Gemeinsamer Bundesausschuss

Justification

on the resolution of the Federal Joint Committee (G-BA) on the initiation of a procedure on the requirement of a routine practice data collection and evaluation according to Section 35a, paragraph 3b SGB V:
Risdiplam (spinal muscular atrophy)

of 7 October 2021

Contents

1. Legal basis

According to Section 35a, paragraph 3b, sentence 9 SGB V, the Federal Joint Committee (G-BA) can demand the pharmaceutical company to submit routine practice data collections and evaluations for the purpose of the benefit assessment within a reasonable period of time for the following medicinal products:

1. in the case of medicinal products authorised to be placed on the market in accordance with the procedure laid down in Article 14, paragraph 8 of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1). L 136, 30.4.2004, p. 1), as last amended by Regulation (EU) 2019/5 (OJ L 4, 7.1.2019, p. 24), or for which a marketing authorisation has been granted in accordance with Article 14-a of Regulation (EC) No 726/2004; and
2. for medicinal products authorised for the treatment of rare diseases under Regulation No 141/2000.

2. Key points of the resolution

With the present resolution, the G-BA initiates a procedure for the requirement of a routine practice data collection according to Section 35a, paragraph 3b, sentence 1 SGB V for the active ingredient risdiplam (Evrysdi®).

According to Chapter 5, Section 51 of the Rules of Procedure of the G-BA (VerfO), the procedure for the requirement of routine practice data collection and evaluations is divided into

1. the assessment of necessity according to Section 54,
2. the resolution of the plenary session initiating proceedings under Section 55 and evaluations under Section 56,
3. the preparation of a concept for the requirements of a routine practice data collection and evaluations and evaluations with the participation of expert bodies according to Section 57 and
4. the resolution of the plenum demanding a routine practice data collection and evaluations according to Section 58 to be done by the pharmaceutical company.

According to Chapter 5, Section 54 of the VerfO, the initiation of a procedure for the requirement of a routine practice data collection and evaluations requires that the routine practice data collection is considered necessary for the purpose of the benefit assessment of a medicinal product. The assessment of necessity is based on documents relating to this medicinal product, in particular from a benefit assessment procedure of the G-BA according to Section 35a SGB V, the marketing authorisation procedure at the European Medicines

Agency (EMA), a request for advice according to Section 7 as well as further documents relating to clinical studies.

The active ingredient risdiplam (Evrysdi®) was approved by the European Commission (EC) on 26.03.2021 as a medicinal product for the treatment of rare diseases (orphan drugs) under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 for the treatment of spinal muscular atrophy. The pharmaceutical company has irrevocably notified the Federal Joint Committee that, despite the orphan drug status for risdiplam, a benefit assessment is to be carried out with the submission of evidence in accordance with Section 35a, paragraph 1, sentence 3, numbers 2 and 3 SGB V.

The approved therapeutic indication according to the product information is: "Evrysdi is indicated for the treatment of 5q spinal muscular atrophy (SMA) in patients 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies." The first listing in the directory services in accordance with Section 131, paragraph 4 SGB V took place on 1 May 2021.

The assessment of the necessity of a routine practice data collection was made on the basis of the ongoing or completed studies on risdiplam considered for the marketing authorisation.

The marketing authorisation of risdiplam is based on data from the pivotal studies BP39056 (FIREFISH), study part 2 and BP39055 (SUNFISH), study part 2.

Study parts 1 of the FIREFISH and the SUNFISH studies were considered in support of the marketing authorisation.

The FIREFISH study is a 1-arm study that included patients with genetically documented 5q SMA, age at the time of enrolment ≤ 7 months, age at symptom onset between 28 days and ≤ 3 months, and 2 SMN2 gene copies. In the first part of the study, 21 patients in 2 cohorts were treated with different doses of risdiplam; in the second part of the study, 41 patients were treated with the approved dose of risdiplam. Both parts of the study have a treatment duration of 24 months, followed by an open-label extension phase. At the time of marketing authorisation, the treatment phase of the second part of the study had not yet been completed, and the primary analysis was conducted at treatment month 12.

