vfa. Die forschenden Pharma-Unternehmen
Research-Based Pharmaceutical Companies

Statement

Evaluation of the Impact of the SHI Financial Stabilization Act on Patient Access to Medicines and on Germany as a Business Location

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Executive Summary

Starting point

Germany's new legislation to stabilize statutory health insurance funding (GKV-FinStG) introduced extensive changes to the existing AMNOG (Pharmaceutical Market Reorganization Act) assessment and pricing system. The law represents a watershed moment for the German pharmaceutical industry from the perspective of globally operating companies. Given the short evaluation period of only six months, there is a risk of underestimating the implications of the legislative interventions. It is therefore all the more important for political decision-makers to take notice of the first signs of unintended harmful consequences. vfa bases its assessment on various primary data sources, secondary data analyses, and past experience to provide a broader initial assessment of the impact of the new legislation.

Results

The first negative impacts of the new legislation on patient care and Germany's innovative research and production capabilities are showing after just a few months.

- Launches of innovative medicines in Germany have been seriously delayed or canceled until further notice. Some innovative drugs are not being approved in Europe (for a new indication) or have been withdrawn from the market after the G-BA (Federal Joint Committee) decision. A vfa member survey indicates that 30 drugs/approvals could potentially be affected in this way over the next two years – that's a very high risk ratio. Four innovative drugs are currently not available for patient care in Germany due to the new legal requirements.

- The planning horizon for corporate decisions on investments in research and development or expanded production capacities is long-term. Many companies have adjusted their longer-term plans for investment, R&D and new job creation. The legislation seems likely to cost around 5000 highly skilled jobs in Germany.

It is alarming that harmful consequences for the pharmaceutical industry – more specifically, for patient access to pharmaceuticals – are already showing within this very short evaluation period. The full effects will become manifest in the coming years unless corrective action is taken now.

Need for action

- Strengthen negotiations in the AMNOG process — abolish the anti-innovation "guard rails" of the GKV-FinStG and the combination discount
- Refine and evolve AMNOG for novel therapeutic approaches and the new European health technology assessment process
- Ensure reliable framework conditions to support Germany and Europe as hubs of innovative research and production

Preliminary remarks

Evaluation process

The statutory evaluation mandate (section 130b(11) SGB V [German Social Code, Book 5) on the effects of the GKV-FinStG is laudable in principle, but the time period provided is clearly too short for effective legislative impact assessment. This is evident from the fact that since the law came into effect in November 2022, not a single new drug has completed the AMNOG process in its entirety, as the section 35a SGB V health technology assessment and subsequent reimbursement negotiation process takes a minimum of 12 months. Moreover, companies have a significantly longer planning horizon for market launch, staffing and investment decisions than the one-year impact assessment period specified by the legislature.

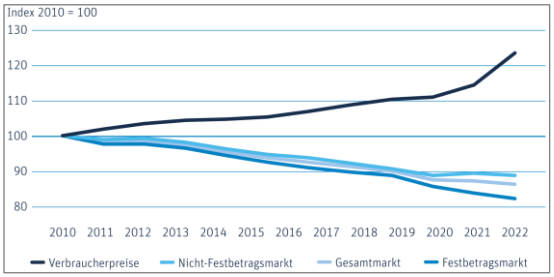
Another point of criticism is the fact that the call for the industry association's statement was issued as early as August 2023, leaving just six months to collect data for the evaluation and essentially further curtailing the evaluation period. It is therefore all the more concerning that adverse trends are already identifiable. The negative impact is likely to increase the longer the measures remain in effect. The statutory evaluation mandate should therefore be extended.

The vfa would also like to see more transparency regarding the evaluation process, including early involvement of the Federal Ministry of Economic Affairs and Climate Protection. Right at the start of the year, the vfa suggested in a letter to the Ministry of Health that the evaluation process should be accompanied by external scientific support, but received no reply. A scientific study by an independent body on the impact of GKV-FinStG both on patient access to medicines and on Germany and Europe's status as hubs of pharmaceutical innovation and production is desperately needed. Consulting the industry associations alone is not sufficient.

Starting point

The aim of the GKV-FinStG was to stabilize the financial situation of the statutory health insurance funds in the short term. However, structural reforms are needed to ensure sustainable funding. The cost-cutting measures on the expenditure side disproportionately affect the pharmaceutical sector. There was no viable justification for this. Contrary to widespread public perception, pharmaceutical price trends – unlike consumer prices – have been declining overall since 2011 and cannot be the cause of the SHI deficit.

Figure 1: Pharmaceutical price trends since 2010



Source: vfa based on WIdO (SHI drug price index), destatis

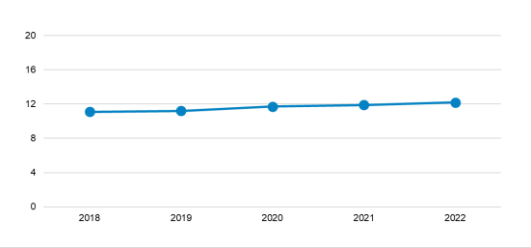
At the same time, the cost pressure on companies has recently increased disproportionately. Unlike other industries, the pharmaceutical industry is unable to pass on upstream price hikes (energy, raw materials) to the end consumer.[1]

Pharmaceutical expenditure as a proportion of the SHI spend was 12% last year, excluding distribution costs and value-added tax.[2] A similar trend has applied over the past number of years.[3]

[1] see figure 7 in MacroScope Pharma Economic Policy Brief 07/2023: Energy prices down: Inflationary wave gradually subsiding, available online.
[2] IGES based on BMG 2022 (KV45), ABDA

[3] See also Bundesrat(Federal Council of Germany) Opinion 366/1/22 (p. 32): "The Bundesrat notes that pharmaceutical costs as a percentage of total statutory health insurance costs

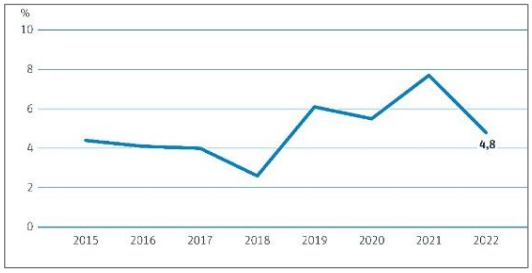
Figure 2: Percentage share of drugs in SHI expenditure 2018-2022



Source: vfa based on IGES and BMG 2022 (KJ1, KV45), ABDA.

Moreover, the SHI pharmaceutical market returned to normal in 2022 after the Covid-related special effects, and the growth rate is back to the 2020 level of 4.8% according to final data.[4]

Figure 3: Growth rate SHI pharmaceutical market



Source: vfa based on BMG (KJ1).

To sum up: there is no evidence of the alleged rapid increase in spending on pharmaceuticals which was used to justify the cost-cutting measures to the detriment of the pharmaceutical industry.

Lawmakers nevertheless constructed a rigid, contradictory set of requirements for reimbursement negotiations that systematically devalue the benefit assessment decision of the G-BA and undermine the principle of utility-based pricing through negotiations. Moreover, across-the-board price reductions were also imposed, including for all patent-protected drugs used in combination, regardless of price level. This also runs contrary to the established AMNOG pricing system and disproportionately burdens pharmaceutical manufacturers. Instead of seeing the research-based pharmaceutical industry as a key industry for the German economy and healthcare system and strengthening its innovative potential, it was used once again to fill acute financial gaps in the SHI system. In the process, measures outlined in the coalition agreement for sustainable financing of the SHI system were not implemented, in particular the proposed use of taxation to fund non-insurance benefits. One outcome of political action of this kind is to undermine confidence in the reliability of framework conditions in this location.

No economic impact assessment of any kind was implemented to inform the legislative process. This is incomprehensible in view of worsening access shortages, Germany's increasing dependence on China (both in terms of active ingredient production[5] and technological progress[6]) and the fundamental realignment of Germany's economic business model. At a time when major investments are desperately needed to transform the economy, the legislation has caused significant financial harm to the industry. These resources are no longer available. The industry is being drained of liquidity that would otherwise be reinvested in future projects and high-tech production on a scale unparalleled in any other sector[7]. The pharmaceutical industry invests far more than any other industry in research and development and has a far above-average investment ratio, thus contributing significantly to modernizing the industrial hub[8]. As a result, the pharmaceutical sector triggers value creation in other areas of the economy like no other.[9]

[4] Adjusted for inflation, pharmaceutical spending actually decreased in real terms in 2022.
[5] Cf. Francas, D., Fritsch, M., & Kirchhoff, J. (2022). Pharmaceutical supply chain resilience, available online.
[6] Cf. Fraunhofer ISI (2023): Technological Sovereignty of Germany in the Pharmaceutical Industry, study commissioned by vfa, Mimeo.
[7] cf. MacroScope Pharma Economic Policy Brief 04/2022: Innovations as a basis for growth, available online.
[8] cf. MacroScope Pharma Economic Policy Brief 05/2023: Aging capital stock: Competitiveness is on the line, available online.
[9] cf. MacroScope Pharma Economic Policy Brief 02/2023: Pharmaceuticals is a key industry in structural transformation, available online or DIW Econ (2022): The overall economic importance of the pharmaceutical industry against the background of the COVID-19 pandemic, study commissioned by vfa.

