# Justification

Gemeinsamer Bundesausschuss

## to the Resolution of the Federal Joint Committee (G-BA) on an amendment to the Pharmaceuticals Directive (AM-RL): Annex XII – Amendment of Information on the Period of Validity of a Resolution on the Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Cabozantinib

From 06 June 2019

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## 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 a rare disease (orphan drugs) that are approved according to Regulation (EC) number 141/2000 of the European Parliament and of the Council of 16 December 1999, according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medicinal benefit is deemed to be proven through the grant of the marketing authorisation. Evidence of the medicinal benefit and the additional medicinal benefit in relation to the appropriate comparator therapy need not 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, numbers 2 and 3 German Social Code, Book Five (SGB V in conjunction with the 5th Chapter, Sections 5 *et seq.* of the Rules of Procedure, G-BA (VerfO) has not been carried out. Only the extent of the additional benefit has to be demonstrated.

However, the restricted benefit assessment for orphan drugs as linked by law to marketing authorisation does not apply if SHI sales of the medicinal product at pharmacy sales prices including VAT exceed €50 million in the last 12 calendar months. According to Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company must, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, subsection 1–6 VerfO, in particular regarding the additional medicinal benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5, Section 6 VerfO. In this dossier, the pharmaceutical company must also provide evidence of the additional benefit in relation to the appropriate comparative 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). On the basis of the statutory requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is deemed to have been proven through the grant of marketing authorisation, the G-BA modified the procedure for the benefit assessment of orphan drugs at its meeting on 15 March 2012 to the effect that, in the case of orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit provided by the G-BA is evaluated exclusively on the basis of the approval studies.

Accordingly, at its meeting on 15 March 2012, the G-BA amended the mandate given to the IQWiG in its 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 in such a way that, in the case of orphan drugs, IQWiG is only commissioned to carry out a benefit assessment in case of a previously defined comparator therapy when the sales volume of the drug concerned has exceeded the legal limit of €50 million and is therefore subject to an unrestricted benefit assessment (*cf* Section 35a, paragraph 1, sentence 12 SGB V. 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 shall pass a resolution 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.

## 2. Key points of the resolution

In its meeting on 22 January 2015, the G-BA passed a resolution on the benefit assessment of cabozantinib in the therapeutic indication “Treatment of medullary thyroid carcinoma in adult patients with progressive, non-resectable, locally advanced or metastatic disease” in accordance with Section 35a SGB V. The period of validity of the resolution was limited to 1 June 2018. By resolution of 18 January 2018, the period of validity of the resolution was extended to 1 January 2020 at the request of the pharmaceutical company.

The original limitation was based on the fact that the pharmaceutical company is obliged to submit further data on the efficacy and safety endpoints of cabozantinib to the EMA on the basis of its conditional marketing authorisation for the present therapeutic indication in accordance Article 14 paragraph 7 of Regulation (EC) No. 726/2004 in conjunction with Article 4 Regulation (EC) No. 507/2006. The requirements of the EMA relate to the data of the XL-184-401 study in which, in particular, the dosage of cabozantinib and the RET and RAS mutation status of the patients are to be further investigated. By resolution of 18 January 2018, the deadline was extended to 1 January 2020 on the grounds that the pharmaceutical company had shown that the XL-184-401 study was in the extended recruitment phase and that full recruitment, monitoring, and data evaluation could not be implemented by 1 June 2018. In order to further extend the limitation of the period of validity of the resolution, the pharmaceutical company stated that the XL-184-401 study is still in the extended recruitment phase and that the number of events pre-specified in the study protocol to evaluate the study will not be reached by 1 January 2020.

In addition, the EMA has extended the deadline for the submission of data from the XL-184-401 study to 30 September 2020. It is therefore plausible that the data necessary for the new benefit assessment will not be available by 1 January 2020.

To enable a new benefit assessment to be carried out using the required data from the XL-184-401 study, it was resolved to extend the limitation until 1 November 2020.

In accordance with Section 3 number 5 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 1 paragraph 2 number 7 VerfO, the procedure for the benefit assessment of the active ingredient Cabozantinib begins again when the deadline has expired. This requires the pharmaceutical company to submit a dossier to the G-BA at the latest on the day of expiry of the deadline for the benefit assessment of Cabozantinib (Section 4, paragraph 3, number 5 AM-NutzenV in conjunction with Chapter 5, Section 8, number 5 VerfO). In principle, an extension of the limitation may be granted if it is justified and clearly demonstrated that the period of the time limit up to 1 November 2020 is not sufficient.

The possibility that a benefit assessment for Cabozantinib can be carried out at an earlier point in time for other reasons (*cf* Chapter 5, Section 1, paragraph 2, numbers 2, 3, 5, and 6 VerfO) remains unaffected by this.

## 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

The matter was discussed in the medicinal products sub-committee, and an amendment resolution was passed.

At its meeting on 06 June 2019, the plenum resolved to change the limitation of the period of validity of the resolution.

Berlin, 06 June 2019

Federal Joint Committee
in accordance with Section 91 SGB V
Chair

Prof Hecken