



Celgene Position on the proposed Regulation on Health Technology Assessment (HTA)

The Celgene perspective in a nutshell

Celgene generally supports the Commission's proposed Regulation on Health Technology Assessment (HTA) as it can accelerate and improve patient access to innovative therapies across the European Union (EU). Celgene believes some elements will need to be improved to ensure that the regulation effectively delivers the expected results. A set of principles governing the methodology of joint clinical assessments is needed, including a degree of flexibility to enable adequate assessments of and support timely patient access to certain promising medical innovations that Celgene and other biopharmaceutical companies are developing (e.g. highly specialized and potentially disruptive treatments, like cell and gene therapies) and which present a certain degree of evidence uncertainty. The joint clinical assessment system should be mandatory for centrally approved medicines, both in terms of participation and use in national HTA processes. Joint clinical assessments should be carried in parallel with regulatory assessments by the EMA and any duplications between the regulatory process and the clinical assessments should be avoided. Overall, the joint clinical assessment procedures should be set up to avoid any delays in national processes and patient access compared to the current situation.

Celgene strongly encourages EU policy-makers to take a pragmatic approach to EU cooperation on HTA that reflects the national competence for the organization and funding of health systems and the differences between Member States from a socio-economic and health system perspective. The cooperation should be focused on those areas of joint work that can deliver synergies and efficiency gains, truly supporting faster patient access, i.e. joint clinical assessments and joint scientific consultations.

Joint Clinical Assessments

Joint clinical assessments can speed up patient access by reducing duplication, increasing the predictability of evidence generation requirements and ensuring greater consistency in decision-making. For the regulation to deliver on this potential, the following elements should be considered:

1) *Joint assessments should focus exclusively on clinical aspects (Article 6)*

Celgene supports the Commission proposal limiting joint assessments to the clinical aspects of health technologies. HTA processes that inform national pricing and reimbursement decisions currently consist of clinical assessments and, in certain countries, evaluations of economic and ethical considerations. We believe that the strongest synergies among EU countries can be achieved through joint clinical assessments, which should consist of a compilation and analysis of the available scientific evidence of the relative effects of a healthcare technology. The evaluation and appraisal of these effects, as well as non-clinical assessments related to economic and ethical elements, which are dependent on the national context, should be undertaken at Member State level.



2) Clinical assessments should follow a science-based, consistent and appropriate methodology (Articles 22, 23)

The outcomes of joint clinical assessments should be consistent, reliable and transparent. To achieve this, Celgene supports the development of a joint clinical assessment methodology that is used consistently by all Coordination Group members and is flexible enough to enable an adequate assessment of certain innovative and potentially disruptive technologies that require innovative clinical trial designs.

There are several situations where such flexibility in clinical assessment methodology is required:

- Blinded randomized clinical trials are not possible for certain products - e.g. orphan medicines for very small patient numbers, resulting in low statistical relevance of a randomized clinical trial, or cell/gene therapies where a blinded randomized clinical trial is not feasible;
- Clinical trials with medicines for fatal diseases for which patient cross-over between the different trial arms is necessary for ethical reasons;
- Life-prolonging therapies that reveal benefits over a period longer than the duration of the clinical trial, requiring the use of surrogate endpoints;
- Therapies receiving conditional marketing authorization subject to specific obligations to provide confirmatory evidence.

In each of these cases uncertainty about the value of the therapy at the time of marketing authorization and joint clinical assessment is unavoidable. This does not entail that the evaluated therapy has a low value for patients and health systems, but it could require that further evidence is generated post-marketing authorization, an approach commonly used by the regulators to manage uncertainty in regulatory approvals. If only evidence providing the highest level of certainty is accepted for joint clinical assessment, there will likely be significant delays in patient access to promising innovations in areas of high unmet medical needs. Therefore, Celgene believes that the methodology for joint clinical assessments should allow HTA bodies to manage evidentiary uncertainty by taking an open and flexible approach to the data required for joint clinical assessments.

We recognize the complex and technical nature of clinical assessment methodologies and support the development of the methodology through tertiary legislation. However, we would strongly encourage the legislator to include the following principles in the regulation to guide the Commission in the development of the implementing and delegated acts:

- The methodology should enable an adequate assessment of therapies developed through clinical trials with innovative designs or receiving marketing authorization subject to post-marketing authorization evidence generation;
- The most relevant available evidence should be accepted, including real-world observational data, evidence from case control studies etc.
- Indirect treatment comparisons should be possible, to address challenges in agreeing on a common comparator across the Union or changes in the relevant comparator due to the rapid evolution of the standards of care;



- Patient-relevant health outcomes should be identified taking due account of the preferences and respective roles of patients, physicians, regulators and HTA bodies;
- The methodology should be regularly updated to take into account the evolution of science.

In developing the tertiary legislation, the Commission should build on the outcomes of the EUnetHTA Joint Actions and particularly the methodological guidelines and evidence submission templates.

3) Participation and use of the Joint Clinical Assessments should be mandatory (Articles 8, 34)

The new system will only be effective if participation of EU Member States and companies is mandatory for centrally authorized products and if the joint clinical assessment reports are integrated into national HTA processes without duplicating them. However, in certain complex HTA cases, Member States should remain free to carry out complementary clinical analyses required to account for the national context (e.g. for specific target populations or where uncertainty remains), which are not part of the joint assessment. They should also remain fully responsible for assessing non-clinical elements and drawing conclusions on the overall added value and, in some cases, cost-effectiveness, to inform pricing and reimbursement decisions.