The legislation has stripped this key industry of growth opportunities, resulting in long-term prosperity losses.

The alarming conclusion is that the consequences for Germany as a pharmaceutical hub and in particular for patient access to medicines are already visible now. The full extent of the impact will become evident in the coming years – unless corrective action is taken now. The undesirable developments need to be counteracted as quickly as possible. The course needs to be reset to encourage the development and availability of innovative medicines and promote investment to boost the economy.

Evidentiary basis
vfa bases its assessment on a variety of sources. Where available, primary data sources from official statistics and survey results of third-party institutions are assessed first. This includes results of the ifo Business Survey, data from regulatory authorities, and assessment of public sources on market entries. These sources generally do not provide specific information on the impact of the GKV-FinStG and can at best point toward undesirable trends.

This prompted vfa to monitor the potential impact of the GKV-FinStG in detail from the outset to serve as an early warning system for potential adverse access and economic implications. The data is obtained from a structured survey of association members conducted regularly since January 2023 and implemented by a trust center. The pseudonymized data from this survey of members of the vfa, representing the interests of 48 of the world's leading research-based pharmaceutical companies, constitutes the second cornerstone of the GKV-FinStG impact assessment presented in the following.

However, significant effects of the legislation are not immediately reflected in hard performance indicators and will only become visible bit by bit in the coming years. For this reason, guided interviews on the medium- to long-term consequences of the legislation were conducted with leading experts at vfa member companies in June and July 2023 with the involvement of the Prognos economic research institute. A synopsis of the results is also provided. In addition, expert opinions from other institutes (IGES, IQVIA) are included in the analysis in order to provide the fullest possible picture at this early stage, particularly in light of the often medium- to long-term impact of the measures on patient access to medicines.

The fourth element of the assessment of potential consequences is the review of the literature on the consequences of previous interventions in the pharmaceutical market. For instance, the consequences of the manufacturer's discount introduced in 2011 may help predict the economic consequences of the current legislation.

Part I: Overall impact of the legislation

Impact on patient access to medicines

Even within the very short period under consideration, two significant supply effects are becoming apparent:

- Delay or cancellation of pharmaceutical launches in Germany
- Delay or cancellation of marketing authorization applications in the EU

Dimensions of the problem
The dimensions become clear in the vfa member survey of June 2023. 21 research-based pharmaceutical companies indicate that they are delaying or canceling new drug launches due to the GKV-FinStG or actively discussing these steps.

Effects of the GKV-FinStG on the supply of drug innovations

30 Drugs/approvals are subject to the risk of not being supplied in Germany in the next two years.

13 Drugs will be significantly delayed or not available at all in Germany.

5 Approvals/extensions of approvals are delayed or not sought at all in the EU - with consequences for all patients in the EU.

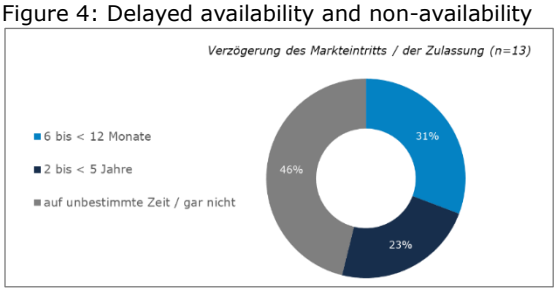
Source: vfa member survey, June 2023

Publicly known case studies

- Nivolumab/Relatlimab for first-line treatment of advanced melanoma in adults and adolescents 12 years of age and older
- Lenacapavir for the therapy of pretreated patients with multidrug-resistant HIV infection
- Teclistamab, for the treatment of multiple myeloma in a late-stage therapy line (one-year delayed launch)
- Spesolimab, as the first approved targeted therapy for acute relapses in generalized pustular psoriasis (market withdrawal)
- Amivantamab against a very rare form of lung cancer (market withdrawal)

vfa member companies were also asked whether the decision was attributable to the GKV-FinStG in each case. The figures exclude market avoidances for other reasons (e.g. production capacity shortages or similar), indicating a causal link to the legislation. The measures most commonly cited as the main reason were the "AMNOG guard rails" for reimbursement negotiations, the combination discount and the elevation of manufacturer's discount. Most of the products affected are oncology drugs but medicines for HIV, diabetes and neurological disorders are affected too. Patient-relevant delays of 6 to 12 months are involved in about one-third of cases. About a quarter of the cases will entail delays of at least 2 years. Almost half of the affected launches are expected to be delayed indefinitely or canceled outright.

Figure 4: Delayed availability and non-availability



Source: vfa member survey in June 2023.

Supply chain slowdowns

The emerging availability gap will have a devastating impact on patient access to medicines, as the five publicized cases indicate.

One example is the non-introduction of the fixed combination of nivolumab and relatlimab for first-line treatment of advanced melanoma in adults and adolescents 12 years and older in Germany. Dual immunotherapy significantly improves progression-free survival (PFS), but the latter is not recognized as a patient-relevant outcome in Germany (unlike in other countries including France, Spain, and the United Kingdom).

In conjunction with the new legal framework, this means the value of this therapeutic advance is not reflected in Germany.[10] With an "additional benefit not proven" AMNOG rating, the manufacturer would even have to "pay on top" for the privilege of marketing the product in Germany, because they would fetch a negative price (-10% versus monotherapy) for the new active ingredient in the fixed combination. The negative impact of the guard rails is demonstrated here in the non-availability of a drug that scores 3 out of a possible 5 points on the current ESMO magnitude of clinical benefit scale.

Another example is the non-launch of the active ingredient lenacapavir for treatment-experienced patients with multidrug-resistant HIV infection.[11] The major clinical benefit that the product offers to patients would most likely not be reflected in an AMNOG assessment process: Conducting benefit assessment-relevant clinical trials in treatment-experienced patients with multidrug-resistant HIV infection using the formal methods required by AMNOG is a major challenge in itself. Since the pivotal trial would not provide evidence of additional benefit that meets these formal methodological requirements (as has already happened in other cases in this population), the reimbursement amount would have to be at least 10% below the price of equally effective innovative drugs. Furthermore, since lenacapavir is indicated for combination with other antiretroviral agents, it can be assumed that an additional 20% combination discount would reduce the reimbursement amount even more.

The examples show that the new GKV-FinStG requirements would make already challenging requirements even more difficult in some situations. Corporate decisions are not informed by any individual measure but by the combination of factors in a given case. This also applies to teclistamab, an agent approved in response to a high unmet medical need for late-line treatment of multiple myeloma. Due to the GKV-FinStG, the manufacturer decided not to market the product in Germany for the time being. Market launch in Germany has not been possible until now, after almost a year's delay.

We can also report that there have been market withdrawals associated with the legislation. Amivantamab, a drug for a very rare form of lung cancer, was withdrawn at an early stage in the legislative process when the negative impacts were becoming apparent. A more recent example is the market withdrawal of spesolimab, the first approved targeted therapy for acute flares of generalized pustular psoriasis, a rare and potentially life-threatening condition. In a formalistic assessment, the G-BA did not consider an additional benefit to be proven, whereas an additional benefit was recognized in France.

Market withdrawals are exceptionally far-reaching decisions because the medicines involved have already been in clinical use. As the statistics show, withdrawals are very rare. Such decisions are taken if continuing to sell the product in the German market is not economically viable, for example. That was a relevant issue in the first AMNOG years until the legislature introduced an "advisory provision" which was applied in justified individual cases by the negotiating partners in compliance with the applicable laws and prevented market withdrawals.[12] The number of market withdrawals might increase again in future due to the rigid negotiation provisions and additional rebates required by the GKV-FinStG.

Leadership in danger

Germany still heads European rankings in terms of access to advanced medicines[13] – but is in

[10] The former chair of the arbitration board, Prof. Wasem, commented that he considers it "*fundamentally wrong to not reward incremental progress*. *It also leads to completely absurd results, for example that the price of a drug administered in combination with the designated appropriate comparator is zero where the additional benefit of this combination is deemed minor. It's clearly nonsense*." (OPG 07/2023 of 10 Mar 2023, p. 13)

[11] See SHI FUNDING STABILIZATION ACT– "Ethically questionable in our view", Tagesspiegel background dated 22 Aug 2023

[12] Evaluation of the vfa-AMNOG database and the Lauer-Taxe (recommended retail price list)

[13] IQVIA 2023, EFPIA Patients W.A.I.T Indicator 2022 Survey

acute danger of losing the top spot, as evidenced by case studies and public databases.[14]

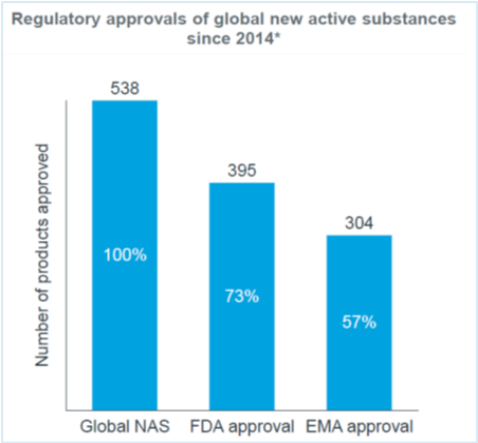
In each of the ten years prior to 2022, on average 88.1% of approved drugs became available in Germany, with a sharper increase in availability toward the end of that decade. In the first half of 2023, however, availability rates of drugs approved in 2022 were 10 percentage points below this average. This finding is backed up by the absolute figures for market launches in Germany: As of August 15, only 20 new drugs had been launched in Germany in 2023, which is 14.5% fewer than in the same period in each of the previous five years.

