THE IMPACT OF INNOVATIVE STATUS ON NEGOTIATION OUTCOMES IN ITALY

HPR12

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Introduction

In Italy, price and reimbursement of medicines is regulated at central level by the Italian Medicine Agency (AIFA) through negotiations with pharmaceutical companies of reimbursement, ex-factory price, confidential discounts on prices, and possible Managed Entry Agreements.[1] Moreover, AIFA evaluates the innovative status that might be requested by companies for drugs already approved by the European Medicines Agency (EMA) and indicated for serious diseases, diseases requiring frequent hospitalization or severely compromising a patient's quality of life.[2] Each application is evaluated by AIFA considering three main factors: added therapeutic value of the drug and unmet need in the therapeutic area using a five-grade scale (maximum, important, moderate, poor, and absent) and quality of evidence using the GRADE methodology which considers a four-levels scale (high, moderate, low and very low).[2]

Depending on AIFA's assessments, a drug may be awarded with a full or conditional innovative status or considered not innovative. Full innovative status, if granted, ensures access to a dedicated fund as well as the removal of temporary 5%+5% reductions on ex-factory prices.

Given the fundamentals of value-based healthcare, full and conditional innovative status should be, in principle, associated with better negotiation outcomes both in terms of negotiated discount as well as duration of the negotiation process. Given the few to none evidence available,[3] this study aims at assessing the impact of innovative status on negotiation outcomes of drugs in Italy in terms of overall discount and negotiation process duration.

Methods

The analysis was conducted on all drugs for which pricing and reimbursement resolution for the first indication was published in the Italian Official Journal (IOJ) between 2016 and 2023.
The panel was selected from an IQVIA proprietary database on negotiation dynamics which collects and integrates data on all new active substances receiving a positive opinion by the EMA's Committee for Medicinal Products for Human Use (CHMP) since 2015. Information related to the pricing and reimbursement process of the drugs in Italy, and negotiation outcomes (e.g., innovative status request assessment's results, overall discount) are included.

The two variables of interest for the analysis were:

- Overall discount: the estimated price reduction identifying the difference between the ex-factory price and weighted average price. The weighted average price represents a statistical elaboration of expenditure data, including discounts negotiated with AIFA, commercial and tender discounts;
- P&R process duration: the number of days between the pricing and reimbursement request's submission date and the publication date of the pricing and reimbursement resolution in the IOJ.

To assess the impact of innovative status on the variables of interest, an analysis was conducted in two steps:

- First, descriptive statistics were estimated to assess the median overall discount and median P&R process duration of drugs granted innovative status (either full or conditional), versus non-innovative drugs;
- Then, inferential analyses were run to investigate the impact of innovative status on overall discount and P&R process duration. Potential control variables (e.g., drug characteristics or factors pertaining to the Italian market) were tested in a univariate beta regression and negative binomial generalized linear model with overall discount and P&R process duration as outcome variables, respectively. Next, the variables with a significance threshold of $p<0.15$[4] were included in the model with innovative status (either full or conditional) as main independent variable of interest. Finally, sensitivity analyses were performed considering the same set of control and a further stratification of innovative status (full innovativeness / conditional innovativeness / not granted / never requested).

Results

A total of 293 drugs for which pricing and reimbursement resolution for the first indication was published in the IOJ between 2016 and 2023 were included in the analysis. Of these, 57 drugs were granted innovative status in the same period, either full or conditional, while the remaining drugs (236) were either found not innovative or did not request innovative status *(Figure 1)*.
Results from the descriptive analysis are presented in *Figures 2 and 3*. The analysis shows that innovative drugs had a median overall discount of 37.9% (IQR 25.4%-48.9%) after the negotiation, similarly to non-innovative drugs (39.0%; IQR 30.0%-50.1%). The median P&R process duration for innovative drugs was 405 days (IQR 348-535), compared to 424 days (IQR 343-527) for non-innovative drugs.
Innovative status defined as either full or conditional was not significantly associated with overall discount *(Table 1A)*. Conversely, when considering a further stratification of this variable in the sensitivity analysis, full innovative status was found significantly associated with a lower discount with respect to drugs which never requested innovative status (-8.8 percentage points; $p<0.01$) *(Table 1B)*.
No significant impact on P&R process duration was observed in both the baseline and sensitivity analyses *(Table 1A and 1B)*.

Conclusions

The analysis shows that drugs that have been granted full innovative status by AIFA between 2016 and 2023 have negotiated a significantly lower discount compared to non-innovative drugs. This may indicate an alignment on value perception between the manufacturers and the regulatory body, which appears to be lacking for drugs that did not fully meet AIFA's criteria for innovativeness. It is worth noting that several companies renounce the economic benefit of not applying the two temporary 5% reductions, which may justify better negotiated conditions. Neither full nor conditional innovative drugs underwent faster negotiation processes likely mirroring the higher complexity of decision making and assessment process when new and innovative healthcare technologies are evaluated within the existing frameworks.

