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Spitzenverband

Amendments to Regulation (EC) No 726/2004: Far-reaching impact on the early benefit assessment

On 10 September 2014, the European Commission submitted a proposal for a regulation of the European Parliament and of the Council amending Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (EMA). On 23 February 2016, the Members of the European Parliament adopted a report on the proposal in the Environment, Public Health and Food Safety Committee, in which they proposed a number of amendments. The proposed amendments were accepted in plenary on 10 March 2016. These amendments would have a far-reaching impact on the early benefit assessment.

1. Benefit assessment in the EMA's market authorisation procedure puts the German Act on the Reform of the Market for Medicinal Products (*AMNOG*) in question.

The amendments that were proposed by the Members of the European Parliament would have the effect of fundamentally questioning the early benefit assessment that was introduced through the Act on the Reform of the Market for Medicinal Products (AMNOG) in Germany. There is provision to implement within the authorisation procedure an evaluation of the comparative efficacy of medicinal products with respect to those that already exist in the same therapeutic class. This comparative evaluation is to be entrenched as a new task for the EMA. According to the proposals put forward by the EP, the Committee for Medicinal Products for Human Use (CHMP) is to enclose a comparative evaluation of the medicinal product for human use with the authorisation, if a positive opinion is issued. The power to set the prices of medicinal products, as well as to include such products in the scope of the national health insurance system, would then only remain unaffected provided that Member States take this comparative reference evaluation of medicinal products for human use into due consideration.

Evaluation by the National Association of Statutory Health Insurance Funds (GKV-Spitzenverband)
The consequence of the implementation of this proposal would be that the assessment of any additional benefit would already be carried out within the EMA's authorisation procedure. This would lead to a considerable degradation of the early benefit assessment carried out by national competent institutions like the German Federal Joint Committee (G-BA). Given that this Committee is currently already bound by the stipulations contained in the EMA's authorisation, the margin of appreciation that is open to it would be minimised. When selecting the expedient comparative therapy within the benefit assessment, the Federal Joint Committee would only be able to derogate from the comparative medicinal products selected by the EMA by stating quite

substantial grounds. The determination of the expedient comparative therapy would transfer a central factor of national price setting to the EU level. The Federal Joint Committee would be able at best to carry out an additional evaluation vis-à-vis an expedient comparative therapy which it selected. This would however impose on it the burden of stating grounds as to why it was necessary to derogate from the actions of the EMA. This would considerably intensify the discussions which are already underway as to the selection of an expedient comparative therapy. It would de facto become much more difficult for the Federal Joint Committee to take national healthcare aspects into account in the benefit assessment. There would be a danger of price-setting powers being transferred to the EU level. It must however also remain ensured that price negotiations are carried out within the responsibility of the Member States and within the framework of national refund systems. This is the only way in which the national particularities of healthcare provision can be taken into consideration.

Moreover, the proposal for a regulation of the European Parliament leaves open the standards which the EMA is to apply when carrying out the benefit assessment. The criteria applied in the national procedures diverge widely at present. A conscious decision was taken when the Act on the Reform of the Market for Medicinal Products was introduced, not to apply the quality adjusted life year (QALY) concept in Germany to the evaluation of medicinal products. It cannot be ruled out that the EMA might nonetheless apply this very concept.

The orientation towards the future EMA criteria will result in the EU-wide harmonisation of the benefit assessment. It can be predicted that this will lead to the high level of requirements under German social law being reduced to the standard of the study accepted within the authorisation procedure. This is to be unambiguously rejected in the view of the community of insured parties and in the interest of the patients.

2. Relaxation of conditions for the authorisation of new medicinal products with potential consequences for patient safety

The European Commission already provides in the proposal for a regulation of 10 September 2014 for extensive regulatory powers to be transferred to itself. This proposal is taken up in the current amendments by the Members of the European Parliament. Accordingly, the power is to be transferred to the Commission to adopt acts stipulating when marketing authorisations can be granted without adequate evidence having been provided as to efficacy, and such evidence can be provided post-authorisation, so as to facilitate the authorisation of new medicinal products.