Impact across Europe

The law also affects access to medicines at the European level. As reported above, the vfa member survey indicates that several companies are significantly delaying or indeed canceling new drug approvals and applications for new indications in the EU because of the new reimbursement conditions under the GKV-FinStG. The German market is hugely important to pharmaceutical companies in Europe, one reason being the reference price effect. Many countries around the world use the German drug price as a reference. If reimbursement conditions deteriorate in Germany, as has recently been the case as a result of the GKV-FinStG, it can unleash a downward price spiral on an international scale ("race to the bottom") which companies need to take into account. So as well as potentially upsetting the fragile balance between (prompt) availability of advanced medicines and cost containment in Germany, the GKV-FinStG risks causing upheaval on an international scale. It considerably weakens Europe as a pharmaceutical hub.

This also needs to be viewed in light of the fact that the number of new drug approvals in the EU falls far short of the US figure. As things stand, one in four drugs approved in the US is not approved in the EU, according to recent IQVIA studies.

Figure 5: EU availability gap



Source: IQVIA New Active Substance database (2014-2023); FDA and EMA websites (accessed 25 Aug 2023).

The absences include drugs such as Casimersen to treat people with a specific genetic expression of Duchenne muscular dystrophy, the most common childhood-onset inherited muscular disorder. The latest datacut confirms the trend, indicating that there were only ten approvals in Europe in the first half of the year, 25 fewer than in the USA. While this may not yet be attributable to the GKV-FinStG, it does show that intra-European availability comparisons do not show the full picture as the statistics only look at medicines approved in the EU. Given that decisions are being made not to approve pharmaceuticals in the EU in the first place because of the GKV-FinStG (as reported above), a broader view is necessary.

Impact on Germany as a business location

The impact on Germany as a hub of innovation and production is part of the evaluation. That is to be welcomed because it indicates that the legislature recognizes the importance of the pharmaceutical industry for German and European innovation and is considerate of the impact of healthcare policy decisions on the economy.

[14] Evaluation of the vfa-AMNOG database and Lauer-Taxe

With good reason, as the innovativeness of the pharmaceutical industry has gone down in history: from the development of the first synthetic painkiller and antipyretic at the end of the 19th century to the first Covid-19 vaccine, many active ingredients were discovered and produced in Germany. Blessed with inventiveness and an excellent infrastructure, Germany has always been an important source of groundbreaking medicines.

As a knowledge-based, productivity-boosting sector, the pharmaceutical industry is a key industry that can help to future-proof the local economy amid demographic change and industrial transformation[15]. It provides highly skilled jobs, and its crisis resilience helps stabilize the German economy. Moreover, it ensures safe and reliable access to medicines with numerous production sites located across Europe. These assets should not be jeopardized by the short-term cost-cutting envisaged with the GKV-FinStG. Instead, the strengths of innovative drug manufacturers can be harnessed to counter supply and access issues, including acute shortages.

The impact of the legislation on the economic activities of the pharmaceutical industry are becoming noticeable in manifold ways. We need to distinguish between effects due to

1. immediate withdrawal of liquidity
2. uncertainty and loss of confidence in political decision-making[16], and
3. changed incentives for innovation.

Withdrawal of liquidity immediately results in corporate cost efficiency programs, affecting operating expenditure, staffing expenditure and investment decisions. Austerity drives result in lower staffing levels, longer vacancies or actual net headcount reductions, lower investment in production plant retention and maintenance, and cancellation or postponement of research projects. Reduced investment and reduced spending on innovation in particular have serious long-term impacts on a production location's competitiveness due to aging plant and machinery.

Political uncertainty is always detrimental to investment, particularly in high-risk areas such as R&D. Policy changes sooner or later result in strategic reorientation of businesses and realignment of global investment priorities, with potentially major effects especially in a globally operating industry.

In response to changes in the expected revenues from innovation projects – for example due to the rigid pricing imposed by the AMNOG "guard rails" or due to the combination discount – spending will be adjusted accordingly. The connections and correlations are clearly documented in the literature around data exclusivity, to give just one example[17]. The long-term outcome is reduced innovation and overall reduced competitiveness of the industry in the international arena.

A little more than six months after the new regulations entered into force, the official statistics likely only give a tiny glimpse of the full impact of the mechanisms described here. It is all the more alarming to note that many impacts are already quite apparent. The qualitative assessments based on case studies also show the direction of travel very clearly.

The consequences for employment, investment, and corporate innovation are discussed in detail in the following.

Staffing plans significantly revised in response to the new legislation

According to conventional wisdom, labor market trends are a very late indicator of trends in a

[15] see vfa article "The opportunities of transformation", available online

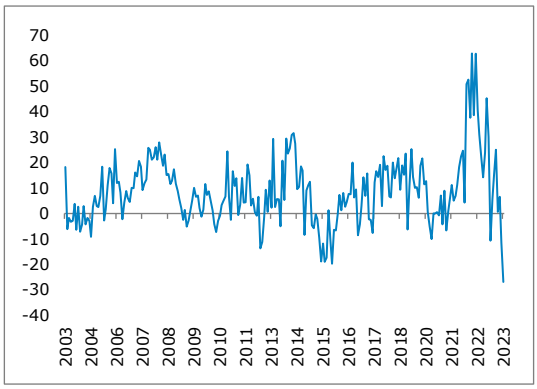
[16] The literature on the relationship between policy uncertainty and investment is very extensive and unanimously concludes that this channel has a starkly negative impact on corporate investment. See, for example, Gulen, H., & Ion, M. (2016). Policy uncertainty and corporate investment. The Review of Financial Studies, 29(3), 523-564, available online.

[17] See e.g. Gaessler, F., & Wagner, S. (2022). Patents, data exclusivity, and the development of new drugs. Review of Economics and Statistics, 104(3), 571-586, available online.

branch of industry.[18] In keeping with the long-standing positive evolution of labor trends in the pharmaceutical industry, companies continued to add to their headcount through the first months of 2023. New facilities were inaugurated based on investment decisions made years ago, in turn resulting in new hirings.

However, corporate polls indicate that staffing plans have been drastically cut back. From an all-time high in early 2022, the outlook of the companies responding to the survey plummeted to an all-time low in July of this year. European Commission, ifo Business Survey and the Association of German Chambers of Industry and Commerce (DIHK) statistics unanimously show this trend.

Figure 6: Employment expectations of the pharmaceutical industry for the coming months; balance of positive and negative responses

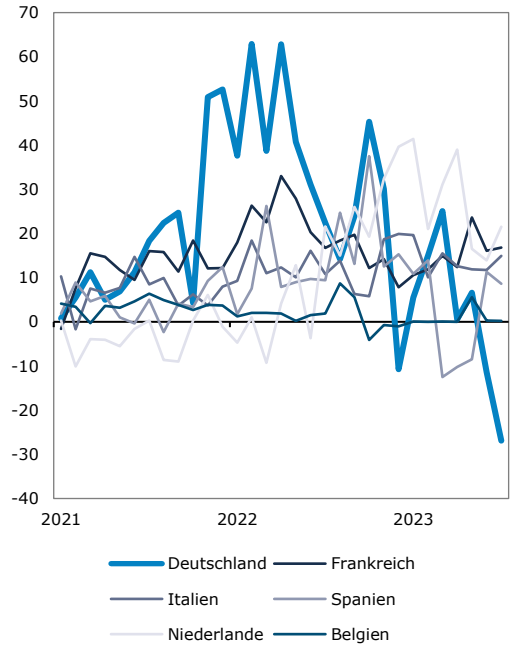


Source: European Commission.

The dispersion of the responses also tells us more about what is happening: A substantial proportion of companies still plan to build employment (about ¼), reflecting global healthcare market opportunities. However, the proportion of companies planning to reduce headcount (over one-quarter) has been well above the long-term average for more than six months. In the 20 or so years of the survey up to the summer of 2022, the proportion of companies with workforce reduction plans averaged 6%, with rare spikes and a peak of 27% in 2012. In December 2022, almost 33% of companies said they planned to cut staff. This is a historical high.

A comparison with neighboring European countries shows that Germany is a negative exception as far as this goes. While other major pharmaceutical locations are largely stable and showing positive trends, Germany slipped from its top-ranking position in terms of employment trends just over a year ago right to the bottom in July 2023.

Figure 7: Employment expectations of the pharmaceutical industry for the coming months in a European comparison; balance of positive and negative responses.



Source: European Commission.

