Moving to a continuous evaluation of value and price in Germany

First therapy to be requested for post-launch real world data for German benefit assessment.

The requirements in case of established data uncertainty for rare disease therapies and therapies under conditional marketing authorisation.

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EVIDENCE AND VALUE INSIGHT

FEBRUARY 2021

1.Managing uncertainty

-In case of **established data uncertainty**, manufacturers of **orphan treatments and products under conditional marketing authorisation** (1) may be requested by the G-BA to collect and submit additional post-launch data.

- The data has to be **submitted within a defined period post-launch** and will be evaluated by the G-BA to establish the level of incremental benefit.

- The G-BA will have to **determine for the manufacturer the mode of data collection and the centres** involved in further data collection.

THE CHANGE

The GSAV (Gesetz für mehr Sicherheit in der Arzneimittelversorgung / Law for increased security in the provision of pharmaceuticals) law passed in 2020 sets out the general framework under which the G-BA can determine post-launch, real-world data collection, and conditional evaluation. (4)

THE EVIDENCE

The detailed specifications, such as the duration, type, and scope of the data collection and evaluation, including the formats to be used, are determined by the G-BA. Priority is given to methodological specifications as well as patient-relevant endpoints and the determination how they are recorded. The G-BA can request indication-related data collection without randomization. (3)

THE PROCESS

The G-BA can request that IQWIG assess the additional evidence needs along PICO. G-BA can set deadlines by which the manufacturer has to submit collected data for re-evaluation, earliest 18 months after the initial data request. During the data collection the G-BA can restrict use of the therapy to those centres that participate in the collection of additional data. (3)

REFERENCES FOR FURTHER READING

(1) 2004000089de1-32 1..1 (europa.eu)
(2) Bundesgesetzblatt Teil I Nr. 30 (bundesgesundheitsministerium.de)
(3) as in (2) page 1212
(4) as in (2) page 1211

G-BA

Gemeinsamer Bundesausschuss - G-BA, the Federal Joint Committee (Reimbursement assessment)

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2.Impact on price agreement

- Initial price evaluation will be conducted along annual therapy costs.

- Price evaluation for products requiring additional data collection (determined by G-BA) will be a continuous process and can be called ad hoc in case G-BA notices no data collection efforts.

- If the G-BA re-evaluation leads to a non-quantifiable benefit, the reimbursed amount has to be lower than the annual therapy costs considered in the previous price agreement.

GKV

Spitzenverband der Krankenkassen - GKV - National Association of Statutory Health Insurance Funds

ONGOING PRICE EVALUATION

For medicinal products (according to Section 35a Paragraph 3b Clause 1 SGB V), the reimbursement amount is regularly renegotiated after the deadline set by the G-BA for carrying out a Real-World Evidence-related data collection, and after another decision on the benefit assessment by the G-BA.

In case the G-BA notices before expiration of the deadline set for supplying additional data, that no data collection efforts have been made or will be made, or due to other reason cannot be made, the GKV can request a re-evaluation of the reimbursement price at any time. The re-evaluated price is to be lower than the previously agreed price. (1)

PRICING WITH ADDITIONAL DATA

If the G-BA established in the re-evaluation *no quantification of the benefit,* a reimbursement amount must be agreed that is appropriately lower than the annual therapy costs considered for the previously agreed reimbursement amount. (1 and 2)

REFERENCES FOR FURTHER READING

(1) Art 130b, paragraph 3
(2) GSAV page 1214: Bundesgesetzblatt Jahrgang 2019 Teil I Nr. 30, ausgegeben zu Bonn am 15. August 2019

3. Process map

MAPPING OF PROCESS STEPS

Price will be re-assessed along data re-evaluation by G-BA.

