

Lump-sum envelopes: high predictability for payers (French healthcare Product Pricing Committee – CEPS) and minor contribution for companies.

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BACKGROUND

The possibility of regulation by lump-sum envelopes (capped total revenue amount) was introduced in the framework agreement of September 25, 2008, with the initial intention of regulating orphan drugs. Such agreements also offer the possibility of securing a prescription framework, when the fields of reimbursement is restricted or indication(s) extended in a short timeframe.

OBJECTIVE

The analysis aimed to describe the contribution of lump-sum envelopes (LSE) to the regulation of healthcare drugs by the CEPS.

METHODS

A retrospective study of medicines with a first indication negotiated by the CEPS between 2014 and 2023 was performed. We focused on the drugs, which presents a reimbursement at least in one indication and a clawback agreement in particular the ones with a LSE. The research was conducted on the clawback payment file, held by the CEPS. Health products presenting a clawback agreement made by LSE for 2021, 2022 and 2023 with a payback rate exceeded 80% above a specified amount were included in the analysis. For each years, revenues and rebates were reported, as well as the activation rate and the contribution rate. LSE can be used for regulatory purposes, where an envelope is set aside to treat a defined number of patients (mainly orphans), or for security purposes. The latter are not intended to be activated and are used to prevent off-label prescribing. An analysis was carried out to identify the variables influencing the activation of the LSE. The variables analysed were the orphan status of the drug, the type of LSE, the presence of a joint remittance mechanism, the clinical added value, the revenue range and the therapeutic area.

RESULTS

LUMP-SUM ENVELOPES IN THE LANDSCAPE OF REGULATION

Respectively for years 2021, 2022 and 2023, the total regulation concerns €13.36M, €15.93M and €18.43M of revenue data and allows €4.58M, €5.68M and €7.10M to be remitted, excluding the safeguard clause. The regulation LSE concerns €1.63B, €1.87B and €2.18B€. Respectively 32.14% and 33.33% and 39.35% of the identified products have seen their capping reached in 2021, 2022 and 2023 contributing in €0.09B, €0.12B and €0.17B of remittance. This represents around 2% of the total contribution of regulated drugs for both years.

