Gemeinsamer Bundesausschuss

Justification

on the Resolution of the Federal Joint Committee (G-BA) on the Suspension of a Consultation Procedure under Section 35a paragraph 3b SGB V
Iptacopan (paroxysmal nocturnal haemoglobinuria); requirement of routine practice data collection and evaluations

of 20 March 2025

Contents

1. Legal basis

According to Section 35a, paragraph 3b, sentence 1 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), as last amended by Regulation 162 Rules of Procedure last revised: 16 December 2020 (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 approved for the treatment of rare diseases under Regulation No. 141/2000.

2. Key points of the resolution

The active ingredient iptacopan was approved by the European Commission (EC) on 17 May 2024 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 paroxysmal nocturnal haemoglobinuria.

The first listing in the directory services in accordance with Section 131 paragraph 4 SGB V took place on 1 July 2024.

On the basis of the ongoing or completed studies on iptacopan considered for the marketing authorisation, the G-BA identified gaps in the evidence, particularly for the following aspects relevant to the early benefit assessment, which justify the requirement of routine practice data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V for the active ingredient iptacopan:

- Data to assess the long-term (additional) benefit and harm of treatment with iptacopan for the approved sub-population of therapy-naïve adults with paroxysmal nocturnal haemoglobinuria (PNH) who have haemolytic anaemia;
- Comparator data of treatment with iptacopan versus existing therapeutic alternatives for the approved sub-population of therapy-naïve adults with PNH who have haemolytic anaemia

The marketing authorisation of iptacopan is based on data from the pivotal phase III CLNP023C12302 (APPLY-PNH) and CLNP023C12301 (APPOINT-PNH) studies.

In the APPLY-PNH study, patients pretreated with C5 antibodies were examined, which is why no data are available for the sub-population of therapy-naïve adults in question.

The APPOINT-PNH study and the phase II studies used to support the marketing authorisation also included therapy-naïve patients, but these were single-arm or non-comparator studies.

The study research only identified non-comparator studies for therapy-naïve adults with PNH. On this data basis, it can be assumed that no comparator data are available for treatment with iptacopan compared to existing therapeutic alternatives for therapy-naïve adults with PNH and that no improvement in the body of evidence can be expected, taking into account the

current study planning. Therefore, the G-BA considered it necessary to examine the extent to which the body of evidence for the assessment of the additional benefit of the present medicinal product can be improved by collecting data from healthcare by initiating a procedure for the requirement of a routine practice data collection.

By resolution of 1 August 2024, 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 iptacopan.

A concept was drawn up in preparation for the resolution on the requirement of routine practice data collection and evaluations. The concept contains in particular requirements for:

1. the type, duration and scope of data collection,
2. the research question (PICO framework: patient/population, intervention, comparison, outcomes) that is to be the subject of the data collection and evaluations, including the patient-relevant endpoints to be collected,
3. the data collection methods,
4. the evaluations by the pharmaceutical company according to Section 50, paragraph 2 of the VerfO.

The G-BA decides whether to prepare the concept itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG) to do so. In the present case, the G-BA commissioned IQWiG to prepare the concept. The expert bodies according to Section 35a, paragraph 3b, sentences 7 and 8 SGB V made a written submission in drawing up the concept. The submission took place in such a way that the expert bodies were given the opportunity in writing to comment on the requirements of routine practice data collection and evaluations in accordance with the concept that had been drawn up. In addition, expert consultation was held.

In preparing the concept, ongoing and planned data collections were taken into account, especially those resulting from conditions or other ancillary provisions imposed by the marketing authorisation or licensing authorities.

The Post-Authorisation Safety Study (PASS) CLNP023C12003 commissioned by the European Medicines Agency (EMA) investigates the safety risk of iptacopan in routine clinical practice based on the International PNH Interest Group (IPIG) registry. This study is designed as a non-comparator study. It can also be assumed that the PMR 4553-1 registry study commissioned by the US Food and Drug Administration (FDA) to investigate long-term safety is designed as a non-comparator study. In addition, the ongoing CLNP023C1US01 study, which uses a health app to collect data from everyday care in the USA, was identified. This study is also unsuitable for closing the existing gaps in the evidence, as no comparison with the comparators was designed and important patient-relevant endpoints (e.g. side effects) were not assessed.

Thus, the further studies on iptacopan for therapy-naïve adults identified when the concept was drawn up are unsuitable for closing the gaps in the evidence in the relevant aspects for the early benefit assessment.

Based on the above-mentioned research question, the G-BA deliberated on the requirements for routine practice data collection and evaluations on the basis of IQWiG's concept and the participation of the expert bodies in the concept.

In principle, the IPIG registry is a suitable data source for carrying out a routine practice data collection. Patients with any PNH therapy are included in this registry, patient-reported endpoints are documented and sufficient recruitment can be assumed due to the global outlook. It also became clear in the expert consultation that the IPIG registry already records

the data listed in the IQWiG concept, which should be collected in the routine practice data collection.

