Gemeinsamer Bundesausschuss

Justification

for the resolution of the Federal Joint Committee for suspension of a benefit assessment procedure in accordance with Section 35a SGB V on brentuximab vedotin (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit; new therapeutic indication: Hodgkin lymphoma, CD30+, stage III, first-line)

of 18 July 2024

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, half-sentence 1 SGB V. Evidence of the medical benefit and the additional medical benefit do not have to be submitted (Section 35a, paragraph 1, sentence 11, half-sentence 2 SGB V). Section 35a paragraph 1 sentence 11, half-sentence 1 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, Nos. 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. Only the extent of the additional benefit has to be proven.

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, 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 of the G-BA and prove the additional benefit in comparison with the appropriate comparator therapy.

2. Key points of the resolution

Brentuximab vedotin was approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999. Brentuximab vedotin was recently designated as an orphan drug for three therapeutic indications (EU/3/08/595, EU/3/08/596, EU/3/11/939), which were entered in the Community Register of Orphan Medicinal Products in accordance with Article 5 paragraph 9 of Regulation (EC) No. 141/2002.

The active ingredient brentuximab vedotin (Adcetris) was listed for the first time on 1 December 2012 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices. The G-BA conducted a benefit assessment in accordance with Section 35a and added the active ingredient brentuximab vedotin to Annex XII of the Pharmaceuticals Directive by resolution of 16 May 2013 (BAnz AT 25.06.2013 B6).

In the subsequent period till 2020, brentuximab vedotin (Adcetris) received marketing authorisation for four additional new therapeutic indications to be classified as a major type 2 variation as defined according to Annex 2 number 2 letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products (OJ L 334 of 12.12.2008, p. 7). A benefit assessment in accordance with Section 35a SGB V was carried out for each of these, taking Section 35a paragraph 1 sentence 11 SGB V into account. The information on the active ingredient brentuximab vedotin was added to Annex XII of the Pharmaceuticals Directive by resolutions of 19 January 2017 (BAnz

AT 08.02.2017 B5), 5 July 2018 (BAnz AT 19.09.2018 B3), 5 September 2019 (BAnz AT 27.09.2019 B1) and 16 December 2021 (BAnz AT 02.02.2022 B2).

Not so long ago on 12 October 2023, brentuximab vedotin (Adcetris) received marketing authorisation for the new therapeutic indication "is indicated for adult patients with previously untreated CD30+ Stage III Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD)". The pharmaceutical company submitted a dossier for this new therapeutic indication in due time in accordance with Section 35a, paragraph 1, sentence 11 SGB V.

If the sales of the orphan drug through the statutory health insurance at pharmacy sales prices and outside the scope of SHI-accredited medical care, including value-added tax, exceed an amount of € 30 million in the last twelve calendar months, the pharmaceutical company must submit evidence in accordance with Section 5, paragraphs 1 to 6 within three months of being requested to do so by the Federal Joint Committee, and in this evidence must demonstrate the additional benefit compared to the appropriate comparator therapy.

Brentuximab vedotin exceeded the EUR 30 million turnover limit no later than 31 May 2023 and has not yet been assessed with evidence of medical benefit and additional medical benefit in relation to the appropriate comparator therapy. By letter of 18 January 2024, the G-BA requested the pharmaceutical company to submit a complete dossier for the six therapeutic indications listed below by 2 May 2024:

<u>Hodgkin lymphoma</u>

- ADCETRIS is indicated for adult patients with previously untreated CD30+ Stage III and IV Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD) (see sections 4.2 and 5.1).
- ADCETRIS is indicated for the treatment of adult patients with CD30+ HL at increased risk of relapse or progression following autologous stem cell transplant (ASCT) (see section 5.1).
- ADCETRIS is indicated for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL), following: 1. ASCT, or 2. at least two prior therapies, if ASCT or multi-agent chemotherapy is not a treatment option.

<u>Systemic anaplastic large cell lymphoma</u>

- ADCETRIS in combination with cyclophosphamide, doxorubicin and prednisone (CHP) is indicated for adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL) (see section 5.1).
- ADCETRIS is indicated for the treatment of adult patients with relapsed or refractory sALCL:

<u>Cutaneous T-cell lymphoma</u>

- ADCETRIS is indicated for the treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) after at least 1 prior systemic therapy (see section 5.1).

The benefit assessment procedure that commenced on 15 November 2023 for the new therapeutic indication approved in October 2023 was temporarily suspended by resolution of 18 January 2024. Following the omission of the procedural simplifications due to the turnover limit being exceeded, the dossier submitted by the pharmaceutical company was unsuitable in relation to the appropriate comparator therapy on the basis of the studies used for the marketing authorisation without proof of additional benefit.

On 2 May 2024, the pharmaceutical company has submitted in due time the dossier in accordance with Section 4, paragraph 3, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 6 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient brentuximab vedotin with the six therapeutic indications mentioned above (Hodgkin lymphoma, systemic anaplastic large cell lymphoma and cutaneous T-cell lymphoma).

On 21 June 2024, the pharmaceutical company informed the G-BA that the orphan designation (EU/3/08/595, EU/3/08/596, EU/3/11/939) for the active ingredient brentuximab vedotin had been withdrawn and that the active ingredient was no longer listed in the European Commission's Community Register of Orphan Medicinal Products with effect from 20 June 2024. At the investor’s request, a medicinal product designated as an orphan drug is deleted from the Community Register for Orphan Medicinal Products in accordance with Art. 5 paragraph 12 letter a) Regulation (EC) No. 141/2000. The announced withdrawal of orphan designations has been completed in the Community Register for Orphan Medicinal Products as of 20 June 2024.

Since the factual prerequisites for a benefit assessment according to Section 35a SGB V are no longer fulfilled upon timely adoption of the resolution on 17 October 2024, the six benefit assessment procedures for brentuximab vedotin according to Section 35a SGB V will be discontinued. The benefit assessment procedure for the therapeutic indication "is indicated for adult patients with previously untreated CD30+ Stage III Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD)", which commenced on 15 November 2023 and suspended by resolution of 18 January 2024, will also be discontinued.

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

On 2 May 2024, the pharmaceutical company submitted a dossier for the benefit assessment of brentuximab vedotin to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 3 May 2024 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient brentuximab vedotin.

The proposed resolution was discussed and approved at the session of the subcommittee on 9 July 2024.

At its session on 18 July 2024, the plenum decided to discontinue the benefit assessment procedure according to Section 35a SGB V.

Chronological course of consultation

Session	Date	Subject of consultation
Working group Section 35a	2 July 2024	Consultancy on the discontinuation of the procedure according to Section 35a SGB V
Subcommittee Medicinal products	9 July 2024	Consultancy on the discontinuation of the procedure according to Section 35a SGB V
Plenum	18 July 2024	Resolution on the discontinuation of the procedure according to Section 35a SGB V

Berlin, 18 July 2024

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

Prof. Hecken