VALUE IN HEALTH 20 (2017) 927–935

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/jval

Pharmaceutical Pricing in Germany: How Is Value Determined within the Scope of AMNOG?

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ABSTRACT

Objectives: To analyze how value is determined within the scope of the German Pharmaceutical Restructuring Act, which came into effect in 2011. **Methods:** Using data from all pharmaceuticals that had undergone assessment, appraisal, and price negotiations in Germany before June 30, 2016, we applied generalized linear model regression to analyze the impact of added benefit on the difference between negotiated prices and the prices of comparators. Data were extracted from the Federal Joint Committee's appraisals and price databases. We specified added benefit in various ways. In all models, we controlled for additional criteria such as size of patient population, European price levels, and whether the comparators were generic. **Results:** Our regression results confirmed the descriptive results, with price premiums reflecting the extent of added benefit as appraised by the Federal Joint Committee. On the substance level, an added benefit was associated with an increase in price premium of 227.2% ($P < 0.001$) compared with no added benefit. Moreover, we saw increases in price premium of 377.5% ($P < 0.001$), 90.0% ($P < 0.001$), and 336.8% ($P < 0.001$) for added benefits that were "considerable," "minor," and "not quantifiable," respectively. Beneficial effects on mortality were associated with the greatest price premium (624.3%; $P < 0.001$), followed by such effects on morbidity (174.7%; $P < 0.001$) and adverse events (93.1%; $P = 0.019$). **Conclusions:** Price premiums, or "value," are driven by health gain, the share of patients benefiting from a pharmaceutical, European price levels, and whether comparators are generic. No statement can be made, however, about the appropriateness of the level of price premiums.

Keywords: early benefit assessment, Germany, price negotiation, value-based pricing.

Introduction

Health systems vary in structure and in the needs and preferences of their populations. As a consequence, the assessment of health technologies and related decisions on the pricing and reimbursement of pharmaceuticals differ across countries as well [1–3].

Invariably, the concept of value plays an important role in health technology assessment. Yet looking at how different stakeholders define what attributes contribute to value [4] and how different countries have used the concept to help determine the prices of pharmaceuticals [5–7] reveals great heterogeneity. Paris and Belloni [6] even describe the application of value-based pricing (VBP) strategies as "more of an art than a science."

In Germany, a fourth-hurdle process, which leads to a change in launch prices after the pharmaceutical's first year on the market, was introduced in 2011 with the German Pharmaceutical Restructuring Act (AMNOG). With this legislation, the German government aimed to ensure that pharmaceutical prices would be economically efficient while not inhibiting innovation [8].

The AMNOG process consists of two phases. First, new pharmaceuticals are assessed to determine whether they have an added therapeutic benefit over the current standard of care, defined as "appropriate comparative therapy" by the Federal Joint Committee (G-BA). (For the sake of simplicity, we use the term "comparator" in this article.) To do so, an initial advisory assessment is made by the Institute for Quality and Efficiency in Health Care, followed by a final appraisal of the G-BA. Second, pharmaceutical prices are negotiated between manufacturers and the National Association of Statutory Health Insurance Funds (GKV-SV). If the negotiations fail, prices are set by an arbitration board [9]. By law, substances that do not have an added benefit over their comparator should not lead to annual treatment costs that are higher than those of the comparator. For substances with an added benefit, however, the annual treatment costs may exceed those of the comparator by a premium that is in line with the extent and certainty of the added benefit specified in the appraisal of the G-BA.

Although the determinants of coverage decision making have been studied well for countries that use formal economic evaluations (e.g., United Kingdom and Australia) [1,10–12], the determinants of decision making and pricing in two-stage administered systems [13], such as Germany, have not. Neither the determinants of decision making in Germany, which have been studied

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1098-3015$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2017.04.006

only descriptively [14,15], nor the determinants of price negotiations' outcomes [16–18] have been analyzed conclusively.

In the present study, we analyzed whether price premiums negotiated in the second phase of the AMNOG process do indeed reflect 1) the G-BA's previous appraisals on the pharmaceuticals' added benefit; 2) the criteria, which are set out in a framework agreement between manufacturers and the GKV-SV [19], such as the size of the patient population; and 3) further aspects, such as the manufacturers' experience in negotiating prices. Furthermore, we explored the magnitude of the price premiums granted for different extents of added benefit.

Methods

Study Setting

We included data on all pharmaceuticals that had completed the second phase of the AMNOG process between January 1, 2011, and June 30, 2016. In cases in which the price of a pharmaceutical had been renegotiated (e.g., because of a re-assessment or an extension to a new indication), we included results from only the first negotiations to eliminate potential bias resulting from strategic behavior of manufacturers. We excluded assessments of so-called orphan drugs because these do not have to demonstrate an added benefit over a comparator and thus do not include data on comparator costs. We also excluded pharmaceuticals for which manufacturers had decided not to start or complete negotiations and had therefore opted out of the German market. Last, we excluded benefit assessments with comparators defined as "best supportive care" because the G-BA does not publish comparator costs in these cases.

