PMU57: Analysis of the evolution in the access to medicines in Italy in the last 5 years (2014-2018)

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Introduction

In Italy, the price setting of medicines reimbursed by the NHS is regulated at the central level by the Italian Medicines Agency (AIFA). The Agency provides, with its scientific authority and autonomy, the clinical, scientific, and economic evaluation of medicines. AIFA's activities are supported by two commissions consisting of well-established experts: the CTS (Technical Scientific Commission), which assesses the national marketing authorization applications, delivers a consultative opinion on them, and provides a classification for reimbursement; and the CPR (Pricing and Reimbursement Committee), which carries out negotiations with pharmaceutical companies for setting prices of medicinal products considered for the reimbursement by the NHS according to transparent methods, timelines, and procedures established by the resolution of the Interministerial Committee for Economic Planning (Comitato Interministeriale per la Programmazione Economia – CIPE) of February 1, 2001.

For a non-orphan drug, companies are allowed to submit a Price and Reimbursement Dossier for the AIFA CTS and CPR evaluation after the European Commission Decision on its marketing authorization. In case of an orphan drug, the related dossier could be submitted immediately after a positive opinion of the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP).

After the dossier submission, the AIFA CTS issues a binding opinion on the therapeutic value of the drug, defining its place in therapy, its delivery regime, and its possible innovative status. The AIFA CPR assesses the economic part, evaluating: cost-effectiveness ratio compared with other available treatments, the lowest price of the medicine in all other EU Member States, price of similar products within the same pharmacotherapeutic group, market share, and the expected impact on NHS expenditures for the next three years, economic models (e.g. BIM). If there is no agreement on the price between CPR and the applicant, the medicine is classified as not-reimbursable and listed in Class C.

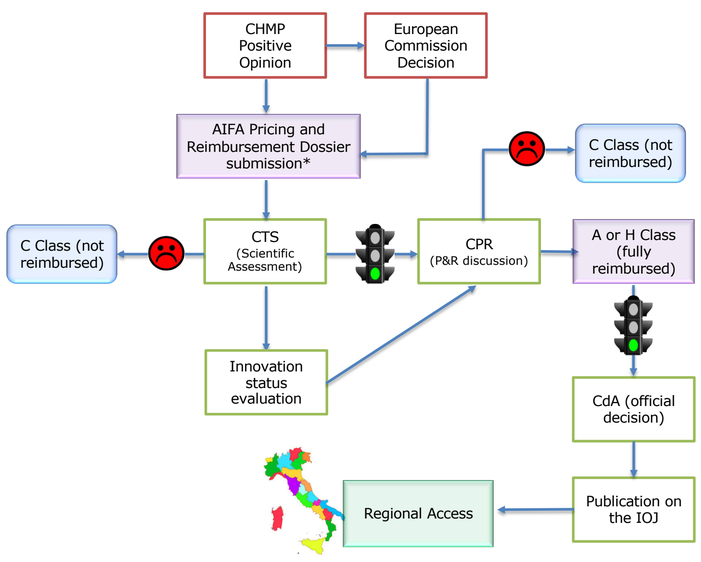

Figure 1 – Key steps for the market access procedure in Italy

Objective

This study aims to assess the changing dynamics of the Italian market access (negotiation conditions, time to reimbursement (TTR), time to patient) for all the new active substances recommended for authorization by the EMA between January 2014 and December 2018.

Methods

We reviewed the EMA's Human Medicines annual Highlights referred to the last 5 years (2014-2018) in order to build our panel, by selecting all the new molecular entities approved by the EMA between January 2014 and December 2018. Then we collected all the information about authorization and reimbursement in Italy, throughout the AIFA's website and the Italian Official Journal (IOJ). The received data were carefully analysed in order to evaluate TTR for different drug categories (negotiation conditions, OD/non-OD, Innovation status, publication year on IOJ).

Results

Between January 2014 and December 2018, 432 drugs, of which 184 represented new active substances, were recommended for the authorization by the EMA.

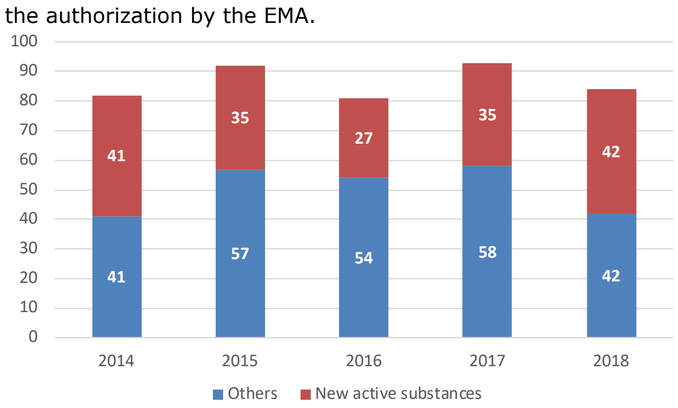

Figure 2 – EMA's recommendations for the authorization of new medicines between Jan 2014 and Dec 2018

In September 2019, 109 drugs (59%) out of these 184 obtained the reimbursement in Italy, with a medium TTR (i.e. days between CHMP positive opinion and P&R publication) of 15 months (446 days, mean 516, range 97-1.260). Out of these 109 drugs 36/62 (58%) orphan drugs (ODs) and 73/122 (60%) non-ODs achieved a reimbursement. Median TTR for ODs was slightly shorter (5%) than for non-ODs (428 vs. 452 days, mean 495 vs. 526, ranges 122-995 vs. 97-1.260, respectively).

