medicines for children and rare diseases (medicines for special populations)[3]

*October 2018*

*"With this open public consultation, the European Commission asks private citizens and healthcare professionals to share their experiences with and perspectives on access to orphan medicines in general, and on the role the EU Orphan Regulation plays in the development of orphan medicines."*[1]

**Few analyses** have been **published** describing European **OMP expenditure** since the **introduction of the OMP regulation**[9]


1. EU Regulation 141/2000. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32000R0141&from=EN
2. Heemstra H. Variations in access and use of orphan drugs among EU Member States. EJHP Practice 2010; 4(16): 25–27
3. European Commission. October 2018. Available at: https://ec.europa.eu/info/law/better-regulation/initiatives/ares-2017-6059807/public-consultation_en Accessed December 2018

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# HOW MUCH DO WE SPEND ON OMPS?: THE OMP SHARE OF TOTAL PHARMACEUTICAL EXPENDITURE HAS CONSISTENTLY INCREASED YEAR-ON-YEAR SINCE 2000

## OMP SHARE OF TOTAL PHARMACEUTICAL EXPENDITURE ACROSS EU MARKETS (2000–2017)

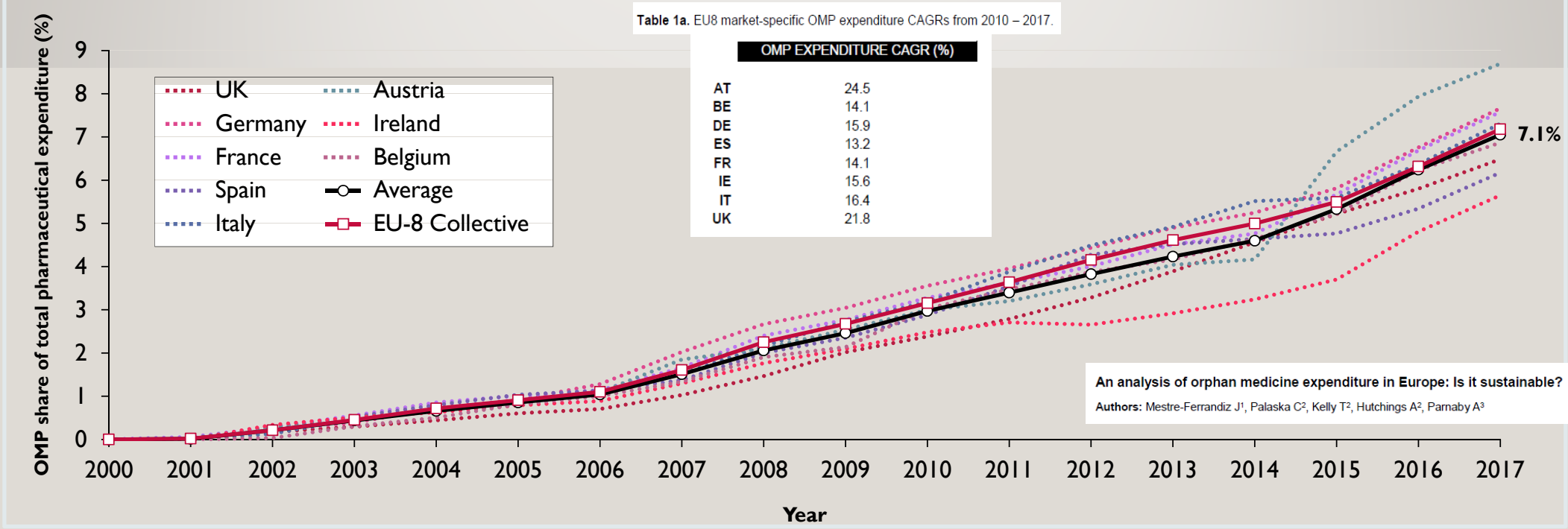


**Table 1a.** EU8 market-specific OMP expenditure CAGRs from 2010 – 2017.

| | OMP EXPENDITURE CAGR (%) |
|---|---|
| AT | 24.5 |
| BE | 14.1 |
| DE | 15.9 |
| ES | 13.2 |
| FR | 14.1 |
| IE | 15.6 |
| IT | 16.4 |
| UK | 21.8 |