1. Products with orphan designation and / or conditional marketing authorisation

2. IQWIG to assess post-launch data needs along PICO, upon request by G-BA

3. G-BA to communicate scope of additional data collection, including population, methods, timelines; G-BA re-evaluation at earliest at 18 months

4. G-BA to request that manufacturer submit study – and analysis plan

4. GKV initial price agreement

G-BA re-evaluation at 18 months at the earliest, and agreed milestones

6. GKV re-agreement on price

G-BA re-evaluation: Data doesn't allow establishment of additional benefit level

No submission of study – and analysis plan: G-BA establishes no intent to collect data

Price lower than initial price

GKV can request a price re-evaluation at any time, and a price lower than initial price

G-BA - Gemeinsamer Bundesausschuss - Federal Joint Committee
GKV - Spitzenverband der Krankenkassen - GKV - National Association of Statutory Health Insurance Funds-
PICO - Patient Population, Intervention, Comparator, Outcome

As of February 2021

Zolgensma® - Onasemnogen-Abeparvovec

The molecule Onasemnogen-Abeparvovec (Zolgensma® by AveXis Novartis Gene Therapies), with orphan drug designation, received conditional Marketing Authorisation by EMA on 18 May 2020, for the treatment of spinal muscular atrophy (SMA).

The G-BA assessment started 1st July 2020. (1)

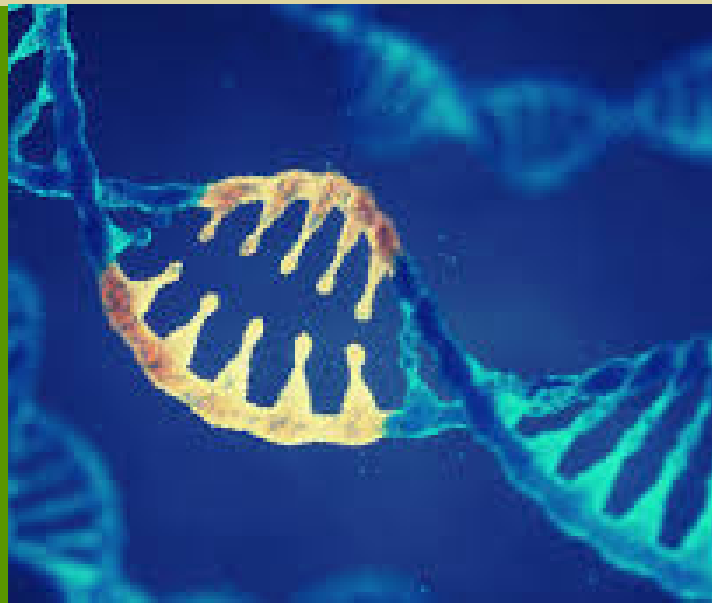
On 4th February 2021, the G-BA set out the requirement for collecting real-world evidence data via a registry, to close identified evidence gaps. (2)

Costs to the GKV per treatment = 2.256.241,75 € (3)

CASE

PROCESS

- Start of the procedure: 1st July 2020
- Start of the written comments procedure: 1st October 2020
- Deadline for submitting written comments: 22 October 2020
- Decision: 3rd December 2020
- Determination of real world data: 4th February 2021
- Proceedings status as of February 2021: Proceedings suspended



1.AVAILABLE DATA

- Outcomes of two open-label, non-randomised, single-group, single-dose clinical studies named STR1VE and START.
- STR1VE is an ongoing/completed Sept 2020 Phase III clinical trial enrolling 21 patients with infant-onset SMA, while START is a Phase I clinical trial. START, a 24-month clinical study, was conducted to evaluate the safety and efficacy of the drug in 15 patients.(4)

2. EVIDENCE GAPS IDENTIFIED BY THE G-BA

The G-BA identified the following evidence gaps as rationale for requesting further data:
- Evidence on the long-term (additional) benefit and harm of the treatment in the approved patient population;
· Comparative data regarding treatment with Onasemnogen-Abeparvovec versus existing therapy alternatives for the approved patient population. Comparator therapy was determined by G-BA as Nusinersen (SPINRAZA®)
· Data from patients with 5q-associated spinal muscular atrophy who were at the time of receiving the therapy older than 6 months or 6 weeks.

