Briefing document template for

HTA Coordination Group (HTACG) Joint Scientific Consultation (JSC) for Medicinal Products (MP)

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HTACG JSC MP

V5.3

21 November 2024

Adopted on 28 November 2024 by the HTACG pursuant to Article 3(7), point (f), of Regulation (EU) 2021/2282 on Health Technology Assessment

[The use of this **briefing document template** is mandatory and standard headings in the template should be used. It is important to follow the template as the document forms the basis of the advice procedure.

The briefing document with annexes and references constitutes the briefing package.

This annotated template should be read in conjunction with the relevant guidance that can be found on the website of the European Commission and of the European Medicines Agency (EMA).

The briefing document should contain all necessary information and function as a 'stand-alone' argument. Cross-references to annexes can be included only when additional detail is needed to support the argument.

Bracketing convention:

[text]: explanation and orientation; can be removed when filling out the template

{text}: required text

<text>: optional text.

References convention:

For citation of literature references in the text, footnotes are preferred, alternatively the format (first author <et al.>, publication year) is recommended. For footnotes, a smaller font size can be used. In addition, references should be presented as a list at the end of the document in alphabetical order.]

[Table to be filled in by the HTD:]

Health Technology Developer (HTD)	

Research Product Identifier (RPI)	
Active substance	
INN (if available)	
Trade name (if available)	
Company product code	
ATC code (broad or detailed if known)	Click to select. or detail here:
Therapeutic field	☐ Cancer ☐ HIV/AIDS ☐ Diabetes ☐ Neurodegenerative disorder ☐ Viral disease ☐ Autoimmune disease/dysfunction ☐ Cardiovascular disease ☐ Other, please specify:
ICD-10 code (if available)	
Proposed intended indication	

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List of Figures

[Create a list of figures with figure number, figure title and page]

List of Tables

[Create a list of tables with table number, table title and page]

List of Abbreviations

[Any acronyms or abbreviations used should be specified the first time they appear in the text.]

Summary

[Summary to be provided by HTD. This summary will inform the summary section of the JSC Outcome Document of the HTACG. An upper limit of 3 pages for the summary is recommended.]

1. Introduction

[The objective of this section is to briefly introduce the disease setting, the product, its regulatory status, the rationale for seeking advice, previous consultations and potential health benefits.]

1.1. Background information on the disease to be treated

[Outline main features of the disease including relevant aetiology, epidemiological data, information on the natural history of the disease and the evolution of disease symptoms and burden.]

1.1.1. Current treatment landscape including current standard of care

[Discuss the evolution of treatment options, including current standard therapy in Europe referencing relevant guidelines and publications and addressing variations between the MS. For future Joint Clinical Assessments (JCA), the availability of treatment alternatives is a critical point. Therefore, describe all technologies (medicinal products, medical devices and procedures) that are relevant alternatives for the treatment of the disease (stage, line of treatment) together with their labelling status in Europe, North America and other non-EU countries. Include information, if applicable, on new treatment options that are in advanced phases of development, including compassionate use programs. This section will inform the summary section of the JSC Outcome Document of the HTACG.]

1.1.2. Current unmet need

[Describe how the product addresses an unmet medical need. Substantiate the claim with a description of the available diagnostic, prevention or treatment options/standard of care (SOC), including all relevant treatment modalities. The effect of available methods should also be described together with a description of how the medical need is not fulfilled by the available treatment options (in-label and off-label). The justification should be based as much as possible on epidemiological data about the disease (e.g., life expectancy, symptoms and duration, health-related quality of life). The claims could be substantiated e.g., by published literature or registries or healthcare databases].

1.2. Background information on the product

[Describe the mode of action (MoA), chemical structure and pharmacological classification, e.g. chemical/biological product; orphan medicinal product; advanced therapy medicinal product (ATMP).

If the administration of the product is associated with the use of a medical device, a companion diagnostic or artificial intelligence, a medical procedure or co-administered with other medicinal product(s), this information should be stated, and adequate information given on the associated test or device. The information can be presented in tabular form.

<Intended indication>

The consultation is carried out on the basis of one intended indication.

Specify the proposed wording for the intended indication for the label including the intended placement of the intervention in the current treatment landscape: (e.g. 1st line, 2nd line, 3rd line, add-on, screening pre-treatment, monitoring during treatment, etc.), posology, and any special precautions or recommendations for use of the product (including a possible risk management strategy). Describe whether it is a combination or a monotherapy. Describe the aim of treatment (preventive, curative, palliative, symptomatic, disease modifying). The target population should be described as precisely as possible, if any population should not be included in the label, this should be clearly indicated. Substantiate the statements with relevant guidelines.]