This assessment is consistent with the results of the vfa member company poll. Overall, the June 2023 location barometer painted a negative picture in the wake of the new legislation: 92% of the companies said Germany has become a less attractive place to do business within the last 12 months. Almost three-quarters indicated complete agreement with the statement that conditions have become more hostile. Responses

[18] Cf. Sauer, S., & Wohlrabe, K. (2020). ifo Handbook of Business Surveys (No. 88). ifo Beiträge zur Wirtschaftsforschung, available online.

concerning the damaging effects of the GKV-FinStG on Germany as a business location are unequivocal too. The immediate impact of the law comes in particular from reimbursement-related measures such as the AMNOG "guard rails". More than half of the responding vfa members believe that the full effects will only become apparent one to five years hence. The evaluation period is far too short to assess the impact on Germany as an industry hub.

Survey respondents also indicate effects on staffing plans. The survey showed that headcount reduction plans have been drawn up and are being implemented for 9% of the total workforce in the polled vfa companies, with 665 jobs originally budgeted for 2023 and 2024 axed in these workforces. The figure corresponds to approximately 8% of headcount in 2022. Job cuts are contemplated for about half the workforce of vfa member companies. Lower headcount reductions in the range of an 8% reduction in total workforce as described above would correspond to around 3850 jobs. The total loss of (additional) jobs extrapolated in this way adds up to approximately 4500 jobs.

The annual gross payroll of these discontinued jobs amounts to approximately 480 million euros based on wages and salaries for the 4th quarter of 2021. The sum is equivalent to the earnings of about 5,000 industrial jobs – or about 0.5 Intel sites. And it translates to an annual shortfall of 130 million euros in income tax and solidarity surcharge alone. Taking social security contributions into account, the total shortfall in public-sector revenue would come to EUR 240 million per annum, not including excise and sales taxes or the second-round effects of induced value creation. This projection helps show the considerable implications of the GKV-FinStG for Germany as a pharmaceutical hub and its impact on the public sector.

The findings are consistent with studies of previous events and projections of potential legislative scenarios, according to which the overall economic losses are considerable and have lasting consequences.[19]

Don't let short-sighted austerity strangle investment in an industry with a big future

Investment decisions generally involve long lead times, while official statistics on investment trends generally take quite a while to appear in sectoral breakdowns. The literature clearly demonstrates the correlation between liquidity withdrawal and investment activity – no matter the assets involved.[20] The pharmaceutical pricing and reimbursement system largely determines economic incentives for innovation and production and is a key factor in determining location investment decisions. Erratic intervention in pricing leaves companies without the security they need to make plans, with a resultant negative impact on location decisions. Companies need planning certainty and confidence-building signals from policymakers.

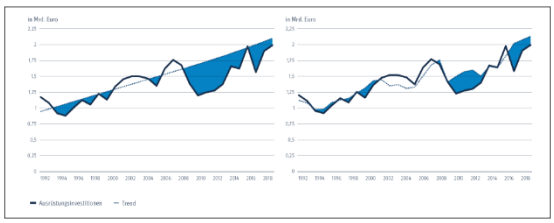
In the pharmaceutical industry as in many other areas, past events show that lower earnings lead to lower investment activity. vfa calculations demonstrate that the increase in the general manufacturer's discount from 2011 to 2014 led to a cumulative reduction of around two billion euros in investment in Germany in the pharmaceutical industry alone. That's not including lack of demand at upstream and downstream stages of the value chain. Lack of investment permanently reduces production potential and future value creation.[21]

[19] See Schneider, M. (2013): The health economic significance of the pharmaceutical industry in Bavaria. BASYS, Augsburg, available online, and Schneider, M. (2022): Macroeconomic and health economic effects of rebates on pharmaceutical products, BASYS, Augsburg.

[20] For examples, see Lichter, A., Löffler, M., Isphording, I. E., Nguyen, T. V., Pöge, F., & Siegloch, S. (2021). Profit taxation, R&D spending, and innovation. ZEW-Centre for European Economic Research Discussion Paper, (21-080), available online for more on the effects of higher business taxation on corporate innovation.

[21] cf. MacroScope Pharma Economic Policy Brief 06/2022: Low investment weighs on Germany's growth, available online.

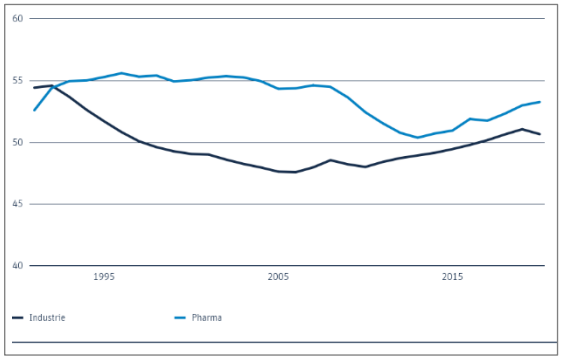
Figure 8: Investment by the pharmaceutical industry (left) in 2015 prices and deviation from the long-term trend (dashed line) / development of a synthetic imitator (right, dashed line) in billion euros.



Source: Federal Statistical Office, vfa calculations.

Another observation is that modernization of capital stock suffered during this period, after having remained very stable in the previous years, contrary to the overall industry trend. This is another clear indication that the changes in reimbursement policy at that time had an immediate impact on the competitiveness of the pharmaceutical industry in Germany.

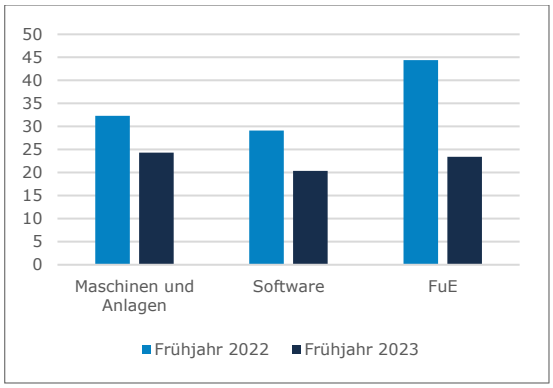
Figure 9: Degree of modernization of the capital stock of plant and machinery versus the industry as a whole



Source: Federal Statistical Office, vfa calculations.

Current developments can only be estimated from company polls. According to the ifo investment database, the pharmaceutical industry's investment readiness has declined significantly compared with the survey conducted the previous year; this relates to investment in machinery and equipment, research and development, and software. ifo investment data indicates that investment in buildings will probably expand more strongly in the current year than in the previous year. This is due to infrastructural adjustment in response to the energy crisis. The findings are in line with the results of the DIHK survey.

Figure 10: Investment intentions of pharmaceutical companies in movable assets and intellectual property, balance of positive and negative responses.



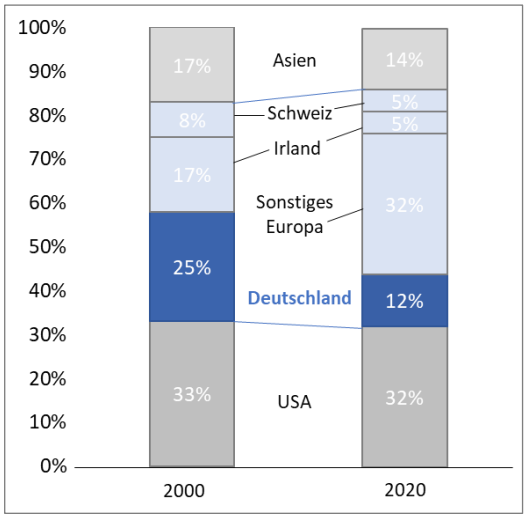
Source: ifo Institute, vfa calculations.

The vfa member survey shows that around half of all the companies polled are making changes to their investment plans in response to the GKV-FinStG. The vast majority of respondents at the last assessment in summer 2023 were unable to cite actual figures yet, which is hardly surprising given the scope and long-term nature of the decisions involved. Regarding R&D investment, more than one-third of the companies polled also said they were planning to make specific changes in response to the legislation.

Given the long-term nature of the decisions concerned (as described above), it is not possible to quantify the magnitude of specific effects of the GKV-FinStG on Germany as an investment location at the present time. The case studies conducted by Prognos AG outlined projects that had already been decided upon and are now being reconsidered. The examples include re-assessment of the planned construction of two new production facilities for highly advanced therapies in the wake of the GKV-FinStG. In another case, a final decision on a planned significant investment in existing production is on hold pending adjustment of the framework conditions set by the GKV-FinStG. The legislation is reinforcing an already apparent trend. Figure 11 shows that Germany has dramatically lost importance as a production location for

biopharmaceutically manufactured active ingredients over the last 20 years.

Figure 11: Production sites for the manufacture of active biopharmaceutical ingredients



Source: vfa based on IW Cologne (2022)

Worsened conditions are harmful in combination – qualitative results

The results of a Prognos AG analysis of the overall innovation and investment climate based on interviews with 15 CEOs of research-based pharmaceutical companies give further insight into the consequences of the new legislation. The medium- to long-term consequences in particular are difficult to quantify at present but now provide the basis for ongoing decision-making processes.