4) The system should generate synergies between HTA and regulatory processes (Articles 6, 11)

The marketing authorization and HTA are different processes with different purposes and requirements. However, over the past 20 years, cooperation between regulatory and HTA bodies has increased and synergies between the two processes can be used to accelerate patient access. Celgene recommends that the EMA regulatory approval process and the joint clinical assessment run in parallel with aligned timelines, so that the joint clinical assessment report is available at the same time as the marketing authorization decision. Celgene also urges policymakers to put in place effective mechanisms for cooperation between the EMA and the Coordination Group, to guarantee relevant information is shared and avoid any duplication of the EMA efficacy or safety assessments as part of the joint clinical assessment. Particularly for orphan medicines, the joint clinical assessment should take into account and not duplicate the significant benefit assessment carried by the EMA, which compares the therapy to all other existing satisfactory treatment methods, unless further analysis is justified by the availability of further evidence.

Joint Scientific Consultations (Articles 12-17)

Celgene supports joint scientific consultations as a key tool for developers to obtain feedback from both regulators and HTA bodies on their evidence generation plans to support decision-making on both marketing authorization and reimbursement of new medicines. This will help to increase predictability and drive greater alignment between EMA and HTA bodies on evidence generation requirements, including the selection of the relevant clinical endpoints and comparators. The latter is crucial to help biopharmaceutical companies generate optimal and robust evidence that satisfies the needs of both regulators and HTA bodies and avoid situations where clinical evidence is considered suitable for marketing authorization processes, but not for HTA purposes. The latter would ultimately result in patient access delays and additional burdens for companies.



Identification of Emerging Health Technologies (Article 18)

Celgene recognizes the value of EU collaboration on horizon scanning, with a view to identify those health technologies that should be subject to joint clinical assessments. Celgene recommends that Article 18 is amended to clarify that, for medicinal products, horizon scanning will form the basis of annual work programmes pursuant to Article 4 only during the 3-year transition period, following which all centrally authorized products should be subject to joint assessments, in line with the scope of the Regulation (see article 5 paragraph 1(a)). Moreover, Celgene encourages policy-makers to further clarify the scope of the horizon scanning exercise (e.g. products in Phase II or III clinical trials) and the content. Celgene recommends that the latter be based exclusively on publicly available information and not include cost or pricing expectations, which are country-specific.

Voluntary Cooperation (Article 19)

Non-clinical aspects, including ethical and economic considerations are highly dependent on the context of each country. Differences exist between EU Member States in terms of disease burden and economic parameters like the cost of comparators, available resources, or the organization of the health system. Therefore, at least until healthcare systems in Europe are more aligned on socio-economic and organizational parameters, Celgene believes that patient access is best served if non-clinical assessments and subsequent price negotiations are handled by Member States. This allows the flexibility necessary to find patient access solutions tailored to the context and needs of each national health system.

Celgene therefore recommends that Article 19 be removed so that the limited resources available to the Coordination Group can be focused on joint clinical assessments, joint scientific consultations and horizon scanning, which have the greatest potential to generate synergies and improve patient access.

About Celgene

Celgene is a global biopharmaceutical company engaged in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases. We focus our efforts on bringing next generation solutions, such as cell and gene therapies (CAR T) and immuno-oncology treatments to our patients with life-threatening and seriously debilitating conditions.

As a company at the forefront of innovation we are committed to pushing the boundaries of science, investing close to 40% of our annual revenue back into R&D. In 2017, Celgene was the company ranked 3rd worldwide and across economic sectors in terms of R&D intensity according to the EU Industrial R&D Investment Scoreboard. Employing over 2,500 people across Europe and Switzerland, the company is committed to investing in Europe, which hosts over 50% of our worldwide clinical studies and our only R&D facility outside the U.S. (Celgene Institute for Translational Research Europe, in Sevilla, Spain).



Annex

Background on the Commission's Proposed Regulation on HTA

On 31 January 2018, the European Commission published its Proposal for a Regulation on Health Technology Assessment. It sets up a framework to strengthen European cooperation on HTA and amends the Cross-border Healthcare Directive (2011/24/EU), which stood at the basis of a voluntary EU-wide network on HTA composed of national HTA bodies and agencies established in 2013.

Rationale for Regulation. The new proposal aims to address a number of gaps and problems that can no longer be sufficiently addressed by the current system of project-based and voluntary cooperation on HTA. These primarily relate to i) **impeded and distorted patient access** for innovative technologies due to differing processes, evidence requirements and interpretation of the evidence in the EU Member States, ii) **duplication** of work by national and regional HTA bodies, as all national market access processes across the EU include a form of clinical assessment and iii) **the need to provide for a permanent system** and funding solution after the end of the EUnetHTA Joint Action 3.

Objectives

- Foster **timely access to innovative health technologies for patients across Europe.**
- **Ensure efficient use of resources** by avoiding duplication
- **Strengthen the quality of HTA across the EU and provide business predictability** by promoting the convergence of HTA tools, procedures and methodologies

Key components of the proposal

The Regulation provides for a mandatory system of joint clinical assessments for both member states and companies, which will become effective after a 3-year transitional period (i.e. 6 years after the adoption of the legislation). The non-clinical components of HTA such as economic, organizational, ethical and legal elements specific to the national context of HTA will remain a Member State responsibility. The proposal also includes early dialogues, horizon scanning and voluntary cooperation beyond clinical assessments in the scope of the joint work.

The proposal also puts forward additional areas of joint work:

- a) joint scientific consultations whereby developers of a health technology can seek parallel advice from HTA authorities and the EMA on relevant data required for regulatory approval and joint clinical assessments,
- b) identification of emerging health technologies and
- c) voluntary cooperation between EU Member States outside the mandatory elements of the proposal.