Briefing book template for Pharmaceuticals

EUnetHTA multi-HTA Early Dialogues

EUnetHTA EMA multi-stakeholder Early Dialogues

Last updated: 25-Jan-17

This template is to be used by companies willing to submit an overview of relevant information necessary to support an Early Dialogue discussion in the frame of EUnetHTA JA3. It is to be used for both EUnetHTA multi-HTA Early Dialogues and EUnetHTA EMA multi-stakeholder Early Dialogues.

Standard headings in the template should be used whenever possible. If it is considered necessary to deviate from the pre-specified headings due to product-specific requirements, alternative or additional headings/domains may be considered.

Colour coding:

Sections shaded in lightblue are of relevance only for EUnetHTA EMA multi-stakeholder Early Dialogues and display mandatory or optional information according to the bracketing convention stated below.

*Bracketing convention:*

*{text}: Required information;*

<text>*: Optional information to be given if applicable;*

*[text]: Explanation and guidance.*

References convention:

For citation of literature references, footnotes are preferred, alternatively the format (first author <et al.>, publication year) is recommended.

The document must be submitted in Word format. The recommended length of the briefing book is approximately 50 pages, not including annexes. Any essential self-standing documents such as study protocols, reports etc. should be placed in the annex (section 5 of this template) or should be submitted as separate documents in a Word or PDF format. Referenced articles should be submitted in full text versions.

The EUnetHTA JA3 has received funding from the European Union, in the framework of the Health Programme.



Briefing book template for Pharmaceuticals

EUnetHTA multi-HTA Early Dialogues

EUnetHTA EMA multi-stakeholder Early Dialogues

Active substance: {}

Product Name: {}

Pharmaco-therapeutic group: {}

Intended indication(s): {}

Applicant (company): {}

Version: {}

Date: {DD/MM/YYYY}

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List of Abbreviations

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

**1. Summary**

[[It is strongly recommended to address all elements outlined below (whenever applicable) for any advice request, regardless of the scope of the questions. This summary will inform the background information section of the final advice letter. An upper limit of 3 pages for the summary is recommended]

## 1.1. Background information on the disease to be treated

### 1.1.1. Overview of the disease

{}

[Relevant epidemiological data, information on natural history of the disease and evolution on treatment should be discussed.]

### 1.1.2. Treatment options

{}

[The company should list all technologies (drugs, devices, procedures) that present relevant alternatives for the treatment of the pathology (stage, line of treatment) and discuss the current standard therapy with regard to the respective labelling status in Europe and North America. In the case of the existence of new treatments that are in advanced phases of development, this information should be included.]

## 1.2. Background information on the product

### 1.2.1. Indication

{}

[The company is asked to specify clearly the intended indication (1st line, 2nd line, 3rd line of treatment; add-on or monotherapy) of the product in development, as well as the aim of treatment (preventive, curative, palliative, symptomatic, disease modifying etc.). The position of the product in the treatment algorithm should be proposed. The target population of the product should be described as precisely as possible.]

### 1.2.2. Form, route of administration, dose, dosage

{}

[Route of administration and the pharmaceutical form of the product should be described. Dose, frequency of administration and the duration of use should be discussed based on the available evidence at the stage of development.

If the administration of the product is associated with the use of a diagnostic test, a medical device or with a medical procedure, this information should be stated and adequate information given on the associated test or device.]

### 1.2.3 Characteristics of the product

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[Chemical/biological product; orphan product; advanced-therapy medicinal product, any special precautions or recommendations for use of the product (including a possible risk management strategy)]

### 1.2.4. Mechanism of action

{}

[Pharmaco-therapeutic group should be indicated. ATC code should be given if applicable. The mechanism of action should be described as well as key information on pharmacodynamics and pharmacokinetics.]

## 1.3. Quality development

<>

[Relevance, and level of detail included may vary depending on the scope of the request. Special pharmaceutical aspects, if any, e.g. novel delivery system, etc.]

## 1.4. Non-clinical development

<>

[Relevance, and level of detail included may vary depending on the scope of the request. Proof-of-concept and main toxicological findings could be informative.]

## 1.5. Clinical development

{}

[This section should contain a summary of clinical development of the product and give a clear idea of the stage of development of the product. Evidence obtained in the field of the required indication should be mentioned. Existence of trials supporting the use of the product in other indications should be mentioned for completeness. A tabulated summary of completed, ongoing and planned clinical trials would be informative. Briefly summarise whether scientific advice has been previously received from any regulator or HTA institution (EU, national or non-EU (e.g. FDA) and provide minutes or indicate if it is planned at any further stage. Outline whether the relevant advice has been followed or if any deviations have been made or proposed.]

[If applicable, indicate applicability and status of the Paediatric Investigation Plan (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.]

### 1.5.1. Clinical development up to date

{}

[Data on efficacy and safety coming from phase I (if relevant) and phase II clinical trials that are completed or ongoing should be presented. For each trial the design, doses and duration of treatment, comparator, number of subjects and description of studied population, results of the trial (or preliminary results of ongoing trials if available) and all other important information should be given. Data and results may be summarized in tables. Detailed information should be available in study reports in annexes. Cross-links to annexes are recommended.]

