Justification

Gemeinsamer Bundesausschuss

to the Resolution of the Federal Joint Committee (G-BA) on the Discontinuation of the Benefit Assessment of Ceftolozan/Tazobactam According to Section 35a SGB V

of 17 September 2020

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. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. Approved therapeutic indications,
2. Medical benefit,
3. Additional medical benefit in relation to the appropriate comparator therapy,
4. Number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. Treatment costs for statutory health insurance funds,
6. Requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment 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 forms part of the Pharmaceuticals Directive.

According to Section 35a, paragraph 1c SGB V, antibiotics that are effective against infections caused by multi-resistant bacterial pathogens for which only limited alternative treatment options are available and for which the use is subject to a strict indication (last-resort antibiotic) can be exempted from the obligation to present the evidence according to Section 35a, paragraph 1, sentence 3, numbers 2 and 3 SGB V. The details of the application procedure are regulated by the Rules of Procedure of the Federal Joint Committee until 31 December 2020. In agreement with the Federal Institute for Drugs and Medical Devices, the Robert Koch Institute shall determine criteria for the classification of an antibiotic as a last-resort antibiotic according to the current state of medical science by 31 December 2020 and publish these criteria on its website.

2. Key points of the resolution

The active ingredient combination ceftolozan/tazobactam (Zerbaxa) was listed for the first time on 1 December 2015 in the “LAUER-TAXE®”, the extensive German registry of available drugs and their prices with the therapeutic indications complicated intra-abdominal infections in adults, complicated urinary tract infections in adults, and acute pyelonephritis in adults.

The active ingredient combination ceftolozan/tazobactam was exempted from the benefit assessment on the basis of insignificance by resolution of 20 August 2015.

On 23 August 2019, Zerbaxa received marketing authorisation for the new therapeutic indication hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP) in adults, which is classified as a major variation of Type 2 according to Annex 2, number 2a to Regulation (EC) No. 1234/2008 of the Commission from 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12 December 2008, p. 7).

On the occasion of an extension of the therapeutic indication for the proprietary medicinal product Zerbaxa, the factual requirements for the continued exemption of the medicinal product were reviewed on the basis of Chapter 5, Section 15 VerfO as amended by the resolution of 16 March 2018.

At its session on 17 October 2019, the G-BA resolved to revoke the exemption of the medicinal product Zerbaxa with the active ingredient combination ceftolozan/tazobactam from the benefit assessment because of insignificance according to Section 35a, paragraph 1a SGB V with effect from 17 October 2019 and requested the pharmaceutical company to submit a dossier for all approved therapeutic indications by 1 April 2020.

On 11 March 2020, the pharmaceutical company submitted a dossier in accordance with Section 4, paragraph, 3 number 2 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient combination ceftolozan/tazobactam in the therapeutic indications of hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP) in adults, complicated intra-abdominal infections in adults, complicated urinary tract infections in adults, and acute pyelonephritis in adults.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 July 2020 on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held on 10 August 2020.

In the light of the above and taking into account the statements received and the oral hearing, the G-BA has arrived at the following decision:

The procedure for the benefit assessment of ceftolozan/tazobactam according to Section 35a SGB V is discontinued because the prerequisites for the benefit assessment according to Section 35a SGB V, old version, no longer apply at the time of the resolution with regard to an application for exemption from the benefit assessment according to Section 35a, paragraph 1c SGB V, which was initially submitted in a letter dated 20 August 2020. With the entry into force of the Act on Fair Competition between Health Insurance Funds in Statutory Health Insurance (Fairer-Kassenwettbewerb-Gesetz – GKV-FKG) of 27 March 2020 (Federal Law Gazette I, p. 587), a paragraph 1c was added to Section 35a SGB, according to which the Federal Joint Committee must exempt pharmaceutical companies from the obligation to submit the evidence according to paragraph 1, sentence 3, numbers 2 and 3 upon request if the antibiotic in question is effective against infections caused by multi-resistant bacterial pathogens for which only limited alternative treatment options are available and the use of which is subject to a strict indication (last-resort antibiotic). This legal situation, which provides for a privileged treatment of last-resort antibiotics in the procedure of early benefit assessment, must be applied by the Federal Joint Committee to all procedures that are concluded after the entry into force of the GKV-FKG because of the lack of a statutory transitional regulation. Although an application for exemption according to sentence 1 is admissible only before the first obligation to submit the evidence according to paragraph 1, sentence 3 the pharmaceutical company submitted this application when submitting the dossier on 11 March 2020. In his written statement, the pharmaceutical company explained the reserve status of ceftolozan/tazobactam and made these considerations also in view of the change in the legal situation and the reserve status to be evaluated by the Federal Joint Committee afterwards. It was possible to decide on the analogously submitted application only when the GKV-FKG entered into force. The decision was subject to the verification of a corresponding application

according to Section 35a, paragraph 1c SGB V as amended by the GKV-FKG. This was completed by the pharmaceutical company in a letter dated 20 August 2020.

In view of the statements made in the written and oral objections in the written statement procedure, which do not exclude the possibility of a reserve status for the antibiotic, there is a sufficient reason to review the reserve status in a procedure according to Section 35a, paragraph 1c SGB V on the basis of the RKI criteria as soon as they are available. According to the legal concept of Section 35a, paragraph 1c SGB V, this procedure anticipates the benefit assessment procedure, which is why the benefit assessment procedure had to be discontinued on the basis of Section 35a SGB V, old version.

3. Bureaucratic costs

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

At its session on 8 January 2019, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 11 March 2020, the pharmaceutical company submitted a dossier for the benefit assessment of ceftolozan/tazobactam to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 12 March 2020 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits 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 ceftolozan/tazobactam.

The dossier assessment by the IQWiG was submitted to the G-BA on 29 June 2020, and the written statement procedure was initiated with publication on the website of the G-BA on 1 July 2020. The deadline for submitting written statements was 22 July 2020.

The oral hearing was held on 11 August 2020.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The draft resolution was discussed and agreed at the session of the subcommittee on 8 September 2020.

At its session on 17 September 2020, the plenum decided to discontinue the benefit assessment of ceftolozan/tazobactam according to Section 35a SGB V and, at the same time, decided to suspend the procedure regarding an application for exemption from the obligation to submit evidence according to Section 35a, paragraph 1c SGB V.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	8 January 2019	Determination of the appropriate comparator therapy
Working group Section 35a	4 August 2020	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	11 August 2020	Conduct of the oral hearing
Working group Section 35a	18 August 2020 2 September 2020	Consultation on the further procedure
Subcommittee on Medicinal Products	8 September 2020	Concluding discussion of the draft resolution
Plenum	17 September 2020	Resolution on the discontinuation of the benefit assessment of ceftolozan/tazobactam

Berlin, 17 September 2020

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

Prof. Hecken