European Confederation of Pharmaceutical Entrepreneurs AISBL

EUCOPE Position on the EC Proposal for a Regulation on Health Technology Assessment

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Executive summary

EUCOPE, the European association for small to medium-sized companies in the field of pharmaceuticals, biotechnologies – many of which are researching and developing rare disease solutions – welcomes the European Commission's (EC) aim to ensure Member States' cooperation on assessing clinical aspects of Health Technology Assessment (HTA) beyond 2020 (COM (2018) 51 final).

The EC proposal contributes to more transparency and convergence in value assessment of health technologies across Europe. EUCOPE considers that a European legislation on HTA, which provides for the mandatory use of the joint clinical assessment reports by Member States, is important and would like to suggest some adjustments, such as:

- **Methodology:** Any future European joint HTA work should follow high quality standards and clear methodological rules, processes and timelines that do not conflict with the existing regulatory frameworks and pathways. The methodologies should provide for a sufficient level of flexibility allowing an adequate management of evidential uncertainty in specific cases, e.g. for Orphan Medicinal Products (OMPs).
  The legislative text should cover more details regarding the methodology, the comparator and endpoints chosen; it should lay out the procedure on scientific advice; the main aspects of relevance for the fuctioning of the system should be described in the Regulation rather than in delegated and implementing acts and guidelines only.
- **Stakeholder involvement**: Manufacturers whose products are included in the HTA collaboration work should also be granted a right to be consulted during the assessment as well as the possibility to appeal against the final joint clinical assessment report. Relevant stakeholders – including the EMA – should be consulted throughout the process.

1. State of play

1.1. Divergences in HTA across Europe and ensuing issues

Despite the efforts encouraging voluntary European cooperation on HTA through EUnetHTA, significant heterogeneity in assessing medical innovation remains across Europe, such as:

- Differences in governance structures, requirements and criteria;
- Differences in methodologies to assess OMPs serving an unmet medical need in small patient populations;
- Differences in appreciation of value.

In addition, the divergence and multiplicity of HTA processes and methodologies across the EU and even within Member States are often a significant time, administrative and financial burden on health technology developers – especially SMEs at the forefront of innovation – as well as national authorities and often lead to a duplication of efforts and uncertainties.

All the above have resulted in discrepancies in HTA outcomes, with subsequent detrimental effects and delays of patient access to innovation.

1.2. The benefits of increased harmonisation of clinical assessments at a European level

As stated in its submission to the EC public consultation on HTA, EUCOPE is convinced that increased harmonisation of clinical assessments at a European level can pave the way towards more transparency and convergence in value assessment. For that reason, EUCOPE supports the principles behind the EC Proposal for a Regulation on HTA which focuses on the clinical part of the HTA only and the necessity for mandatory uptake of joint clinical assessments by Member States.

In particular, increased harmonisation of clinical HTA standards and increased alignment on evidence requirements at a European level, whilst maintaining Member States' prerogative of context-specific economic and ethical assessments and pricing & reimbursement procedures, could contribute to higher-quality assessments, increased availability of innovative treatments for patients while ensuring transparent and evidence-based decisions.

It can also be anticipated that a European legislation, which allows for a convergence of tools, methodologies and procedures, could reduce burdens and compliance costs for small and mid-sized manufacturers, and as such, increase certainty as to how the product will be assessed, business predictability and competitiveness. The possibility to request a joint scientific consultation, thus allowing companies to seek simultaneous advice from various authorities during the development phase of a product on the level of data and evidence needed, would also be favourable to small and mid-sized manufacturers in particular.

The proposal for a sustainable structure for cooperation on clinical assessments of health technologies is also a unique opportunity for national healthcare systems to avoid duplicative efforts and inneficient use of resources, as well as to issue assessments more quickly and based on robust evidence through sharing of expertise.

However, further key issues such as a clear set of rules of procedure, a clear framework for the methodology of the clinical assessments, built on the EUnetHTA methodological guidelines and sufficiently flexible to account for highly-specialised medicines such as OMPs, and stakeholder involvement, remain disregarded by the EC Proposal and should be defined in the Regulation itself in greater detail.