**An analysis of orphan medicine expenditure in Europe: Is it sustainable?**

**Authors:** Mestre-Ferrandiz J[1], Palaska C[2], Kelly T[2], Hutchings A[2], Parnaby A[3]

**Similar trends** have been observed across **all** markets; the average of the EU-8 countries reached 7.1% in 2017

# BUT HOW IS THE OVERALL MARKET EVOLVING? ARE THE DYNAMICS CHANGING THE STRUCTURE OF THE INDUSTRY?

**Table 1.** Market shares and their CAGRs, for the eight countries, from 2010 – 2017.

| | MARKET SHARE (%) | | | | | |
|---|---|---|---|---|---|---|
| | VALUE | | | VOLUME | | |
| | 2010 | 2017 | CAGR | 2010 | 2017 | CAGR |
| ORPHAN | 3.1 | 7.2 | **13** | <0.1 | <0.1 | **11** |
| NON-ORPHAN BRANDED | 62.4 | 57.3 | **-1** | 27.6 | 22.6 | **-3** |
| UNBRANDED | 28.2 | 30.0 | **1** | 52.4 | 58.1 | **1** |
| OTHER EXPENDITURES[a] | 6.3 | 5.5 | **-2** | 20.0 | 19.3 | **-1** |

[a]Other expenditures include over-the-counter (OTC) products and vaccines, which have been omitted from t

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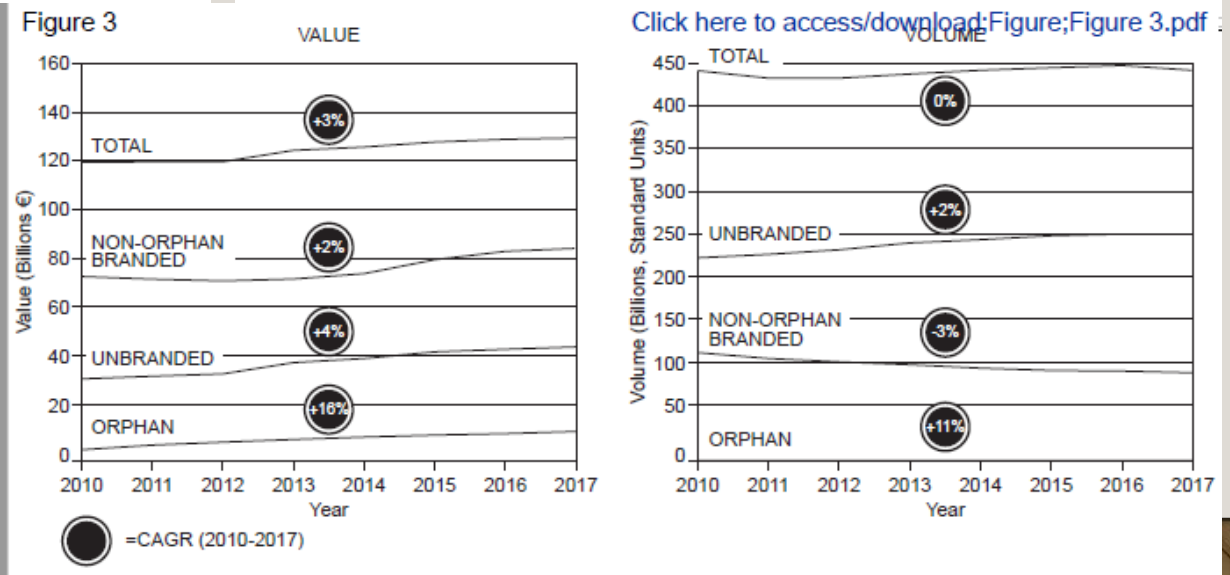
**Figure 3** Aggregated market profile for the eight countries, displayed in value (left) and volume (right).