The SUNFISH study is a randomised, blinded controlled study that enrolled patients with a genetically confirmed diagnosis of 5q SMA and clinical symptoms of type 2 or type 3 SMA (non-ambulatory) and an age range of 2 to 25 years and the ability to sit independently. The first part of the study was a dose-finding study. In the second part of the study, 180 patients are treated with either risdiplam or placebo (in a 2:1 ratio) for 12 months, followed by 12 months of active treatment with risdiplam and 3 years of open-label follow-up treatment with risdiplam. At the time of marketing authorisation, the second part of the study had not yet been completed.

Based on the data basis of the studies mentioned, it can be assumed that no meaningful data are currently available in particular with regard to the following aspects that are relevant for the early benefit assessment:

- Comparative data of treatment with risdiplam versus existing appropriate therapeutic alternatives for patients in the approved therapeutic indication, including data for pre-symptomatic patients

The present indication is a chronic progressive disease that, if left untreated, will lead to death or be associated with progressive disability and reduction in quality of life.

However, in the present therapeutic indication, therapy alternatives are approved for which no direct comparison is available in the current health care context. However, a comparative assessment with regard to patient-relevant endpoints is considered necessary for an adequate assessment of the (additional) benefit and harm of risdiplam. Within the framework of routine practice data collection, data should therefore be collected in comparison with existing appropriate therapeutic alternatives in comparable health care contexts in order to improve the evidence base for a benefit assessment.

Furthermore, no data from pre-symptomatic patients are available on the basis of the studies mentioned. However, the timing of therapy initiation is fundamentally relevant in SMA, as the progressive degeneration of motor neurons begins before the first symptoms appear. Taking into account the earlier identification and treatment of children with SMA due to the inclusion of SMA in newborn screening in Germany, an increase in patients receiving therapy before the onset of symptomatology is expected. Since a possible extrapolation of data from symptomatic to pre-symptomatic SMA patients is associated with great uncertainties, the evidence base for pre-symptomatic patients should be improved by corresponding routine practice clinical data.

Treatment of 5q spinal muscular atrophy (SMA) with risdiplam is currently limited to patients 2 months of age and older. In the event of a corresponding extension of the marketing authorisation, the G-BA intends to extend the data collection within the scope of the routine practice data collection to include patients aged 0 to 2 months.

The G-BA can develop a concept for routine practice data collection itself or commission the Institute for Quality and Efficiency in Health Care (IQWiG) to develop a concept for routine practice data collection. The preparation of a concept should, in principle, not exceed a period of 6 months. In the present case, IQWiG is commissioned to prepare the concept. Given the complexity of the issues to be clarified and for capacity reasons, the preparation of the concept in the present case will exceptionally take more than 6 months. This does not adversely affect the parties to the proceedings.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

In order to prepare a recommendation for a resolution on the initiation of a procedure for the requirement of a routine practice data collection according to Section 35a, paragraph 3b, SGB V, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and the representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The recommended resolution on the initiation of a procedure for the requirement of a routine practice data collection was discussed on 28 Septembe 2021 at the subcommittee session and the draft resolution was approved.

At its session on 7 October 2021, the plenum decided to initiate a procedure for the requirement of a routine practice data collection pursuant to Section 35a, paragraph 3b, SGB V.

Chronological course of consultation

Session	Date	Subject of consultation
Working group Section 35a	2 June 2021 17 August 2021 31 August 2021 14 September 2021 21 September 2021	Consultation on the initiation of a procedure for the requirement of a routine practice data collection and evaluations
Subcommittee Medicinal product	28 September 2021	Discussion and consensus on the draft resolution
Plenum	7 October 2021	Resolution

Berlin, 7 October 2021

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken