A 10-YEAR REVIEW (2009-2018) OF MARKET ACCESS OF PHARMACEUTICALS IN THE EU5 AND US

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OBJECTIVE

- To examine trends in the time between regulatory approval and launch/pricing and reimbursement approval in the EU5 and US, and review EC authorized medicinal products not approved by FDA

METHODS

- New molecular entities, formulations and combinations approved by the European Commission (EC) between January 2009 and December 2018 were included
- Availability and commercialization timelines in US were also analysed for the same products (comparable sample), to establish the number / percentage of medicinal products approved by the EC but not the FDA
  - Cut-off date for data collection was May 31, 2019
- Time comparison for all medicinal products with EC approval vs. orphan and oncology medicinal products was made, including shifts over time
- Data was gathered from official national HTA agencies and P&R bodies; sources for launch date information provided in Table 1

Table 1: Launch Date Information in the EU5 and US

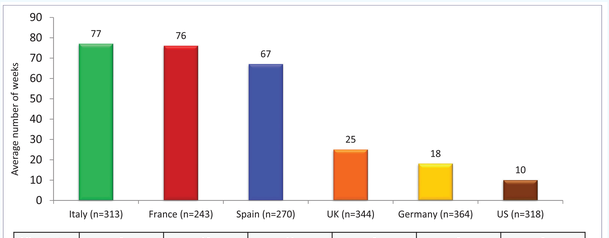
Country	Launch Date Information
France	P&R decision (date published in *Journal Officiel*)
Germany	Product availability/introduction (ABDATA)
Italy	First P&R Decree publication on Official Gazette- Analysis of launch date does not consider initial approval in Class C-nn
Spain	Date of commercialization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

PRODUCT SAMPLE

- **Analysis focuses on 412 new prescription medicinal products, formulations and combinations approved by the EC in the time period January 2009-December 2018 and currently on the market**
  - All other medicinal products (e.g. non-prescription, generics, biosimilars, etc.) were excluded from the analysis
  - 16 medicinal products in scope withdrawn since launch
  - 273 new active substances (including ATMPs)
  - 97 medicinal products for oncology indications
  - 99 medicinal products with orphan designation (OD)
    - 28% of medicinal products with OD are approved for oncology indications
  - Categorization based on route of administration (ROA)
    - 45% (n=185) oral
    - 17% (n=70) IV
    - 9% (n=38) SC
    - 29% (n=119) all other ROA's
  - 46 authorized under accelerated assessment pathway
    - 29 medicinal products with conditional marketing authorizations
      - 11 converted to full MA
      - 18 still have conditional status
    - 17 medicinal products authorized under exceptional circumstances

RESULTS

Figure 1: Average Time to Market Post Regulatory Approval (EC Approvals Jan 2009 - Dec 2018)



	Italy (n=313)	France (n=243)	Spain (n=270)	UK (n=344)	Germany (n=364)	US (n=318)
Min. weeks	9	16	11	0	0	0
Max. weeks	282	276	328	418	222	87*
# Not yet launched	99	169	142	68	48	94

*US: 2 outliers (decitabine; pentosan polysulfate sodium) removed

Cut-off date for data collection was May 31, 2019

Table 2: Number of Weeks to Launch Post Regulatory Approval in US and EU5 for Same EU-Based Sample of Medicinal Products (Jan 2009 – Dec 2018)

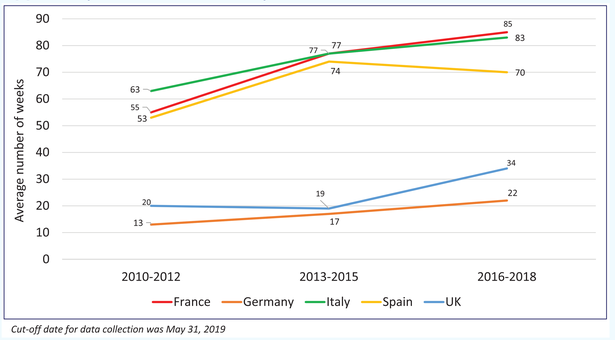
Country	All Products (n=412)		Oncology (n=97)		Orphan (n=99)^^	
	# of Weeks	*% of all EC approved products*	*# of Weeks*	*% of all EC approved oncology products*	*# of Weeks*	*% of all EC approved orphan products*
France	76	59%	76	65%	85	53%
Germany	18	88%*	12	92%	18	93%
Italy	77	76%**	74	76%	91	73%
Spain	67	66%	72	68%	91	39%
UK	25	83%	14	93%	30	81%
US ^	6	77%	2	81%	2	71%

