MARKET ACCESS TRENDS ACROSS THE EU5 AND US: 2009 TO 2018 - AN UPDATE

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OBJECTIVE

- To examine the time between regulatory approval and launch/pricing and reimbursement (P&R) approval (as defined in Table 1) in the EU5 and US
  - Illustrate any differences between all medicines with EC approval, oncology and orphan drugs within and across the countries
- To analyze potential changes in market access timelines in the EU5 countries and US between 2009 and 2018

METHODS

- New molecular entities, formulations and combinations approved by the EC between January 2009 and September 2018 were included in the analysis
  - Commercialization timelines in US were also analysed for the same products (comparable sample)
  - Cut off date for data collection was December 15, 2018
- Time comparison for all medicines with EC approval vs. orphan and oncology medications was made including shifts over time
- It should be noted that marketers may decide not to pursue P&R in any country or reach agreement with authorities if they do and this can only be "measured" based on EMA approval offering the opportunity and the variability in actual results
- Data was gathered from official national HTA agencies and P&R bodies
- Sources for launch date information provided in Table 1 below-

Table 1: Launch Date Information in US and EU5

Country	Launch Date Information
US	MediSpan
UK	Product introduction (MIMS/NHS SPS/NHS DMD)- Launch date does not consider HTA decisions
Germany	Product availability/introduction (ABDATA)
France	P&R decision (date published in *Journal Officiel*)
Italy	First P&R Decree publication on Official Gazette- Analysis of launch date does not consider initial approval in Class C-nn
Spain	Date of commercialization (Portalfarma)

RESULTING SAMPLE

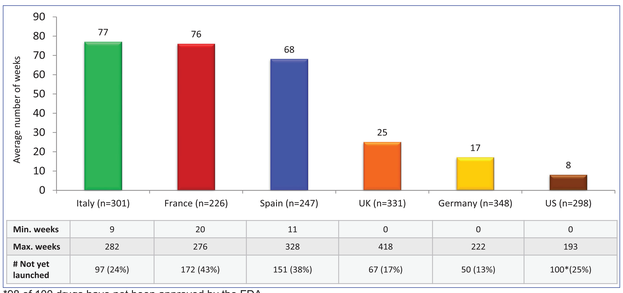
- 435 drugs approved by the EC between Jan 2009 and September 2018
  - This does not include generics/biosimilars or drugs approved based simply on informed consent
  - Drugs such as Nexium Control that received non-prescription status were also not included
- 37 drugs withdrawn/suspended since launch
- **Analysis focuses on remaining 398 drugs currently on the market**
  - 265 new active substances (including ATMPs)
  - 94 drugs for oncology indications
  - 95 drugs with orphan designation (OD)
  - Categorization based on route of administration (ROA)
    - 47% (n=186) orally
    - 20% (n=78) IV
    - 10% (n=40) SC
  - 46 authorized under accelerated assessment pathway
    - 29 drugs with conditional marketing authorizations
      - 11 converted to full MA
      - 18 still have conditional status
    - 17 drugs authorized under exceptional circumstances

RESULTS

Timing and launches by country: All EC approved drugs between January 2009 and September 2018

- Time to market is the quickest in the US at ~8 weeks; however only 75% of EC approved drugs are FDA approved
- Germany has the fastest access (17 weeks) while Italy is the slowest (77 weeks)
  - Although the time to launch in the UK is only 25 weeks, reimbursement is dependent upon decision of national HTA bodies which could considerably extend timelines (time taken for NICE/SMC decisions not analysed as part of this study

Figure 1: Average time to market post regulatory approval (EC approval: Jan 2010 to Sep 2018)



	Italy (n=301)	France (n=226)	Spain (n=247)	UK (n=331)	Germany (n=348)	US (n=298)
Min. weeks	9	20	11	0	0	0
Max. weeks	282	276	328	418	222	193
# Not yet launched	97 (24%)	172 (43%)	151 (38%)	67 (17%)	50 (13%)	100*(25%)

*98 of 100 drugs have not been approved by the FDA

Cut off date for data collection was December 15, 2018

- Germany also has the highest percent of drugs launches at 87% of whereas only 57% are launched in France
  - 6% of drugs (22 products) launched in Germany have however been subsequently withdrawn from the market
- In Italy, P&R decree is published for 301 drugs (76% of all EC approved medications); however 41 of these drugs (13.6%) were authorized as Class C (not reimbursed) drugs at launch and an additional 55 drugs are currently class C-nn available for out of pocket/private pay patients

Timing and launches across countries: Oncology and orphan drugs approved between January 2009 and September 2018