Figure 3

Click here to access/download;Figure;Figure 3.pdf




**Relative spending** on OMPs has **increased** over the last 20 years, but this has been **almost completely compensated for** by **flat expenditure for non-OMPs and increased volumes of generics**

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# ACCESS TO OMPS: EU COMPARISONS

Zamora et al. Orphanet Journal of Rare Diseases (2019) 14:95
https://doi.org/10.1186/s13023-019-1078-5

Orphanet Journal of Rare Diseases

RESEARCH Open Access

## Comparing access to orphan medicinal products in Europe

Bernarda Zamora*, Francois Maignen, Phill O'Neill, Jorge Mestre-Ferrandiz and Martina Garau

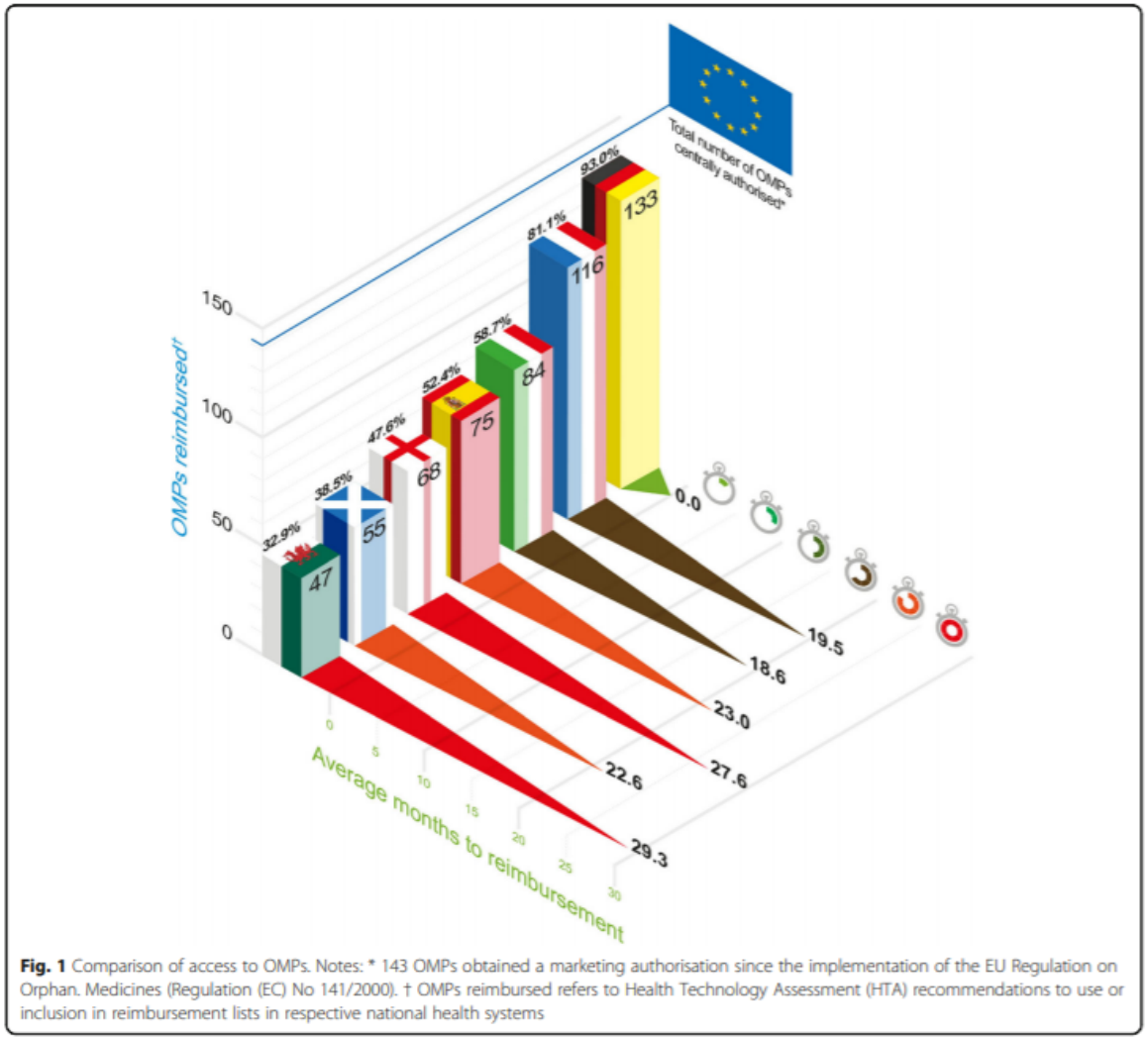


**Fig. 1** Comparison of access to OMPs. Notes: * 143 OMPs obtained a marketing authorisation since the implementation of the EU Regulation on Orphan. Medicines (Regulation (EC) No 141/2000). † OMPs reimbursed refers to Health Technology Assessment (HTA) recommendations to use or inclusion in reimbursement lists in respective national health systems

## Conclusions

Our study suggests that one of the intended effects of this regulation, to grant equal availability to OMPs to patients in the EU via the implementation of the OMPs Regulation, was partially achieved with important variations in availability and access across the selected countries. We found that more than a half of centrally authorised OMPs were available in the five selected countries, but that access to patients was further restricted by different national reimbursement policies, especially in the UK, Italy and Spain. Our study focused on the five largest economies of the 28 EU member states. It highlighted the potential role of a number of national policies, such as the extended remit to HTA in France facilitating pre-authorisation access, and a two-stage administered system in Germany which prioritises reimbursement over price negotiations. More research is recommended to collect reliable data on use of OMPs in clinical practice and assess the impact of individual policies (orphan and non-orphan specific) on access.

# ACCESS TO OMPS - NUMBER: SPAIN


G Model
GACETA-1710; No. of Pages 8
ARTICLE IN PRESS
Gac Sanit. 2019;xxx(xx):xxx–xxx
Original
Análisis de la evolución en el acceso a los medicamentos huérfanos en España
Jorge Mestre-Ferrándiz[a,*], Margarita Iniesta[b], Marta Trapero-Bertran[c], Jaime Espín[d,e,f] y Max Brosa[g]

