REGULATORY APPROVAL TO PATIENT ACCESS, AN EVALUATION OF EU5 AND US NATIONAL TIMING DIFFERENCES: AN UPDATE

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OBJECTIVES & METHODS

- Examine the time between regulatory approval and launch/pricing and reimbursement (P&R) approval in the EU5 and US
  - Illustrate any differences between general medicines, oncology and orphan drugs within and across the countries
  - Look for changes in these timelines over a 5 year period (January 2009 to May 2014)
  - Additional analysis of trends for products launched between April 2013 and May 2014
- New molecular entities, formulations and combinations approved by the EMA (EC centralized approval) between January 2009 and May 2014 were included in the analysis. FDA approval dates were retrieved.
- Time comparison for general medicines vs. orphan and oncology indications was made including shifts over time
- Drugs with time to market >1000 days were considered outliers and removed from the analysis
- Timing differences were NOT weighted by the number of products not available by country and category

Table 1: Launch date information in the US and EU5

Country	Launch date information
US	Date wholesale acquisition cost was effective
UK	Product availability/introduction (UKMI/MIMS)
Germany	Product availability/introduction (ABDATA)
France	P&R decision (Agrément collectivités/date published in Journal Officiel)
Italy	First P&R Decree publication on Official Gazette
Spain	Date of commercialization (Portalfarma)

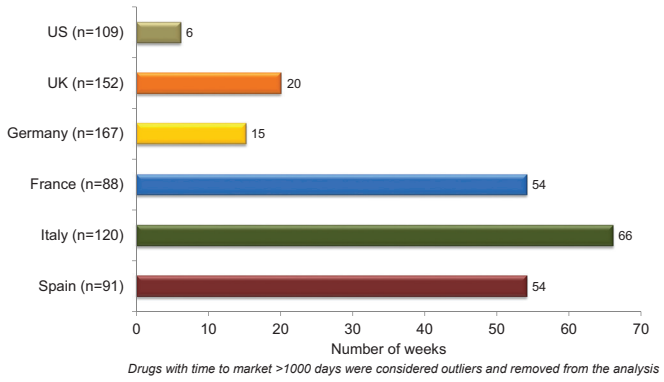
INTRODUCTION

- Increasing divergence between regulatory and P&R approval and a dearth of literature on time to market access in recent times makes this topic both a relevant and interesting issue for analysis
- Since 2006 the regulatory and reimbursement landscape has changed dramatically
- Trials sufficient to gain regulatory approval are now in a vast number of cases not seen as adequate for reimbursement by national authorities
- MME presented a review of time to market access for new molecular entities, formulations and combinations approved by the EMA (between January 2009 and December 2013) at ISPOR Beijing in September 2013
- This poster includes EC centralized approvals from January 2009 to May 2014 and examines any changes in trends for products launched in the previous year (between April 2013 and May 2014)

RESULTS

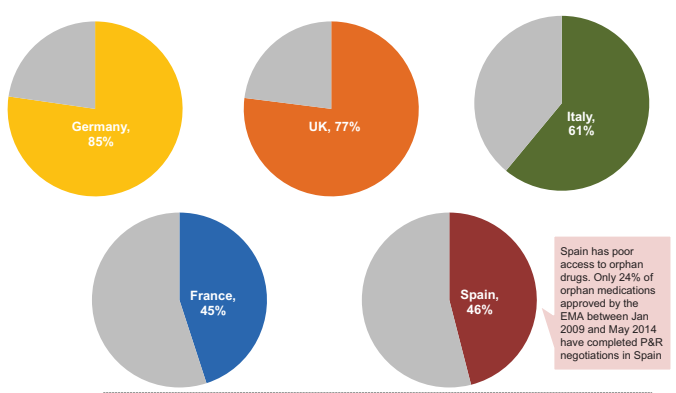
- Analysis of US and EU5 launches of all medications approved by the EMA between January 2009 and May 2014 shows (refer to Figure 1 and Figure 2 below):
  - Average time from FDA approval to US launch was 6 weeks (oncology 4 weeks; orphan drugs 2 weeks) which is much faster than all EU5 countries
  - Although time to market in the UK appears short (20 weeks), HTA assessments often mean significant access delays
  - ~85% of all EMA approved medications in this time period were available in Germany, whereas only 45% had completed P&R negotiations in France
    - 60% of medications that had completed P&R in France were available across the EU5 and 91% were available in at least 3 of the other markets (in most cases the medication had not completed P&R in Spain but was available in Italy, Germany and the UK)
  - Spain has the poorest access for orphan drugs; only 24% of orphan medications approved by the EMA in this time period had completed P&R negotiations as of May 2014
- Analysis of new products launched between April 2013 and May 2014 shows (refer to Figure 3)
  - France is the only country with a decline of 4 weeks in time to market although fewer drugs completed P&R in this time
  - No real difference is seen in Germany and the UK (modest increases of 1 and 2 weeks respectively)
  - Time to access for all medications in Spain has increased in the last year when compared to previous years (75 vs. 50 weeks)
  - Only one orphan drug has completed P&R in Spain between April 2013 and May 2014, taking 106 weeks to complete the process
  - Italian average time to complete P&R is 66 weeks, while average time to be listed in Class C-nn, without national reimbursement, is only 18 weeks