In the short term, the companies – or their German operations – are interested in balancing national earnings and losses. The aim is to achieve as good a balance as possible even if some companies have significant foreign operations and generate major revenue there. Corporate managements monitor earnings and losses at the various sites and base future investment and site development decisions on their observations. The vast majority of respondents expect the GKV-FinStG to have a medium to long-term impact on their organizations and German operations.

The executives responding to the survey say their corporations would decide against Germany as a location of operations case by case, for example where research and development or new production capacities are concerned. The planning horizon of these companies is long-term. Organizations have an infrastructure planning horizon of 5 to 10 years, for instance. A gradual process of erosion is expected, the consequences of which will only become apparent in the long term, with the migration of the generic drug sector serving as a precedent. The relevant discussions in research-based organizations have already begun, however. A recent vfa-Kearney report (*Pharma-Innovationsstandort Deutschland* [*Germany as a location for pharmaceutical innovation*]) confirms that company representatives are unanimous in their agreement that Germany is in danger of losing much of its importance as a hub of innovation.[22]

Corporate headquarters around the globe are taking careful note of the deterioration of conditions for doing business in Germany. Factors cited include lower profitability, the impact on international pricing, and planning uncertainty within Germany. These uncertainties arise from the fact that it is unclear how certain aspects of the law will be interpreted and implemented, making it impossible to calculate potential revenue losses in advance. Some measures require strategic decisions of significant magnitude in a very short window of time. Moreover, fundamental legal and political uncertainty is inherent in the many constitutional weaknesses of the law and the legislative intentions visible therein. It is also not clear how companies are supposed to make provisions for future eventualities if the implementation of the law is not clarified and still subject to interpretation. The situation is exacerbated by repeated attempts in the past - the GKV-FinStG being the latest in a long line - to solve structural challenges of the statutory health insurance system at the expense of the innovative pharmaceutical industry, in particular by imposing manufacturer discounts. Each of these adjustments and their oftentimes delayed reversal (or non-reversal) is

[22] cf. vfa and Kearney: Pharma-Innovationsstandort Deutschland, 2023, available online

registered very closely in other countries as an erratic intervention in stable market conditions.

Business leaders conclude that politicians do not (or no longer) appreciate the pharmaceutical sector and attach little value to it as an industry, employer and innovation driver in Germany. The restrictions imposed on the negotiating freedoms intended by AMNOG, which the respondents view as an established and proven instrument, is seen by some as a clear breach of trust. Existing rules are being cast off unilaterally to the detriment of the industry.

Business leaders in Germany are at pains to point out that the companies based here face competition from other affiliates in their corporations. At corporate level, very close attention is paid to how the individual national or regional sites are performing. Site conditions are analyzed in detail and compared against each other when planning for the future and making strategic decisions, for example when launching new drugs or investing in new production facilities.

Even companies that traditionally have their roots in Germany are thinking about investing abroad or already doing so[23]. While these organizations many not be thinking of abandoning Germany entirely, their German operations are nonetheless in competition with other countries.

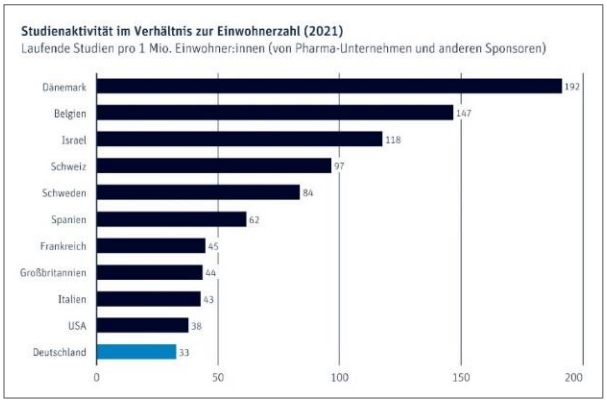
Location deprioritazion is happening on a European scale too, for example through planned regulatory reform (data exclusivity is a prime example) and patent protection reform. As a consequence, Europe's attractiveness as a location and as a market is declining, adding factors into the mix that further reduce Germany's attractiveness.

Both the vfa location barometer and the Prognos report show that location factors have deteriorated significantly from the perspective of research-based pharmaceutical companies, making Germany less attractive as a place to do business.

No future for research "Made in Germany"?

Declining attractiveness also applies to research and development. Germany is already falling behind on R&D and the GKV-FinStG is likely to accelerate the decline. A study published in July 2023 by vfa and the Kearney consulting firm "*Pharma-Innovationsstandort Deutschland*" (*Germany as a location for pharmaceutical innovation*) highlights the challenges facing clinical research. In terms of research study activity, Germany is already lagging behind the USA, France, Israel and Belgium, among others (see Figure 12).

Figure 12: International comparison of study activity



Source: Kearney analysis based on GlobalData, in: Philipp et al (2023).

The GKV-FinStG (AMNOG "guard rails" in particular) is already impacting strategic decisions, for example causing companies not to seek approvals for or market late-line cancer drugs supported by evidence from single-arm studies in Germany. This will result in Germany not being involved in the underlying research studies. German involvement in a number of multinational study programs has already been canceled outright. As a result, Germany stands to lose out on industry-funded early access to innovative therapeutic options and the associated compassionate use programs, notably in oncology, immunology and rare diseases.

[23] See for example the announcements by Bayer AG (Handelsblatt of 16 Jan 2023) and the BioNTech decision (Tagesschau.de of 07 Feb 2023).

All this will serve to make cutting-edge research "Made in Germany" increasingly rare in the pharmaceutical industry as in other areas. Yet research is Germany's best medicine. The pharmaceutical industry is one of the most productive, crisis-proof and innovation-driven sectors of the economy and must be strengthened rather than exploited and undermined for the sake of short-termist cost reduction. Moreover, the austerity approach runs contrary to the Ministry of Health's recently expressed aspiration to significantly improve location factors for pharmaceutical research and production in Germany. A first step in this direction would be to correct the GKV-FinStG and its misguided direction of travel.

Part II: Impact of the individual measures

Any evaluation of the individual measures – an undertaking expressly desired by the Ministry – must address the fact that they are usually applied in combination and can add up to non-viable price reductions, ultimately resulting in a product being withdrawn or not marketed in the first place, as outlined in Part 1.

"Guard rails" for negotiating reimbursement rates

(section 130b(3) SGB V)

Measure

The "guard rails" were introduced as mandatory requirements for reimbursement negotiations where a medicinal product receives an HTA rating of no, minor or non-quantifiable additional benefit if the designated "appropriate comparator" is patent-protected. Hard price ceilings were defined for such cases which leave the contracting parties with no room to negotiate and are a departure from the AMNOG benefit-based pricing system. With the "guard rails" system, a higher additional benefit (minor or non-quantifiable) is no longer rewarded with a higher price, and an "equal benefit" rating in fact leads to lower prices.