Figure 1. ***Analysis sample, by innovative status (2016-2023)***

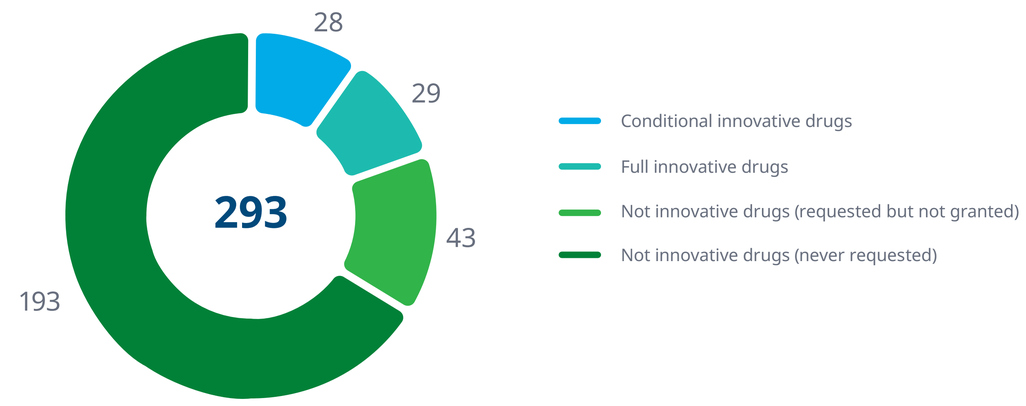

Figure 2. ***Median overall discount for first indications, by innovative status (2016-2023)***

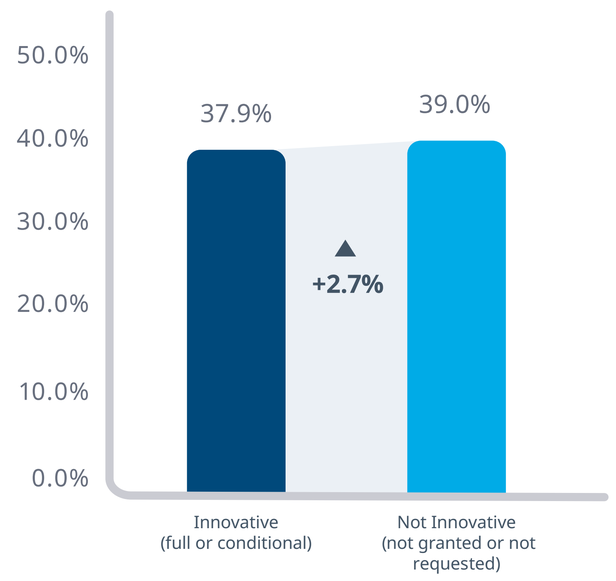

Figure 3. ***Median overall P&R process duration for first indications, by innovative status (2016-2023), n of days***

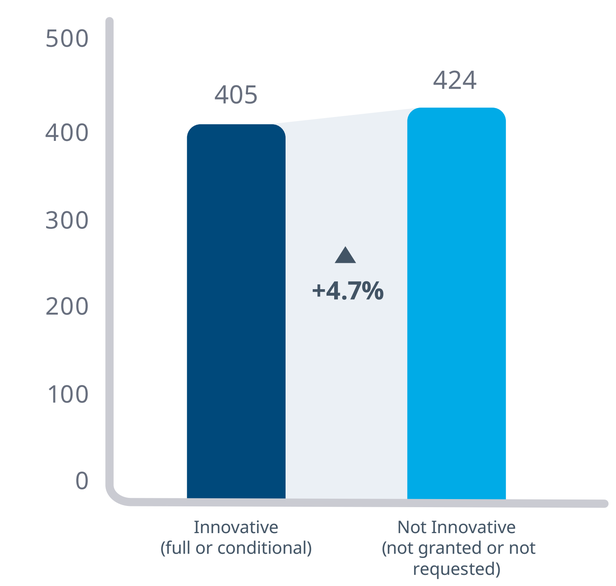

Table 1. ***Main (A) and sensitivity analysis results (B) - Impact of innovative status on overall discount and process duration for first indications (2016-2023), coefficient***

	Overall discount	Process duration
A)		
Innovative status (full or potential vs not innovative)	-0.032 *(0.022)*	-0.017 *(0.048)*
B)		
Innovative status		
Full (vs never requested)	**-0.088*** *(0.024)**	-0.096 *(0.063)*
Conditional (vs never requested)	0.025 *(0.029)*	0.081 *(0.063)*
No but requested (vs never requested)	0.015 *(0.021)*	0.023 *(0.050)*

Robust standard errors in parentheses. *** p < 0.01, ** p < 0.05, * p < 0.1

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