	ODs (N = 38)	Non ODs (N = 73)	All (N = 109)
Median	428	452	446
Mean	495	526	516
Range	122-995	97-1.260	97-1.260

Table 1 – TTR (in days) for ODs, non-ODs, and for the entire panel

The 109 considered drugs have been negotiated by AIFA as follows: 1/109 in 2014, 10/109 in 2015, 25/109 in 2016, 38/111 in 2017, 26/109 in 2018 and 9/109 in 2019. As expected the TTR for the negotiated drugs in 2014 (284 days) and 2015 (median 398, mean 390, range 184-530) are significantly shorter than the TTR for drugs negotiated from 2016 (median 504, mean 493, range 122-952) onwards, due to the small sample size. A similar reasoning can be done for the data related to 2019 (median 563, mean 610, range 350-1.260). However, by concentrating on the data from 2016 onwards, TTR seems to progressively decrease in 2017 (median 477, mean 528, range 97-1.128) and in 2018 (median 449, mean 545, range 250-1.167) with a strong change of this tendency in 2019.

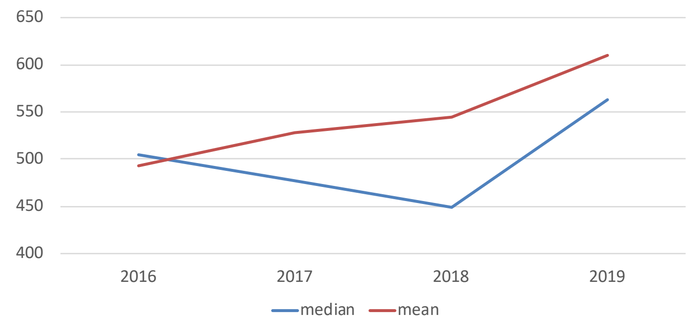

Figure 3 – Median (blue) and mean (red) TTR (in days) in 2016-2019

21/109 (19%) drugs have been negotiated through a Managed Entry Agreement (MEA), 76/109 (70%) with an hidden discount (with or without other conditions), 11/109 (10%) with a cap (sometimes in a combination with other conditions), one with a non-hidden discount and one with a flat price. 16/109 (15%) were reimbursed without specific negotiating conditions and 14/109 (13%) with more than one negotiating conditions.

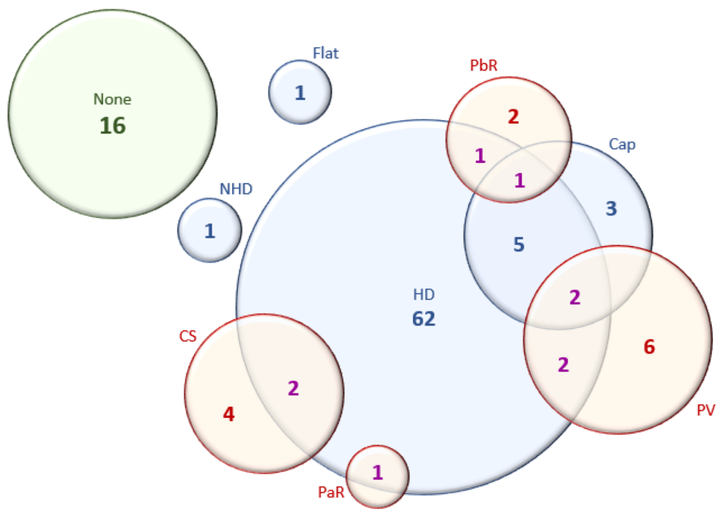

Figure 4 – Number of drugs reimbursed through each kind of negotiation condition between 2014 and 2019. Drugs reimbursed without specific negotiating conditions are in green, drugs reimbursed through the MEA (PbR=Payment by Result, PV=Price Volume, PaR=Payment at Result, CS=Cost Sharing) are in red, drugs reimbursed through negotiation conditions other than the MEA (Cap=Capping, HD=Hidden Discount, NHD=Non-Hidden Discount, Flat=Flat price per patient) are in blue.