- *412 products (New molecular entities, formulations and combinations) approved by EC between Jan 2009-Dec 2018*
- ** Germany: although 88% (364) of all EC approved medicinal products were launched, at least 22 of them have later been withdrawn post-AMNOG assessment*
- *** Italy: 60 products – approved as Class C-nn – are theoretically available but not reimbursed (not included in the 76%)*
- *^ US: 2 outliers (Elmiron; Dacogen) removed from time to market calculations*
- *^^ 28% medicinal products with orphan designation have oncology indications*

Cut-off date for data collection was May 31, 2019

- **Timing by country:**
  - US: Fast overall time to market at 6 weeks – even faster for oncology and orphan medicinal products (2 weeks) - with no significant change over the years of analysis
    - However, 23% of EC authorized medicinal products are not launched in the US; reasons identified include
      - Stricter intellectual property protection in the US, infrastructure limitations for smaller ex-US companies, greater acceptance of off label use and different evidence requirements
  - Across the EU5, Germany has the fastest access (18 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
- **Results across countries:** Comparing time to market (Table 2) for all medicines with EC approval vs. orphan and oncology indications highlights that oncology medicinal products launch faster in Germany and the UK
  - Approval of oncology medicines is faster than orphan drugs in all EU5 countries and also generally faster than approval for standard medicinal products, with the exceptions of France (same timing) and Spain (standard products are slightly faster)
  - Time to market for orphan medicinal products is significantly higher in Spain, France and Italy
  - 88% of all EC approved medicinal products between 2009 and 2018 launched in Germany, whereas only 59% launched in France
    - In Italy, P&R decree is published for 313 medicinal products (76% of all EC approved medications); however 44 of these (14%) were authorized as Class C (not reimbursed) at launch
      - An additional 60 medicinal products are currently in Class C-nn with negotiations ongoing/pending; these medicinal products are available in Italy for out-of-pocket/private pay patients
    - Spain has the poorest access for orphan medicinal products: only 39% of orphan medications approved by the EMA in this time period had completed P&R negotiations, with average time to market being 91 weeks
    - Although average time to market in the UK is 25 weeks, this does not necessarily mean reimbursed access (this analysis does not take into account time taken for decisions by HTA bodies such as NICE/SMC)

Figure 2: All Medicinal Products- EU5 Time to Launch Post Regulatory Approval (Jan 2010 – Dec 2018)



Cut-off date for data collection was May 31, 2019

- **Trends over time:** Analyses of trends over time (Figure 2) demonstrate:
  - Consistently fewer annual medicinal product launches in France, with similar numbers observed in Italy/Spain and Germany/UK
  - Increasing time to market in all countries, especially in France (55 weeks in 2010/2012 to 85 weeks in 2016/2018), Italy (63 weeks in 2010/2012 to 83 weeks in 2016/2018) and Spain (53 weeks in 2010/2012 to 70 weeks in 2016/2018)

CONCLUSIONS

- US time between approval and launch is considerably shorter than in any EU5 country and this has been the case for the entire 10 years of data covered
  - 23% of EC authorized medicines are currently not launched in the US
  - Potential reasons include more stringent intellectual property laws in the US and limited resources of smaller European companies
  - Further analysis must be conducted to determine underlying factors for differences in launches between US and Europe
- Wide disparity exists in the number of EMA approved medications commercially available in each of the EU5 countres, yet time to market in each country is increasing
- Faster approval of oncology medicinal products in the EU5 potentially a result of cancer being a political priority
- System differences likely to explain the gap in launch timing between Germany and the UK on one hand, and France, Italy and Spain on the other
  - Slower launch timing in France, Italy and Spain may possibly be a result of a more challenging P&R negotiation process than in Germany and the UK
- Cost of medicinal products and affordability are potential drivers for rising time to market (through standard P&R routes) in all countries except Germany, where reimbursement is implicit at launch, and pricing negotiations are conducted 6-12 months post-launch
  - In case of orphan drugs, partial availability of clinical evidence also contributes to delay in access
- Despite rising time to market and seemingly poor access in France via standard P&R pathway, patients may benefit from a number of innovative therapies via ATU early access programs
- Although in Spain only a third of EC-approved orphan products are reimbursed at the national level, so far Regions have been able to provide access on a nominative basis to patients; however this is likely to evolve based on recent new legislation
- Time to market needs to be monitored, given growing budget pressures and anticipated changes in regulations
  - In particular, in the UK, Brexit may impact manufacturers' decision to launch new medicines due to uncertainties in regulatory and economic environment

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