2. Procedural rules for joint clinical assessments and joint scientific consultations should be further defined

The EC has issued a Proposal that provides a general legislative framework for increased cooperation on clinical assessments at EU level, and for which the most significant aspects would be dealt with in implementing and delegated acts.

While EUCOPE understands the necessity to address some technicalities in tertiary legislation, basic principles need to be enshrined in the Regulation in order to avoid uncertainty for manufacturers, HTA bodies and patients and pave the way for an absolute degree of acceptance of the joint clinical HTA outcomes by all individual Member States.

In order to offset the levels of ambiguity and uncertainty in the current EC Proposal, EUCOPE would recommend to provide a legal frame in the Regulation for the methodology for joint clinical assessments and scientific consultations, the integration of the joint clinical assessments with the regulatory procedures, and the consultation of stakeholders throughout the value assessment of health technologies. The methodologies should provide for a sufficient level of flexibility allowing an adequate management of evidential uncertainty in specific cases, eg for OMPs.

2.1. Timeliness of the joint clinical assessments

According to the detailed explanation of the specific provisions of the EC Proposal (page 12), joint clinical assessment reports would be made available at the time or shortly after the final EC decision granting marketing authorisation. The foreseen timing would directly prevent health technology developers from submitting their application for pricing & reimbursement as early as it is currently done in some Member States. In particular, this would go against some national procedures whereby a company can submit an application for pricing and/or reimbursement at the time of the opinion of the EMA Committee for Human Medicinal Products (CHMP) – such as in Belgium, Italy, Sweden or the UK – or at the EC decision to grant the marketing authorisation.

In order to avoid both patient access delays and uncertainties for manufacturers, EUCOPE recommends making the joint clinical assessment reports available at latest by the EC decision to grant the marketing authorisation to a product. Further, clear guidelines on subsequent submission of new developing evidence for product re-evauation must also be pre-specified.

2.2. The scope for joint clinical assessments

According to Article 4(2) and (3), the selection of medicines that will undergo the joint clinical assessments is to be done at the sole discretion of the Coordination Group, based on a set of criteria, and to be published in the annual work programme, a year before the joint work. With such vague timelines, the proposal brings further unpredictability and uncertainties for manufacturers.

In order to ensure a timely selection of health technologies – e.g. during phase III clinical trials – and the preparedness of developers for upcoming joint assessments, the annual work programme should systematically build on the Horizon Scanning joint work.

2.3. Alignment between the EU joint work on HTA with the regulatory framework

EUCOPE considers that the current EC Proposal can only lead to an improvement of the status quo if the following guarantees are provided in the legislative text:

- Joint clinical assessments will not delay early access to breakthrough medicines that benefit from the PRIME or orphan designation or are eligible for accelerated assessment.
- Joint clinical assessments for OMPs, whereby their added value needs to be demonstrated, would not be duplicative of the significant benefit demonstration over existing alternatives required by the EMA for approval.

Granting a more prominent role to the EMA in the consultation process would also help ensure that joint HTA work is well-integrated with the existing regulatory framework.

2.4. Acknowledging the specificities of OMPs in the EU HTA legislation

Due to the rarity of the diseases OMPs are intended for, available evidence and data are limited. Furthermore, when an unmet medical need exists, the study design might be unable to be comparative (no alternative), leading to ratings of current submitted evidence as in-adequate or sub-standard. Therefore, a "one-size-fits-all" methodology not considering the specificities of OMPs would ultimately lead to considerable delays in or even hinder patients' access to those medicines across the Member States.

Currently, certain national legislation has distinct processes for OMPs in place, thereby duly recognising the specificities of these medicines (e.g. in England, Scotland, and Germany, where specific HTA processes provide for a greater acceptance of evidential uncertainty in the assessments of OMPs) whilst there are no EUnetHTA guidelines on how the value of OMPs should be assessed.

As identified by the Commission in its proposal, European coordination of OMP value assessment processes can guarantee more consistency in the definition and assessment of clinical value and a pooling of data and epidemiology. European cooperation on OMP-specific clinical assessment would also deliver opportunities for more systematic collection and assessment of data. However, it is important to ensure that any new approach should not result in worsening conditions for OMP assessment or in unnecessary delays compared to the current situation. In addition, it should not undermine favourable national pathways for OMPs and should acknowledge the principle of differentiated assessment. It should be in particular respected that the European Commission's decision to designate a medicinal product as an OMP includes the acknowledgement of a significant benefit over existing methods as it is, *inter alia*, laid down in the German legislation. The German law rightfully provides that for most OMPs the additional benefit is assumed by law while for other medicines, this benefit is graded in the HTA.