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Were the proposal to be transposed, this would mean that the Commission would be granted the regulatory power to also adopt acts stipulating when marketing authorisations can be granted without adequate evidence having been provided as to efficacy, and when such evidence can be provided subsequent to authorisation. Such a power would make it easier to water down the existing requirements as to the evidence that is to be submitted in the authorisation procedure. The National Association of Statutory Health Insurance Funds considers this to be out of place, given the existence of adaptive authorisation procedures. In particular, authorisation on the basis of incomplete data entails risks for patients. The conditions for the further generation of evidence are currently not fully satisfied in practice, or are subject to delay. This engenders an urgent need to ensure that the facilitation of authorisation does not lead to patients being subject to new risks owing to medicinal products which have not undergone adequate trials.

Annex

Report on the proposal for a regulation of the European Parliament and of the Council amending Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Committee on the Environment, Public Health and Food Safety): Amendments 8, 9, 13 and 16.

No.	Amendment
8	***(6e) Member States have developed an evaluation of the comparative efficacy of medicinal products aimed at positioning a new medicinal product with respect to those that already exist in the same therapeutic class. Similarly, the Council, in its conclusions on medicinal products and public health, adopted on 29 June 2000, emphasised the importance of identifying medicinal products that presented an added therapeutic value. That evaluation should be conducted in the context of the marketing authorisation.***
9	***(2a) In Article 1, the second paragraph is replaced by the following:*** "The provisions of this Regulation shall not affect the powers of Member States' authorities as regards setting the prices of medicinal products or their inclusion in the scope of the national health system or social security schemes on the basis of health, economic and social conditions***, provided that Member States take into due consideration the reference comparative evaluation of human medicinal product as referred to in Article 9(4).*** In particular, Member States shall be free to choose from the particulars shown in the marketing authorisation those therapeutic indications and pack sizes which will be covered by their social security bodies."
13	***(5a) In Article 9(4), the following point is inserted:*** ***"(da) the comparative evaluation of the human medicinal product;"***
16	***(10c) In Article 57(1), the first subparagraph is replaced by the following:*** "1. The Agency shall provide the Member States and the institutions of the Community with the best possible scientific advice on any question relating to the evaluation of the quality, safety***,*** efficacy ***and comparative assessment*** of medicinal products for human or veterinary use which is referred to it in accordance with the provisions of Community legislation relating to medicinal products."

Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL amending Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (COM/2014/0557 final)

	Article 1 **Regulation (EC) No 726/2004 is amended as follows:** (7) Article 10b(1) is replaced by the following: 'The Commission shall be empowered to adopt measures, by means of delegated acts in accordance with Article 87b, to determine the situations in which post-authorisation efficacy studies may be required under point (cc) of Article 9(4) and point (b) of Article 10a(1).'; (8) Article 14(7) is replaced by the following: '7. In the interests of public health a marketing authorisation may be granted subject to certain specific obligations, to be reviewed annually by the Agency. Those obligations and, where appropriate, the time limit for compliance shall be specified in the conditions to the marketing authorisation. The summary of product characteristics and the package leaflet shall clearly mention that the marketing authorisation for the medicinal product has been granted subject to those obligations. By way of derogation from paragraph 1, such authorisation shall be valid for one year, on a renewable basis. The Commission shall be empowered to adopt delegated acts in accordance with Article 87b in order to lay down provisions and requirements for granting such marketing authorisation and for its renewal.' ; (9) Article 16(4) is replaced by the following: '4. The Commission shall be empowered to adopt delegated acts in accordance with Article 87b establishing procedures for the examination of applications for variations to the terms of marketing authorisations and for the examination of applications for the transfer of marketing authorisations.';