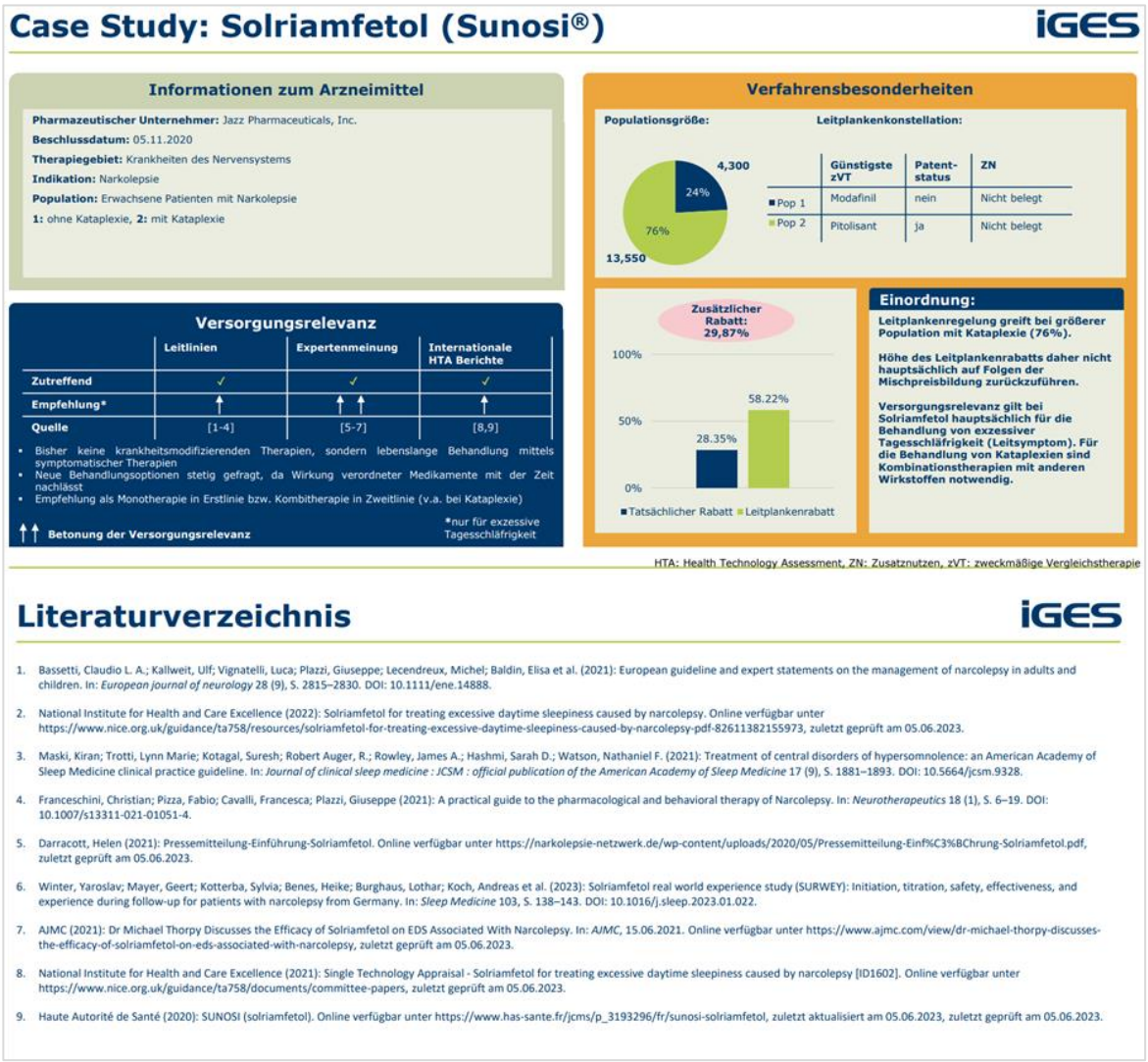
Commentary

The new statutory "guard rails" constitute far-reaching interventions in the tried-and-tested AMNOG process and are the most common reason for delayed or canceled market launches cited by vfa member companies.

A good example of the misguided effect of the "guard rail" requirements is the recent outcome of HTA assessment of trastuzumab-deruxtecan, a drug to treat advanced breast cancer. This drug comes with very clear evidence of benefits in terms of overall survival and severe side effects in second-line treatment. According to former G-BA practice, a "considerable additional benefit" might have been expected. Unexpectedly, however, the G-BA issued a "non-quantifiable" benefit rating. This classification means that this second-line drug is subject to the new rigid price regulations of the GKV-FinStG, preventing the additional benefit from translating into an appropriate price. This will be a major obstacle to successful price negotiations for this internationally recognized drug – and sends out a terrible signal to would-be investors in new drug R&D.

To grasp the implications of this instrument and its potential unwanted consequences, it helps to take a little look back. If the "guard rails" had been introduced in 2017, it can be assumed that a number of current therapeutic advances would no longer be available or would never have made it into clinical use. One example is solriamfetol for the treatment of narcolepsy, which according to the IGES institute would have been saddled with an additional discount of almost 30% if the "guard rails" had applied (see Figure 13). That's not all. A higher manufacturer's rebate would also have applied, and the reimbursement amount would have taken retroactive effect from the seventh month after placement on the market, in addition to various other effects of the GKV-FinStG. It seems unlikely that the reimbursement amount emerging after application of all those measures would have been worth it for the manufacturer, especially against the backdrop of international price referencing and the resulting downward price spiral. A market withdrawal or cancellation of market entry would probably have been inevitable. End result: patients do not get access to an advanced medicine of proven clinical benefit as assessed by experts and designated as such in medical guidelines.

Figure 13: Retrospective effect of "guard rails" using Solriamfetol as an example.



Source: IGES Institute (2023)

The guard rails also pose risks for orphan drugs, i.e., medicines for rare diseases. Let's look at CAR-T cell therapy. Typically, cell therapies are initially developed as last-line treatments for small patient populations. For that reason, classical randomized clinical trials (RCTs) are often neither possible nor ethical. According to G-BA assessment practice to date, an absence of RCT data generally results in a "non-quantifiable" benefit rating. In AMNOG, drugs costs are calculated by comparing annual cost of treatment. This model is not expedient even now for one-time treatments such as cell therapies because it involves comparing the cost of one-time treatment against the long-term annual cost of treatment of other therapies. If the now-lowered annual revenue threshold for orphan drugs of EUR 30 million is exceeded, the permanent therapies will be used as a price cap for the AMNOG guard rails. The annual treatment cost of long-term therapies is typically significantly lower than for a one-time CAR-T therapy and does not even cover the production cost of a CAR-T therapy. Novel treatments to satisfy

the unmet medical needs of vulnerable patient populations will hardly make it to market under these reimbursement conditions.

Prof. Greiner et al. conducted a retrospective analysis of the "guard rail" effect.[24] This involved modeling the reimbursement amounts that would have emerged if the guard rails had already applied in 2019-2021. The results can be summarized as follows: During this period, 106 active ingredients underwent early benefit assessment, of which 70 would have been affected by the AMNOG guard rail approach. The "guard rail discount" would have averaged 42%, i.e. 15 percentage points/1.5 times higher than the discount applicable at the time. In fact, the guard rail discount would have been above 60% for 26 active ingredients, i.e., one in four of the active ingredients undergoing AMNOG assessment in the 2019-2021 period. Discounts in excess of 60% will likely make distribution in Germany economically non-viable, forcing drug makers to withdraw their product or waive market entry for financial reasons.

It seems clear that the guard rails will continue to affect a not inconsiderable proportion of drugs in the future to the point where they will simply not be available in Germany. The legislation is likely to have similar consequences for new indications. Pharmaceutical companies do not have the option to choose whether or not to place a new indication to the German market. The subsequent "race to the bottom" described above can result in extreme situations where a company introduces a swathe of new indications and ends up serving more patients than before while generating lower overall revenue. The logical consequence for companies – especially in indications involving complex methodological or medical challenges and resulting in a "minor or non-quantifiable benefit" rating –would be to not do pivotal studies.

As the name suggests, the guard rails act as pricing boundaries. Unlike the guard rails used in road traffic, AMNOG guard rails do not increase safety, quite the opposite: they jeopardize patients' safe access to medical advances – which has been secure in Germany up to now – which is tantamount to reducing their health insurance benefits.

Discount for pharmaceuticals used in a combination therapy

(section 35a(3)(4), section 35a(1d) and section 130e SGB V)

Measure

The GKV-FinStG introduces a mandatory flat-rate deduction for combination therapies. This additional discount amounting to 20% of the reimbursement amount is to be levied if drugs with new active ingredients are used in a combination designated by the G-BA and are dispensed at the expense of statutory health insurance providers. Implementation of the new regulation is still unclear in many parts, making conclusive evaluation impossible at this point.

Commentary

The introduction of an additional combination discount was neither necessary nor appropriate. Combined use of drugs and the costs thereof had already been fully addressed in the existing AMNOG price negotiations prior to the introduction of the GKV-FinStG. Even where new drugs from different manufacturers are involved, combined administration was and is governed by the respective reimbursement rate negotiations and routinely results in lower reimbursement rates. At no time has there been a regulatory gap. Against the backdrop of the existing AMNOG pricing rules, the combination discount for the combined administration of innovative drugs is yet another ultimately unjustified burden.

Approved combination therapies meet an important clinical need. In many indications, they make outcomes possible that would have been unthinkable just a few years ago. Medical guidelines reflect this. Combination therapies have become an indispensable part of the standard of care in oncology and many other areas too, including HIV, hepatitis C, diabetes and neurological disorders.

[24] Cf. AMNOG Report 2023, available online.

Especially with medications given in combination, the new price reductions accumulate into a downward spiral, significantly impeding the economic viability of these drugs. This also jeopardizes future research and market entry of additional combination partners, limiting patient access to advanced treatment options. New indications that would result in a combination discount being applied to an already marketed product lose their appeal and may no longer be pursued on a European scale. In this manner, the combination discount will also jeopardize future access to medicines in the EU.

In general, the combination discount represents a disproportionate interference with the constitutionally protected freedom of practice for pharmaceutical companies (Article 12(1) of the German Basic Law). The proportionality of the combination discount is highly questionable especially in light of the significant additional burdens placed on pharmaceutical companies by the provisions of the GKV-FinStG. Several constitutional complaints have already been filed, and more are expected.

G-BA implementation

The negative impact of the combination discount is further exacerbated by the current designation practices of the Federal Joint Committee (G-BA), and this is cause for serious concern. Since June 1, 2023, the G-BA has been publishing benefit assessments along with drafts for the designation of drugs with new active ingredients according to section 35a(3)(4) SGB V that are indicated for on-label use in combination therapy with the drug under assessment for the indication under assessment. The G-BA has also released a draft decision on amendment of the designation of combinations involved in decisions made up to November 12, 2022. The approach taken by the G-BA raises serious legal concerns and must be revised.

First and foremost, it should be noted that the G-BA's approach to (non)designation is opaque. It is unclear which drugs were evaluated and what conclusion the G-BA reached in each case. Section 35a(3)(4) SGB V stipulates that combination designation only applies to drugs that are pharmaceutically approved for a specific combination therapy, in the sense of an in-label combination. The decisive factor is the explicit permission for use in combination granted by the approval. However, in cases where the SmPC lacks this information, the G-BA – contrary to these principles – includes drugs with overlapping indications but not explicitly indicated for combination use, calling them "open combinations." In fact, the vast majority of the combinations listed in the draft of June 27, 2023, came about through this unacceptable practice. Therefore, the designation clearly contradicts the fundamental principles of pharmaceutical regulatory approval.

