



October 2025

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

Background

Part 2 of our analysis of German data from the RAre Disease Assessment Review (RADAR) database revealed a significant increase in manufacturer-set list prices for new orphan drugs (ODs) over time.¹ While GKV rebates seemed to have increased as well, their increase was less pronounced than the increases in list prices, resulting in rising reimbursed annual treatment costs. However, the earlier analyses in Parts 1² and 2 of our series did not provide a rationale for increasing list price levels. One might argue that list price increases reflect increasing product value or that manufacturers are increasing list prices to offset what they expect will be higher rebates negotiated with the statutory health insurance system (GKV).

To understand the evolution of list prices for ODs in Germany, as presented in Part 2 of the research, we must first understand how manufacturers anchor their list prices and enter into GKV negotiations. In 2021, I published a CRA white paper analysis that looked at the possibility of achieving prices equal or close to the US wholesale acquisition cost (WAC) in five European markets. At the time, we identified 16 products with similar list prices in the US and Germany, predominantly indicated for rare diseases and different oncology indications. The results of the research suggested that several manufacturers use the earlier established US WAC to set list prices for their products in Germany, which they then try to defend in GKV rebate negotiations.

1 ¹ Evolution of manufacturer-set list prices and GKV rebates for orphan drugs – Part 2 of an analysis for Germany using the RADAR database; A. Ruppert; Charles River Associates; www.crai.com

2 ² 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

If that's true—if manufacturers use the earlier established US WAC to set the German list price as the starting point for GKV negotiations—then manufacturer-set prices in Germany are based on value perceptions in the US and not in Germany. To fully understand how much that matters for orphan drugs, this article tries to answer the following questions:

- How close are the €-denominated US WACs and manufacturer-set list prices in Germany's Lauer Taxe for the same OD, indication, formulation and pack size?
- Do manufacturer-set list prices for ODs in Germany follow the same trajectory as the US WACs over time, both overall and for different drug indication groups?

In case the data confirm that there is a link between manufacturer-set US WAC and German list prices, we also analyse the impact of GKV negotiations on achieved net prices.

RADAR database and methodology

The RADAR database includes orphan drugs that received European Medicines Agency (EMA) marketing authorisation between July 1, 2013, and September 30, 2024. RADAR is a multi-country database, including not only European data but also data from the US and other ex-EU markets.

For the analysis of price correlation between the US and Germany, we screened the database for products that:

- Are registered with a manufacturer-set list price for their first-listed indicated use in Lauer Taxe
- Received a benefit assessment by G-BA (Gemeinsame Bundesausschuss)
- Finished the GKV rebate negotiations, resulting in a GKV rebate and negotiated reimbursement price published in Lauer Taxe before September 30, 2024

One hundred fifteen ODs met the criteria for the analysis; these were further screened 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
- 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 (note: no US net prices were analysed) before the appearance of a list price for the same OD in Lauer Taxe

In total, 79 of the 115 ODs fulfilled all of the above 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 used annual treatment cost calculations and pack-by-pack price comparisons. Annual treatment cost for the US was calculated using WAC and the FDA-approved prescribing information. German annual treatment cost was calculated using manufacturer-set list prices in combination with prescribing information from the EMA summaries of product characteristics (SmPC). Lauer Taxe manufacturer list prices were converted into US dollars (USD) using the exchange rate at the date of the product's EMA marketing authorisation. To compare US and German price levels, the US WAC was set at 100%, and the German price level was calculated

