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 and statistical analysis plan and start of RPDC

of 18 July 2024

At its session on 18 July 2024, 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 stated that the implementation of the requirements for routine practice data collection and evaluations in the study protocol and statistical analysis plan prepared by the pharmaceutical company and submitted to the G-BA for review are considered fulfilled under the condition that the pharmaceutical company is obliged to make the following further adjustments to the study protocol (version 3.0, 23 May 2024) and the statistical analysis plan (SAP; version 3.0, 23 May 2024)that are considered necessary:

a) Data source: Collection of baseline data

The fact that the baseline data are checked for timeliness on the index date is to be added to the study documents.

b) Data source: Completeness of the data

Financial incentives alone are not sufficient to increase the completeness of the documentation of data that is not subject to mandatory collection in the DHR.

Incentivising the enrolled patients in the PRO instruments is inappropriate and should be deleted.

Information on how to deal with possible missing values for data not subject to mandatory collection, or how these could be avoided in the best possible way (e.g. intensification of monitoring), must be added to the study documents.

c) Data source: Source Data Verification

A 100% source data verification for the data field "Patient participates in RPDC and fulfils all necessary inclusion criteria and none of the exclusion criteria" must be ensured by the pharmaceutical company with regard to all inclusion and exclusion criteria defined in the study protocol.

The planned definition of event-related monitoring visits at 4 study sites is incomprehensible and must be adjusted accordingly.

d) Data source/ study design: Confounders

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 must be addressed as uncertainty in the study documents and the consideration of this must be described in the interpretation of the results.

e) Study design: Discontinuation criteria

Information on specific discontinuation criteria must be added to the study documents.

f) Data evaluation: Sensitivity analyses

A sensitivity analysis taking into account the entire control group must be added.

g) Data evaluation: Confounder adjustment

The description of the respective patient population (total, included in the analysis, excluded from the analysis) should be based on the baseline characteristics and not only on the confounders. This must be revised in the study documents.

h) Data evaluation: shifted hypothesis boundary

In the study protocol and SAP, it is to be specified, taking into account the non-randomised study design, that a shifted hypothesis boundary of 0.2 to 0.5 is used for the evaluation and interpretation of the results data, depending on the quality of the data collection and evaluation. In addition, a section should be added to the study protocol and SAP that addresses the interpretation of the results of the data, taking into account the non-randomised study design and using an appropriate shifted hypothesis boundary (in the range between 0.2 and 0.5).

i) Data evaluation: Subgroup analyses

For the subgroup analysis of the factors of joint status and annualized bleeding rate (ABR) 12 months prior to enrolment in the study, a justified cut-off value must be defined a priori in each case, which does not depend on the study results.

The subgroup analysis for the AAV5 antibody is redundant and should therefore be deleted.

In order to avoid inconsistencies, the pharmaceutical company must check whether the need for changes in the study protocol described here leads to corresponding subsequent changes in the SAP and vice versa.

II. The routine practice data collection starts on 30 August 2024.

III. The revised study protocol and the revised SAP are to be submitted to the G-BA by 2 March 2026.

IV. The resolution will enter into force on the day of its publication on the website of the G-BA on 18 July 2024.

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

Berlin, 18 July 2024

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

Prof. Hecken