September 2025

Evolution of manufacturer-set list prices and GKV rebates for orphan drugs

Part 2: Decision analysis using the CRA RADAR database

Background

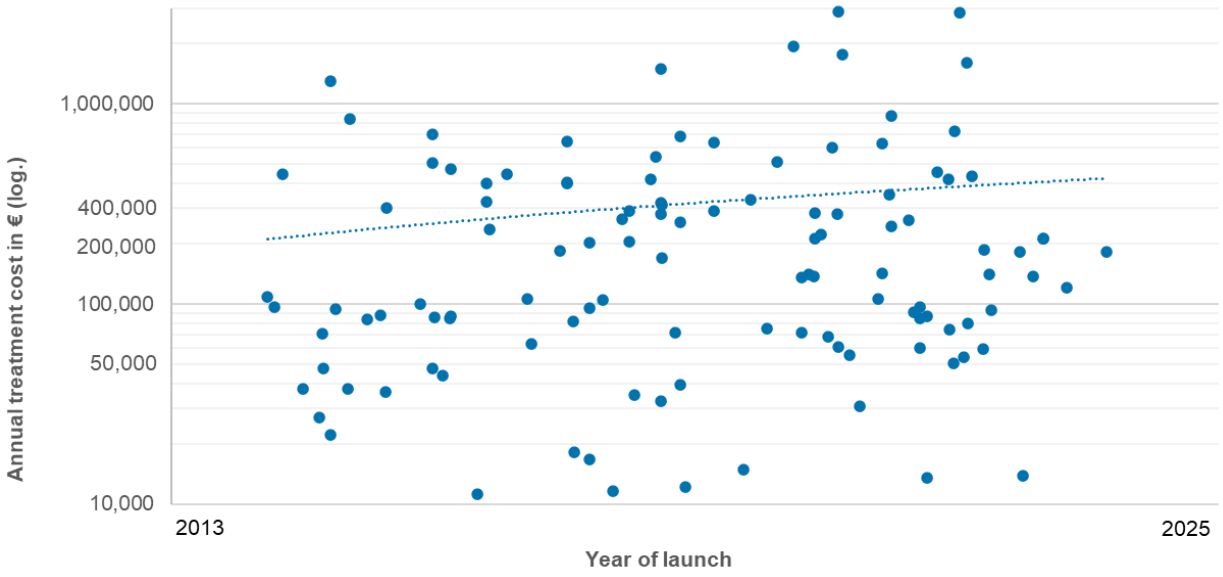
Recently, we published an analysis of German data from the RAre Disease Assessment Review (RADAR) database, developed at Charles River Associates. RADAR includes all orphan drugs (ODs) that received European Medicines Agency marketing authorisation between July 1, 2013, and September 30, 2024. For our analysis, we focused on 115 ODs (1) that were registered by the manufacturer with list prices set freely in the Lauer Taxe pharmaceuticals database, (2) that underwent German Federal Joint Committee (G-BA) benefit assessment, and (3) for which GKV (the statutory health insurance system) negotiations were finalised with rebates and net prices published in Lauer Taxe (for a detailed description, please see Part 1).

Although RADAR includes nearly 12 years of German data, we initially performed a cross-sectional, static analysis. In Part 2 of the research, we performed a longitudinal (dynamic) analysis to assess how the German Medicines Market Reorganisation Act (AMNOG) process has impacted over time manufacturers' price setting and negotiation of GKV rebates for drugs with orphan designation. We undertook this analysis by dividing all OD launches into two equal, six-year time periods: 2013–2018 and 2019–2024. Within each period we examined the progression of mean (SD, or standard deviation) annual cost based on manufacturer-set list prices and negotiated rebates for the ODs' first-listed indicated use in Lauer Taxe.

