Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a (SGB V)
Crizanlizumab (repeal of the resolution of 20 May 2021)

of 19 October 2023

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V). Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a, paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 30 million in the last 12 calendar months. According to Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, paragraphs 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5, Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation, the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the turnover limit according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit assessment. According to Section 35a paragraph 2 SGB V, the assessment by the G-BA must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient crizanlizumab was first approved as a medicinal product on 28 October 2020 (Adakveo). The marketing authorisation was granted for the therapeutic indication: "Adakveo is indicated for the prevention of recurrent vaso-occlusive crises (VOCs) in sickle cell disease patients aged 16 years and older. It can be given as an add-on therapy to hydroxyurea/hydroxycarbamide (HU/HC) or as monotherapy in patients for whom HU/HC is inappropriate or inadequate." This marketing authorisation received a conditional marketing authorisation for a medicinal product for the treatment of an orphan disease.

After the active ingredient crizanlizumab was placed on the market for the first time on 1 December 2020, the G-BA conducted a benefit assessment according to Section 35a and supplemented Annex XII of the Pharmaceuticals Directive with the active ingredient crizanlizumab by resolution of 20 May 2021.

The benefit assessment was based on the results of the phase 2 SUSTAIN study. Against the background that the medicinal product Adakveo was granted conditional marketing authorisation, the European Medicines Agency EMA required that the results of the phase 3 study STAND be submitted with regard to the evidence to be provided by the pharmaceutical company. The submission of the primary analysis of the results of this study to the EMA was expected by December 2025.

The G-BA limited the validity of its resolution on the benefit assessment of crizanlizumab until 1 December 2025 and stipulated submission of the results on all patient-relevant endpoints used for the proof of an additional benefit, including the results of the STAND study for the new benefit assessment after the expiry of the deadline.

End of May 2023, the EMA recommended that the marketing authorisation for the medicinal product Adakveo be repealed. This recommendation was based on the assessment of the results of the phase 3 STAND study, according to which crizanlizumab did not lead to a reduction in pain crises compared to placebo.

On 3 August 2023, the marketing authorisation for Adakveo was repealed by the European Commission due to the facts described above. With this repeal of the marketing authorisation, the basis for the benefit assessment according to Section 35a paragraph 1 SGB V by the G-BA no longer applies. Consequently, the resolution on crizanlizumab dated 20 May 2021 (BAnz AT 24.06.2021 B5) must be repealed.

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

Session	Date	Subject of consultation
Working group Section 35a	6 September 2023	Consultation on the draft resolution
Subcommittee Medicinal products	12 September 2023	Consultation and consensus on the draft resolution on the repeal of the resolution
Plenum	19 October 2023	Adoption of the repeal of the resolution

Berlin, 19 October 2023

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

Prof. Hecken