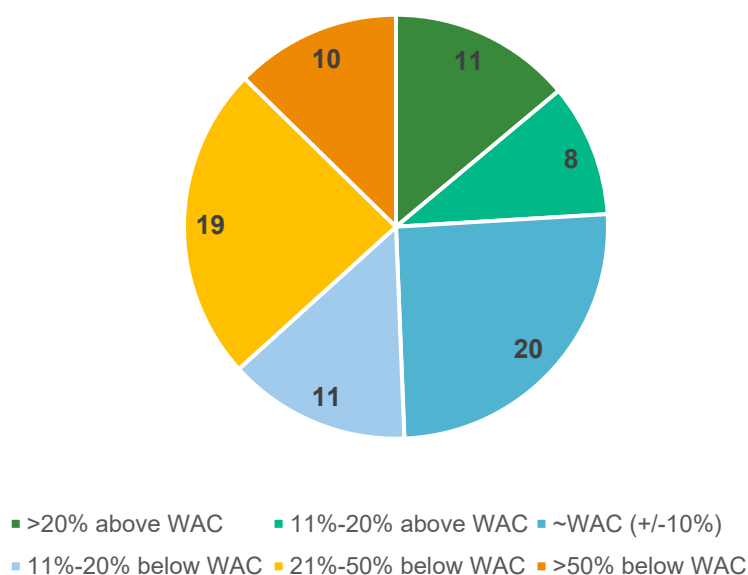
as a percentage of the US WAC denominated in €, using the exchange rate as of each OD's date of EMA marketing authorisation.

To describe the progression of list prices, we divided the launches into two equal, six-year time periods: 2013–2018 and 2019–2024. Within each period we examined the progression of mean (SD) annual costs based on manufacturer-set list prices. For Germany, we also examined the negotiated rebates for each OD's launch indication in Lauer Taxe.

How close are US WACs and manufacturer-set list prices in Germany's Lauer Taxe for ODs?

As a first step, we compared the US WAC and German list price levels of all 79 products.

Figure1: German manufacturer-set OD list prices relative to WAC (n=79)



To account for small inconsistencies when adjusting for exchange rates and pack sizes, we divided the 79 products in Figure 1 into six price clusters relative to WAC, from more than 50% below WAC to greater than 20% above WAC.

Across all 79 products, the mean manufacturer-set list price in Lauer Taxe is 89% (SD 34) of the US WAC (€-denominated). Figure 1 provides further details: a quarter of the products (20) are within a 10% range of the US WAC, and 50% of the products (39) are within 20% of the US WAC. For 14% of products (11), the manufacturer set a premium price of 20% or more above the €-denominated US WAC.

How does the GKV react to these prices in rebate negotiations?

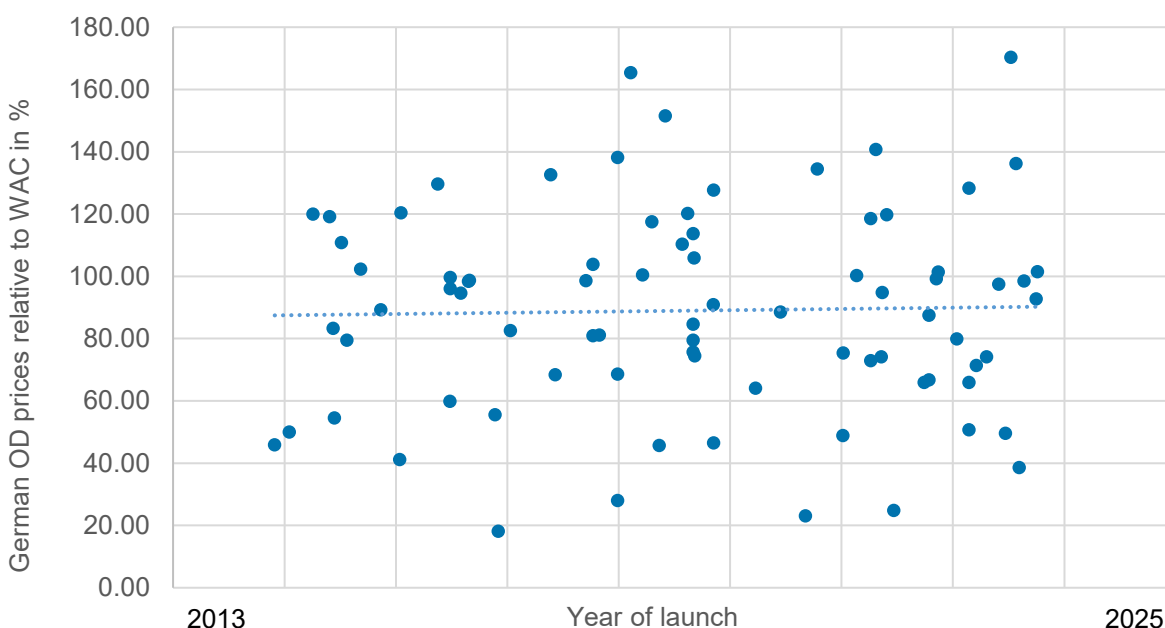
For all 79 ODs, the mean GKV rebate is 22.7% (SD 12), and the mean negotiated GKV net price for ODs is 69% of the US WAC. However, for those products in Figure 1 that are priced at launch in