(1) HTTPS://WWW.G-BA.DE/BEWERTUNGSVERFAHREN/NUTZENBEWERTUNG/561/
(2) PRESSEMITTEILUNGEN UND MELDUNGEN - GEMEINSAMER BUNDESAUSSCHUSS (G-BA.DE
(3) 2020-06-25_MODUL1_ONASEMNOGEN-ABEPARVOVEC.PDF (G-BA.DE) PAGE 48
(4) SINGLE-DOSE GENE REPLACEMENT THERAPY CLINICAL TRIAL FOR PATIENTS WITH SPINAL MUSCULAR ATROPHY TYPE 1 - FULL TEXT VIEW - CLINICALTRIALS.GOV AND ZOLGENSMA FOR THE TREATMENT OF SPINAL MUSCULAR ATROPHY, NOVARTIS (CLINICALTRIALSARENA.COM)

3. PROCESS TO DETERMINE DATA REQUEST

1. IQWIG was requested by the G-BA to develop a concept for the collection of real-world data, including:
a. the type, duration and scope of the data collection
b. The main objective (along PICO scheme) of the data collection and for the evaluation including the patient-relevant endpoints,
c. The methodology of data collection
d. Data analyses and evaluations by the pharmaceutical company.
2. G-BA determined data request and timing to manufacturer. (1)

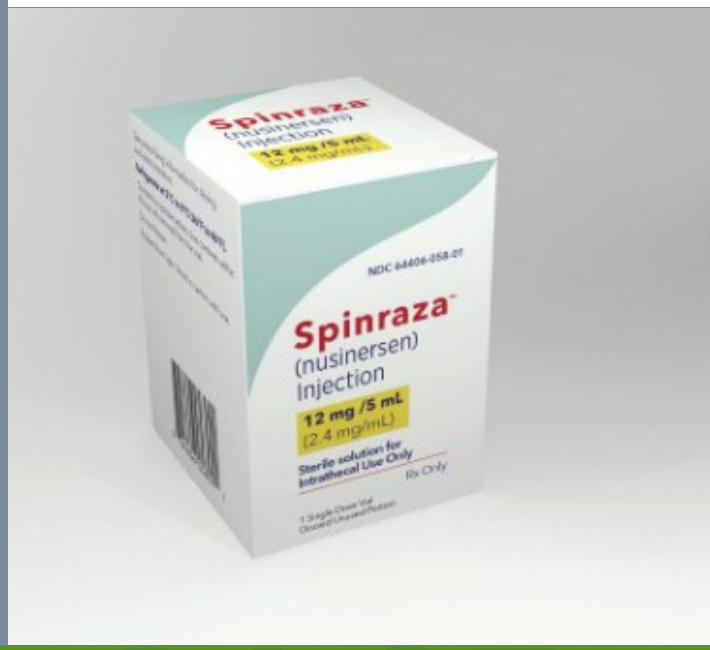
(1) TRAGENDE GRÜNDE ZUM BESCHLUSS DES GEMEINSAMEN BUNDESAUSSCHUSSES ÜBER DIE ÄNDERUNG DER ARZNEIMITTEL-RICHTLINIE (AM-RL): ANLAGE XII – NUTZENBEWERTUNG VON ARZNEIMITTELN, MIT NEUEN WIRKSTOFFEN NACH § 35A SGB V, ONASEMNOGEN-ABEPARVOVEC (SPINALE MUSKELATROPHIE); FÖRDERUNG EINER ANWENDUNGSBEGLEITENDEN DATENERHEBUNG UND VON AUSWERTUNGEN

4. DATA REQUEST

Based on IQWIG analysis, the G-BA requested the following from the manufacturer (non-exclusive):
- A non-randomized comparison of Onasemnogen-Abeparvovec and Nusinersen using parallel and non-parallel control in one data source.
- Data sources are indication registries that meet IQWIG and international quality criteria, and which match the German treatment reality, specifically. SMArtCARE-Registery was recommended
- Guidance on data analysis
- Data collection over 5 years with defined milestones (1)

5. NEXT STEPS

- Manufacturer to submit draft study protocol and analysis plan to G-BA by 15 August 2021
- Assessment of study protocol by G-BA within 4-6 weeks
- Submit data to G-BA at least every 18 months and after at 36 months and 60 months
- Price agreement with GKV ~ July 2021 and re-evaluation of price along G-BA data assessment milestones (1)



IQWIG: Institute for quality and efficiency in health care
PICO - Patient Population, Intervention, Comparator, Outcome

Come in for a virtual chat

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