Figure 1. The impact of lump-sum envelopes in terms of revenue and remittance

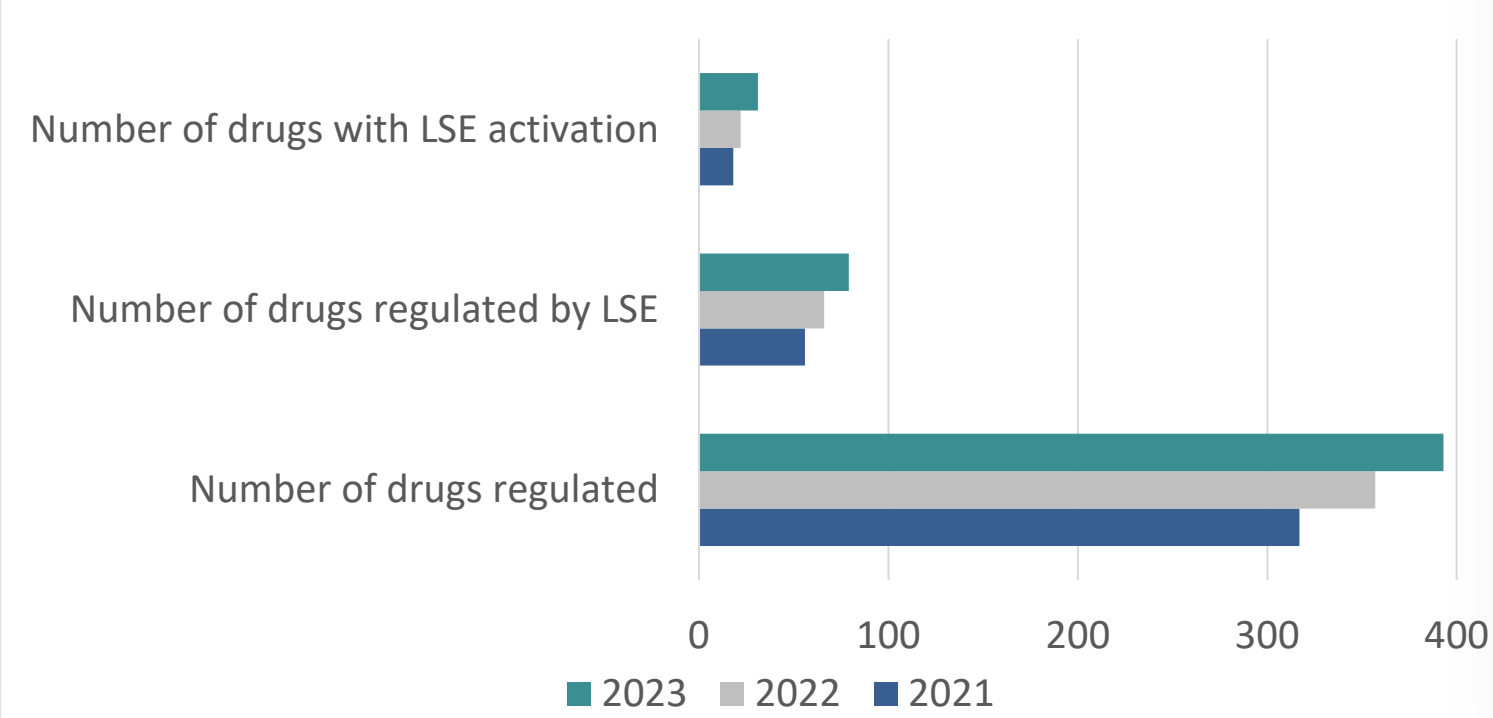


Figure 2. The impact of lump-sum envelopes in terms of revenue and remittance

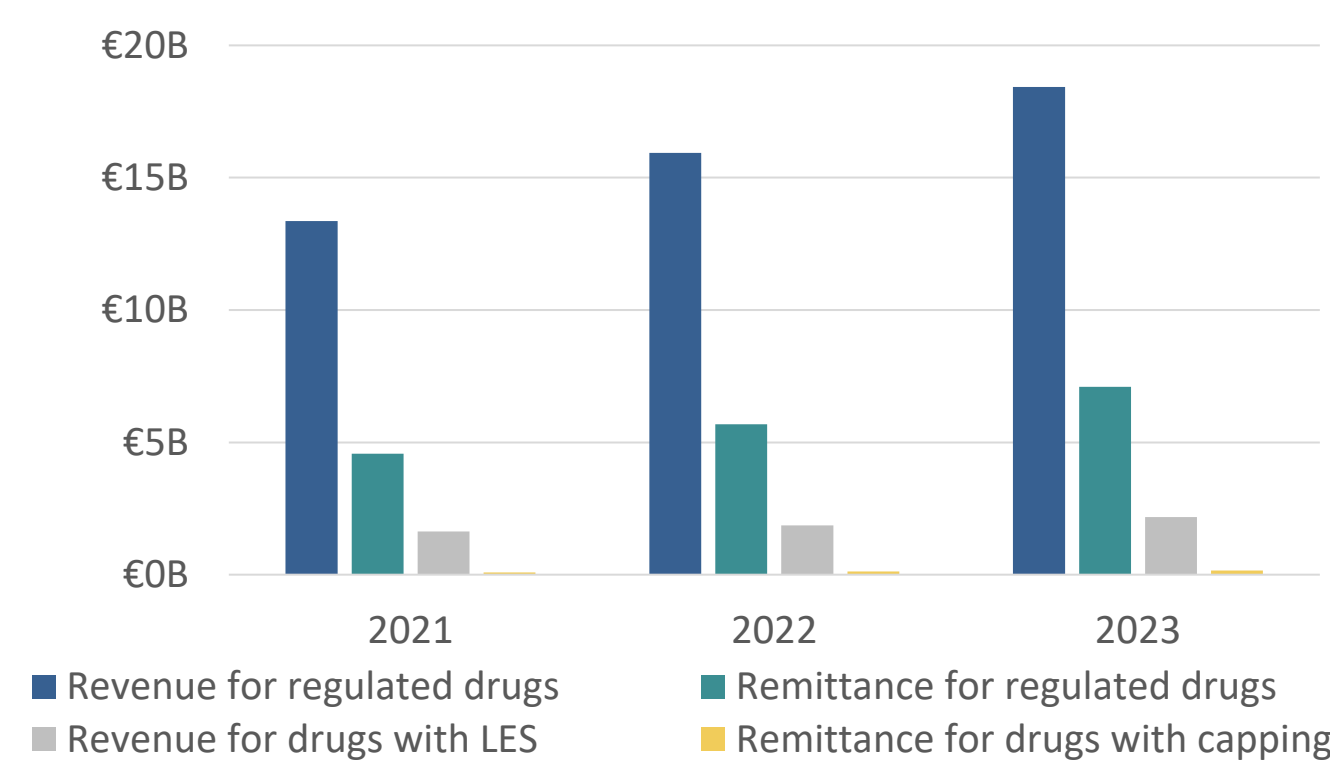
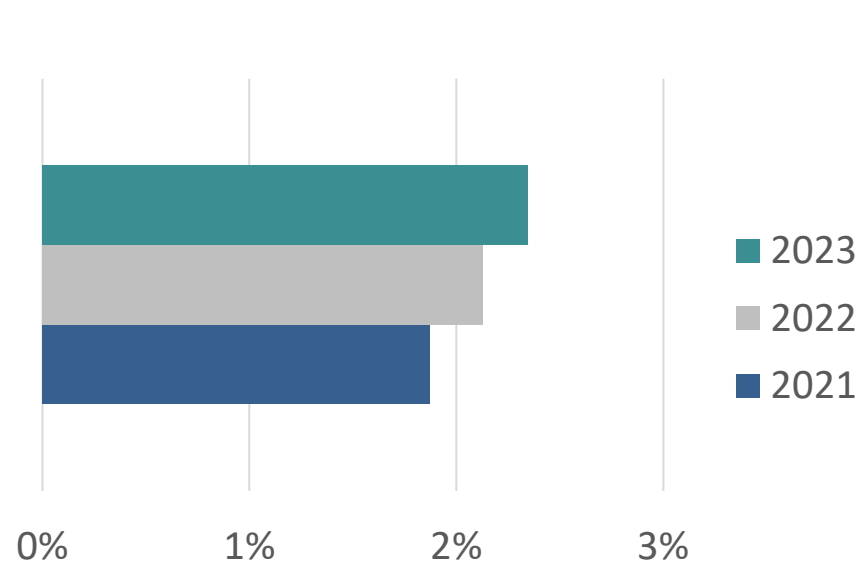


Figure 3. Contribution rate of the lump-sum envelopes



- Although the number of lump-sum envelopes among regulatory mechanisms remains limited, their incidence increases in correlation with the growth in the number of regulated products.
- Revenues and rebates, including those associated with lump-sum envelopes, show growth between 2021 and 2023. The activation rate for rebates is also experiencing a slight increase.
- Consequently, the contribution of lump-sum envelopes is also increasing.