Around 50% of OMPs authorised by EMA are commercialised and reimbursed in Spain

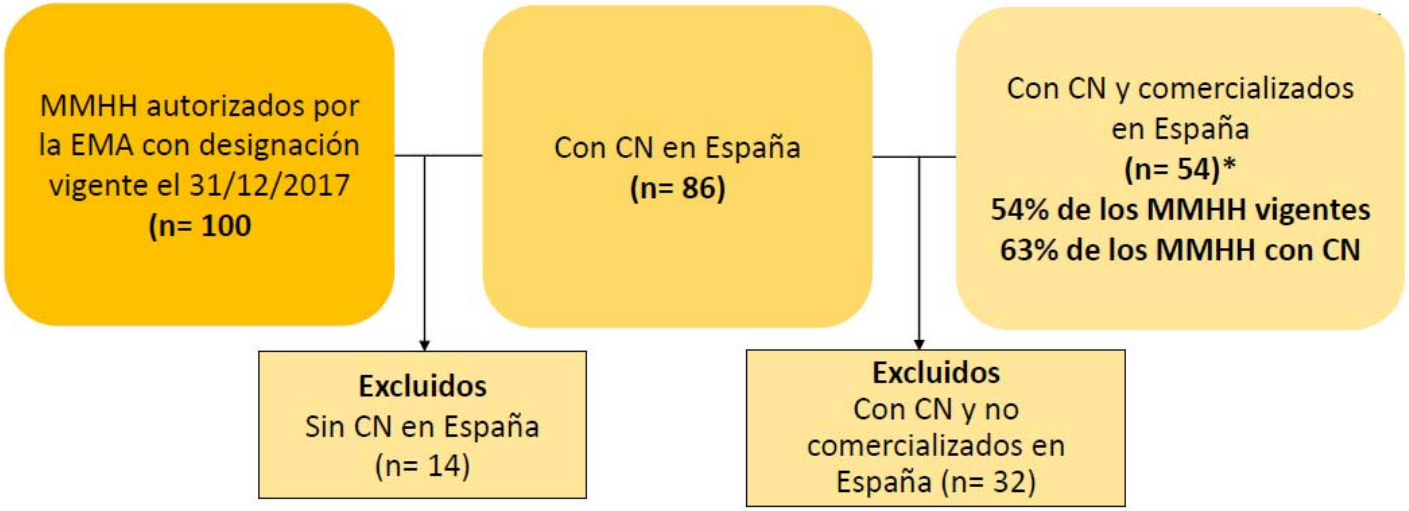


**Diagrama de flujo del número de MMHH cuantificados con fecha 31/12/2017**

CN: código nacional; EMA: Agencia Europea del Medicamento; MH: medicamento huérfano.

* 3 no financiados