1.3. Regulatory status

[Describe the worldwide regulatory status of the product (e.g. any existing marketing authorization (MA), or planned marketing authorization application (MAA) timelines), indicating planned type and timelines of MAA (e.g. full/mixed dossier; advanced therapy, biosimilar, generic/hybrid MA legal basis; conditional or exceptional circumstances MA, if relevant) or variation.

If the product has received Orphan Drug Designation (ODD) related to the intended indication, state the orphan indication, the criteria on which the ODD was based and, if applicable, the development plan to support similarity or clinical superiority.

Indicate if scientific advice has been previously requested from the CHMP, national or non-EU (e.g., FDA) regulatory authorities.

Indicate if relevant CHMP guidance/CHMP advice has been followed or if any deviations have been made or proposed.

Indicate applicability and status of the plea (with or without deferral or waiver). Indicate availability and need for development in other special populations such as the elderly, male/female and ethnic minorities.

Clarify whether the product was deemed eligible for the PRIME (priority medicines) scheme launched by the EMA Committee for Advanced Therapies (CAT) classification for Advanced Therapy Medicinal Products (ATMPs), if applicable.

In case of follow-up advice, summarise the previous recommendations by the CHMP, indicate changes made to the development plans further to that advice and highlight points where follow-up is requested. A tabular presentation of this information can be considered.]

1.4. Rationale for seeking advice

[Describe the scope of the questions and the rationale for the advice request (e.g., for regulators: clinical/non-clinical/quality/significant benefit/similarity/conditional approval/exceptional circumstances).]

1.5. Previous consultations (HTA and/or Parallel)

[Briefly summarise the following aspects:

- If scientific advice has been previously requested and provided from national HTA bodies or via a European advice procedure (Early Dialogues (ED) during EUnetHTA JA3, JSC during EUnetHTA 21, Parallel EMA/HTAb Scientific Advice during the interim period, JSC under HTA Regulation).
    - If yes, please include the full advice documents for the European procedures as an annex to the briefing document.

Summarise the previous recommendations received, indicate changes made to the development plans further to that advice and highlight points where follow-up is requested.

Indicate if relevant guidance has been followed or if any deviations have been made or proposed. The information can be presented in tabular form.]

1.6. Potential health benefits

[Describe with substantiated statements where the product may be positioned in the treatment pathway and how the trial evidence will be used to support this positioning. Reference to section 4 Health economic assessment can be made to further outline the potential benefit.]

2. Overview of product development

[This section should give a comprehensive scientific overview of the product development program, providing relevant systematic information in sufficient detail, together with a critical discussion. However, it should be kept in mind that any information essential for the justification of a given question should also be sufficiently discussed in the corresponding HTD's position. The proposed list of subsections is not meant to be exhaustive nor mandatory, since the relevance or applicability of each subsection may vary depending on the scope of the advice request. In this respect, the potential direct or indirect relevance of the information covered in relation to the questions posed should be considered. It is strongly recommended to address all elements outlined below related to the area of the scientific advice. For areas not within the scope of the advice, it is acceptable to include only high-level information. The briefing document should contain all necessary information and function as a 'stand-alone' argument. Cross-references to annexes can be included only when additional detail is needed to support the argument. The use of tabulated overviews and graphs is encouraged.]

2.1. Clinical background information

[A tabular overview of all clinical studies including study number, main design features, patient number and characteristics, and current study status (completed, ongoing, planned) design, doses and duration of treatment, comparator, results of the trial (or preliminary results of ongoing trials if available) etc. should be provided. Detailed information can be provided in study reports as an annex, or relevant extracts from these reports. Cross-references to annexes are recommended. Also provide information on Post-Launch Evidence Generation (PLEG, if planned).

Whilst the focus should be kept on the intended indication, the development in other indications could be briefly summarised, where relevant. Data from early phases are also necessary as they serve as basis of the development plan.

Whilst the focus should be kept on the intended indication, the development in other indications could be briefly summarised, where relevant.]