We extracted data from publicly available G-BA appraisals as well as from the German price database Lauer-Taxe® and various international, publicly accessible price databases [20–31].

Outcome Variable

We computed the relation between the annual treatment costs of a pharmaceutical and those of its comparator from the statutory health insurer's perspective (i.e., using pharmacy retail prices, including value-added tax minus manufacturer and pharmacy rebates as regulated by law):

$$\text{Relation of costs} = \frac{\text{Annual treatment costs of pharmaceutical}}{\text{Annual treatment costs of comparator}} \times 100$$

If the pharmaceutical and its comparator have equivalent costs, the relation amounts to 100%. The relation of costs can be transformed into a proportional price premium by subtracting 100 for descriptive analysis or by calculating marginal effects when used in regression models.

To calculate the annual treatment costs of a pharmaceutical, we used the expected treatment duration and dosage given in G-BA's appraisals in combination with postnegotiation prices from the German price database Lauer-Taxe. We also extracted annual treatment costs for the comparators directly from G-BA's appraisals. When applicable, we additionally extracted costs for concomitant medication and for procedures associated with the use of the pharmaceutical or its comparator from G-BA's appraisals.

Treatment costs were collected at a patient subgroup level. In cases in which several interchangeable comparators were eligible for the same patient subgroup, we calculated an average of their costs. When the comparator varied between patient subgroups, the population-weighted mean was calculated to determine a pharmaceutical's comparator's cost. We obtained patient population sizes from G-BA's appraisals.

Variable of Interest

When determining the level of a pharmaceutical's added benefit for each patient subgroup, the G-BA considers the following end points: mortality, morbidity, adverse events, and quality of life. We therefore specified the G-BA's appraisal of a pharmaceutical's added benefit in our six regression models in the following ways.

In model A.1 we considered whether an added benefit ("not quantifiable," "minor," "considerable," or "major") had been assigned for at least one patient subgroup or not ("less benefit" or "no added benefit"). In cases in which no added benefit has been assigned, the annual treatment costs of the new substance should not exceed those of its comparator. In model A.2 we took into account differences in added benefit across patient subgroups, specifying the share of the patient population that had been appraised as experiencing an added benefit.

For models B.1 and B.2 we differentiated between "no added benefit" and the four categories of added benefit. We distinguished between the greatest extent of added benefit that had been assigned at the substance level (model B.1) and the particular shares of the patient population that had been assigned a major, considerable, minor, or not quantifiable added benefit (model B.2).

Models C.1 and C.2 reflect whether the G-BA decided that the pharmaceutical showed beneficial effects in particular end point categories (mortality, morbidity, adverse events, and quality of life) (model C.1) as well as the corresponding shares of the patient population (model C.2).

Control Variables

The selection of control variables is based 1) on the framework agreement [19] between manufacturers and the German statutory health insurance and 2) on previous literature on coverage decision making [1]. First, we included the total number of patients eligible for a new pharmaceutical as specified in its marketing authorization [11,19,32,33]. This was obtained from G-BA's documentation. Second, as required in the framework agreement, the annual treatment costs of so-called comparable medication are to be taken into account [19]. According to the framework agreement, a comparable medication is authorized within the same medical indication as the new pharmaceutical and its usage is appropriate according to international standards of evidence-based medicine. Yet, it is unequal to the G-BA–defined "comparator" (standard of care). Because no information on the comparable medication used is disclosed after price negotiations are completed, we used an approximation by specifying a binary variable that captures whether a comparable medication is available at the fourth level of the Anatomical Therapeutic Chemical Classification System. In addition, the comparable medication had to be 1) listed in the German Lauer-Taxe price database at the time of completed price negotiation and 2) authorized for the same medical indication as the new pharmaceutical [19]. The presence of alternative treatments or the "innovativeness" of a new pharmaceutical has also been used as a control variable in the literature [10–12,33–35].

Last, price negotiations must take account of the new pharmaceutical's actual sales prices in other European countries [19]. We therefore attempted to extract the pharmaceutical's ex-factory prices for 14 European countries from publicly available European databases, and were able to do so for the Czech Republic [21] and France [22]. Because ex-factory prices were not always available, we surveyed the pharmaceutical's price to pharmacy for Ireland [23] and Sweden [24], and the pharmacy retail prices for Belgium [25], Denmark [26], Finland [27], Italy [28], the Netherlands [29], Portugal [30], and Slovakia [31]. To calculate the ex-factory prices, we used average wholesaler and pharmacy margins estimated by Kanavos et al. [36]. The framework