GSAV - A New Law for More Safety in the Supply of Pharmaceuticals in Germany

As a reaction to the recent drug safety scandals in Germany (including drugs contaminated with potentially carcinogenic substances, illegal drug imports, and incorrect drug dosing by a pharmacist), the German Ministry of Health introduced a draft "law for more safety in the supply of pharmaceuticals" (GSAV) in November 2018, including increased evidence requirements. The bill is still to be voted on in both chambers of the German Parliament and, if accepted, will come into effect 1 July 2019. The key points are summarised below.

A New Revenue Threshold and Evidence Regulation for Orphan Drugs

Full AMNOG benefit assessment; additional evidence required, likely against active comparator

- Annual turnover threshold is €50 million in total revenue, including retail, hospital, etc. (compared to current standard of €50 million in retail sales only)
- No assumed benefit after €50 million threshold is met (currently orphan drugs receive the advantage of assumed benefit, where, at worst, findings from a health technology assessment (HTA) would indicate a non-quantifiable benefit)
- This could affect several drugs and give the G-BA* legal ability to reassess orphan assets
- Additional evidence can be demanded by G-BA at the initial assessment for assets with conditional approval (given due to missing evidence) and all orphan drugs (where evidence is considered low)
- New demands would be for real-world evidence
- Evidence reviewed yearly; can trigger yearly reevaluation of benefit assessment outcome
- Failure to comply or a negative reassessment based on evidence allows the GKV** to discount drug price *(Note: favourable evidence cannot lead to price increase due to the existing price moratorium in force until end of 2022)*

Supply Contracts Between Health Insurance Companies and Haemophilia Centres

- Genetically engineered blood components and monoclonal antibodies for the treatment of specific coagulation disorders will become available via the pharmacy (like other genetically engineered medicines).
- Health insurance companies are to agree on supply contracts with the manufacturer and specialised haemophilia centres to guarantee drug supply and medical monitoring of patients with haemophilia.

National Implementation of Biosimilar Quotas

- The G-BA can regulate the exchangeability of biosimilars and their biologic counterparts from a national level, similar to the current regulation of brand and generic drugs.
- This could result in national prescription quotas for biosimilars, already in effect at the regional level.
- General expectations are that biosimilars, where available, will have increasingly preferred reimbursement status.
- The automatic replacement of biologics for biosimilars by the pharmacist, as is common practice with generics, is only permissible if the G-BA previously explicitly stated the interchangeability between biologic and biosimilar. There will also be a three-year period (until 2022) during which the exchange can only be made if explicitly permitted by the treating physician.

Enhanced Drug Monitoring and Safety

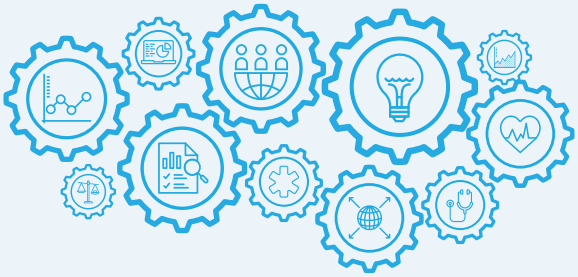
- The higher federal authorities will receive additional monitoring and drug recall powers.
- Drug recalls are possible in all cases where a quality defect is present or counterfeit medicines are suspected.
- Better cooperation is anticipated between the Federal Institute for Drugs and Medical Devices and the Paul-Ehrlich-Institute in coordinating any recall actions.
- Federal authorities can participate during inspections of manufacturer sites in third-party (including non-EU) countries.
- Unannounced inspections of drug manufacturing pharmacies and businesses in Germany are possible.

*G-BA = Federal Joint Committee
**GKV = German statutory health insurance system

U.S. +1 301 654 9729 EUR +44 (0) 208 576 5000 info@evidera.com evidera.com

A Growing Need for Real-World Evidence

Real-world evidence of safety, effectiveness, and value is necessary to achieve successful market access and product uptake. In addition to robust early development clinical trial programs, payers and other key stakeholders, such as patients, physicians, and caregivers, demand evidence of benefits and risks in a real-world setting.



Evidera's team of researchers offers leadership in the design and execution of studies to meet payer and regulator evidence requirements. We offer diverse scientific methods and high quality project and data management expertise. Methods include analytics of secondary data sources, bespoke multinational data collection, hybrid studies, and pragmatic/adaptive studies.

We Can Help You

- Delineate the natural history and course of a disease (e.g., incidence, prevalence, standard(s) of care)
- Determine unmet clinical and humanistic needs by characterizing the burden of illness
- Collect robust data from rare disease populations
- Quantify real-world, product-specific, and/or comparative safety, effectiveness, adherence, and other outcomes
- Evaluate country-specific treatment patterns, quantify associated costs of care, and populate health economic models

Excellence in Study Design and Execution

Extensive experience
Dedicated real-world, non-interventional study operations, regulatory, and global clinical supply teams with over 25 years of experience across ~116,000 patients and ~15,000 sites globally in the past five years

20+ year track record
Have designed and implemented health-related quality of life, treatment satisfaction, adherence, resource use, epidemiological, burden of illness, and safety outcomes studies

Specialist medical affairs team
Rapid study start-up and patient recruitment when working under an early engagement partnership model

Therapeutic area experts
Capabilities across a wide range of indications, and ability to leverage our network of clinicians and global operations professionals

Integrated partnership model
Flexible and proactive operating and governance model customized to unique needs

Innovative methodologies
Application of innovative methods (e.g., pragmatic studies) resulting in optimal study design, endpoint selection, and statistical analyses

Expertise in study design and protocol development
All studies governed by a scientifically robust protocol that is reviewed and quality controlled by an in-house, industry-recognized research team