- Comparing time to market for all medicines with EC approval vs. orphan and oncology indications highlights that oncology drugs launch faster in the US, Germany and the UK
- While time to market is quicker for orphan drugs in the US (2 weeks), it is significantly higher in Spain, France and Italy
- Spain has the poorest access for orphan drugs; only 36% of orphan medications approved by the EMA in this time period had completed P&R negotiations
- Although average time to market in the UK is 25 weeks, this does not necessarily mean reimbursed access ((time taken for NICE/SMC decisions not analysed as part of this study)

Table 2: Number of weeks to launch post regulatory approval in US and EU5 for same EU based sample of products (January 2009 to September 2018)

Country	All drugs (n=398)		Oncology (n=94)		Orphan (n=95)	
	# of Weeks	*% of all EC approved drugs*	*# of Weeks*	*% of all EC approved oncology drugs*	*# of Weeks*	*% of all EC approved orphan drugs*
France	76	57%	74	62%	83	53%
Germany	17	87%*	11	91%	16	91%
Italy	77	76% **	73	74%	90	73%
Spain	68	62%	76	64%	96	36%
UK	25	83%	14	91%	30	80%
US	8	75%	2	81%	2^	67%^

398 drugs (New molecular entities, formulations and combinations) approved by EC between Jan 2009-Sep 2018

* Although 87% (348) of all EC approved drugs were launched in Germany, 20 of these drugs have later been withdrawn post AMNOG (326 currently available)

** 55 drugs approved as Class C-nn, that are theoretically available in Italy (not included in the 76%)

^ Drugs with EU orphan drug designation

Cut off date for data collection was December 15, 2018

Trends over time: All EC approved drugs between January 2010 and September 2018

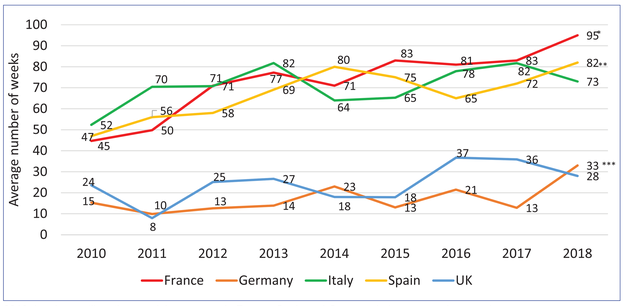
- Consistently fewer annual drug launches in France with similar numbers observed in Italy/Spain and Germany/UK
- Increasing time to market in all countries, especially in France (45 weeks in 2010 to 95 weeks in 2018) and Spain (47 weeks in 2010 to 82 weeks in 2018)

Table 3: Number of drugs launched post regulatory approval in the EU5 from 2010 to September 2018

Number of drugs launched	2010	2011	2012	2013	2014	2015	2016	2017	2018 (9 mo.)	Total
France	21	10	19	23	30	24	33	31	32	**223**
Germany	25	25	28	26	51	45	41	41	42	**324**
Italy	25	26	11	35	35	40	43	61	33	**309**
Spain	22	24	11	23	31	44	41	29	18	**243**
UK	23	22	28	27	52	39	48	49	27	**315**

Cut off date for data collection was December 15, 2018

Figure 2: All drugs- Time to launch post regulatory approval in EU5 for same sample of products from 2010 to September 2018



2018 data has outliers that result in averages in France, Spain and Germany being greater than previous years

* Insulin degludc (Tresiba) and lomitapide (Lojuxta) in France

** Lidocaine / prilocaine (Fortacin) in Spain

*** Lidocaine / prilocaine (Fortacin) and bupropion hydrochloride / naltrexone hydrochloride (Mysimba) in Germany

Cut off date for data collection was December 15, 2018

CONCLUSIONS

- US time between FDA approval and launch is considerably shorter than time to launch following EC approval in any of the EU5 countries and this has been the case for the entire 9 years of data covered
  - Interestingly however 25% of drugs approved by the EC are not available in the US
    - Given the size of the US market reasons for this need to be examined in future research
- Wide disparity exists in the number of EC approved medications commercially available in each of the EU5 countries as well as time to market
  - While 87% of all medications approved by the EC are available in Germany, only 57% have completed P&R negotiation in France
    - ~6% of drugs (22 products) launched in Germany have been subsequently withdrawn from the market
    - Dramatic access issues for orphan drugs in Spain are highlighted by the fact only 36% of medications approved by the EMA are available
- Trend analyses across the EU5 suggests a modest increase in time to price launched products in all countries which may be due to additional data requirements (e.g. pharmacoeconomic dossiers in France), increasing number of resubmissions and budget pressures
  - 2018 trend for timing increases seem to be influenced by outliers in Germany, France and Spain but need to be monitored/tracked
- It is important to recognize variation in ability to launch and timing disparities when analyzing market access timelines and their implications on the availability of new drugs to patients

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