# ACCESS TO OMPS: EVOLUTION SPAIN

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Original

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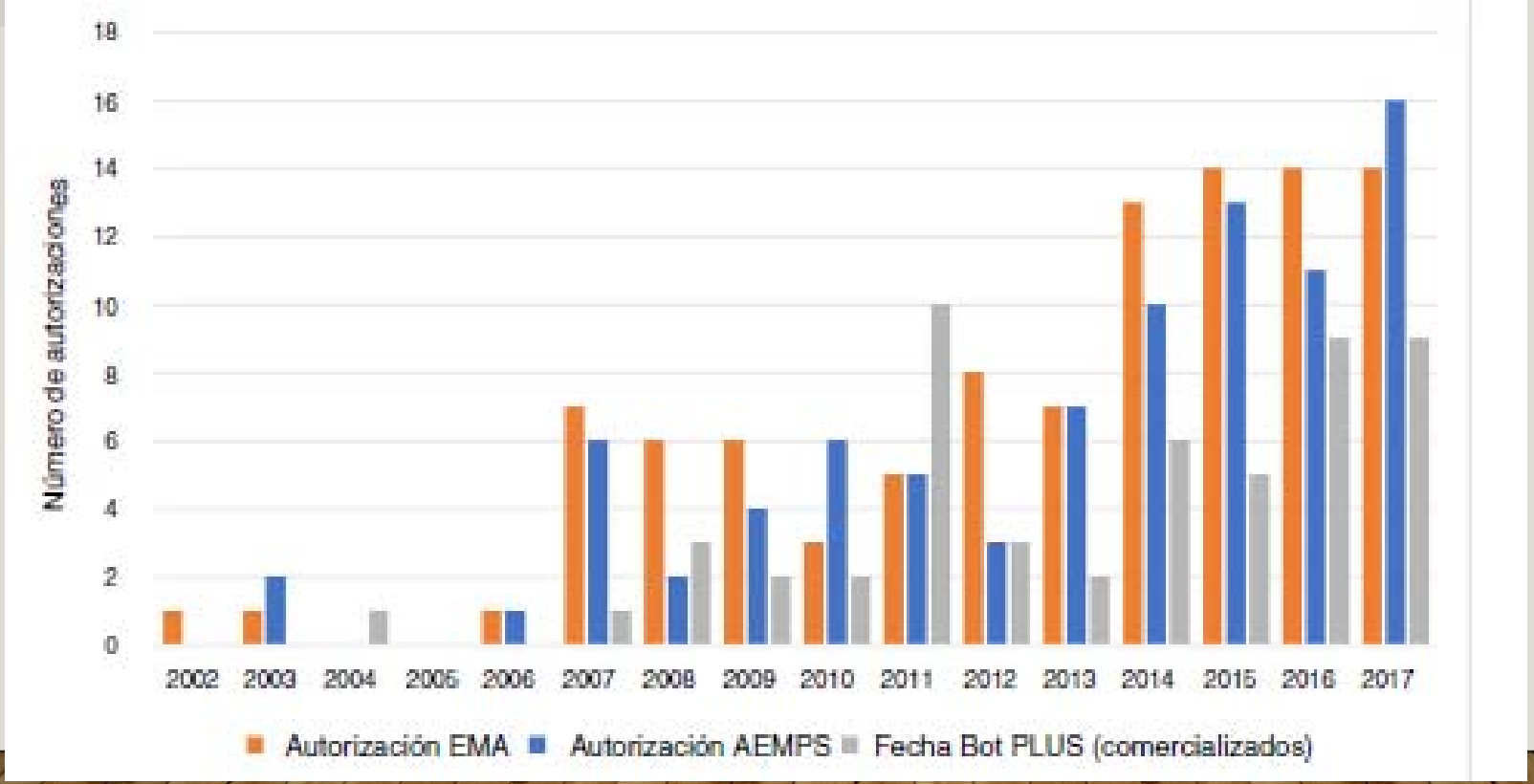
Jorge Mestre-Ferrándiz[a,*], Margarita Iniesta[b], Marta Trapero-Bertran[c], Jaime Espín[d,e,f] y Max Brosa[g]

