IMPACT OF AIFA MONITORING REGISTRIES CLOSURE ON DRUGS' TURNOVER TRENDS IN ITALY

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Introduction

The Italian Medicine Agency (AIFA) Monitoring Registries platform is an IT system adopted by the Italian National Health Service (NHS) since 2005, to guarantee the prescribing appropriateness of medicines and the sustainability of NHS. In most cases, drugs monitored are high-cost drugs, often biologicals, with uncertainty regarding efficacy, safety, appropriate use in clinical practice and cost-effectiveness. Therefore, data collected during monitoring provided real world evidence on the drugs' use, to measure uncertain clinical outcomes or monitor the application of the Managed Entry Agreements (MEA). The monitoring registry activation follows the marketing authorization of the drug or the authorization of an extension of therapeutic indication. In some cases, registries also monitor drugs reimbursed by NHS through the inclusion in the list ex Law 648/96.[1-3]

This study aimed to assess the use of monitoring registries in Italy and the possible impact of their closing on drugs' sales and related turnover trends.

Methods

The analysis was conducted on the latest update of the AIFA report,[4] dated 5th June 2023, containing all closed web-based registries and therapeutic plans, since the introduction of the platform (N=181). Registries related to drugs authorized and reimbursed (N=121) were selected and descriptive statistics were performed. In particular, the analysis evaluated average and median duration of the registries, possible reasons of their closure and related renegotiations with AIFA (including negotiations for new indications or packages).

Information regarding medicines and their negotiation history were collected from a proprietary IQVIA database on Italian negotiation dynamics and integrated with public sources (i.e., Official Journal, European Medicines Agency website and AIFA website).[5-7]

The analysis explored the impact of registries closure on drugs' sales, considering the 3 Moving Annual Total (MAT) preceding and the 3 MAT following the closure. The research focused on registries lasted for a period lower than the overall median duration, 7.0 years (N=61). Moreover, registries of medicines with characteristics that might impact sales values and lead to bias in the results were excluded (residual registries: N=29):

- Medicines used in clinical practice for more than 10 years (for other therapeutic indications);
- Medicines with a MEA ended at the same time as the registry;
- Medicines with new reimbursed indications in the 3 MAT following the closure of the registry.

Sales data were collected from a proprietary IQVIA database that gathers information from a panel of hospital pharmacies located throughout the Italian country,[8] and expressed both in terms of net ex-factory price and weighted average price. The weighted average price represents a statistical processing of expenditure data, including discounts negotiated with AIFA, commercial and tender discounts.

The cut-off date to collect sales data was April 30th, 2023. Incomplete MAT (including months after the cut-off date) were considered only in the case of availability of data for at least 6 months, re-proportioning them over the whole year.

In order to obtain comparable results, drugs that did not comply with the following conditions were subsequently excluded from the analysis (residual registries: N=20):

- Sales data availability for at least 1 MAT after the closure of the registry.
- Stable turnover trend in the 3 MAT preceding the closure of the registry, defined as annual Compounded Average Growth Rate (CAGR) above -10%.

Results

From the 181 closed web-based registries and therapeutic plans in the latest update of the AIFA report, the analysis excluded all treatment plans (N=14) and considered only authorized and reimbursed drugs, thus defining a panel of 121 registries. Among them, in 34 (28%) cases, monitoring continued with a different tool (mostly multi-drug prescription form). Of the remaining 87 (72%) registries, in 58 (66%) cases a specific reason was identified as a possible cause for monitoring ending (55% for a concomitant closure of a MEA and 11% for an over-10-years use in clinical practice). The median duration of the registries was 7.0 years, the average duration was 7.2 years. In 92 (76%) cases the closure of the registry coincided with a renegotiation with AIFA, including renegotiations for new indications or new packs *(Figure 1)*.