When LSE is combined with another rebate mechanism, the latter is applied to the net revenue of the first rebate, thus justifying a lower activation and contribution in comparison to LSE as unique rebate mechanism.

Figure 6. Activation rate when association to another rebate mechanism (RM)

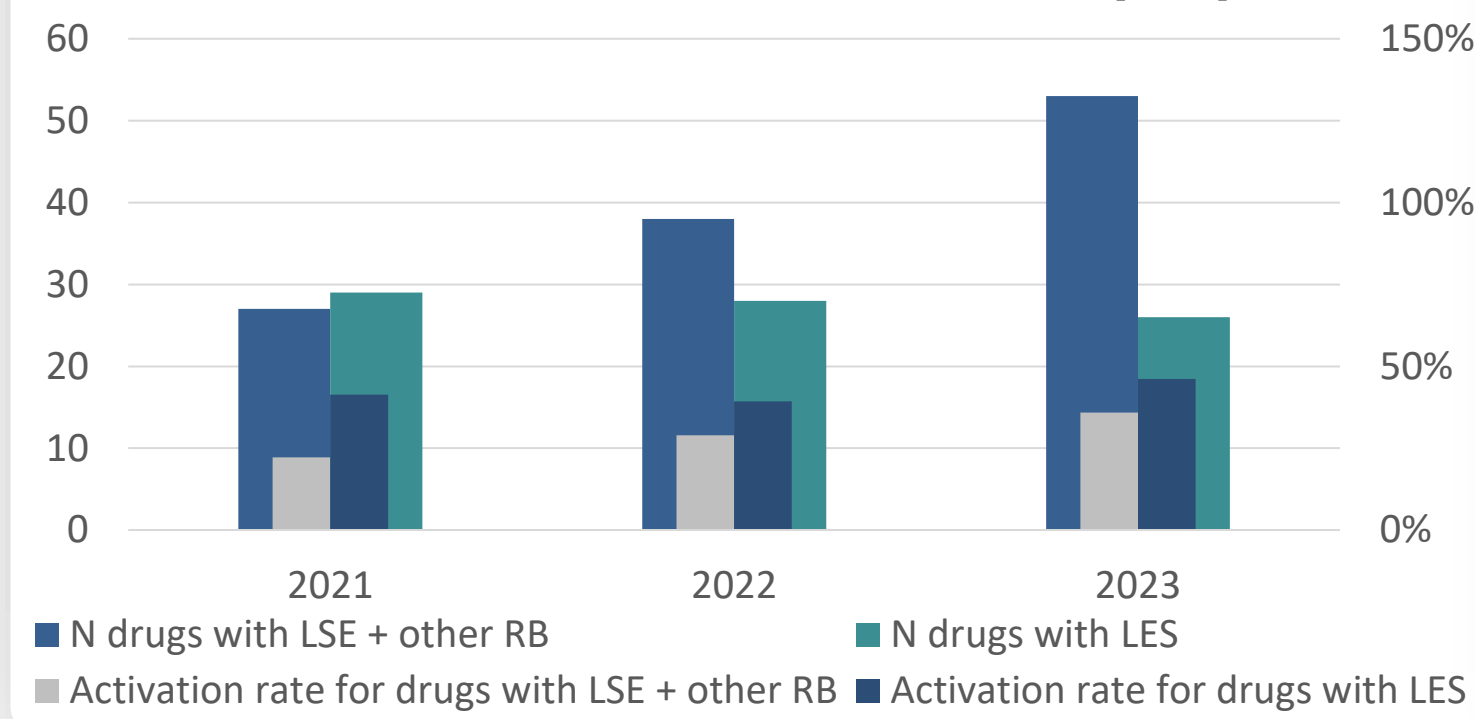
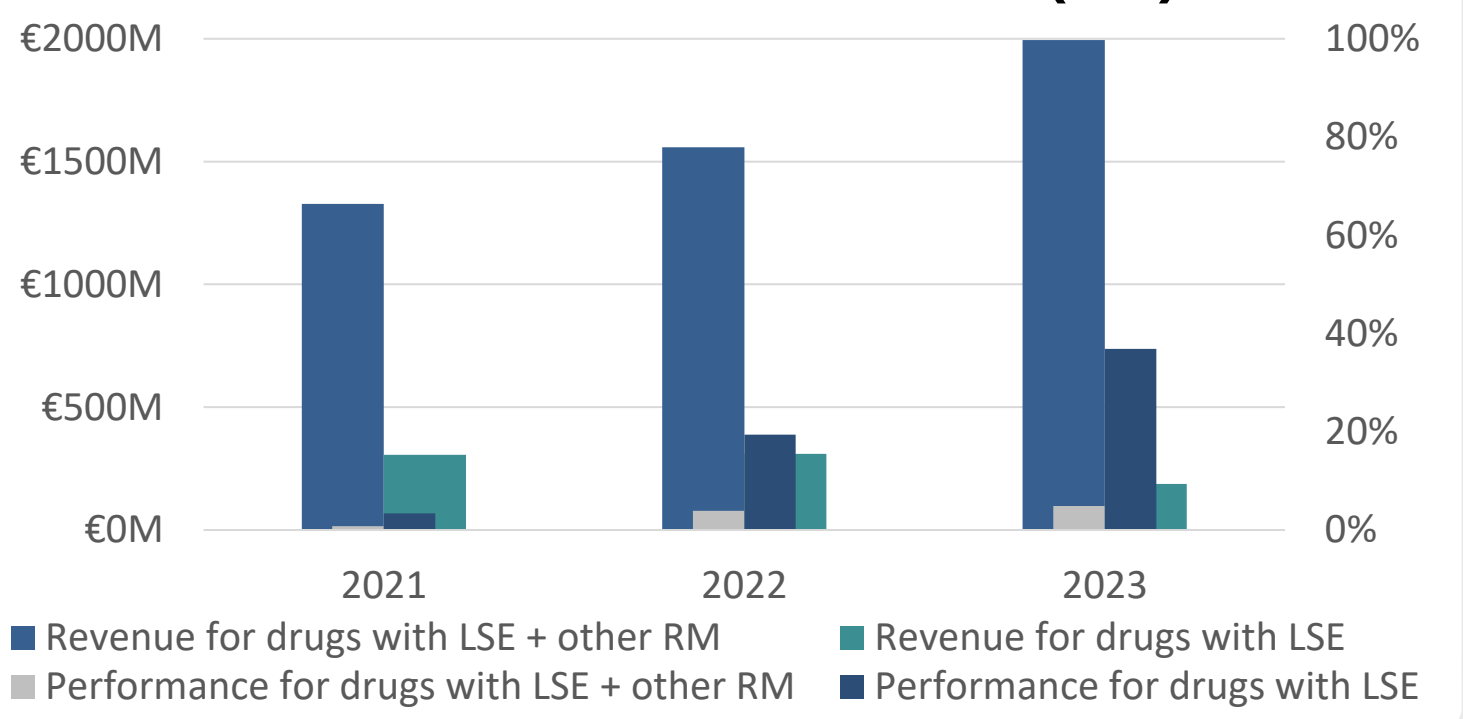
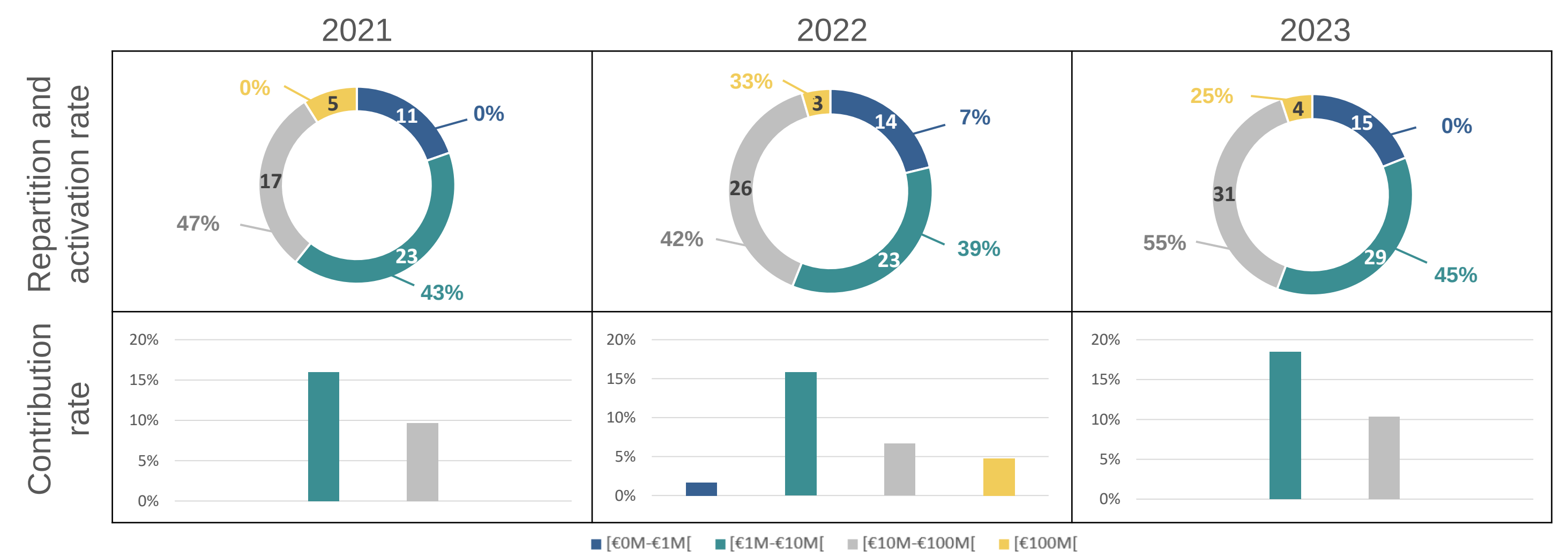


