Negotiation Agreements with AIFA from January 2016 to May 2021 – FOCUS on Orphan Drugs

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INTRODUCTION/BACKGROUND

The Pricing and Reimbursement (P&R) negotiation of a medicinal product between the Company and AIFA is a very important and complex process, involving the evaluation of the AIFA HTA office and of two Consulting Commissions, Commissione Tecnico-Scientifica (CTS) and Comitato Prezzi e Rimborso (CPR).

At the end of the negotiation, the medicinal product can be classified in class A or H and consequently reimbursed by the Italian National Health Service (SSN); if the Company and AIFA can't reach an agreement, the medicinal product will not be reimbursed by the SSN and classified in C. The reimbursement agreement does not only define a class and a price; it often includes other reimbursement conditions which are known as Managed Entry Agreements (MEAs).

MEAs allow to reimburse new treatments by managing uncertainty around their efficacy and/or financial impact, and can therefore be outcome-based or financial-based.

Outcome-based agreements negotiated by AIFA include several schemes, such as:

- Payment by results
- Payment at results
- Risk sharing
- Success fee

Financial-based schemes may include:

- Cost sharing
- Treatment cost capping at patient level

Other conditions include for example: definition of a discount for sales to the SSN, definition of a budget cap at product level; changes in the duration of the agreement; stipulation of a safeguard clause.

The management of MEAs requires the implementation of an AIFA Monitoring Registry (MR). A MR can also be implemented in the absence of MEAs, to verify prescriptive appropriateness.

Furthermore, AIFA Technical-Scientific Committee (CTS) evaluates, according to Determination No. 1535/2017, the request for Innovation Status (IS) recognition, if submitted. This evaluation is based on three main criteria: unmet need, incremental therapeutic value and quality of evidence. The possible outcomes are: Full IS, Conditional IS and No IS.

The P&R Determination published on Italian Official Journal (OJ) details qualitatively all agreement defined during the negotiation and, if applicable, the Innovation Status (IS); on the other hand, the Determination often maintains confidential the quantitative elements of the agreements.

OBJECTIVES

The aim of the present work is to investigate on the agreements for orphan drugs, as designated by EMA, between Company and AIFA following P&R negotiation.

P&R determinations published in the Italian Official Journal in the period January 2016 – May 2021 were analyzed.

METHODS

The data were extrapolated from an internal database, where all the first P&R determinations for each OD, published from January 2016 to May 2021, are collected.

The analysis was focused on agreements reached during the first negotiation with AIFA. Data analysed were: reimbursement classification (A, H or C); Innovation status (IS) recognition; presence of MEAs (financial and/or outcome-based); presence of monitoring registers; other negotiation conditions.

Before AIFA Determination 1535/2017 publication, AIFA didn't publish on website the assessment report, therefore for products with P&R determination published before July 2017 (AIFA Determination 1535/2017 publication month), we had to analyze also the CTS assessment reports, even if not all the data are available compared to the assessment reports.

A sub-analysis on ODs was conducted on ODs which are also Advanced Therapy Medicinal Products (ATMPs), given their innovativeness and potential high impact for patients.

RESULTS

From January 2016 to May 2021, 73 ODs P&R determinations were published; 59 (81%) ODs achieved reimbursement (class A or H), of which 22 (37%) for oncology indications, and 37 (63%) for non-oncology indications. No agreement was reached for 14 (19%) ODs, which were classified in C (Figure 1).

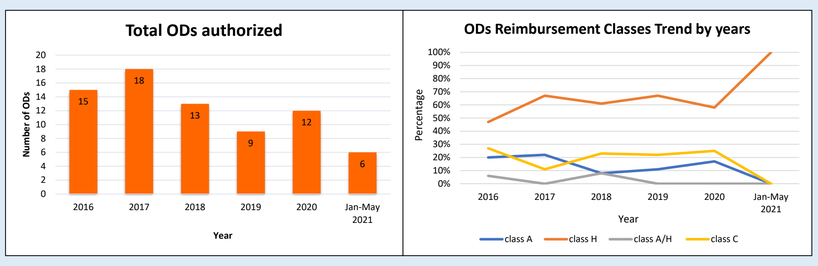

Figure 1 – Orphan drugs reimbursement - trend by year

Across the considered period, 28 (47.5%) ODs obtained Innovation Status: 15 Full IS and 13 Conditional IS (Figure 2). Referring to therapeutic area, 14 (38%) non-oncology ODs and 14 (64%) oncology ODs have been considered Innovative.

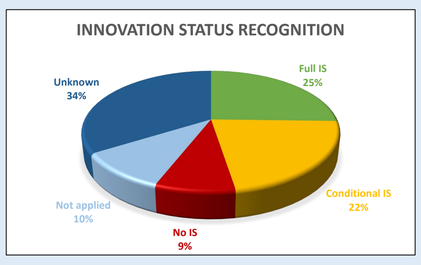

Figure 2 - Innovation Status recognition January 2016 - May 2021

From January 2016 to May 2021, 50 (84.7%) ODs obtained financial agreements during the P&R negotiation, 2 (3.4%) ODs had an outcome-based one and 4 (6.8%) obtained both, financial and outcome-based agreements. 3 ODs hadn't an agreement (5.1%). In addition, 41 (69.4%) ODs required a monitoring register.

Focusing on financial agreements, the results showed that these are predominantly agreements other than MEAs (87%). The most common was the discount, in fact in total 46 (78%) out of 59 orphan drugs obtained the discount which was almost always confidential (only in one case the discount has been specified); 8 (14%) ODs obtained the budget cap. Note that 7 drugs had both agreements, discount and budget cap (Figure 3).