2.1.1. <Clinical efficacy (total overview)>

[A general overview of the clinical development program should be based on a comprehensive discussion of e.g., the main clinical results so far, dose-response, exploratory trials, special populations, supportive and pivotal clinical studies, and any analyses performed across trials (pooled and meta-analysis). The discussion should identify the most important findings and challenges in the clinical development program, and its compliance with legal requirements, relevant clinical guidelines, previous scientific advice (sufficiently justifying any deviations), etc. Information on the geographical distribution of centres participating in the pivotal clinical studies can be reflected in this section.]

2.1.2. <Clinical safety (total overview)>

[A general overview of the safety profile of the product should be based on a comprehensive discussion of e.g., patient exposure (safety database), adverse events observed so far, serious adverse events and deaths, laboratory findings, safety-related discontinuations, specific safety findings, immunological events, safety in special populations, etc.]

2.2. Overview of clinical evidence subject to the JSC

[This section should focus on the information directly relevant to the requested JSC and give a comprehensive scientific overview of the product development programme, providing relevant systematic information in sufficient detail, together with a detailed discussion. However, it should be kept in mind that any information essential for the justification of a given question should also be sufficiently discussed in the corresponding HTD's position. The proposed list of subsections is neither meant to be exhaustive nor mandatory, since the relevance or applicability of each subsection may vary depending on the scope of the consultation request. In this respect, the potential direct or indirect relevance of the information covered in relation to the questions posed should be considered. Additional details can be provided with study protocols, study reports or investigators' brochures as annexes with cross-references in the background information and the HTD´s position. The use of tabulated overviews and graphs is encouraged.]

2.2.1. Planned clinical trial(s) subject to the JSC

[For the trial that is to be the subject of the JSC, a rationale and a short study synopsis (Section 5) of the protocol is to be provided. The short study synopsis should contain key information on the objectives of the trial, study design, patient population (inclusion and exclusion criteria), patient subgroups and stratification (if applicable), sample size estimation, line of treatment, comparators, endpoints (primary, secondary, etc.), measures used to assess endpoints, patient reported outcomes (PRO), patient flowchart, follow up, methods of statistical analysis multiplicity, etc.). If more trails are subject to the JSC, also provide study synopses for these studies. All relevant information should be given at a sufficient level of detail, together with a justification for the choices made and a critical discussion of key issues.

Provide sufficient information on Post-Launch Evidence Generation (PLEG) (if planned) for which the developer also requests advice, i.e. anticipated evidence gaps, remaining research questions, high level design of the study, core data set and data source details if use of an existing data source is planned.]

2.2.1.1. <Clinical efficacy proposed in the trial(s) subject to the JSC>

2.2.1.2. <Clinical safety proposed in the trial(s) subject to the JSC>

2.2.1.3. <Patient-Reported Outcomes (PROs), Health-Related Quality of Life (HRQoL) proposed in the trial(s) subject to the JSC>

[Provide a general overview of the planned Patient-Reported Outcomes (PROs) and Health-Related Quality of Life (HRQoL) measures being collected in the trial(s).

Explain the choice of PROs and patient reported outcome measures (PROMs) including a systematic literature review of existing PROs in the disease along with justification of the appropriateness of the questionnaire(s) chosen and the frequency of collection of this data. If patient preference data are planned to be collected alongside clinical development, detailed methodology should be given.]

2.2.1.4. <Relative effectiveness proposed in the trial(s) subject to the JSC>

[Provide considerations regarding generation of evidence on relative effectiveness (based on clinical trial efficacy). In particular, the points not addressed in the sections above can be explained in more detail. It may contain (as bullet points):

- Population,
- Choice of comparator,
- Study design,
- Study duration,
- Evidence synthesis (including indirect comparisons/NMA) – if applicable,
- Trial endpoints (including minimal clinically important differences),
- Predictive modelling of effectiveness from surrogate endpoints,
- Transferability of trial data,
- Evidence for sub-groups,
- Other relevant statistical issues (e.g. stratification),
- Choice of measures of health-related quality of life – if applicable]

2.3. Evidence gaps identified

[Describe the evidence gaps identified, particularly with respect to the information, data, analyses and other evidence that are likely to be required for JCA, and, if applicable, elaborate further in section 4 Health economic assessment on any evidence gaps which may be relevant for the health economic assessment. Please note, discussions on PLEG during the consultation can be facilitated only in conjunction with a request for discussion of pivotal trial design and when contextualised with clinical data expected from the pivotal (phase II/III) studies. Evidence gaps need to be identified as early as possible in the development of a product and therefore an early exchange on this topic, when discussing the pivotal study design, is encouraged.]