Figure 7. Contribution rate when association to another rebate mechanism (RM)



An increase in the activation rate is observed with higher revenue range. The results in the highest range are difficult to interpret due to the low sample size. The activation rate is slightly higher for drugs presenting a revenue [€10M-€100M] in comparison to drugs presenting a revenue [€1M-€10M], while the opposite is observed for the contribution rate.

Figure 8. Activation rate and contribution by revenue range



DESCRIPTIVE ANALYSIS OF LUMP-SUM ENVELOPES

Both years, around 75% of drugs with a lump-sum envelope were strictly regulated (marginal rate of 100%), while around 25% had a marginal payout rate of between 80% and 100%.

Figure 4. Total or marginal LSE: repartition

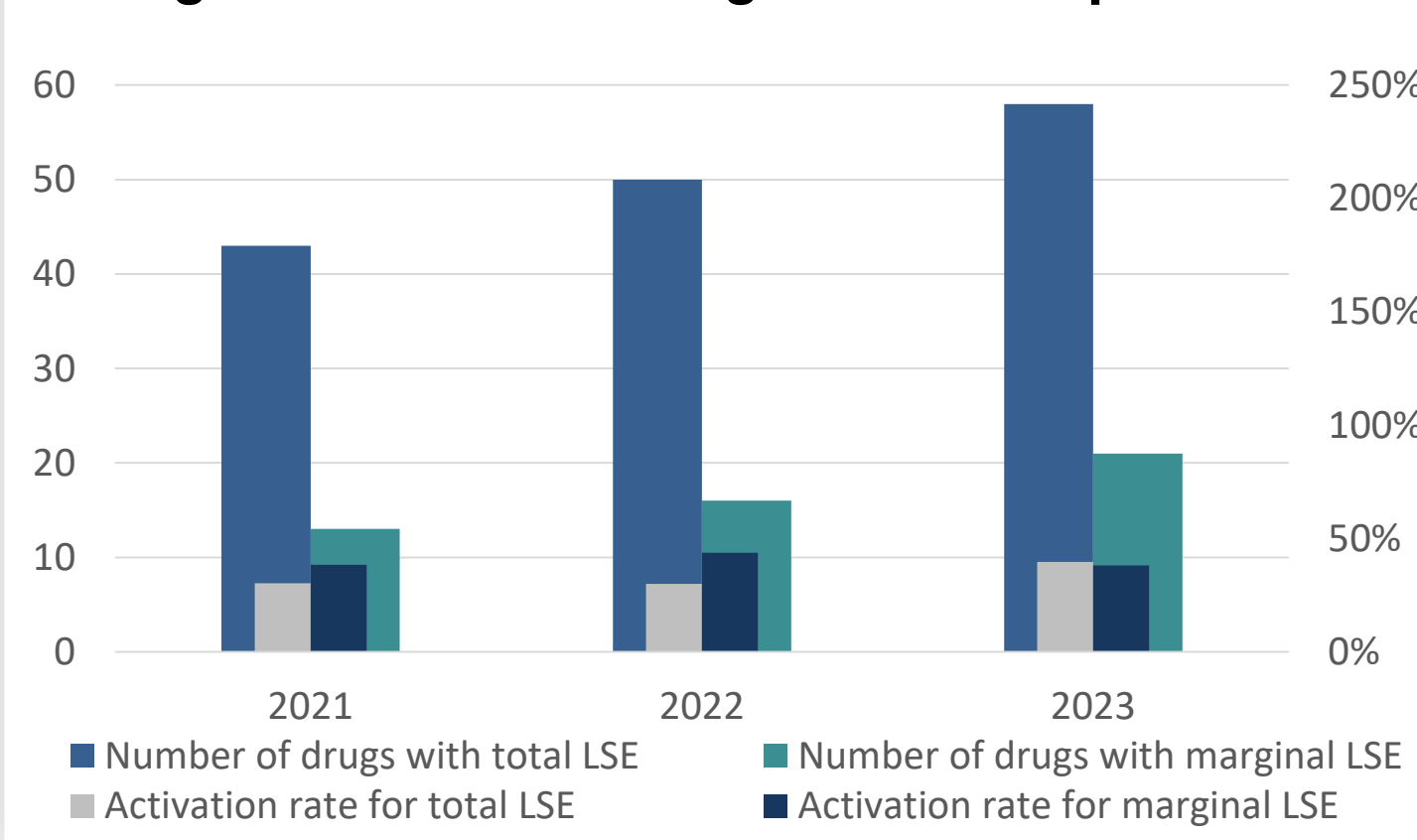
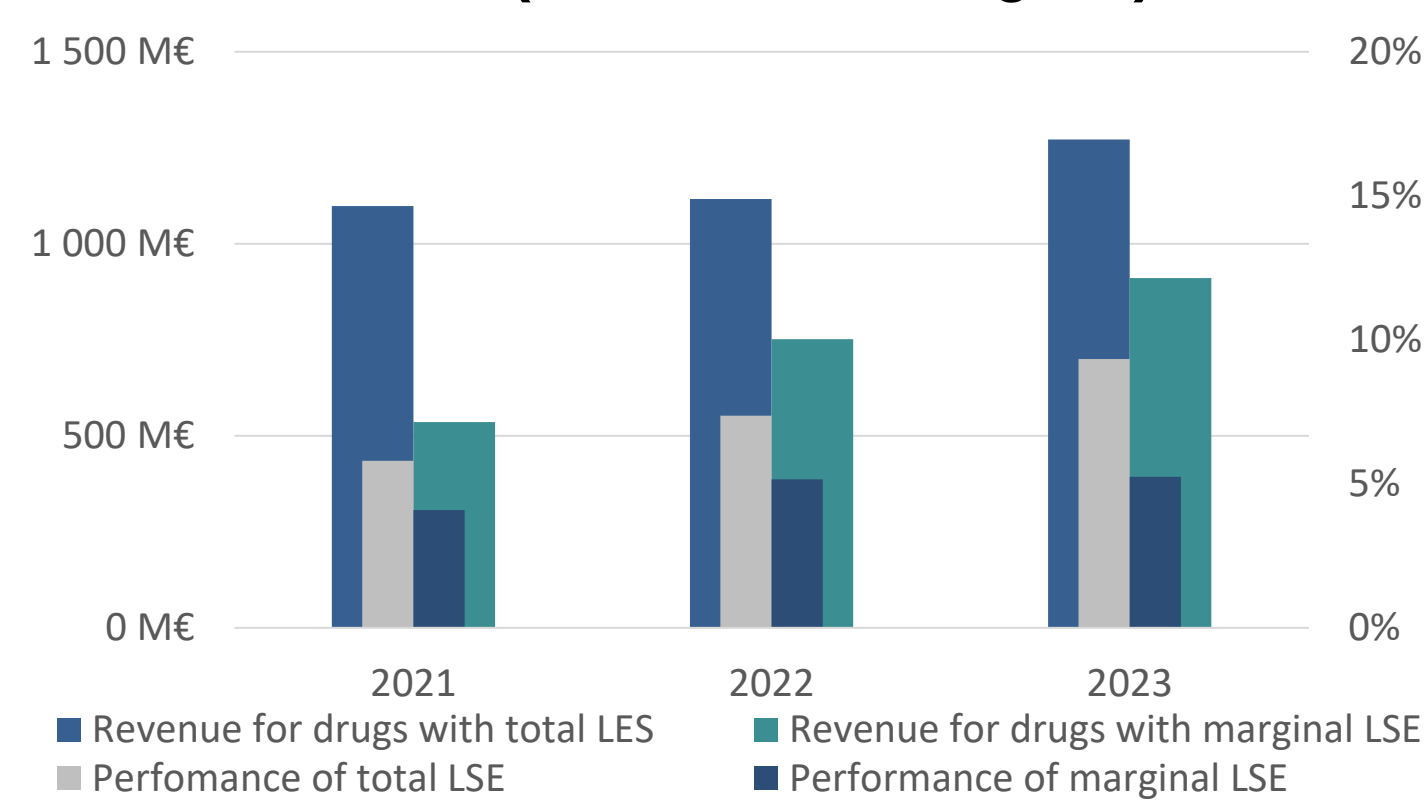