**Figura 2.** Número de autorizaciones por la Agencia Europea de Medicamentos (EMA) (n = 100) y por la Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) (n = 86), e inclusión en Bot PLUS, por año (n = 53, + 1 sin fecha no incluido), para medicamentos huérfanos con designación vigente a 31 de diciembre de 2017. Fuente: análisis de los autores, basado en la información pública disponible sobre los medicamentos huérfanos autorizados por la EMA[10], sobre los autorizados por la EMA con designación huérfana vigente[11], sobre la fecha de asignación del CN[12] y sobre la fecha de comercialización efectiva en España[13].

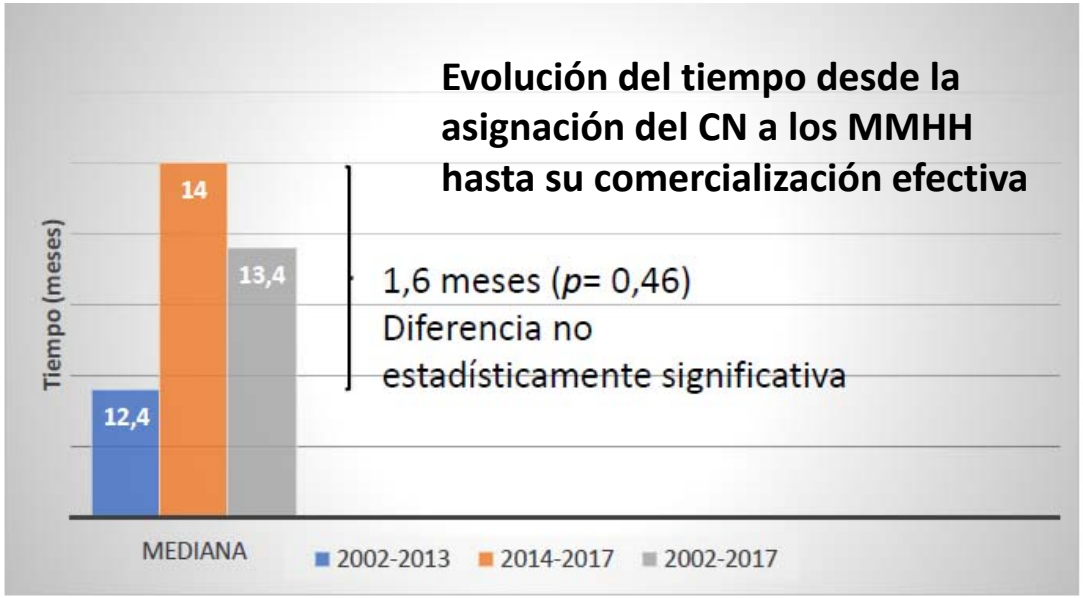


# ACCESS TO OMPS: DURATION OF P&R NEGOTIATIONS SPAIN

**Tabla 1**
Tiempo medio y mediana desde la asignación de código nacional por la Agencia Española de Medicamentos y Productos Sanitarios para un medicamento huérfano hasta su comercialización en España (Bot PLUS)

