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: Onasemnogene Abeparvovec (spinal muscular atrophy) – Review of Study Protocol and Statistical Analysis Plan

of 20 October 2022

At its session on 20 October 2022, 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 onasemnogene abeparvovec (spinal muscular atrophy):

I. It is noted that the pharmaceutical company has 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 3.01 of 13 July 2022) as stated in the declaratory resolution of 20 January 2022. The revised study documents also contain far-reaching changes that go beyond the requirements of the G-BA in the declaratory resolution of 20 January 2022. The routine practice data collection can therefore only be carried out under the condition that the following adaptations to the study documents (version 3.01 of 13 July 2022), which are deemed mandatory for the implementation of the requirements pursuant to Section 58, paragraph 1, no. 1 VerfO, are made:

1. The following adaptations are to be made to the study protocol and the SAP (version 3.01 of 13 July 2022):

a) Study design: *Selection of confounders*

In the declaratory resolution of 20 January 2022, the pharmaceutical company was instructed to classify the confounder "age at symptom onset" as "very important" instead of "less important" in the sub-populations of symptomatic patients. The requirement was not implemented in the present study protocol (version 3.01 of 13 July 2022)

The defect must be remedied.

b) Evaluation of data collection: *Analysis of the endpoints*

With regard to the examination of the suitability of non-parallel data on nusinersen, the pharmaceutical company was instructed in the declaratory resolution of 20 January 2022 to use the respective other sample for sensitivity analyses in central evaluations of the samples of the data collected in parallel and not in parallel. The required planning for sensitivity analyses regarding the data collected in parallel and not in parallel is missing in the present SAP, as well as in the study protocol (version 3.01 of 13 July 2022).

The defect must be remedied.

c) Changes that go beyond the conditions in the declaratory resolution of 20 January 2022

The submitted versions 3.01 of the study protocol and the SAP of 13 July 2022 not only include changes that resulted from the requirements of the G-BA in the declaratory resolution of 20 January 2022. The pharmaceutical company has not clearly and completely labelled all changes. In addition, there are significant inconsistencies in the study protocol and SAP due to the changes made within the documents and between the documents, also with regard to central points of content[1]. The impact of these changes on the RPDC study using the SMArtCARE registry as the primary data source therefore remains unclear.

All changes that go beyond the requirements of the G-BA in the declaratory resolution of 20 January 2022 must be reversed accordingly.

When resubmitting the revised version of the study protocol and the SAP, the pharmaceutical company must ensure that the changes made can be completely and clearly understood.

Amendments that do not result from the need for adjustment set out in this declaratory resolution and the associated justification must be justified separately and must be submitted in a separate addendum to the study protocol or SAP.

III. The resolution will enter into force on the day of its publication on the website of the G-BA on 20 October 2022.

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

Berlin, 20 October 2022

1 IQWiG report – No. 1417: Routine practice data collection of onasemnogene abeparvovec: Review of the study protocol and statistical analysis plan 3rd addendum to the mandate A20-61, addendum A22-84, last revised: 06.09.2022.

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

Prof. Hecken