Spitzenverband

Comments by the National Association of Statutory Health Insurance Funds from 13.02.2017

to the stakeholder consultation on the experience acquired with the Paediatric Regulation

GKV-Spitzenverband
Reinhardtstraße 28, 10117 Berlin
Telefon 030 206288-0
Fax 030 206288-88
politik@gkv-spitzenverband.de
www.gkv-spitzenverband.de
Transparency Register Number
839750612639-40

I. Comments for the consultation

Consultation item No 1: Do you agree that specific legislation supporting the development of paediatric medicines is necessary to guarantee evidence-based paediatric medicines?

A specific legislation seems to have substantial positive influence concerning the investigation of the paediatric application of active substances primarily developed for the use in adults.
Its influence on the development of medicines for paediatric diseases alone seems less prominent. From the perspective of GKV-Spitzenverband, this is directly connected to the fact that legislative incentives cannot compensate for economic success. This view is supported by prices requested for such medicines regardless the existence of the current legislative framework and the still relatively low numbers of new paediatric products compared to the time before or shortly after the paediatric regulation came into force.

Consultation item No 2: Do you have any comments on the above? To what extent and in which therapeutic areas has the Regulation contributed to the availability of important new treatment options?

The GKV-Spitzenverband agrees that achievements of the Paediatric Regulation are not the same across all therapeutic areas. We are of the view that this cannot be influenced by legislation as one important reason is differences in price levels that can be reached in different areas of disease. The same differences can also be observed in the development of medicinal products for adults, where trends seem to influence the direction of research.

Consultation item No 3: In your experience, has the number of new paediatric medicines available in Member States substantially increased? Have existing treatments been replaced by new licensed treatments?

The GKV-Spitzenverband is not able to comment on this issue on a proper database.

Consultation item No 4: Do you have any comments on the costs for pharmaceutical companies to comply with an agreed paediatric investigation plan?

The GKV-Spitzenverband is not able to comment on this issue except for one general comment. In the view of the GKV-Spitzenverband, ownership comes with responsibility and in case of pharmaceutical companies this includes a societal responsibility.

Consultation item No 5: Do you agree that the reward system generally functions well and that early, strategic planning will usually ensure that a company receives a reward?

The GKV-Spitzenverband is not commenting on this topic.

Consultation item No 6: How do you judge the importance of the orphan reward compared to the SPC reward?

The GKV-Spitzenverband is not commenting on this topic.

Consultation item No 7: Do you agree that the Regulation's implementation has improved over time and that some early problems have been solved?

The GKV-Spitzenverband is not commenting on this topic.

Consultation item No 8: Do you have any comments on the above? Can you quantify and qualify missed opportunities in specific therapeutic areas in the last ten years?

Although the 'mechanism of action' principle is tempting, its applicability has to be investigated in every single case. Hyman and colleagues reported about the investigation of vemurafenib in several nonmelanome cancers with BRAF V600 mutations in 2015 and showed mixed results: The existence of a BRAF V600-mutation, the mechanism of action, alone seems not to be sufficient for positive results and other disease specific factors seem to also exert substantial influence. Therefore, it might be appropriate to further investigate the possibility of incentivising paediatric research based on the mechanism of action principle. The current scientific debate on the validity of mechanism-based treatment approaches indicates that there might be a trend towards accepting inappropriate evidence transfers when searching for new treatments, be it in paediatric or adult diseases. If proper research was to be conducted, evidence-based decisions would be pos-

sible. Nevertheless, it is agreed that due to the heterogeneity of possible results, the selection of research topics might be challenging and need further scrutiny.

Consultation item No 9: Do you agree with the above assessment of deferrals?

The GKV-Spitzenverband is not commenting on this topic.

Consultation item No 10: Do you have any comments on the above?

The GKV-Spitzenverband is not commenting on this topic.

Consultation item No 11: Do you have any comments on the above?

The GKV-Spitzenverband deems the regulations already put in place to sufficiently ensure the availability of products adapted to children in the face of biosimilar competition.

Consultation item No 12: Do you share the view that the PUMA concept is a disappointment? What is the advantage of maintaining it? Could the development of off-patent medicines for paediatric use be further stimulated?

It cannot be disputed that the number of PUMA has not come up to expectations. Nevertheless, the low number of PUMA reflects the generally low number of extensions of marketing authorisations for off-patent medicines, regardless the fact that evidence might be generated in investigator initiated trials. It seems like one has to acknowledge that incentives that can be given by legislation cannot compensate for economic success. Therefore, the need to further uphold this specific regulation needs to be evaluated taking into account possible different measures like public licensing or regional regulations on off-label use.

Consultation item No 13: Do you have any comments on developments in clinical trials with children following the adoption of the Regulation and in view of the above discussion?

The GKV-Spitzenverband agrees with the observation that special difficulties are to be overcome in the conduct of paediatric trials. The recruitment of children for clinical trials not only needs to take into account legal aspects, but also needs to overcome emotional hurdles, especially for parents. In order not to overburden the limited number of volunteers unnecessarily, cooperation of companies in the conduction of clinical trials needs to be enhanced. Consideration should be given to investing in additional manufacture-independent research activities and facilitation of their implementation in order to specifically address the existing care gaps in the medicinal treatment of children.

Consultation item No 14: Do you have any views on the above and the fact that the paediatric investigation plan process is currently exempt from the fee system?

The GKV-Spitzenverband is not commenting on this topic.

Consultation item No 15: How do you judge the effects of the Paediatric Regulation on paediatric research?

The GKV-Spitzenverband is not commenting on this topic.

Consultation item No 16: Are there any emerging trends that may have an impact on the development of paediatric medicines and the relevance of the Paediatric Regulation?

The GKV-Spitzenverband generally is critical of the concept of adaptive pathways and has expressed his concerns regarding a lowering of evidential standards for marketing authorisations and the lack of a proper reflection of the need for and the scope of the concept. Nevertheless, if adaptive pathways were to be become reality, one has to come to a social decision on the discrimination between cases in which a new medicine may not be withheld from children despite high uncertainty and cases in which an additional hazards due to this uncertainty are unbearable.

With regards to stratified medicines (so called personalised medicines), the focus on the mechanism of action need further scrutiny e.g. in the light of intra-tumoural heterogeneity and differences due to tissues harbouring the diseases.

Consultation item No 17: Overall, does the Regulation's implementation reflect your initial understanding/expectations of this piece of legislation? If not, please explain. Are there any other issues to be considered?

The GKV-Spitzenverband is not commenting on this topic.