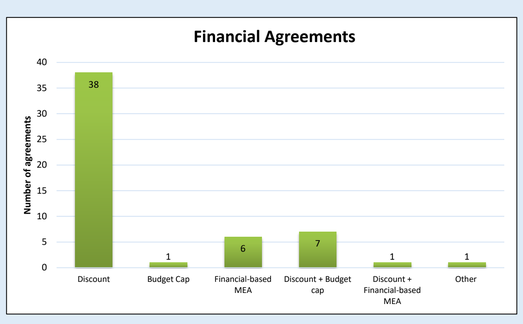

Figure 3 - Financial Agreements January 2016-May 2021

In general, during the period analyzed, the MEAs arranged were few: total of 9 (17%) (financial and outcome-based). As showed by Figure 4, 67% are outcome-based MEAs.

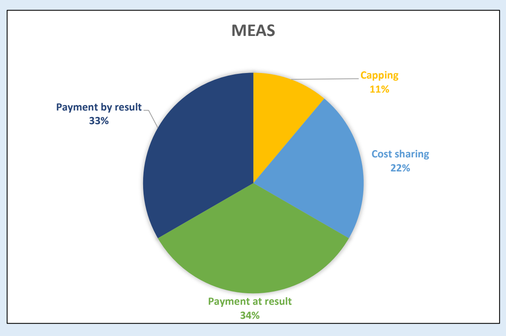

Figure 4 - MEAs arranged from January 2016 to May 2021

Concerning to therapeutic area, only 3 (8%) non-oncology ODs had a MEA, all outcome-based. On the other side, 6 (27%) oncology ODs had a MEA: 3 had outcome-based ones and 3 had financial-based ones.

From January 2016 to May 2021, the results showed a greater tendency to sign financial agreements than outcome-based ones. In 2018 and 2020, 100% were financial agreements, in 2019 71.4% of ODs had a financial agreement and 28.6% of ODs arranged both, financial and outcome-based agreements (Figure 5).

In the last years there have been no more financial MEAs (from 2018 no financial MEAs were arranged), but for all ODs reimbursed it has been stipulated other types of financial agreements. In addition, from 2018 no OD P&R negotiations closed without a financial and/or outcome-based agreements (Figure 5).

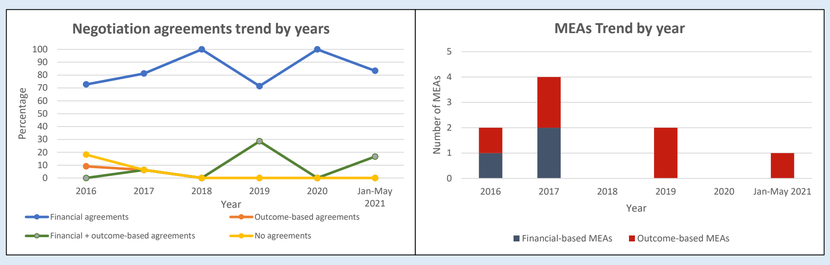

Figure 5 - Trend of agreements by year

During negotiations, for 7 (12%) ODs a change in the duration of the agreement from the 24 months required by law was arranged: 18 months for 5 drugs and 12 months for 2. In addition, for 5 (8%) ODs a safeguard clause was stipulated.

To sum, considering all the negotiation clauses achieved during the analyzed timeframe (MEAs, confidential discount, budget cap or other financial agreement, monitoring register, safeguard clause, change in the duration of the agreement), it was observed that the majority (75%) obtained more than one negotiation clause. In particular, between 2017 and 2019, 4 ODs obtained 4 negotiation clauses and in the last years it was observed a decrease of negotiation ended with a single clause (Figure 6).

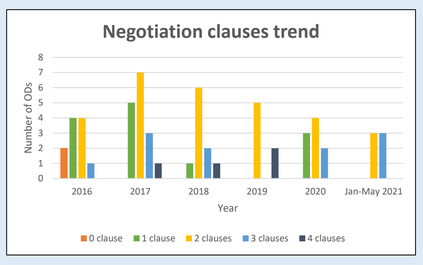

Figure 6 - Negotiation clauses trend from January 2016 to May 2021

A sub-analysis with focus on ATMPs observed that from January 2016 to May 2021, 8 ATMPs, designated also orphan drugs by EMA, were approved in Italy; for 1 (12.5%) no agreement was reached and it has been classified in C.

Of the 7 reimbursed ATMPs, 5 (71%) obtained Full IS recognition. The majority of ATMP reimbursement agreements (5/7, 71%) included an outcome-based MEA; three of those also included a financial-based MEA. In addition, all ATMPs presented a monitoring register.

CONCLUSIONS

From January 2016 to May 2021, the majority (81%) of ODs assessed by AIFA achieved reimbursement, most of them with one or more financial and/or outcome-based agreements. In fact, in the last years there were no negotiations without stipulating an agreement and the majority ended with multiple negotiation clauses achieved.

In particular, the results of the analysis showed a greater tendency to sign financial agreements than outcome-based ones. The financial agreements arranged are predominantly agreements other than MEAs (87%) and the most common was the discount. Furthermore, it was noted that from 2018 there have been no more financial MEAs, but other types of financial agreements have been adopted.

On the other hand, the majority (71%) of ATMPs presented an outcome-based MEA.

During the period considered, the analysis showed that the therapeutic area has an impact on MEAs and on IS recognition; in fact, there was a higher percentage of oncology ODs which received IS recognition (64% vs 38% of non-oncology ODs) and MEAs (27% vs 8% of non-oncology ODs).

AIFA https://www.aifa.gov.it/web/guest/registri-farmaci-sottoposti-a-monitoraggio Last access: 7th October 2021
Wenzli M., Chapmani S. Performance-based managed entry agreements for new medicines in OECD countries and EU member states. OECD Health Working Papers. 2020.