

Introduction and Objective

A recent analysis (ISPOR 2025, Poster HPR92)² introduced the CRA-developed RARE Disease Assessment Review (RADAR) database. RADAR includes all orphan drugs (ODs) that received European Medicines Agency marketing authorization between July 1, 2013, and September 30, 2024. The research, a cross-sectional, static analysis, tried to identify and quantify if and how factors such as G-BA benefit rating, clinical comparator, prevalence, manufacturer (MNF)-set list prices, and different groups of indications (oncology vs non-oncology) impact the outcome of rebate negotiations between manufacturers and the GKV.

With 12 years of available German data, it is possible to performed a longitudinal (dynamic) analysis to assess how the German Medicines Market Reorganization Act (AMNOG) process has impacted over time manufacturers' list-price setting and negotiation of GKV rebates for ODs.

Additionally, we tried to understand how manufacturers develop their list-price strategy for ODs in Germany. Earlier research¹ suggested that US WAC prices might serve as a starting point for OD price strategies in Germany. Our research tries to validate the hypothesis and to quantify its effect.

Methodology

For the evolution of OD list-prices and GKV rebates over time, we used the same 115 ODs as in the static analysis:² We divided all 115 OD launches into two equal, six-year time periods: 2013–2018 and 2019–2024. Within each period we examined the progression of mean annual cost, based on MNF-set list prices and SmPC dosing schemes, and negotiated rebates for the ODs' first-listed indication. We also analyzed if and how G-BA ratings, indication, and prevalence impact negotiated GKV rebates.

For the analyses if and how US WAC impacts German MNF-list price setting and GKV rebates, we screened the 115 ODs for products that:

- were approved by the US Food and Drug Administration (FDA) after July 1, 2013, for the same launch indication as approved by EMA later
- were provided for the same population and had the same formulation and strength as the US product and a comparable pack size
- had a publicly available WAC for their first indication before the appearance of an MNF-set list price for the same OD in Lauer Taxe

In total, 79 of the 115 ODs fulfilled all criteria. Of these, 34 were ODs with oncology indications and 45 were ODs with non-oncology indications.

For the US–Germany list price comparison, we calculated annual treatment cost, using SMPC / FDA dosing regimen and pack-by-pack price comparisons. Lauer Taxe manufacturer list prices were converted into US dollars (USD) using the exchange rate at the date of the product's EMA approval. For the analysis of German list price as percentage of US WAC, the US WAC was set at 100%, and the German list price level was calculated as a percentage of the US WAC denominated in €, using the exchange rate as of each OD's date of EMA marketing authorization.⁴

Increase of negotiated GKV rebates did not match increase of manufacturer-set list prices for ODs in the period 2013-18 vs 2019-2024

Evolution of annual treatment cost* based on manufacturer-set prices 2013-2024

Evolution of GKV rebates as percentage of list price 2013–2024

	Mean annual cost at MNF-set list prices	Mean negotiated GKV rebate
Time Period 2013-2018 (n=61)	€248,785	21%
Time Period 2019-2024 (n=54)	€397,477	24.1%
Increase 2013/18 vs 2019/24 by	60%	15%

The analysis shows that the mean negotiated GKV rebate of 22.5% for all 115 ODs across the 12-year period is the result of increasing price and rebate levels of successive launches

The analysis indicates that mean MNF-set list prices and the mean GKV rebates increased over time, but the increase in the former (60%) was four times larger than in the latter (15%). Consequently, negotiated reimbursed annual treatment costs for ODs increased substantially between the time periods. G-BA benefit ratings, which impact GKV rebate levels, cannot explain the difference, as G-BA rating distribution is similar across both time periods. The answer must be found elsewhere.

Mean price increase for ODs in Germany is driven by higher MNF-set list prices for recently launched oncology ODs

Mean annual OD cost by indication based on mnf-set list prices

Mean GKV negotiated rebate by indication group

Period 1 shows significantly higher price levels for non-oncology vs oncology ODs (>160%; p<.03). In period 2, MNF-set list prices for oncology ODs increased vs period 1 by 190% (p<.04) vs 30% for non-oncology ODs. GKV rebates increased between period 1 and 2 for oncology ODs by 22% vs.12% for non-oncology ODs. Again, no differences were observed for G-BA benefit outcomes or clinical evidence between time periods and indications. Period 2, however, saw the arrival of new therapies in oncology, such as gene therapy (CAR-T), potentially leading to significantly higher MNF-set list price levels.