The analysis showed that in some cases registries of drugs belonging to the same pharmaceutical class were closed simultaneously (e.g., drugs for chronic autoimmune diseases, drugs for eye diseases, etc.). In these cases, generally there was not a renegotiation related to the closure of the registries in the absence of new therapeutic indications. When the closure of the registries coincided with a renegotiation with AIFA, it resulted in an increase in the overall discount between 5% (generally drugs for rare diseases) and 15% (generally oncological drugs).

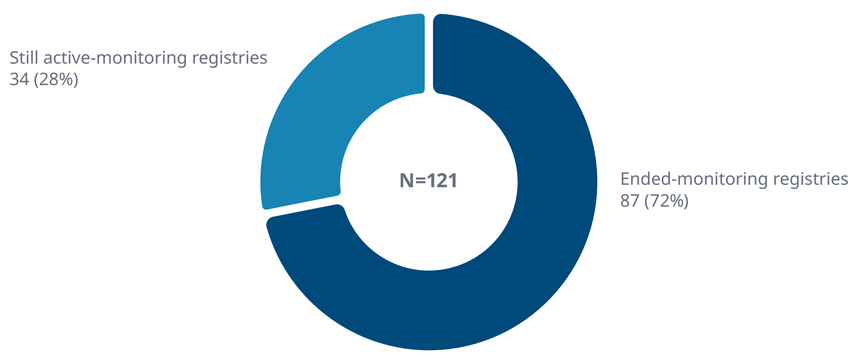
The analysis of drugs sales compared the 3 MAT preceding and the 3 MAT following the closure of the registries of 13 drugs, corresponding to 20 registries *(Figure 2 and Figure 3)*:

- In 5 cases the turnover, which increased in the period before the closure of the registry, showed a decrease following the closure;
- In 1 case the turnover, slightly decreasing in the period before the closure of the registry, continued to show a decreasing trend;
- In 6 cases the turnover continued to grow, albeit with a lower trend than in the period before the closure of the registry;
- In 1 case turnover continued to grow with a higher trend than in the period before the closure of the registry. This case was related to an orphan drug.

Conclusions

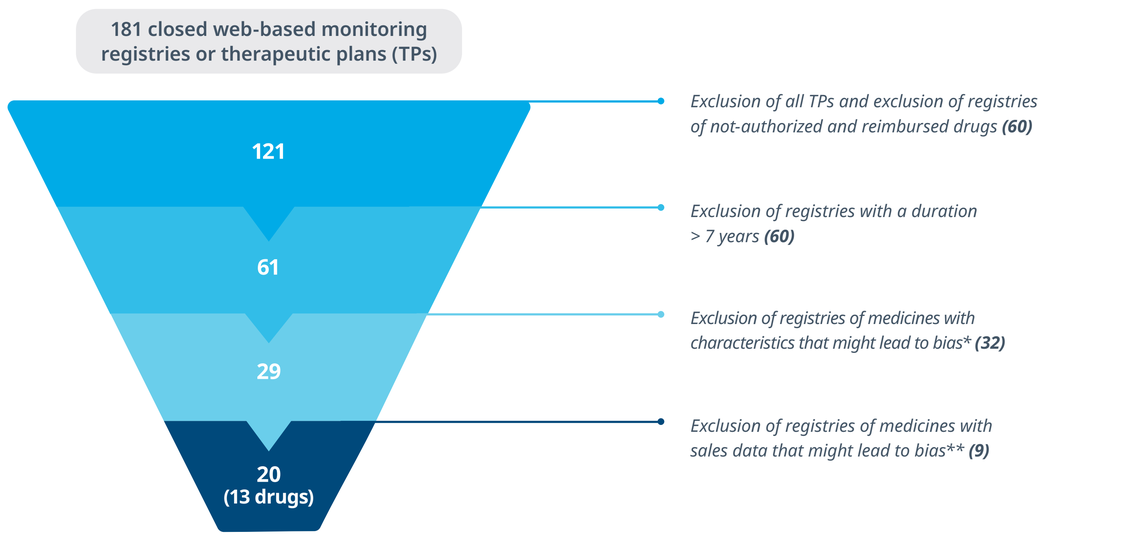
The analysis showed that the closure of a registry after a monitoring < 7 years does not lead to an increase in turnover trends of non-orphan drugs, even in absence of renegotiation. Thus, it can be assumed that a 7-year period is enough to monitor prescribing appropriateness through registry and ensure it even after registry closure.
This study broads the horizons towards new analyses on the subject. The impact on prescribing appropriateness of closing registries after different timing might be explored in further analyses.