| Medicamentos huérfanos autorizados por la EMA, con designación vigente, con CN y comercializados en España (con fecha Bot PLUS) | Tiempo transcurrido entre CN (AEMPS) y Bot PLUS, promedio (meses) | Tiempo transcurrido entre CN (AEMPS) y Bot PLUS, mediana (meses) | Deviación estándar (mínimo-máximo) |
|---|---|---|---|
| Total comercializados (n = 53) | 20,1 | 13,4 | 17,0 (2,1-91,7) |
| Comercializados en 2014-2017 (n = 29) | 19,5 | 14,0 | 14,0 (2,1-53,5) |
| Comercializados en 2002-2013 (n = 24) | 20,8 | 12,4 | 20,4 (2,7-91,7) |

AEMPS: Agencia Española de Medicamentos y Productos Sanitarios; CN: Código Nacional; EMA: Agencia Europea de Medicamentos.
Fuente: análisis de los autores, basado en la información pública disponible sobre la fecha de asignación del CN[12] y sobre la fecha de comercialización efectiva en España[13].





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Original

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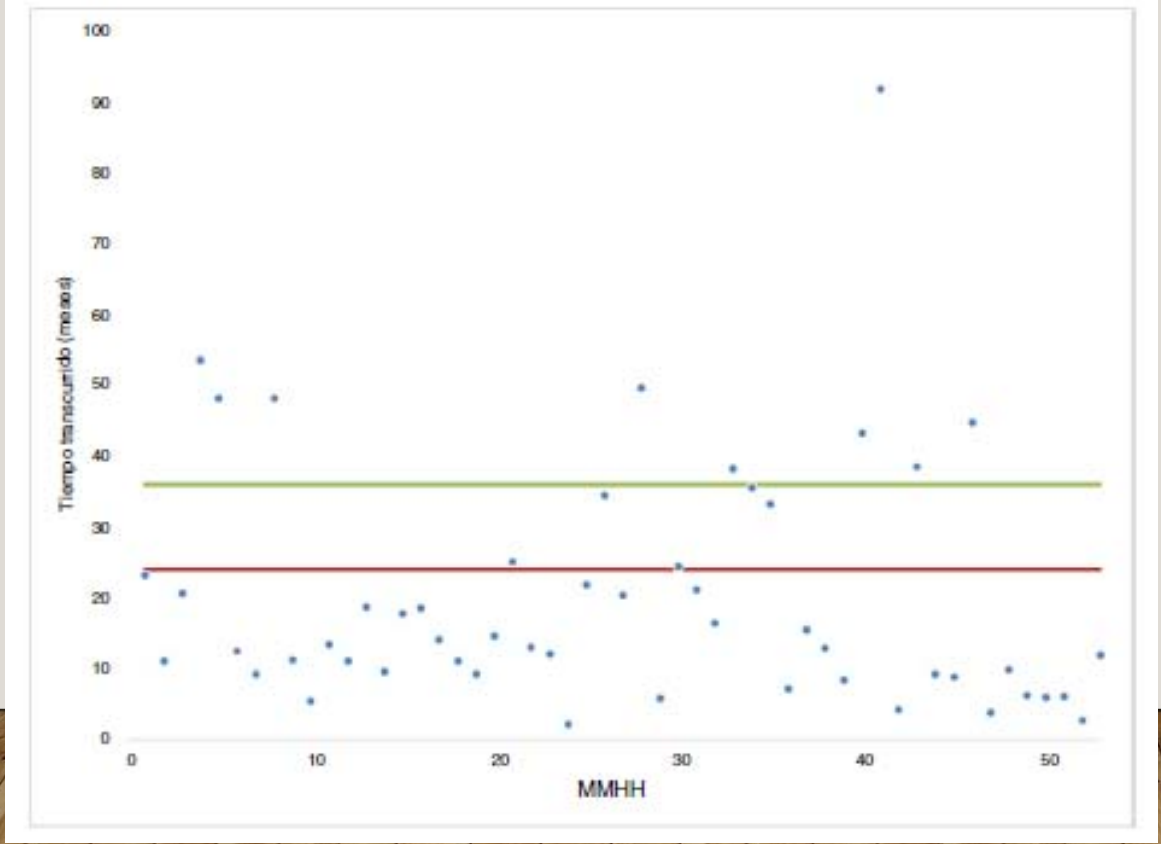
# ACCESS TO OMPS: DURATION OF NEGOTIATIONS SPAIN