Evolution of list prices and GKV rebates for orphan drugs in Germany 2013–2024

The dynamic analysis focuses on the same 115 ODs that were included in the static analysis. To accurately compare the rebates and prices of different products, we calculated the annual treatment cost per product using the manufacturer-set unit list prices from Lauer Taxe and applying dosing information from the summaries of product characteristics (SmPC). For weight-based dosing schemes, we used average weight measurements for adults, children and infants.

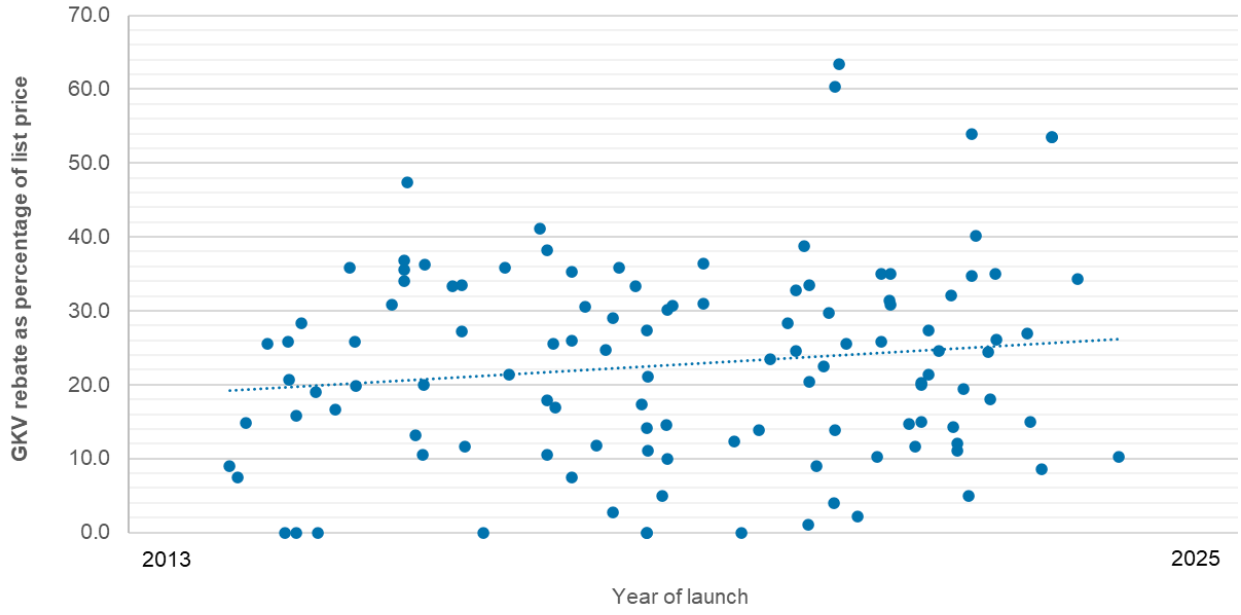
Figure 1: Evolution of annual treatment cost based on manufacturer-set prices for 115 ODs in € (logarithmic scale)



The static analysis for all 115 products showed a mean annual treatment cost of €319,899 (SD 489,130) based on manufacturer-set list prices at launch. The logarithmic trend line in the dynamic analysis shown in Figure 1 suggests an increase over time (see Table 1 for more details).

The two-step AMNOG process, using a health technology assessment (HTA) by G-BA to define added benefit ratings, followed by rebate negotiations with GKV, aims to adjust manufacturer-set prices/treatment costs based on societal willingness to pay for the added value ODs provide. Figure 2, below, shows how the negotiated GKV rebate levels changed during the observation period.

Figure 2: Evolution of GKV rebates as percentage of list price for 115 ODs, 2013–2024



The dynamic analysis indicates that the mean negotiated GKV rebate of 22.5% for all 115 ODs over the entire 12-year period is the result of seemingly increasing rebate levels over time.

As the analysis shows, both manufacturer-set list prices and negotiated rebates seem to increase over the observation period. However, the manufacturer-set list prices increased much more than the rebates did. The table below shows the mean change of manufacturer-set prices and GKV rebates, comparing the periods 2013–2018 and 2019–2024.