3. Questions for HTACG and HTD's positions

[**Questions** should conform to the **scope** of the Procedural Guidance for JSC on MP. It is recommended that questions are phrased in a way to allow for an unambiguous understanding of the question. The scope should be carefully considered in order to avoid too broad or too narrow questions. For a given development programme, it is recommended that clinical questions are posed foremost about population(s), comparator(s) and outcomes. The intended placement of the intervention in the treatment pathway should be clear.

The wording of the question should be clear and concise, avoiding extended reference to the justifications (which should be discussed in the HTD position) and starting with, for example, "Does the HTACG agree that/with…?". Questions concerning the future appraisals and/or reimbursement/coverage decision will not be considered by the HTACG, in accordance with the general principles of JSC.

It is recommended to limit the number of questions (maximum 10) in order to focus the discussion on the relevant aspects of the briefing document. It is highly recommended to ask focused questions with a maximum of one or two sub-questions.

IMPORTANT INFORMATION

Each question should be followed by a corresponding, separate HTD's position including a comprehensive justification of the chosen approach.

All key information about the topic should be sufficiently discussed, so that the HTD's position can function as a 'stand-alone' argument. Issues to be covered could include the following: context and proposal, other options (potentially) considered together with a critical discussion on the relative merits and drawbacks of various approaches, possible consequences and eventual measures to ameliorate these. Statements regarding the properties (e.g., type I error control) of novel and/or complex statistical procedures should be justified with reference to the relevant scientific literature, or otherwise. In general, an extension of 1 to 3 pages for each HTD position is recommended.

Cross-references to the relevant parts of the briefing document or annexes can be included if additional detail is needed to support the argument.]

[There are no mandatory areas for discussion. However, several areas are recommended:

- Population, including potential deviation between study population vs targeted indication, biomarkers, subgroups, extrapolation, generalizability;
- Intervention, including dosing, concomitant, add-on, monotherapy, duration, label/indication induction, life-long therapy;
- Comparator;
- Outcomes, including primary & secondary endpoints, PROs, Adverse Events (AEs);
- Study design, including randomisation, blinding, duration, statistical methods, time points of data collection.

Justified proposals for each of them should appear in the HTD's position if they are to be discussed during the meeting. Otherwise, they should be clearly stated in section 2.2.1 Planned clinical trial(s) subject to the JSC.

All relevant questions must be submitted in this briefing document. Questions should be presented following the topics as described above. Any other questions on clinical development can be placed after those topics.

The suggested question categories are a recommendation and can be adapted or expanded as required.]

3.1. <Questions regarding population(s)>

Question {X}

Does the HTACG agree that/with {}?

HTD's position: {}

3.2. <Questions regarding intervention>

Question {X}

Does the HTACG agree that/with {}?

HTD's position: {}

3.3. <Questions regarding comparator(s)>

Question {X}

Does the HTACG agree that/with {}?

HTD's position: {}

3.4. <Questions regarding outcomes>

Question {X}

Does the HTACG agree that/with {}?

HTD's position: {}

3.5. <Questions regarding study design>

Question {X}

Does the HTACG agree that/with {}?

HTD's position: {}

3.6. <Questions regarding Post-Launch Evidence Generation (PLEG)>

[There are no mandatory areas for discussion. However, several areas are recommended:

- Anticipated evidence gaps and unanswered research questions at the end of pivotal trials
- Post-launch study design with sufficient information on additional data planned to be collected, for example population targeted, comparative data, choice of outcomes, timeframe
- Quality of data source: study is based on a disease registry or another existing database. For discussion on quality of disease registry.
- Please note, discussions on PLEG can be facilitated only in conjunction with a request for discussion of pivotal trial design and when contextualized with clinical data expected from the pivotal (phase II/III) studies.]

Question {X}

Does the HTACG agree that/with {}?

HTD's position: {}

4. Health economic assessment (optional)

Advice on health economic assessment may be provided as part of the voluntary cooperation on health technology assessment pursuant to Article 23 of the EU HTA Regulation.

4.1. Product development programme

4.1.1. Information on health economic assessment for HTA

[Describe the scope of the planned economic analysis, clearly defining the research questions. Evidence gaps and model assumptions should be described. In this section the external validity needs to be explored.