Lauer Tax at a premium of 10% or more above the €-denominated US WAC (mean list price at 131% of WAC), the mean GKV rebate is 24% (SD 12). The resulting mean reimbursed net price for these products in Germany is 107% (SD 27) of the US WAC, which results in a mean negotiated GKV net price for these products that is slightly above the US WAC (all €-denominated).

How does the relationship of launch list prices in Germany and US develop over time?

To answer this question, we must analyse the launch list prices for the 79 ODs over time.

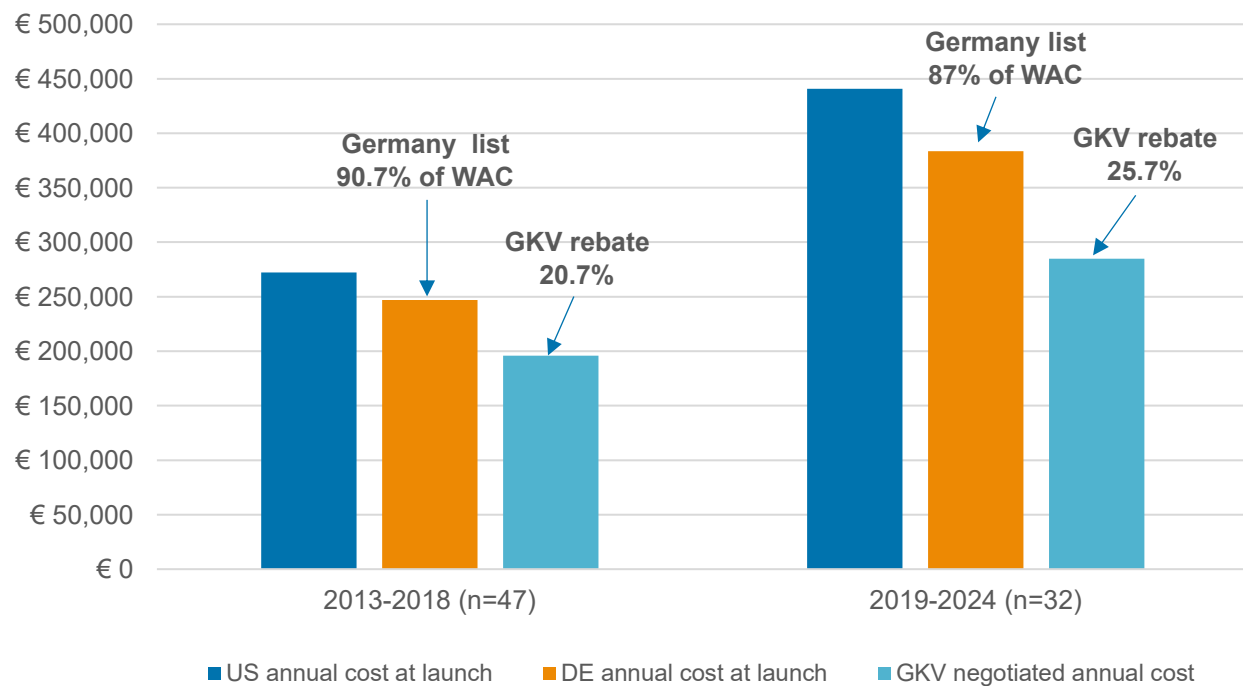
Figure 2: Evolution of German OD list prices relative to US WACs (WAC=100%)



The trend analysis shows that the correlation between the €-denominated US WAC and manufacturer-set German list prices remains relatively steady over time. 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 the manufacturer-set list prices at launch.

