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 – Ingenol Mebutate (Repeal of the Resolution of 21 February 2019)

of 20 August 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.

2. Key points of the resolution

The active ingredient ingenol mebutate was first approved as a medicinal product on 14 November 2012 (Picato®). The marketing authorisation was granted for the therapeutic indication: “Picato® is indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults.”

After the active ingredient ingenol mebutate was first placed on the market on 15 January 2013 with the present therapeutic indication, the G-BA carried out a benefit assessment of this active ingredient according to Section 35a SGB V and added the active ingredient ingenol mebutate to Annex XII of the Pharmaceuticals Directive by resolution of 4 July 2013.

At its session on 21 June 2018, the G-BA decided to grant an application of the pharmaceutical company for a renewed benefit assessment on the basis of new scientific

knowledge according to Section 35a, paragraph 5 SGB V. The G-BA decided on the renewed benefit assessment of ingenol mebutate on 21 February 2019. Accordingly, the active ingredient ingenol mebutate was added to Annex XII of the Pharmaceuticals Directive by the resolution of 1 February 2019.

The renewed benefit assessment was based on the results of the Phase III "LP0041-1120" study at week 17. Because of the lack of long-term data on the development of squamous cell carcinoma and the ongoing LP0041-1120 study, the G-BA limited the period of validity of its resolution on the benefit assessment of ingenol mebutate until 28 February 2022 and imposed the condition that long-term data on patient-relevant endpoints, in particular on the occurrence of squamous cell carcinoma and the complete regression of lesions, must be submitted for the renewed benefit assessment after the deadline for assessing the sustainability of the effects in the dossier.

On 20 January 2020, the European Commission provisionally suspended the marketing authorisation for the medicinal product Picato® because of safety concerns. This recommendation was based on an ongoing review by the Pharmacovigilance Risk Assessment Committee (PRAC) at the request of the European Commission in accordance with Article 20 of Regulation (EC) No. 726/2004.

On 11 February 2020, at the request of the marketing authorisation holder, the European Commission withdrew the marketing authorisation for ingenol mebutate as the active ingredient of the medicinal product Picato®. The review by the PRAC was completed on 17 April 2020. The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has completed its review of Picato® with the conclusion that the medicinal product may increase the risk of skin cancer and that the risks outweigh the benefits. On 30 April 2020, the CHMP recommended the suspension of the marketing authorisation of Picato®. On 6 July 2020, the European Commission issued a legally binding decision that the marketing authorisation of Picato® had been revoked.

With the revocation 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 ingenol mebutate of 21 February 2019 (BAnz AT 8 March 2019 B1) is to be repealed.

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

Session	Date	Subject of consultation
Working group Section 35a	3 June 2020	Consultation on the draft resolution
Subcommittee on Medicinal Products	28 July 2020	Consultation and consensus on the draft resolution to repeal the resolution
Plenum	20 August 2020	Resolution on the repeal of the resolution

Berlin, 20 August 2020

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

Prof. Hecken