Figure 1: Average time to market post regulatory approval (January 2009 to May 2014)



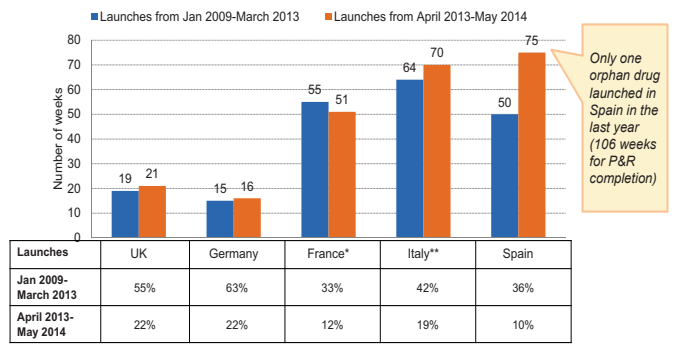
Drugs with time to market >1000 days were considered outliers and removed from the analysis

Figure 2: Percent of EMA approved medications (January 2009 to May 2014) available in the EU5



German analysis includes 8 drugs that were withdrawn from the German market post launch either after G-BA assessment and/or reimbursement price negotiation with the GKV (Xiapex, Rasilamlo,Trobalt, Livazo, Yellox, Trajenta, Fycompa, Constella were withdrawn as of May 2014).

Figure 3: Comparison of time to market for latest year vs. previous years



Launches	UK	Germany	France*	Italy**	Spain
Jan 2009-March 2013	55%	63%	33%	42%	36%
April 2013-May 2014	22%	22%	12%	19%	10%

**France analysis does not include 6 drugs that are available as of last year without a reimbursement agreement (Spedra, Bosulif, Mirvaso, Zoely, Iclusig and Resolor)*
***Italy analysis does not include drugs currently classified as C-nn. (Cnn listing takes only 18 weeks on average)*

Table 2: Number of weeks to P&R completion post EMA approval (January 2009 to May 2014)

Country	All drugs	Oncology	Orphan
US	6 (n=109)	4 (n=30)	2 (n=19)
UK	20 (n=152)	16 (n=39)	23 (n=30)
Germany	15 (n=167)	13 (n=38)	16 (n=32)
France	54 (n=88)	45 (n=22)	53 (n=16)
Italy	66 (n=120)	59 (n=24)	61 (n=21)
Spain	54 (n=91)	59 (n=15)	71 (n=9)

Drugs with time to market >1000 days were considered outliers and removed from the analysis

CONCLUSIONS

- Average time to market in the US is considerably shorter than in the EU5 countries
- Wide disparity exists in the number of EMA approved medications available in each of the EU5 countries and the time to market
  - While ~85% of all medications approved by the EMA are available in Germany, only 45% have completed P&R negotiation in France
  - Dramatic access issues for orphan drugs in Spain are highlighted by the fact that patients only have access to a quarter of medications approved by the EMA
  - In the EU5, the German and UK launches on average were within 4 to 6 months of authorization, while France, Italy and Spain are >1 year
  - Although time to P&R post-regulatory approval has stayed the same in most countries, it has increased by ~6 weeks in Italy and ~25 weeks in Spain for products launched in the latest year vs. those launched previously
- It is important to recognize variation in ability to launch and timing disparities when analysing market access timelines and their implications on the availability of new drugs to patients