In Figure 3, we compare changes over time in manufacturer-set list prices at launch in the US and Germany by dividing the data into two time periods: 2013–2018 and 2019–2024. To accurately compare the rebates and prices of different products, we calculated the annual treatment cost per product based on manufacturer set list prices and dosing information as described above. US WAC dollars were converted into € using the exchange rate at the date of each product's EMA marketing authorisation.

Figure 3: Evolution of pre- and post-negotiation cost levels in Germany relative to €-denominated WAC, 2013–2018 vs 2019–2024



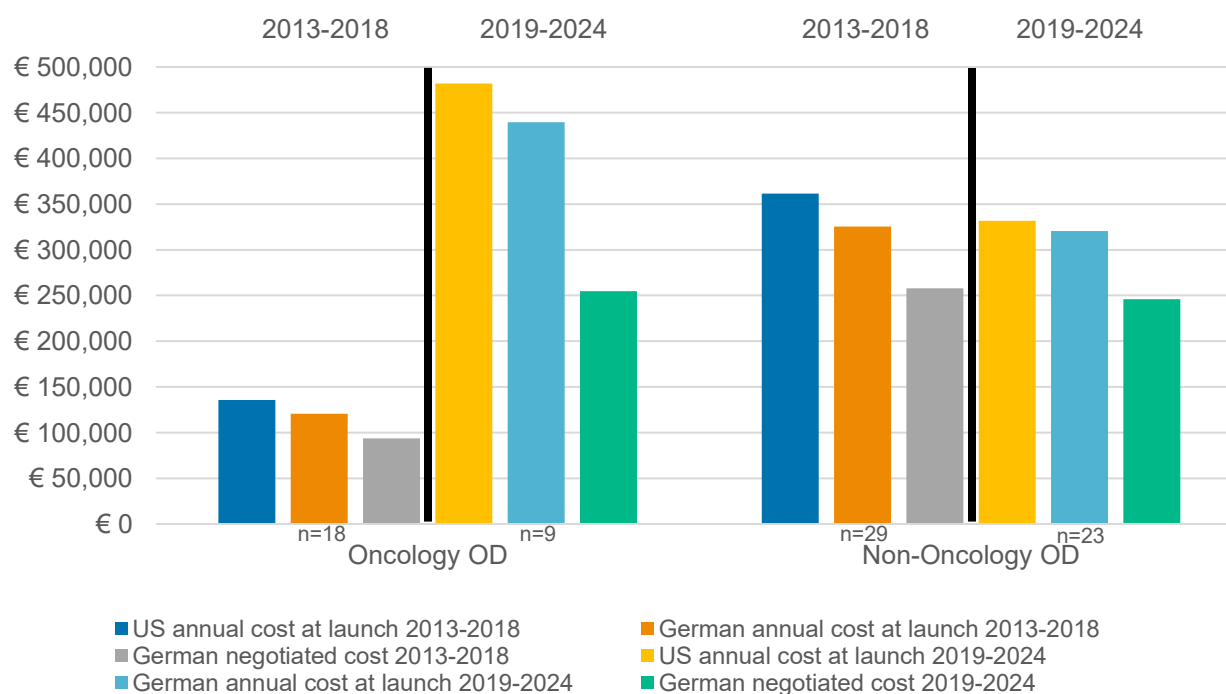
The analysis in Figure 3 suggests that the average €-denominated US WAC increased for newly launched ODs between the two time periods. Manufacturer-set list prices at launch in Germany's Lauer Tax seem to follow a similar pattern. In the period 2013–2018, the mean manufacturer-set prices in Lauer Tax were 91% of €-denominated US WAC; in 2019–2024, these prices slightly decreased, to 87%. Still, the increase in manufacturer-set list prices for ODs in Germany looks similar between the two time periods.