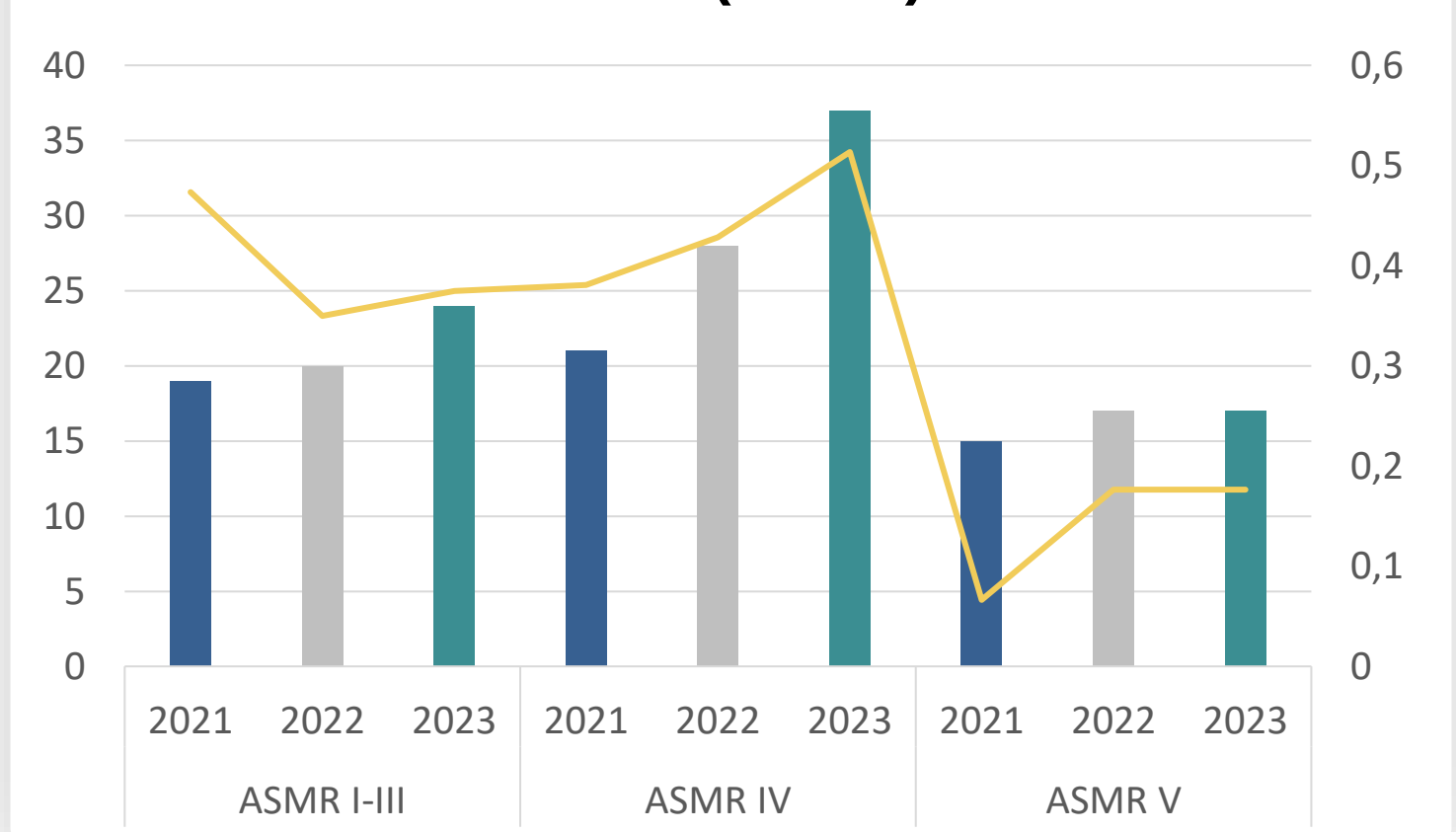
Figure 5. Revenue and remittance by type of LSE (total versus marginal)



Activation rates appear to be comparable for strict and marginal LSE. However, strict LSE offer a slightly higher return (9% versus 5% in 2023), consistent with full repayment above the envelope.