Figure 1. ***Descriptive statistics of authorized and reimbursed drugs registries***



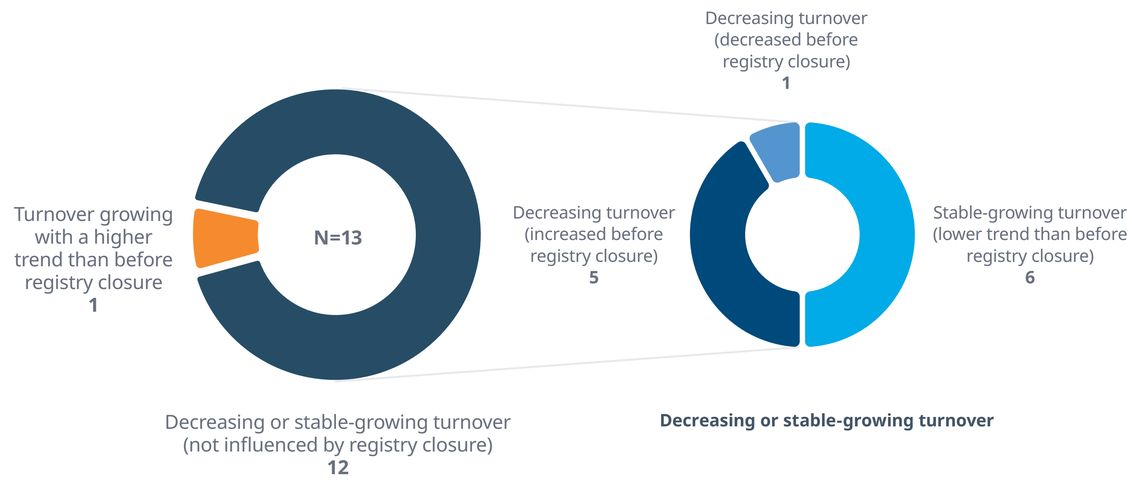
DURATION		RENEGOTATION			REASON		
ENDED MONITORING		**ENDED MONITORING**			**ENDED MONITORING**		
Average	**7.7** (years)	Yes	**89%**	n=77	End of a MEA	**55%**	n=48
Median	**7.9** (years)	No	**11%**	n=10	10+ yrs use in clinical practice	**11%**	n=10
					Not attributable	**33%**	n=29
STILL ACTIVE MONITORING		**STILL ACTIVE MONITORING**			**STILL ACTIVE MONITORING**		
Average	**5.9** (years)	Yes	**44%**	n=15	Paper-based prescription form	**12%**	n=4
Median	**5.3** (years)	No	**56%**	n=19	Multi-drug prescription form	**76%**	n=26
					Paper-based therapeutic plan	**12%**	n=4
ALL		**ALL**					
Average	**7.2** (years)	Yes	**76%**	n=92			
Median	**7.0** (years)	No	**24%**	n=29			

Figure 2. ***Selection of the drugs for the analysis of registries closure's impact on sales***



** 10+ years use in clinical pratice and/or with a MEA ended at the same time as the registry and/or with new reimbursed indications in the 3 MAT following the registry closure*
*** no data available for at least 1 MAT after the registry closure and/or turnover's CAGR below -10% in the 3 MAT preceding registry closure*

Figure 3. ***Sales trends after (vs before) registry closure***



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