Table 1: Evolution of manufacturer-set prices and GKV rebates for ODs, 2013–2024

	Mean annual treatment cost at manufacturer-set prices	Mean negotiated GKV rebate
2013–2018 (n=60)	€248,785 (SD 294,679)	21% (SD 12.29)
2019–2024 (n=55)	€397,477 (SD 631,233)	24.1% (SD 14.1)
Increase 2013–2018 vs 2019–2024	**60%**	**15%**

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

Evolution of manufacturer-set OD prices in Germany, 2013–2024, by indication group

In an earlier static analysis of factors that affected GKV rebate and list price levels for ODs,[1] indications of ODs seemed to be relevant. The analysis indicated that mean manufacturer-set price levels for non-oncology products were higher than for products with oncology indications, although there was great variability.

For the dynamic analysis, we similarly divided the products into two groups: ODs for non-oncology indications (n=81) and ODs for oncology indications (n=34). The increase in mean annual treatment cost during the study period is shown below for non-oncology ODs in Figure 3 and for oncology ODs in Figure 4, all based on manufacturer-set list prices.

1 Factors impacting GKV rebates for Orphan Drugs in Germany – Part 1 of a deep dive decision analysis using the CRA RADAR database; A. Ruppert; Charles River Associates; www.crai.com.

Figure 3: Evolution of annual treatment cost based on manufacturer-set prices for 81 non-oncology ODs, 2013–2024, in € (logarithmic scale)

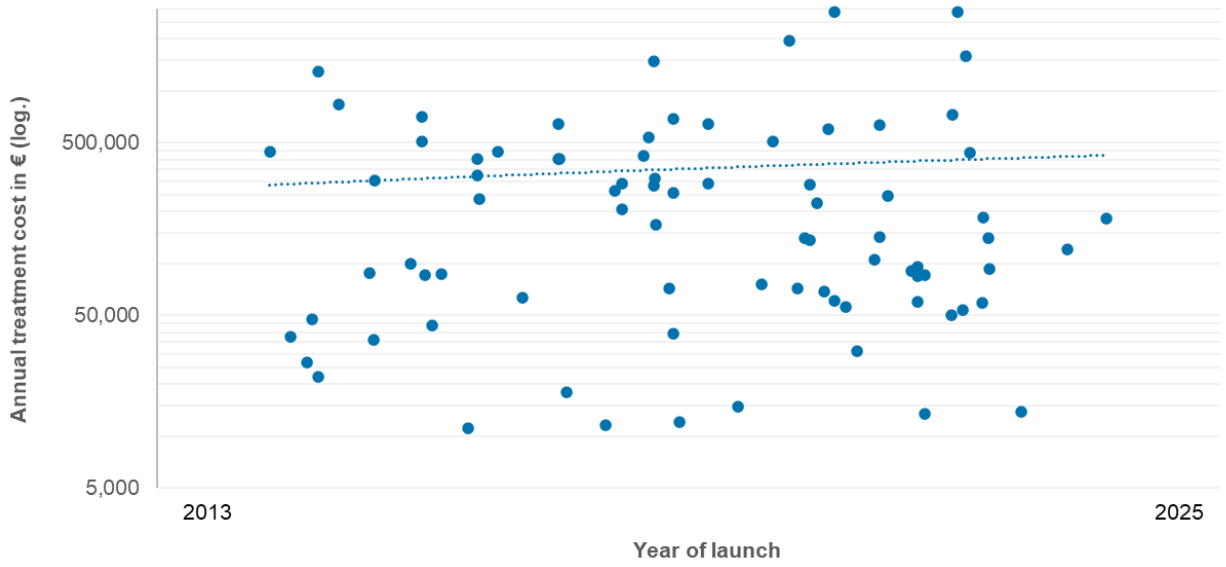


Figure 4: Evolution of annual treatment cost based on manufacturer-set prices for 34 oncology ODs, 2013–2024, in € (logarithmic scale)