- Most OMPs are available within a maximum period of 2 years after obtaining the CN – acceptable period.
- However, of the 14 OMPs with times greater than 2 years, for 9 (64%) the delay is greater than 3 years
  - ✓ Over and above, various reasons: 'challenges' during price negotiations, strategic decisions of companies…





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# A 30 de septiembre de 2019, 58 medicamentos huérfanos, que mantienen la designación, están comercializados en España

AELMHU
ASOCIACIÓN ESPAÑOLA DE LABORATORIOS DE MEDICAMENTOS HUÉRFANOS Y ULTRAHUÉRFANOS

**151**
MMHH con designación huérfana por la EMA[1]

**108**
MMHH con autorización de comercialización (AC) en UE[2]

**97**
MMHH autorizados en España (CN)[3]

**58**
MMHH comercializados en España[3]

*AELMHU - Boletín informativo*
*II Edición - 30 -09.2019*

Análisis de todos los medicamentos con nombre comercial **que tienen vigente la designación huérfana** a fecha de 30 /09/19

# Por tanto, sólo el 54% de MMHH aprobados en UE se comercializan en España, siendo el 60% de los que tienen CN

AELMHU
ASOCIACIÓN ESPAÑOLA DE LABORATORIOS DE MEDICAMENTOS HUÉRFANOS Y ULTRAHUÉRFANOS

108
con AC[2]

vs.

58
comercializados [3]

**53,7%**
**COMERCIALIZADOS**

97
con CN[3]

vs.

58
comercializados[3]

**59,8%**
**COMERCIALIZADOS**

AC= autorización comercial.
CN= código nacional



Análisis de todos los medicamentos con nombre comercial **que tienen vigente la designación huérfana** a fecha de 30 /09/19

# AGENDA

1. Setting the context - OMPs
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# (SOME) FINAL REMARKS…

- Relative spending on OMPs has increased over the last 20 years, but this has been almost completely compensated by flat expenditure for non-OMPs and increased volumes of generics….
- Perhaps reflecting a shift towards expenditure in higher cost, lower volume patient populations…
- … and a shift in drug development towards more specialised targeting of diseases.
- Impact of legislation? (pull incentives seems to have worked)
- But inconsistency across Member States – different access:
  - Pricing and reimbursement systems are national competency
  - Different access might reflect different needs, but there needs to be further coordination at European level for OMPs in particular
- Is there a willingness to pay a price premium for OMPs (vs non-OMPs)?

Thanks for your attention!

Dr Jorge Mestre-Ferrándiz

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Honorary Visiting Lecturer, Department of Economics, City University London

Views expressed are my own

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