If plans for the health economic assessment are provided, these should include to the extent possible:

- Description of the proposed model (diagram, modelling approach, time horizon, perspective, type of analysis)
- Information on data collection plans to inform the model:
  - Evidence synthesis/meta-analysis – sources of evidence
  - Comparators – Mixed Treatment Comparisons (MTC) and indirect comparisons and evidence available
  - Trial endpoints used to derive health outcomes in the model
  - Quality of life – source and methods, tools used to measure quality of life
  - Incorporation of adverse effects
  - Resource use – sources and methods, tools used to measure resource utilisation
- Information on methodological approaches:
  - Extrapolation – assumptions and data sources
  - Continuation rules
  - Use of surrogate outcomes
  - Planned sensitivity analyses
  - Expected (key) limitations
- Information regarding external validity/internal validity]

4.2. Questions and HTD's positions

4.2.1. <Questions regarding health economic assessment to the HTACG>

[There are no mandatory areas for discussion. However, several areas are recommended based on their importance for HTA. Proposed areas are the following:

- Time horizon
- Population
- Choice of comparator
- Model structure
- Model assumption and planned scenario model outcomes
- Clinical data and other data sources used to populate the model
- Extrapolation hypothesis
- Perspective (societal, healthcare related etc.)
- Utility values
- Collection of resource utilisation data
- External validity
- Internal validity

The topics listed above are essential for the discussion with the HTACG. Therefore, justified proposals for each of them should appear in the HTD's position if they are to be discussed during the discussion meeting. Otherwise, they should be clearly stated in section 2.2.1 Planned clinical trial(s) subject to the JSC.]

Question {X}

Does the HTACG agree that/with {}?

HTD's position: {}

5. Short Study Synopsis

Date of the information provided: **- *Date* -**

[Please specify/delete as necessary.]

(Planned) Phase-II/III-study NAME – Short Study Information	
Short description	[Open/(double)blind, randomized, placebo/active control, Intervention, study population
Study objective	Comparison of effectiveness and safety of intervention vs. comparator in description of study population, quality of previous specific therapy
Centres	Number of Centres, nations/continents
Size of study	estimated number of randomized patients
Inclusion criteria	- - - -
Exclusion criteria	- - - -
Design	Parallel-group/cross over/factorial design
Randomization	N:M
Stratification	Disease severity, prior therapy, ethnicity, geographic region
Blinding	Blinding for Intervention, outcome assessment
Intervention	Substance INN, Dose, application, duration
Additional intervention	Substance INN, Dose, application, duration
Comparator	Substance INN, Dose, application, duration
Additional Comparator	Substance INN, Dose, application, duration
Start/End Date	(Planned) start and end date of patient inclusion and of study treatment. (Planned) date of analysis of primary outcome
Study periods	Duration of pre-randomization, study, post-treatment periods
Interim analyses	Methods and Procedures used
primary hypothesis to be tested	superiority/non-inf/equivalence; which arms will be compared
Outcome measures	
Primary	Primary outcome measure (and timing of assessments)
Secondary	Secondary outcome measure (and timing of assessments)
Quality of life	All QoL measures not yet listed (and timing of assessments)
Supplementary	Additional outcome measure (and timing of assessments)

List of References

[In general, all relevant publications included in the list of references should be annexed in full text (in PDF format, either collated as a single document or, if provided as single files, clearly identified and whenever possible compiled in one or more compressed files, for convenience). In case a relevant publication is not included at the time of validation, it should be ensured that it can be made available upon request.]

List of Annexes

[Annexes (to be submitted as separate files) should include any information potentially relevant to the questions, e.g.

- Investigators' brochure
- Study protocols (final, draft or outline/synopsis, statistical analysis plan)
- Study reports (final/draft/synopses)
- Pharmacokinetic modelling and simulations reports
- Previous scientific advice received relevant for the present JSC (e.g. CHMP Scientific Advice/Protocol Assistance, any relevant official correspondence and meeting minutes with National Competent Authorities in EU-Member States, FDA and other non-EU Authorities as well as with national HTA bodies or previous European advice procedures)
- Relevant guidelines (non-EMA)
- Documents related to Orphan Drug Designation (e.g. COMP summary report)
- Documents related to Paediatric Investigation Plans (e.g. PDCO summary report, opinion)
- Contract/agreement consultant/CRO - sponsor
- Literature references]

Contact points

Any question or comment concerning this document or any other point related to the JSC should be directed to the HTA secretariat.