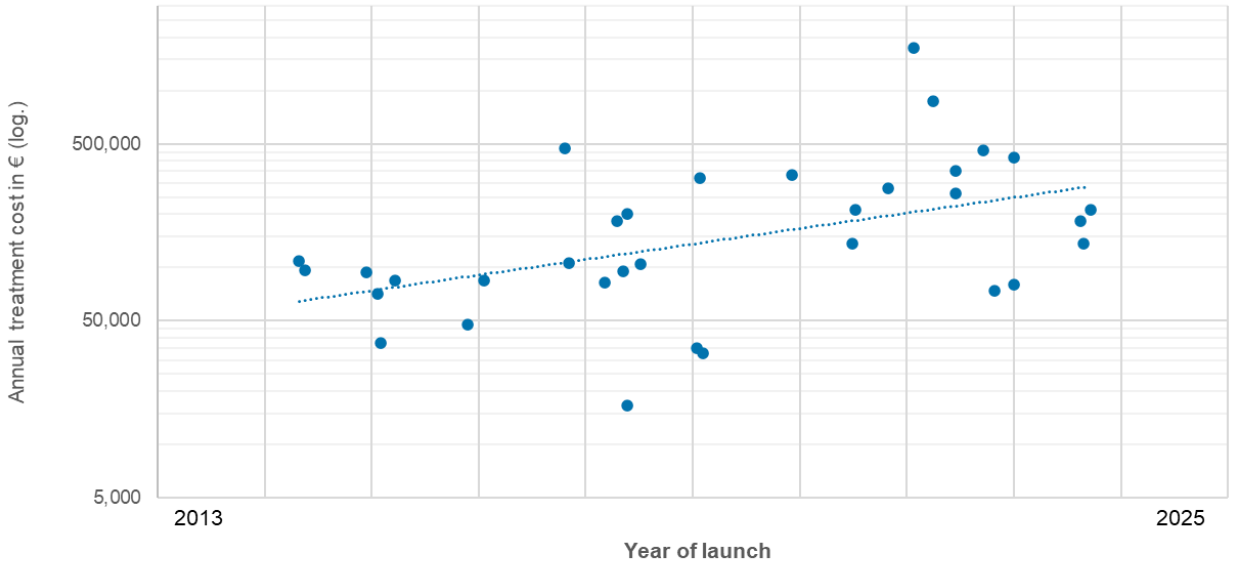


Figure 3 indicates that manufacturers historically have priced non-oncology ODs higher than oncology ODs, as shown in Figure 4. While in Figure 3 there is no consistent trend of increasing prices observable for non-oncology ODs, the trend of increasing prices for oncology ODs in Figure 4 is significant ($p<.02$), to the point where the prices for both indication groups are nearly equal at the end of the observed period.

Table 2: Mean annual cost of ODs by indication group at manufacturer-set list prices

Non-Oncology Orphan Drugs	
2013–2018 (n=41)	€308,699 (SD 333,079)
2019–2024 (n=40)	€402,568 (SD 697,035)
Increase 2013–2018 vs 2019–2024	**30%**
Oncology Orphan Drugs	
2013–2018 (n=16)	€117,683 (SD 105,184)
2019–2024 (n=18)	€341,447 (SD 404,471)
Increase 2013–2018 vs 2019–2024	**190%**

Table 3 uses the data from Figures 3 and 4 by dividing the observed time and events into two time periods. In the earlier observation period, 2013–2018, we see significantly higher price levels ($p<.03$) for non-oncology ODs compared to oncology ODs, with a difference of over 160%. This difference between oncology OD and non-oncology OD prices has decreased to less than 20% for the period 2019–2024. The reason for the converging price levels is the statistically significant 190% increase in prices for oncology ODs between the 2013–2018 and 2019–2024 periods ($p<.04$).