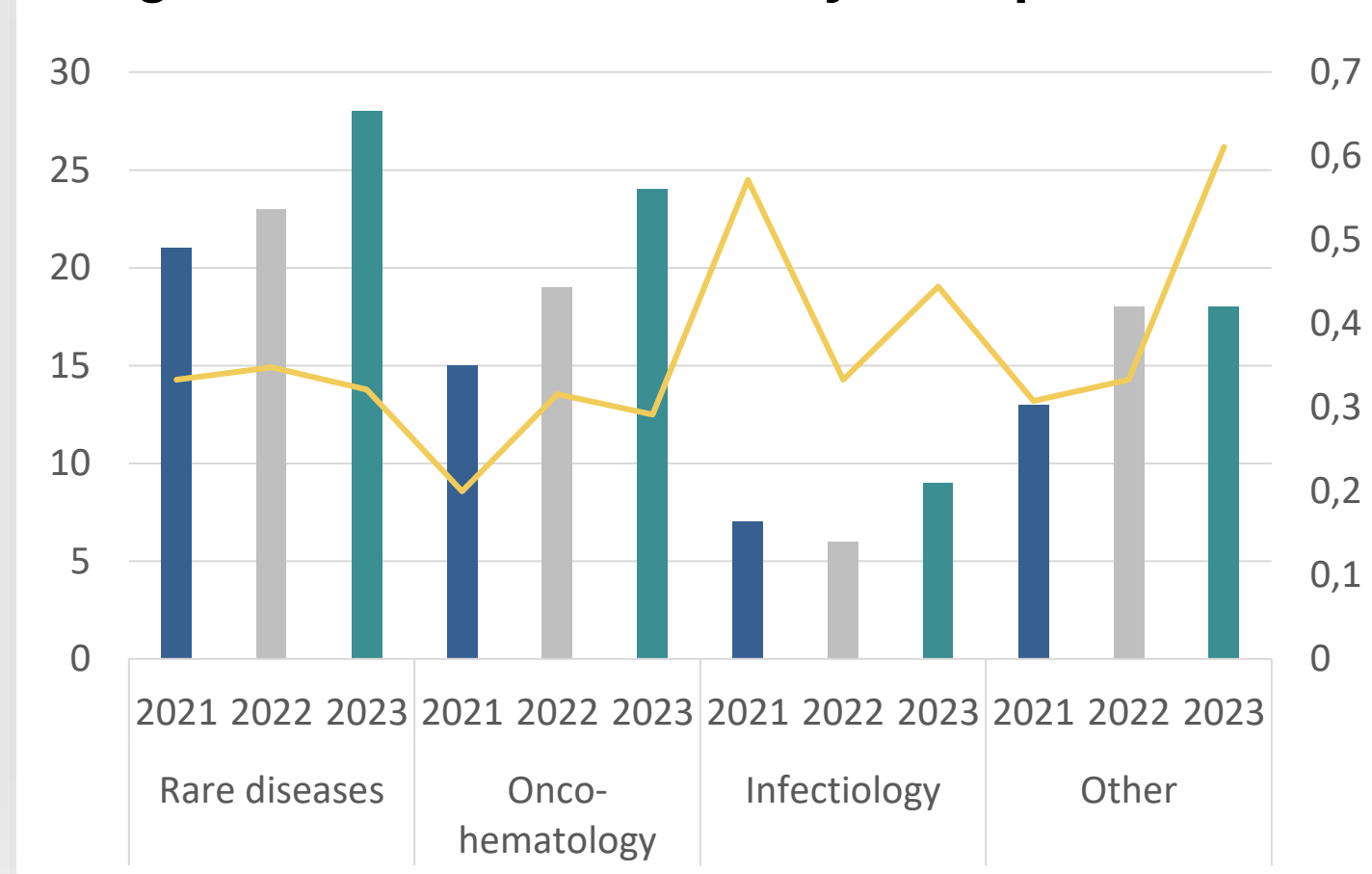
Drugs with no clinical added value (ASMR V) present a lower activation rate. We suppose that LSE are introduced more for securing than regulation.

Figure 9. Activation rate by clinical added value (ASMR)



The activation rate appear to be consistent across therapeutic areas, except for infectiology where LSE seems to be more sensitive to variations of treatment modalities.

Figure 10. Activation rate by therapeutic area



KEY FACTORS INFLUENCING THE ACTIVATION OF LUMP-SUM ENVELOPES

The activation of LSE was investigated as of 2022, assessing whether each drug had been activated at least once during the period from 2014 to 2022. Drugs registered in 2023 were excluded to mitigate bias from the average activation delay typically observed in the second-year post-registration. Although a Cox regression analysis, which accounts for time, was considered, it was excluded due to the introduction of new entrants each year, leading to a substantial amount of censoring. The dependent variable, defined as whether the LSE were activated, is binary, allowing an assessment of each drug's status at the time of observation. A series of explanatory variables were tested using logistic regression to analyze their impact on the likelihood of LSE activation.