Consequently, it needs to be already laid down in the text of the Regulation that the implementing and delegated acts on the procedural rules (Article 11(1)) will provide for a sufficient level of flexibility allowing an adequate management of evidential uncertainty in specific cases, in particular for OMPs.

2.5. Ensuring the right level of stakeholder involvement

In order to ensure a thorough, transparent, independent and inclusive joint work, the proposed Regulation provides for 'appropriate involvement of stakeholders' in the Coordination Group's work (Article 3). This includes:

- The opportunity to input in joint clinical assessment and scientific consultation reports by thealth technology developers, patients and clinical experts,
- The creation of a Stakeholder Network (Article 26), which shall take part in ad-hoc meetings with the Coordination Group.

According to Articles 16 and 17, the Commission shall be given the power to develop implementing acts on the consultation of the above-mentioned stakeholders for both activity sets. The Commission will also select participating organisations to the Stakeholder Network based on criteria to be later defined.

The provisions, as such, do not provide enough clarity on stakeholders' – and more particularly industry's, patients and experts – involvement. Similarly, procedures and timing for stakeholders' comments along the joint clinical assessments are not detailed enough. EUCOPE considers it important for developers whose technology is included in the HTA collaboration work to be consulted during the assessment of their health technology and by the time the joint clinical assessment report is finalised. Finally, active stakeholder participation

should also be ensured in identifying emerging technologies so as to optimise their introduction into health care systems.

EUCOPE suggests that rules be laid out in the Regulation to clarify how stakeholders will input throughout the process. A regular dialogue with the stakeholder network, which shall inter alia contribute to the identification of experts in joint clinical assessments, should also be set up. The industry's role in the third pillar of the activities (horizon-scanning) should also be specified.

2.6. Voluntary cooperation

Article 19 provides Member States with the opportunity to further cooperate on non-clinical aspects of health technology assessments, thus including economic aspects. The need for such a provision is unclear as Member States may cooperate on certain issues at any time. Given the circumstance that existing voluntary cooperation often touches upon pricing & reimbursement issues, this should remain in the remit of Member States thus avoiding to divert focus and resources from the identified priority areas, namely joint clinical assessments and joint scientific consultation and ensuring avoidance of unnecessary processes with consequent delays on time to patient access.

EUCOPE therefore recommends that Section 4 on voluntary cooperation of the proposal be removed.

3. Conclusion

Supportive of the EC proposal for mandatory uptake of joint clinical assessments by Member States, EUCOPE considers that the below points need to be addressed in the text of the Regulation and not in tertiary legislation:

- Any future European joint HTA work should follow high quality standards and clear methodological rules, processes and timelines that do not conflict with the existing regulatory frameworks and specific pathways.
  The methodologies should provide for a sufficient level of flexibility allowing an adequate management of evidential uncertainty in specific cases, in particular for OMPs.
- Manufacturers whose products are included in the HTA collaboration work should also be granted a right to be consulted during the assessment of their health technology and by the time the joint clinical assessment report is finalised.
- Similarly, stakeholders – including the EMA and patients – should be consulted at the right level throughout the process.

EUCOPE remains available and ready to enter into discussions with the EU Commission, the European Parliament and the Council, in order to identify most effective suitable terms for future cooperation of European Member States on joint clinical assessments of centrally-authorised medicines as well as joint scientific consultations and horizon scanning.

About EUCOPE

The European Confederation of Pharmaceutical Entrepreneurs (EUCOPE) gives voice to small-to-medium sized innovative companies in the field of pharmaceuticals, biotechnologies and medical devices.

EUCOPE represents 900+ mid-sized innovative pharma and biotech companies, directly and via national trade associations such as British EMIG, French France Biotech, German BPI or Swedish IML.

EUCOPE membership includes innovative family-owned companies as well as innovative companies active in the field of biotechnology and rare diseases.

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