The 190% increase in the mean annual treatment cost for oncology ODs over the 12-year observation period raises the question of how German oncology OD manufacturers set their list prices. Do they adjust their prices based on non-oncology OD manufacturers' price levels in the Lauer Taxe? Or do they increase the list prices over time in anticipation of and/or as pre-compensation for anticipated high GKV rebates?

Evolution of GKV rebates 2013–2024 by indication group

How did the GKV react to the increasing manufacturer-set list prices of ODs, and can we see similar differences in the two indication groups? Table 3 provides a possible answer.

Table 3: Mean GKV rebates negotiated for ODs by indication group and time period

Non-Oncology Orphan Drugs	
2013–2018 (n=41)	20.4% (SD 12.5)
2019–2024 (n=40)	22.9% (SD 12.8)
Increase in % 2013–2018 vs 2019–2024	**12%**
Oncology Orphan Drugs	
2013–2018 (n=16)	22.4% (SD 12)
2019–2024 (n=18)	27.3% (SD 17.3)
Increase in % 2013–2018 vs 2019–2024	**22%**

Although the negotiated GKV rebates increase over time in both indication groups, the increase in rebate levels for the oncology OD group does not mirror the significant increase in manufacturer-set price levels. Because the increase in rebates does not offset the greater increase in manufacturer-set prices for newly launched ODs, the eventual result is a substantial increase in negotiated reimbursed (net) prices, more for oncology than for non-oncology ODs.

Our static analysis in Part 1 of this series might suggest a relationship between negotiated GKV rebates and G-BA benefit ratings. An examination of the benefit ratings within each of the two indication groups and time periods should provide answers regarding to what extent G-BA ratings also increased over time. However, the data reveal no relevant differences between the benefit ratings in the different periods that could explain such a significant price increase over time.

Evolution of prevalence of newly launched ODs, 2013–2024, by indication group

Prevalence was identified as a key impact factor in the Part 1 static analysis, with statistically significant differences in mean rebates between the upper and lower halves of the distribution. Table 4 compares prevalence by indication group and time period. The prevalence of oncology indications, for which ODs were launched, was substantially lower in the later period compared to the earlier period and compared to the non-oncology ODs at any point. The prevalence difference between the earlier and later period for oncology ODs is close to statistical significance (p=.059).

Table 4: Comparison of OD indication prevalence by indication group and time period

Non-Oncology Orphan Drugs	
2013–2018 (n=41)	0.22 per 10,000 patients (SD 0.47)
2019–2024 (n=40)	0.26 per 10,000 patients (SD 0.39)
Oncology Orphan Drugs	
2013–2018 (n=16)	0.21 per 10,000 patients (SD 0.25)
2019–2024 (n=18)	0.09 per 10,000 patients (SD 0.07)

The considerably lower prevalence of oncology ODs in the later period might explain why the GKV is willing to pay significantly higher net prices for newly launched oncology ODs.

Summary

Through the dynamic analysis of different time periods, and of the overall 12-year period covered by RADAR, we have gleaned greater insight into price setting for ODs in Germany overall and for the analysed indication groups, as well as into the evolution of GKV rebates.

The analysis suggests that average manufacturer-set list prices for new ODs in Germany seem to have increased over time. The main driver for the price evolution is a significant increase in list prices

for oncology ODs over time. While average GKV rebates seem to have increased as well, and for oncology ODs more than for non-oncology ODs, the increase in GKV rebates does not offset the increase in manufacturer-set list prices. The results indicate increased net prices for ODs for GKV.

The willingness to pay higher prices for oncology ODs might in part be justified by the substantially lower prevalence of diseases treated by more recently launched oncology ODs. However, the data do not explain why list prices and net prices of non-oncology ODs seem to have increased as well. G-BA benefit ratings, clinical evidence and prevalence of non-oncology ODs have not changed over time.

To understand the rationale for increased oncology OD prices over time, one might need to investigate more specifically the OD manufacturers' pricing and negotiation strategies and to interview GKV negotiators about their motivations in accepting the continually increasing reimbursement price levels for ODs seen in recent years.

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