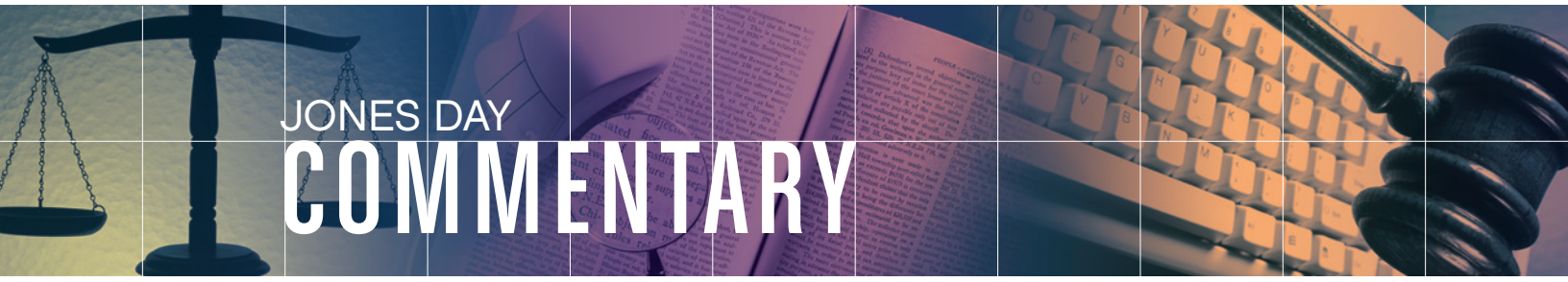
JANUARY 2011



A REVOLUTION OF REIMBURSEMENT IN GERMANY

New legislation effective January 1, 2011, will revolutionize reimbursement for pharmaceuticals in Germany. Pharmaceutical and biotechnology companies currently developing products need to take a "fourth hurdle" into account, in addition to demonstrating quality, safety, and efficacy. They will also have to demonstrate an additional clinical benefit over the standard therapy. This will need to be taken into account when designing clinical trials during drug development.

FROM FREE MARKET ACCESS TO NEGOTIATED MARKET ACCESS

From a business perspective, Germany was for a long time an attractive market for innovative pharmaceuticals (including biopharmaceuticals), as reimbursement by the public health system in general occurred at the prices set by the pharmaceutical companies. The legislator had introduced rebates in favor of the public health system, and increased them earlier this year to 16 percent, at the same time extending this rebate to pharmaceuticals distributed to patients in private health insurance plans. Nevertheless, the originators had been free to set the initial asking price, with the added advantage that this list price in Germany was referenced in reimbursement price calculations by a range of other European countries.

This is about to change as of January 1, 2011. On December 17, 2010, the act introducing this change passed the last legislative approval required. One day earlier, the German Federal Government had approved the implementing regulation. The law is entitled "Act on the reorganization of the pharmaceutical market in the public health insurance" (*Gesetz zur Neuordnung des Arzneimittelmarktes in der gesetzlichen Krankenversicherung* or *Arzneimittelmarktneuordnungsgesetz*, or "AMNOG"). In fact, the act fundamentally changes reimbursement in Germany, and thus can be described as a revolution rather than a reorganization. In the best case, reimbursement prices have to be negotiated. In the worst case, reimbursement is limited to that which is granted to comparable products.

THE PROCEDURE

The originator has to file documentation on the benefits of a product at the latest by the first time of

placing a product on the German market. The same applies for new indications. For existing products, such documentation may be requested on a case-by-case basis. The documentation has to be filed with the Joint Federal Committee (*Gemeinsamer Bundesausschuss*, or "G-BA"), a body of the German public health system. It has to include, in particular, data on the additional medical benefit in relation to the "appropriate comparator therapy," on the number of patients and group of patients for which of a significant additional therapeutic benefit exists, and on the costs of the therapy for the public health system.

Within three months, the G-BA is required to assess the benefit of the product and to publish this assessment. The G-BA may carry out the assessment itself or may delegate it. The stakeholders both from the medical and the industry side shall be heard on the assessment in writing and/or in oral presentations, before the assessment is published. Within a further three months, the G-BA has to decide on the benefit assessment. In particular, the G-BA has to determine whether an additional benefit exists.