However, the IPIG registry is subject to several limitations with regard to its governance structures.

The IPIG registry is not designed to make the elaborately collected data available for comparative analyses. This is due to the governing confidentiality agreements and the specified registry structure (consisting of a core dataset and substance-specific data silos). Various pharmaceutical companies are part of the supervisory bodies of the registry, which limits scientific autonomy to some extent. Each pharmaceutical company has an 18-month exclusivity right to the data collected in their substance-specific data silo. Iptacopan and the comparators eculizumab and ravulizumab are sold by different pharmaceutical companies, so that the pharmaceutical company of iptacopan does not have access to the data silos of the comparators. The data silos also differ in the endpoints assessed, which are defined and collected specifically for each active ingredient in addition to the core dataset. At the end of the 18-month period, some of the data collected from the data silos is transferred to the core dataset. According to the explanations in the expert consultation, comparative analyses would only be possible based on the provided, aggregated reports of the individual data silos as no comparative analyses can be carried out from the core dataset either. The provision of aggregated data alone is inadequate for the proper implementation and evaluation of a routine practice data collection by the pharmaceutical company; instead, data is required on a patient-individual level. This is not possible due to the current registry structure.

Due to this registry structure and the strict confidentiality agreements, a data platform to be set up specifically for the routine practice data collection (study-specific data collection) would be the only way to realise the routine practice data collection (including comparative analyses for the benefit assessment). The set-up of a parallel structure to a fundamentally well-suited registry with a comprehensive endpoint assessment is considered disproportionate by the G-BA due to the circumstances of the individual case.

In the overall assessment, the generation of routine practice data, which would improve the existing body of evidence sufficiently for the purpose of the benefit assessment, is considered infeasible in the present case.

Therefore, the G-BA suspends the consultation on the requirement of routine practice data collection and evaluations for the active ingredient iptacopan in the treatment of therapy-naïve adults with paroxysmal nocturnal haemoglobinuria who have haemolytic anaemia.

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 (amendment of Annex XII of AM-RL) according to Section 35a, paragraph 3b SGB V, the Subcommittee on Medicinal Products commissioned a working group (WG routine practice data collection (RPDC)) 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. In addition, the competent higher federal authority, the Paul Ehrlich Institute, was involved in the consultation to assess the requirement of a routine practice data collection according to Section 35a, paragraph 3b, sentence 1 SGB V.

The recommended resolution on the initiation of a procedure for the requirement of a routine practice data collection was discussed on 23 July 2024 at the subcommittee session and the draft resolution was approved.

At their session on 1 August 2024, the plenum resolved to initiate a procedure for the requirement of a routine practice data collection.

In conjunction with the resolution of 1 August 2024 regarding the initiation of a procedure for the requirement of a routine practice data collection, the G-BA commissioned IQWiG to scientifically develop a concept for routine practice data collection and evaluations for the purpose of preparing a resolution.

IQWiG's concept was submitted to the G-BA on 4 November 2024. On 5 November 2024, the written submission of the expert bodies according to Section 35a, paragraph 3b, sentences 7 and 8 SGB V was initiated. The deadline for making the written submission was 3 December 2024.

The expert consultation within the framework of the submission by the expert bodies took place on 27 January 2025.

The evaluation of the written submissions received and of the expert consultation was discussed at the session of the Subcommittee on 11 March 2025, and the proposed resolution was approved.

At their session on 20 March 2025, the plenary decided on the suspension of consultations on the requirement of routine practice data collection and evaluations.

Chronological course of consultation

Session	Date	Subject of consultation
WG RPDC	7 September 2023 5 October 2023 2 November 2023 5 January 2024 15 July 2024	Consultation on the initiation of a procedure for the requirement of a routine practice data collection (amendment of Annex XII of the AM-RL), involvement of the higher federal authority
Subcommittee on Medicinal Products	23 July 2024	Concluding discussion of the draft resolution
Plenum	1 August 2024	Resolution on the initiation of a procedure for the requirement of a routine practice data collection (amendment of Annex XII of the AM-RL)
WG RPDC	20 January 2025	Information on written submissions received, preparation of the expert consultation
Subcommittee on Medicinal Products	27 January 2025	Implementation of the expert consultation
WG RPDC	6 February 2025 17 February 2025 6 March 2025	Consultation on IQWiG's concept and on the specifications for the review of the obligation to conduct and submit evaluations, evaluation of the submission procedure
Subcommittee on Medicinal Products	11 March 2025	Concluding discussion of the draft resolution
Plenum	20 March 2025	Resolution on the suspension of the consultation procedure on the requirement of a routine practice data collection

Berlin, 20 March 2025

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

Prof. Hecken