Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on a Finding in the Procedure of Routine Practice Data Collection and Evaluations according to Section 35a, paragraph 3b SGB V: Etranacogene dezaparvovec (haemophilia B) – Review of study protocol, statistical analysis plan and interim analyses

From 2 July 2026

At their session on 2 July 2026, the Federal Joint Committee (G-BA) decided the following in the procedure of routine practice data collection and evaluations according to Section 35a, paragraph 3b SGB V for the active ingredient etranacogene dezaparvovec (haemophilia B):

I. It is noted that the pharmaceutical company have not fully implemented the requirements for the implementation of the routine practice data collection (RPDC) and evaluations in the submitted, revised versions of the study protocol and the statistical analysis plan (SAP) (version 4.0 of 27 February 2026) as stated in the declaratory resolution of 18 July 2024. Furthermore, the submitted, revised versions of the study protocol and the SAP as well as the review of the approach taken in the 1st interim analysis indicate that further adaptations are required. The routine practice data collection can therefore only be continued under the condition that the following adaptations to the study protocol and the statistical analysis plan (version 4.0 of 27 February 2026), which are deemed mandatory for the implementation of the requirements pursuant to Section 58, paragraph 1, number 1 Rules of Procedure (VerfO), are made:

a) Interpretation of the data: Confounder

The exclusion of potentially relevant confounders must be justified in the study documents with regard to content. The missing collection of confounders classified as relevant (in the absence of an adequate reason for exclusion) must be addressed as uncertainty in the study documents and the consideration of this must be described in the interpretation of the results.

b) Study design: Discontinuation criteria

The two criteria for study discontinuation, as defined in the study documents, must be revised due to uncertainties.

Changes that go beyond the conditions in the declaratory resolution of 18 July 2024:

c) Start of monitoring for the endpoints of haemorrhage and Factor IX infusions:

Unlike previous versions, the current study documents state that the start of monitoring for the endpoints on haemorrhage and Factor IX infusions in the intervention arm has been postponed to day 21 following the infusion of etranacogene dezaparvovec. No adjustment was made to the comparator arm in the study documents, meaning that monitoring of these endpoints in the comparator arm commenced from the index date, as originally planned for both treatment groups. However, it must be ensured that analyses are carried out consistently for both treatment arms from the index date onwards. Postponement of the start of monitoring for the endpoints on haemorrhage and Factor IX infusions in the intervention arm to day 21 following the infusion of etranacogene dezaparvovec must therefore be cancelled.

d) Operationalisation of the responder analyses for the patient-reported endpoints and joint function:

In the previous version of the study documents (version 3.0 of 23 May 2024), the adjustment made to the operationalisation of the responder analyses for the patient-reported endpoints and joint function was deemed appropriate. However, the current version of the study documents (version 4.0 of 27 February 2026) still contains, in some instances, the original operationalisation of a responder (a patient who, on at least two occasions, shows a change in score by ≥ 15% of the scale range compared with baseline), which cannot be meaningfully interpreted. Any passages that still contain the original definition of a responder should be revised accordingly.

e) Evaluation of side effects:

In the report on the 1st interim analysis, the pharmaceutical company provided no data in the methodology section regarding the collection and evaluation of specific adverse events (AEs) (formation of Factor IX inhibitors, thromboembolic events, symptomatic liver damage, malignant neoplasms). However, side effects must be collected and evaluated for the following interim analyses and the renewed benefit assessment, as required by the G-BA's resolution and as planned in the study documents (overall rate of SAEs and specific AEs, specifying the respective severity grade).

f) Presentation of pre-specified patient characteristics:

It is unclear why the pre-specified patient characteristics "History of Factor IX inhibitors" and "Known advanced liver fibrosis or cirrhosis" – the presence of which leads to exclusion from the study – were not presented for the 1st interim analysis, particularly as these are included in the DHR data record. In particular, given that the individual inclusion and exclusion criteria for the routine practice data collection cannot be fully recorded in the DHR, and that compliance with the inclusion criteria and non-compliance with the exclusion criteria are only documented using a single field, at least those inclusion and exclusion criteria that can be recorded individually must be presented for the following interim analyses and the renewed benefit assessment.

II. The revised study protocol and the revised SAP must be submitted to the G-BA by 30 April 2028.

III. The resolution will enter into force on the day of its publication on the G-BA website on

2 July 2026.

The justification for this resolution will be published on the G-BA website at www.g-ba.de.

Berlin, 2 July 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Dr Optendrenk