If the determination denies an additional benefit, the product is immediately included into a group of comparable pharmaceutical and therapeutic characteristics, for which maximum reimbursement prices have already been set. If there is no such group, because the product is a pharmaceutical novelty, the reimbursement price has to be negotiated, but it may not exceed the annual costs of the "appropriate comparator therapy." The originator may only request a new assessment one year after the publication of the negative determination.

If the determination acknowledges an additional benefit, the originator has to negotiate the reimbursement price with the Federal Head Association of the Public Health Insurances (*Spitzenverband Bund der Krankenkassen* or *Spitzenverband Bund*). The negotiations have to be concluded within six months of the publication of the determination. Technically, the result of the negotiations is a rebate for the public health care system on the list price.

If the negotiations fail, an arbitration body has to determine the reimbursement price within a further three months. The arbitration body is composed of an independent chairman, two independent co-arbitrators, and two arbitrators for each of the public health care system and the pharmaceutical industry. The arbitrators representing the industry shall be appointed by the German federal industry associations. The arbitration body shall take into account the actual prices applicable in other European countries. The price determined by the arbitration body applies one year after the first placing of the product on the market (possibly retroactively, if the decision of the arbitration body is issued thereafter).

The originator may file suit against the price determination; however, the action does not stay the determination pending the outcome of the suit.

THE ADDITIONAL BENEFIT

The benefit of a product is further defined in the implementing regulation as the "patient relevant therapeutic effect." This includes the improvement of health, the shortening of the time of an illness, the prolongation of survival, the reduction of side effects, or the improvement in quality of life. Economic benefits, in particular macroeconomic benefits (*e.g.*, indirect costs like work stoppage, rehabilitation, or reduced requirement for home care), are not taken into account. The additional benefit is one that is quantitatively or qualitatively superior to that of an "appropriate comparator therapy."

To the extent the product is comparable pharmacologically and therapeutically to existing products, the additional benefit has to be demonstrated as therapeutic improvement over such existing products. If the product is not comparable pharmacologically and therapeutically to existing products, the "appropriate comparator therapy" has to be determined according to the standards of evidence-based medicine. In case of alternatives, the more cost-efficient therapy shall be used, preferably one for which a fixed limit of reimbursement exists. The "appropriate comparator therapy" has to be an appropriate therapy in accordance with generally accepted standards of medical science, preferably a therapy for which endpoint trials exist and that has been proved and tested in clinical practice.

The starting point of the additional benefit assessment are the trials submitted for regulatory approval. However, the G-BA may request further trials. If data on patient-relevant endpoints cannot exist at the time of the assessment (*e.g.*, demonstrating additional benefit in patient survival), the G-BA may set a deadline by which such data has to be submitted. The data is classified according to the categories of evidence-based medicine.

The additional benefit is classified by the implementing regulation according to six categories, from great improvement of the benefit of a therapy, to a benefit lower than that of the "appropriate comparator therapy." The statute does not require such categories, but it is to be assumed that the categories—in case an additional benefit is determined—will affect the price negotiations and any eventual determination by the arbitration body.

Originators may seek advice from G-BA on the data required to demonstrate the benefit of a drug under development, including on the "appropriate comparator therapy," as early as prior to entering phase III of clinical trials. The German authorities responsible for approving the applications for marketing authorizations may participate in such advice. The advice shall be documented in writing. Participation by the European Medicines Agency, which is responsible for evaluating applications for central marketing authorizations, is not provided for under the statute.

ORPHAN DRUGS

For drugs designated as orphan drugs under the European regulation 141/2000, the additional benefit is deemed to be demonstrated by the marketing authorization. This special provision reflects the requirement for orphan drugs to demonstrate additional benefit over existing therapies in order to obtain orphan drug designation in the first place.

However, once an orphan drug generates annual gross sales of €50 million or more at the cost of the German public health system, the G-BA may request current data on the additional benefit, which the originator has to provide within three months. The procedure outlined above is then also applicable to orphan drugs.

LAWYER CONTACT

For further information, please contact your principal Firm representative or the lawyer listed below. General email messages may be sent using our "Contact Us" form, which can be found at www.jonesday.com.

Christian B. Fulda
Munich
+49.89.20.60.42.200
cfulda@jonesday.com