Lower prevalence of more recent launched oncology ODs might provide some rationale for lower negotiated GKV rebates for these ODs

Evolution of OD prevalence by indication and time period

Period 1 shows similar mean prevalence for oncology ODs (0.21 p.10,000) and non-oncology ODs (0.22 p. 10,000). While in period 2, the mean prevalence slightly increased for new non-oncology ODs (0.22 to 0.26 p. 10,000), prevalence for oncology ODs launched in period 2 decreased significantly compared to the period before 2018, from 0.21 to 0.09 p. 10,000 (p=0.59), which might explain willingness to pay more for recently launched oncology ODs.

Data suggests a relationship between manufacturer-set list prices of ODs in their launch indication in Germany and the previously established US WAC for the same OD

Evolution of German OD list prices relative to US WACs (WAC=100%)

The trend analysis shows the correlation between the €-denominated US WAC and MNF-set German list prices to remain relatively steady over time between 88-90%. This suggests that whatever the list price dynamics are in the US, where all included products launched ahead of Germany, these will spill over to Germany through MNF-set list prices at launch.

Time-period and indication comparison identified behavioral patterns of manufacturers that strengthen the argument of list-price transfer from the US to Germany for ODs*

2013-20182019-20242013-20182019-2024

In period 1, mean WAC for oncology ODs in the US and mean MNF-set list prices in Germany are very close (German mean list price ~94% of US WAC). Period 2 saw an increase of mean US WAC for new oncology ODs of >250% (p<0.005) compared to period 1. Data shows the same increase in MNF-set list prices of >250% (p<0.016) in Germany. The pattern suggests that manufacturers used the US WAC of their oncology ODs to set the list prices in Germany. Mean GKV rebates of new oncology ODs in period 2 were 30%, vs 23% in period 1.

*The analysis was performed with annual treatment cost using MNF-set list prices and FDA/SmPC dosing for the calculation.

Using US WAC as pre negotiation list price in Germany seems to result in higher net prices post negotiation compared to using a lower starting point

German manufacturer-set OD list prices relative to €-denominated US WAC (n=79)

Of all 79 ODs within the US/German analysis, 25% show a German list price within a +/- 10% range of US WAC, half of them are within a +/- 20% range of US WAC. For 29 of the 79 OD, the German list price was <80% of US WAC, while 11 ODs show a German list price >20% above US WAC. For all 79 ODs, the mean German list price was 89% of US WAC, and the mean GKV rebate was 22.7%.

For those 19 products in the figure that were prices by the manufacturer in Germany at a premium of >10% over €-denominated US WAC (with a mean list price at 131% of US WAC), the mean GKV rebate was 24%. The resulting mean reimbursed net price for these 19 products in Germany is 107% of the US WAC.

Conclusions

Main driver for a significant increase in MNF-set list and net-prices of ODs in Germany over time are a) significantly higher list prices set by manufacturers for oncology ODs, and b) a higher GKV willingness to pay for innovative (gene) therapies within oncology, targeting indications with substantially lower prevalence. While G-BA ratings have not changed over time, MNF-set list prices have, often by using earlier established US WAC prices as initial list price in Germany. The data cannot provide any conclusions to what extent this list price import is justified by non-quantifiable product characteristics that might lead to a higher GKV willingness to pay. What the analysis does show is that it seems an appropriate price optimizing strategy for Germany: Those manufacturers who used US WAC as list price in Lauer Taxe or even set the German list price above US WAC, seem to have achieved higher net price levels than those who do not, as increasing GKV rebates do not seem to offset list prices / premiums imported from the US. It also looks like if list-prices in US and Germany are closer than one might have thought - at least for ODs.

References

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4. Impact of US pricing strategies for orphan drugs on price levels in Germany - Part 3: Analysis using German and US data from the RADAR database; 2025, A. Ruppert, Charles River Associate, www.crai.com

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