Furthermore, the G-BA's draft designations also raise concerns from a legal systematics point of view. Section 35a(1d) SGB V explicitly states that pharmaceutical companies can apply for a determination that a combination therapy is expected to provide at least substantial additional benefit. This allows them to achieve an exemption from the combination discount. However, this regulation is rendered ineffective by the G-BA's new practice. The right to exemption from the combination discount is undermined by the G-BA's approach, as it designates combinations that are not subject to regulatory approval and therefore not subject to HTA. As a result, pharmaceutical companies cannot present studies suitable for demonstrating additional benefit. Moreover, such studies would contradict the generally accepted state of medical knowledge, grossly so in some cases.

It is important to note that the G-BA's approach generates entirely hypothetical and medically absurd designations, as (among other things) it forgoes assessment of the recognized state of medical knowledge. This is evident from the explanation in the statement of reasons for the benefit assessment decision. According to the latter, the designation is not associated with any statement as to the extent to which treatment with the drug under assessment in combination with the designated drugs corresponds to the generally accepted state of medical knowledge. The non-assessment of the generally accepted state of medical knowledge as a benchmark is not tenable. The designation as combination therapy and the examination of the criteria for the designation are components of the benefit assessment decisions in accordance with section 35a(1d) and (3) SGB V. According to section7(2) of the AM-NutzenV,

the generally accepted state of medical knowledge is the benchmark for assessment purposes. In addition, the G-BA's approach leads to medically absurd and impractical designations with devastating signal effects. For example, there are nonsensical designations in the field of chronic hepatitis C treatment (combinations of multiple fixed combinations) and in other therapeutic areas as well, including rare cancers (combination of CAR-T cell therapies) and more common conditions such as chronic heart failure and metabolic disorders (combination of two agents of the same drug class). The extent and radiating effect of such medically absurd determinations are inestimable.

Discount implementation
vfa fundamentally opposes the introduction of combination discounts, as elaborated above. If the legislature chooses to persist with this, a fair and practical implementation is necessary at the very least.

In this context, vfa believes that the negotiation-based approach selected in the GKV-FinStG for implementing combination discounts is the best way to achieve a fair, legally sound, and practical realization of the legislative requirements. Furthermore, the combination discount constitutes a significant encroachment on the constitutionally guaranteed freedom of professional practice for pharmaceutical companies. The GKV-Spitzenverband (national association of statutory health insurance providers) should not have the authority to make regulatory decisions in a substantive sense. Additionally, the potential for disputes between health insurance providers and manufacturers regarding the interpretation and necessary evidence for a combination prescription is significantly reduced when essential principles are consented to beforehand in a model agreement by the associations. The "by mutual agreement" provision now amended by the Pharmaceutical Supply Shortage Control and Improvement Act (ALBVVG) does not ensure a reasonable balance of interests and has no legal or practical benefit.

The vfa views the currently beginning technical implementation phase with great concern. The current designation practice of the G-BA is not only medically absurd but also carries the risk of wrongly including treatment sequences and treatment switches in the combination discount. This would be disproportionate and has no basis in law.

Quantity-related aspects in reimbursement agreements
(section 130b(1a) SGB V)

Measure
With the entry into force of the GKV-FinStG, the legislature replaced the previous option ("*can*") with an obligation ("*must*") to include "quantity-related aspects" when negotiating the price of new drugs in accordance with section 130b SGB V.

Commentary
Quantity aspects have always played a role in the reimbursement negotiations between pharmaceutical companies and the GKV-Spitzenverband in accordance with the framework agreement. The contracting parties determined the expected prescription quantity and agreed on regulations, particularly for quantity overruns. If actual quantities deviated from expectations, the GKV-Spitzenverband usually had an extraordinary right of termination to adjust the higher-than-expected SHI spend in a new agreement.

According to the legislative rationale, the new regulation is intended to be limited to individual cases and aims to mitigate the financial burden on the payers in the event of a general increase in quantity, or approval of new therapeutic indications in a targeted way. However, the intended significance of the new provision has sparked heated debate. The GKV-Spitzenverband aimed to make "price-quantity models" a key determinant in pricing. In practice, this would have completely undermined the benefit-appropriate pricing model in Germany. Basing drug prices mainly on sales or prescribed quantities would disregard the clinical benefit of the drug in question and be yet another breach of the AMNOG system.

Increase in manufacturer's discount
(section 130a(1a) SGB V)

Measure
The general manufacturer's discount was temporarily increased by 5 percentage points for 2023.

Commentary
In principle, the GKV-FinStG does not provide for an evaluation of the increase in the manufacturer's discount. This is appropriate insofar as it is intended as a one-time, time-limited measure. However, since the Federal Ministry of Health (BMG) has asked for comments on the measure, we are stating our position nevertheless.

The measure is by no means justified given that pharmaceutical spending is not to blame for the SHI deficit. The federal government itself has pointed out that the reduced growth in revenue from health insurance contributions since 2020 has significantly contributed to the growing funding gap in the SHI system. The gap in question is due to Covid-related special effects. Current analysis shows that the SHI is in better financial shape than originally thought. The latest financial results show that revenue from health insurance contributions has stabilized and the predicted catch-up effects on the expenditure side have not materialized. What's more, even before the GKV-FinStG came into force in 2022, the pharmaceutical industry made a significant cost-cutting contribution to the tune of €23 billion through various cost containment instruments.[25]

There was no constitutional basis for the increase either. The pharmaceutical industry is not responsible for expenditure trends in other areas. The manufacturer's discount should not be misappropriated as a "shunting yard" to shift funds elsewhere. Pharmaceutical companies have long passed their limit of endurance, one reason being that – unlike other sectors – they cannot simply pass on significantly increased production costs to the consumer.

The manufacturer's discount affects all therapeutic areas equally and had to be implemented directly. No other measure directly impacted pharmaceutical companies to quite the same extent. The economic climate changed overnight to one of general uncertainty, delayed investment and staffing decisions, and loss of trust in political decision-makers.

The vfa takes a very critical view of the increase. Companies are now under pressure not only on the cost side (energy prices and other inputs) but on the revenue side as well (manufacturer's discount and other measures in the GKV-FinStG). Studies show that higher (tax) burdens significantly affect investment in physical capital and also in research and development.[26] It is apparent from the current financial results of the BMG for the first quarter of 2023 that the increase in the manufacturer discount has already caused a significant additional burden compared to the same period last year. An additional burden of approximately EUR1.3 billion is estimated for 2023 as a whole.[27] The increased manufacturer's discount seriously and durably jeopardizes innovative strength and new drug development. The phasing out of the increased manufacturer's discount (which is regulated by law anyway) is therefore right and proper.

Reduction of revenue threshold for orphan drugs
(Section 35a(1)(12) SGB V)

Measure
The sales threshold for orphan drugs in the benefit assessment process has been lowered from EUR 50 million to EUR 30 million. The G-BA has the authority to be flexible in the procedures to implement the new provision.

[25] IGES based on BMG statistics (KJ1, KV45), NVI (Insight Health), ABDATA. Reference prices: GKV-SV (National Association of Statutory Health Insurance Organizations) (press release 19 Jun 2019).
[26] For examples, see Lichter, A., Löffler, M., Isphording, I. E., Nguyen, T. V., Pöge, F., & Siegloch, S. (2021). Profit taxation, R&D spending, and innovation. ZEW-Centre for European Economic Research Discussion Paper, (21-080), available online for more on the effects of higher business taxation on corporate innovation.
[27] vfa, extrapolation based on BMG financial statistics

Commentary

With regard to the progress on implementing the new regulation, it is important to note that a G-BA decision dated February 2, 2023, temporarily suspended the orphan drug procedures for drugs that exceeded the new revenue threshold as of December 1, 2022. Each manufacturer will be asked to submit a dossier after a staggered deadline, extending in some cases into 2024. At present, however, due to the deadlines correctly indicated in the Rules of Procedure, no procedure with a new benefit assessment decision has yet been completed. This makes it impossible to comply with the legislature's desire for assessment of the new regulation based on initial results and experiences. Moreover, there was no transition period for this regulation. In fact, it even applied retroactively in 2022, with no planning security whatsoever[28]. As already stated in the preliminary remarks, an extension of the statutory evaluation is necessary in light of these (and other) circumstances.

The vfa continues to view the reduction of the revenue threshold as inappropriate. This and other measures only serve to jeopardize the previously well-functioning system to ensure patients with rare diseases can access the medicines they need and may potentially delay the development of drugs for unmet medical needs. This would be devastating given that approved drugs currently exist for only about 2% of the approximately 8,000 known rare diseases. There is a vast unmet need for effective drugs in this area. While 90% of all orphan drugs approved in Europe are available in Germany, only 79% are available in France, for example. The time span between EU approval and availability (89 days) is shorter in Germany than anywhere else in Europe. The current high level of access to orphan drugs may be about to deteriorate.