In 2014, only one drug concluded negotiations; no specific negotiating conditions were set up by AIFA in its case. Between 2015 and 2017, a low percentage of the drugs concluded negotiations without application of specific negotiating conditions (2015: 10%; 2016: 28%; 2017: 18%); both in 2018 and in 2019 there were no drugs concluding negotiations without application of specific negotiating conditions. Even if between 2015 and 2017 the percentage of drugs negotiated through the MEA seems to progressively increase (2015: 20%; 2016: 24%; 2017: 32%), none of the 26 new active substances reimbursed in 2018 were negotiated throughout the MEA. In 2019, only one drug was negotiated through the MEA; in particular, it is a new kind of the MEA, never used before, named "Payment at Result" (PaR). PaR is similar to the current PbR approach, aimed to manage uncertainty for drugs with unfavourable benefit to risk ratios by requiring the manufacturer to pay-back treatment costs for non-responsive patients (the response is monitored throughout the AIFA's Registries system). The payment at results approach is characterized by the payment provided gradually in three different instalments and only in case of efficacy: 1. upon enrolment in the treatment programme; 2. whilst treatment is ongoing (after 3 months); 3. after 12 months. This is the key difference compared to the classical PbR, where the full drug costs are paid in advance.

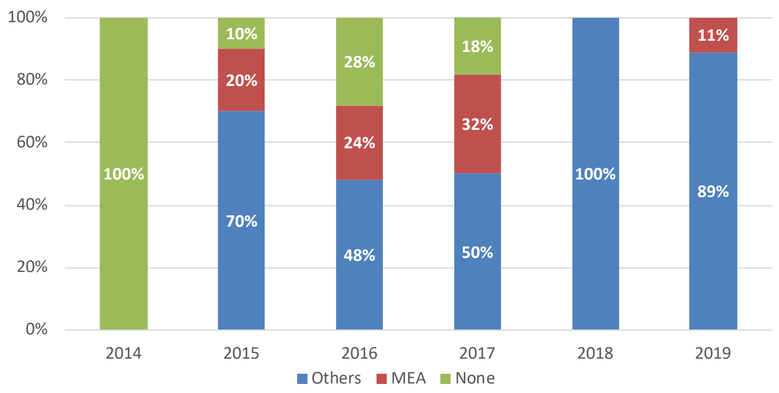

Figure 5 – Percentage of drugs reimbursed between 2014 and 2019 without specific negotiating conditions, through the MEA and through negotiation conditions other than the MEA

Median TTR for drugs reimbursed through the MEA (383 days, mean 419, range 19-984) was shorter than for drugs reimbursed through other negotiation conditions (461 days, mean 541, range 204-1,260) and for drugs reimbursed without specific conditions (475 days, mean 528, range 160-1,128). In particular, reimbursement through the MEA reduced TTR by 17% compared to those reimbursed through other negotiation conditions and by 19% compared to drugs reimbursed without specific conditions.

	MEA (n=21)	Conditions other than MEA (n=72)	No specific condition (n=16)
Median	383	461	475
Mean	419	541	528
Range	19-984	204-1.260	160-1.128

Table 2 – TTR (in days) for drugs reimbursed through the MEA, through negotiation conditions other than MEAs and without specific conditions

32/109 evaluated drugs were classified as "innovative" by AIFA, showing a median TTR significantly shorter than "non-innovative" drugs (353 vs. 540 days, mean 359 vs. 581 days, range 97-617 vs. 130-1.260, respectively). In particular, for innovative drugs, TTR is 35% less than TTR for non-innovative drugs. Moreover, drugs granted the "full innovative status" (21/32) show a median TTR shorter than drugs granted the "conditional/potential innovative status" (335 vs. 431 days, mean 323 vs. 426, range 97-617 vs. 302-563, respectively). In particular, for drugs with a full innovative status, TTR is 38% less than TTR for non innovative drugs, while for conditional/potential innovative TTR is 20% less than TTR for non-innovative drugs.

	Innovative drugs (full status) (N = 21)	Conditionally/potentially innovative drugs (N = 11)	Non-innovative drugs (N = 77)
Median	335	431	540
Mean	323	426	581
Range	97-617	302-563	130-1.260

Table 3 – TTR (in days) for innovative (full status), conditionally/potentially innovative and non-innovative drugs.

Conclusions

This analysis allows to observe trends and dynamics in the access to new active substances in Italy in a consistent timeframe. Even if our results don't show a clear time trend in reduction or increase of time to reimbursement, they clearly show that the adoption of the MEA, helping to manage possible uncertaintes, leads to a quicker completion of the negotiation procedure. Likewise, the innovation status granted by the AIFA CTS allows drugs to be made available in a shorther time than non innovative drugs (mainly when a «full» instead of a «conditional» innovation status is recognized). Despite the increasing interest in MEAs, in the last months hidden discounts seem to be preferred to these - more sophisticated - regulatory tools. This may depend on the complexity of their management. It will be estremely interesting to observe the future developement of the performance based schemes, which role will be essential in granting access to the new coming innovative medicinal products. Unexpectedly, the drug's orphan status does not seem to have a significant impact on the time to reimbursement, even if the Italian regulation allows P&R Dossier to be sumbitted immediately after the CHMP positive opinion (instead of waiting for the European Commission Decision, as for the non-orphan drugs).

References

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