Figure 11. Analysis of Odds Ratios for Factors Influencing the Activation of LSE

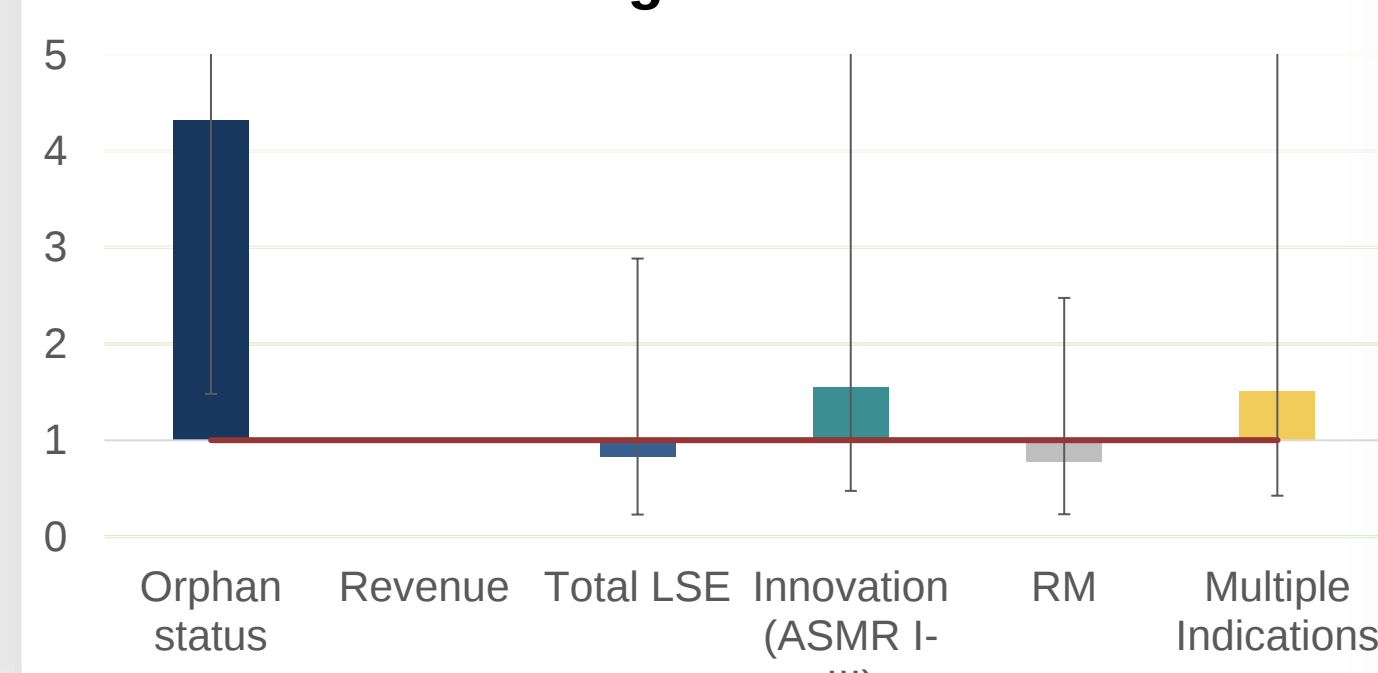
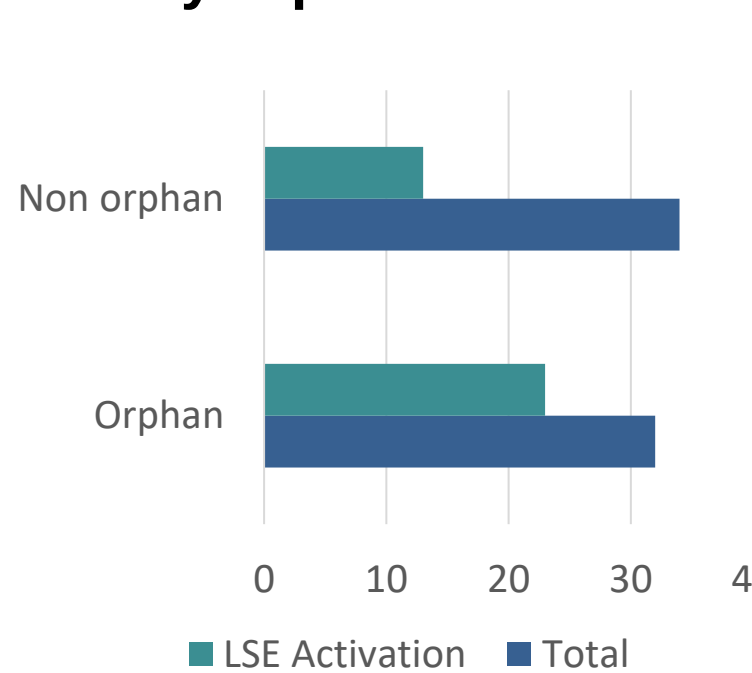


Figure 12. LSE activation by orphan Status



- The orphan status of the product is the only statistically significant variable.
- In a simple regression, the orphan status is significantly associated with an increased probability of activating LSE, with a coefficient of 1.4178 ($p = 0.00728$).
- The probability of activating LSE is 71.9% for orphan drugs, compared to 38.2% for non-orphan drugs.

Table 1. Average activation delay by status

Status	Average Activation Delay (Years)
Orphan	1.2
Non orphan	2.1
Total	1.5

On average, the LSE for orphan drugs is activated in the second year, while for non-orphan drugs, it occurs in the third year after the LSE introduction.

Table 2. Orphans in terms of volume and remittance in total LSE

	2021	2022	2023
Proportion of orphan drugs	46%	48%	53%
Orphan weight in total remittance	88%	69%	75%
Orphan remittance rate	17%	11%	11%
Non-orphan remittance rate	1%	3%	4%

Orphan LSE are activated more frequently than non-orphans, leading to higher remittance, while a trend of increasing remittance for non-orphan LSE is observed.

CONCLUSION

Lump-sum envelopes account for only a minority of clawback agreements, as they do in terms of performance and contribution reviews. The analysis showed that the activation of LSE is depended on the orphan status of the drug. This aligns with the intention to regulate orphan drugs through LSE, where an envelope is assigned to a defined volume. The introduction of LSE for non-orphan drugs is primarily aimed at risk management. The trend toward an increasing yield rate of non-orphan drugs may, beyond these two scenarios, indicate a growing frequency of an uncertain factor that could involve an increase in sales volume related to variations in dosage or treatment duration. This may also reflect an intent to introduce regulatory capping for non-orphan drugs. However, these agreements are tending to be more widely used and accepted by the companies as they provide both security and predictability.