The vfa already pointed out during the legislative process that the Act for Greater Security in the Supply of Medicines (GSAV) was effectively lowered only recently by expansion of the assessment basis to include the inpatient sector. Further lowering of the revenue threshold to EUR 30 million risks making the AMNOG an insurmountable hurdle for many orphan drugs. It is uncontested that evidence generation and evaluation in rare diseases is exceptionally challenging for all parties concerned. Randomized controlled trials of orphan drugs are often difficult to perform, or produce inconclusive results due to the very small patient populations involved. These special features are currently not taken into account in the comprehensive benefit assessment process. There is currently no provision for appropriate adjustment of the evaluation methodology for special therapies. Many orphan drugs, including those already in clinical use, run the risk of not being able to demonstrate their additional benefit according to the strict AMNOG methodology for non-orphan products, thereby depriving them of a fair starting position for benefit-based price negotiations. This increases the risk of subsequent market withdrawal for introduced orphan drugs. Pharmaceutical companies also lose an important economic incentive to invest in research and development of drugs for small patient populations with rare diseases and to give patients in Germany rapid access to those medicines.

Retroactive application of the reimbursement amount

(Section 130b(3a) SGB V)

Measure

The GKV-FinStG has implemented a retrospective validity of the reimbursement amount from the seventh month after the initial market launch. Retroactivity also applies to any new therapeutic indications. A compensation requirement also

[28] The manufacturers concerned find themselves in a precarious accounting situation with disproportionately long reimbursement periods, entailing immense provisioning. Take, for example, a staggered call for dossier submission in early 2024. In this case, the re-negotiated reimbursement amount under non-orphan terms will be available 12 months later, i.e., in early 2025. However, the retroactive validity of this new reimbursement amount is six months after the new law came into effect and the associated 30 million euro threshold was exceeded, i.e., June 2023. Provisioning for a period of 20 months is required, which is all but impossible from an accounting point of view and not feasible for an international corporation.

applies in the inpatient sector. Additionally, due to an amendment to the Pharmaceutical Supply Shortage Control and Improvement Act (ALBVVG) alien to AMNOG, pharmaceutical companies have been obligated to compensate for trade margins and the amount of value-added tax.

Commentary
The retroactive validity of the reimbursement amount is another serious intervention in the AMNOG regulatory framework. Up until now, the contracting parties were able to regulate this themselves case by case in reimbursement negotiations. Now, it is specified by hard and fast rules. The procedure even provides for repeated backdating of negotiated reimbursement amounts in the absence of a free pricing situation. If a drug with a new therapeutic indicate goes through the AMNOG procedure again, the previous reimbursement amount still applies to it. The new benefit assessment outcomes for the new indication and the quantity changes were already prospectively taken into account in the renegotiation of the reimbursement amount before the GKV-FinStG came into effect.

Moreover, the retroactive compensation of trade margin costs by the manufacturer, which are regulated in the Medicinal Products Price Ordinance and outside the control of the manufacturer, raises significant legal concerns. Contrary to the justification provided for the amendment, this change in the ALBVVG is not a mere legal clarification, but in fact constitutes the introduction of a new discount obligation, which does not logically arise from the retroactivity to the seventh month within the applicable legal system. Pharmaceutical companies are neither at fault, nor do they help cause the overpaid trade surcharges. Finally, reimbursement by the pharmaceutical company is out of the question because the pharmaceutical company simply never received the amounts to be collected. Therefore, they cannot be required to compensate for the trade surcharges paid by the health insurance companies and sales tax in addition to compensating for the price difference. This new discount requirement in the guise of something else places a considerable burden on pharmaceutical companies, also due to the high administrative effort leading to additional costs for the companies. This is another clear example of the lack of predictability and transparency in the legal framework.

The vfa considers the retroactive validity of the reimbursement amount to be problematic and not very effective. The reimbursement rules in place to date provided positive incentives for swift market entry and access to innovative drugs for patients – a hallmark of German pharmaceutical policy in the international arena. Rapid availability is jeopardized by the retroactive validity of the negotiated or fixed reimbursement amount, as this results in a significantly increased entrepreneurial risk for the market-introducing pharmaceutical company. This applies in particular to new therapeutic indications where availability exists as soon as the marketing authorization is granted and where the pharmaceutical company has no choice but to introduce the new indication to the German market. In individual cases, the extension of marketing authorization to include new indications may no longer be economically viable. Especially for new indications, supply risks of this magnitude are disproportionate in relation to the projected cost savings.

Consideration of waste in reimbursement negotiations
(Section 130b(1b) SGB V)

Measure
In pricing, drug waste in excess of 20% due to uneconomical pack sizes is supposed to be taken into account as a price-reducing factor.

Commentary
This provision leads to inappropriate across-the-board price reductions. For production reasons, a patient-specific range of pack sizes (to enable weight-dependent dosage) can rarely be provided economically by a company. It is unrealistic to think otherwise. Concerns about waste could already be agreed case by case by contract within the existing negotiation framework. This would give the contracting parties the necessary leeway to include potential waste when setting prices. In the case of preparations, the auxiliary tax also ensures that the SHI does not incur any avoidable costs.

Part III: More extensive reform needed

The underlying AMNOG principle, i.e., benefit- and negotiation-based pricing for innovative medicines, is based on the premise that a higher price than the existing standard treatment is justified if the new drug represents an improvement over the standard of care in the German healthcare setting. This logic, constitutionally enshrined in Article 3 of the Basic Law ("principle of equality"), has been undermined with the introduction of the "guard rails". The new legislation also introduces extraneous price reductions for combination therapies.

These structural interventions have put the AMNOG process in a precarious position. They are affecting the availability of new therapies in Germany just a few months after coming into effect and are the very opposite of a sustainable location policy for research-based pharmaceutical companies. Legislative adjustments are needed. The AMNOG principle must be reinstated and negotiation-based solutions must be strengthened. Abolition of the "guard rails" and combination discounts is desperately needed for this purpose.

vfa is presenting the following suggestions[29] in the hope of making a constructive contribution to the current reform debate and lending strong support to AMNOG's further evolution.

Recognition of special treatment situations
New therapies are becoming increasingly targeted in nature. Scientific progress can make benefit assessment challenging because the patient populations targeted by a therapy are smaller than before. Classical randomized controlled trials (RCTs) designed to study larger patient populations and which continue to be considered the gold standard are difficult or impossible for some new therapeutic approaches for practical reasons, and also for ethical reasons if very serious conditions are involved. Research in those areas relies on other types of investigation. Regulatory agencies have been addressing this trend for a number of years, with a focus on situational, case-by-case assessment of what constitutes an appropriate study design. In AMNOG benefit assessment, on the other hand, only classic RCTs are routinely accepted as a basis for assessment. The "guard rail" situation only serves to exacerbate the situation. Little to no consideration is given to the special features of treatment situations, with all the consequences one might expect for reimbursement rate negotiations further down the line. As a result, AMNOG is no longer able to fulfill its original purpose as an instrument for fair and reasonable pricing. There is a risk of an increasing disconnect between healthcare provision in Germany and scientific progress in medicine. This is not an acceptable situation.

The vfa proposes making the AMNOG evaluation criteria more fit for purpose in the face of medical progress. More effective consideration must be given to the special features of specific treatment settings in order to assess study designs and results. This enables case-specific assessment and consideration of additional benefit. Especially in special treatment situations, categorical rejection of evidence is unacceptable. Instead, joint agreement is needed on how the available evidence can best be used for HTA.

Scope for new contract models
Pay for performance reimbursement models are currently difficult to implement in reimbursement rate negotiations with the GKV-Spitzenverband, not least due to legal framework conditions**.** In practice, such models have not played a major role in Germany to date. In contrast to rigid requirements, flexible solutions can also lead to savings in the healthcare system without endangering access to medicines.

vfa suggests expanding the legal framework and creating the legal foundations for the implementation of such models. In special treatment settings with justifiably limited evidence, for example in the case of highly innovative one-time therapies, contracting parties should have more leeway for fee structuring than the traditional normative

[29] See also vfa position paper "AMNOG 2025 – Current Areas of Action", available online.

framework of the Social Security Code currently allows (in particular section 130b SGB V).

Priority for European health technology assessment

European HTA begins on January 12, 2025 for the first products, including advanced therapy medicinal products (ATMPs) and oncology drugs. This is intended to improve access to innovative therapies in Europe, reduce red tape for pharmaceutical companies and national HTA authorities, and boost the quality of clinical evaluation across the EU. Efficient collaboration at the European level should also enhance and sustain Europe as a successful biotechnology hub. To achieve these goals, clear priority rules for the results of European HTA are necessary in AMNOG.

vfa suggests establishing a mandatory consideration of joint European work results in the national process. This will help avoid redundancy and contradictory assessments that would necessitate additional effort and confuse patients. In addition, national processes must connect seamlessly to European groundwork without delaying rapid market access in Germany. Adequate involvement and consultation of pharmaceutical companies at the critical interfaces of these processes needs to be ensured through new provisions.

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