One can argue that list prices in Germany—as in the US—are only a starting point for negotiations over reimbursement prices in the GKV system. And indeed, Part 2 of our series on RADAR analysis findings indicated that negotiated GKV rebates seem to increase over time in parallel with increasing list price levels. However, the rebates have not increased in proportion to prices; the average list price increase seems more pronounced than the corresponding average GKV rebate increase in the same period, suggesting a substantial increase of reimbursed GKV net prices between these two periods.

How are the overall dynamics reflected in different OD indication groups?

In Part 1 of our series on RADAR analyses, we divided the products into two groups—ODs for oncology indications and ODs for non-oncology indications—to understand any indication-specific impacts on the overall result. Of the 79 ODs in this analysis, 52 were for non-oncology indications and 27 were for oncology indications. As previously, we examined the two indication groups by time period: 2013–2018 and 2019–2024. Figure 4 shows the number of ODs in each analysis segment, the €-denominated US WAC and the German list price-based mean annual cost, as well as mean annual costs in Germany after GKV rebate negotiations.

Figure 4: Evolution of mean €-denominated WAC in the US and list and net prices in Germany for oncology and non-oncology ODs



For the period 2013–2018, the mean annual cost of oncology ODs based on €-denominated US WAC and the mean annual cost based on manufacturer-set list prices for Germany are very close at 94%. The period 2019–2024 saw a significant increase in mean €-denominated WAC for newly launched oncology ODs in the US of more than 250% ($p<0.005$) compared with the mean price level in 2013–2018. A similar significant price increase of more than 250% ($p<0.016$) between the periods 2013–2018 and 2019–2024 appeared in Germany when manufacturers listed these nine oncology ODs in Lauer Taxe. The pattern suggests that manufacturers may have used their US list prices for oncology ODs to set their pre-negotiation list prices in Germany.

While GKV rebates for these nine products were 30%, on average, compared with 23% in the earlier period, mean net prices for the nine oncology ODs launched in 2019–2024 are significantly higher than for the 18 oncology ODs launched in 2013–2018 ($p<0.004$).

For non-oncology ODs in Germany, the average manufacturer-set list prices as percentages of €-denominated US WAC in both time periods are relatively close: 88% of €-denominated US WAC for 2013–2018 and 90% for 2019–2024. A small mean decrease in €-denominated WAC from the earlier to the later period in the US can also be observed in German manufacturer-set list prices for non-oncology ODs, suggesting that several manufacturers may have used their US list price strategy to set the pre-negotiation list price in Germany.

With the average GKV rebate increasing for non-oncology ODs from 19% in 2013–2018 to 24% in 2019–2024, the GKV seem to have achieved a small mean net price reduction for more recently launched non-oncology ODs.

Summary

The analysis, especially the sub-analyses of indication groups with different list price patterns over time, suggests a correlation between manufacturer-set prices in the US and in Germany. It seems that many OD manufacturers may have used the US WAC as a starting point for GKV negotiations since the implementation of AMNOG (German Medicines Market Reorganisation Act). Our analysis also suggests that for those ODs with a list price of 10% or more above the €-denominated US WAC, the mean list price premiums translated into mean net price premiums over €-denominated US WAC. It seems, therefore, advisable for manufacturers to use €-denominated US WAC when setting the initial list price in Germany, as it potentially ensures higher net prices after GKV negotiations.

GKV negotiators seem to have reacted to increasing or continued high manufacturer-set list prices by negotiating higher rebates, especially for oncology ODs.

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