Justification

Gemeinsamer Bundesausschuss

to the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Ropeginterferon Alfa-2b (Number of Patients)

of 16 July 2020

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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. According to Section 35a, paragraph 6 SGB V, the G-BA may also arrange for a benefit assessment according to Section 35a, paragraph 1 SGB V for reimbursable medicinal products containing an active ingredient that is not a new active ingredient within the meaning of Section 35a, paragraph 1 SGB V if a new marketing authorisation with new data protection is granted for the medicinal product. 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 Chapter 5, Section 20, paragraph 4 of the VerfO, the Subcommittee on Medicinal Products may, in the event of a need for change in the sense of a factual and mathematical correction with regard to the information according to Chapter 5, Section 20, paragraph 3, no. 2 (number of patients or demarcation of patient groups eligible for treatment) or no. 4 (treatment costs) of the VerfO, make the corresponding changes by mutual consent.

2. Key points of the resolution

At its session on 5 March 2020, the G-BA passed a resolution on the benefit assessment of ropeginterferon alfa-2b in accordance with Section 35a SGB V. Following publication of the resolution on the website of the G-BA, the G-BA concluded that there is a need to adapt the information on the number of patients presented in the resolution or the demarcation of patient groups eligible for treatment.

In the resolution, the patient group “b) Adult patients with polycythaemia vera without symptomatic splenomegaly pre-treated with hydroxyurea who are resistant or intolerant to hydroxyurea” was based on patient numbers from the previous resolution on ruxolitinib in the therapeutic indication polycythaemia vera (15 October 2015). The information on the number of patients is based on the target population in statutory health insurance (SHI).

In the course of the written statement procedure on ropeginterferon alfa-2b, the pharmaceutical company had presented a new calculation with regard to the criticism raised in the benefit assessment (i.e. that the proportion of patients who received hydroxyurea in the first line was not taken into account) and made reference to two studies. These were the studies of Tefferi et al. (2013) and Jentsch et al. (2016). The pharmaceutical company had taken the value of 73% as the lower limit for the proportion of patients who had been pretreated with hydroxyurea from the study of Tefferi et al. (2013).

However, it should be noted that this proportion also includes patients who have received cytoreductive therapy other than hydroxyurea. Taking into account only those patients in the study of Tefferi et al. (2013) who had received therapy with hydroxyurea ± a non-leukemogenic substance or with busulfan + hydroxyurea results in a proportion of 53%, which is used as the lower limit in this new calculation. On the other hand, the value of 64.4% cited in the study by Jentsch et al. (2016) is used as an upper limit for the proportion of patients who have previously been treated with hydroxyurea.

Taking into account the other values presented in the dossier, (i.e. a prevalence of polycythaemia vera of 5–30/100,000 patients, a range of 0–36% as an approximation of the proportion of patients with symptomatic splenomegaly, a proportion of 24.1% of patients with resistance or intolerance to hydroxyurea, and a SHI proportion of 87%, this results in 300–3360 patients for patient group b). Because information on the proportion of patients with symptomatic splenomegaly is missing in the dossier, a range was formed. In the lower limit, all patients with splenomegaly (36%) were removed. For the upper limit, it was assumed that this proportion is negligible and no patient was removed.

In accordance with patient group b), also for the recalculation of patient group a) “Adult patients with polycythaemia vera without symptomatic splenomegaly not pretreated with hydroxyurea or pretreated with hydroxyurea who are not resistant or intolerant to hydroxyurea”, proportional values of the studies of Tefferi et al. (2013) and Jentsch et al. (2016) are used. Taking into account the 73% of patients with cytoreductive pre-treatment and the aforementioned range of the proportion of patients with symptomatic splenomegaly and SHI insurance results in 624–5850 patients who have not yet received any cytoreductive treatment. For those patients who have been pre-treated with hydroxyurea and who are not resistant or intolerant to it, a number of 933–10591 patients is calculated taking into account the aforementioned percentage values of 53–64.4% for a hydroxyurea pretreatment and subtracting the 24.1% of patients who are resistant or intolerant to hydroxyurea. After adding the patients who have not received cytoreductive treatment and the patients who have been treated with hydroxyurea but are not resistant or intolerant to it, there are approx. 1560–16440 patients in patient population a). Because the underlying unit values are predominantly taken from a single study (Tefferi et al. 2013), there are uncertainties overall.

3. Written statement procedure according to Section 92, paragraph 3a SGB V

The Pharmaceuticals Directive does not require the submission of a written statement procedure according to Section 92, paragraph 3a SGB V. Pharmaceutical companies will not be adversely affected by the correction of the information on patient numbers for the active ingredient ropeginterferon alfa-2b. The change for the reasons mentioned under 2. is legally necessary.

4. 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.

5. Process sequence

Following the adoption of the resolution, the necessity of the adjustment in the resolution with regard to the patient numbers in the resolution of 5 March 2020 on an amendment of the Pharmaceuticals Directive Annex XII – Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V – ropeginterferon alfa-2b has become apparent.

The matter was discussed in the Working Group Section 35a as well as in the Subcommittee on Medicinal Products.

At its session on 16 July 2020, the plenum unanimously adopted the amendment to the AM-RL with regard to an adjustment to the number of patients stated in the resolution of 5 March 2020.

Chronological course of consultation

Session	Date	Subject of consultation
Working group Section 35a	19 May 2020 4 June 2020 17 June 2020	Consultation on the facts of the case
Subcommittee Medicinal Products	7 July 2020	Consultation on an amendment to the resolution of 5 March 2020 regarding the indication of number of patients
Plenum	16 July 2020	Resolution on an amendment to the resolution of 5 March 2020 regarding the number of patients

Berlin, 16 July 2020

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

Prof. Hecken