### 1.5.2. Planned trials

{}

[This section should provide a comprehensive overview of all planned trials with the product in the intended indication. The company should clearly state which of the planned trials (if there are more than one) will be the subject of the Early Dialogue and a rationale and a synopsis of the protocol should be provided. The synopsis should contain key information on objectives of the trial, trial design, patient population (inclusion and exclusion criteria), comparators, endpoints (primary, secondary etc.), flowchart, follow up, methods of analysis etc. All relevant systematic information should be given at a sufficient level of detail, together with justification for the choice made and a critical discussion of key issues.]

## 1.6. Economic aspects

<>

[If the company desires to discuss economic assessment as a part of the Early Dialogue, then all relevant information about the planned economic analysis should be provided. The company should state the scope of the planned economic analysis, clearly defining the research questions. The company should describe the main aspects of the economic analysis, in particular the type of analysis, the perspective, the time horizon, the population and the comparator(s).

An outline of the structure of the model could be provided if available. Relevant published papers could be provided as annexes to the briefing book. Expected data sources and planned sensitivity analyses should be described. Trial endpoints used to derive the model health outcome should be stated where relevant. Tools used to measure resource utilization should be described.]

## 1.7. Regulatory status

{}

[Information should be given on the worldwide regulatory status of the product (e.g. any existing marketing authorisation (MA), or planned marketing authorisation application (MAA) timelines), indicating planned type and timelines of MAA (e.g. full/mixed dossier; advanced therapy, biosimilar, generic/hybrid/ product) or variation. The company should indicate whether a scientific advice has been received from any regulator (EU, national or non-EU (e.g. FDA) and provide minutes or indicate if it is planned at any further stage. Estimated timelines for market entry may be given if this information is available.

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.]

## 1.8. Rationale for seeking advice

{}

[The scope of the questions and the rationale for the advice request should be elaborated (e.g. clinical/non-clinical/quality/significant benefit/similarity/conditional approval/exceptional circumstances).]

## 1.9. Discussion on added benefit

{}

[The company should provide arguments supporting the added benefit of the product in the target population in comparison with the standard of care and with a pharmacologically similar product aimed to be replaced (if adequate).]

# 2. Questions and Applicant’s positions

The company should list all questions they wish to address. 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. The wording of questions should be clear and concise, avoiding extended reference to the justifications (which should be discussed in the Applicant position). Open questions are not acceptable. Given the timeframe, a high number of questions (i.e. more than 10) is not feasible to be discussed during the meeting. Questions should be ordered in the corresponding section according to the expertise required for the assessment, and numbered sequentially. Each question should be followed by a corresponding, separate Applicant’s position including a comprehensive justification of the chosen approach. All key information about the topic should be sufficiently discussed, so that the Applicant 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. Each position description should not be longer than 3 pages. Cross-references to the relevant parts of the briefing document or to annexes can be included if additional detail is needed to support the argument.

All scales and scores that will be used for endpoint measurement should be presented and their validity should be commented.]

## 2.1. Questions on Chemical, Pharmaceutical and Biological development

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## 2.2. Questions on Toxico-Pharmacological development

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## 2.3. Questions on Clinical development

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

* population
* comparator
* trial design and duration
* endpoints
* statistical issues (stratification, subgroups etc.)

The topics listed above are essential for the discussion with HTA bodies. Therefore, justified proposals for each of them should appear in the Applicant’s position if they are to be discussed during the meeting. Otherwise, they should be clearly stated in section 1.5.2 Planned trials.]

## 2.4. Economic questions

<>

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

* population
* choice of comparator
* choice of economic model
* data used to populate the model
* time horizon and extrapolation hypothesis
* perspective (societal, healthcare related etc.)
* utility values
* resource utilisation data

The topics listed above are essential for the discussion with HTA bodies. Therefore, justified proposals for each of them should appear in the Applicant’s position if they are to be discussed during the meeting. Otherwise, they should be clearly stated in section 1.5.2 Planned trials.]

## 2.5. Questions on Significant Benefit

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[For Protocol Assistance, the questions should be within the scope of the designated orphan indication.]

# 3. Background information

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 Applicant’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 advice 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 included in study protocols, study reports, investigators’ brochure provided as annexes. The use of tabulated overviews and graphs is encouraged.]

## 3.1. Quality background information

<Active substance>

<Finished product>

## 3.2. Non-clinical background information

<Pharmacology>

<Pharmacokinetics>

<Pharmacodynamics>

<Toxicology>

[It is recommended to include a tabulated overview of all non-clinical studies (completed, ongoing and planned), including study number, main design features and GLP status. Main findings and safety margins may be described in the narrative.]

## 3.3. Clinical background information

<Clinical pharmacology>

<Pharmacokinetics>

<Pharmacodynamics>

 [A tabular overview of all clinical studies (completed, ongoing and planned), including study number, main design features, patient number and characteristics, etc. could be informative, if not provided elsewhere. Whilst the focus should be kept on the intended indication, the development in other indications could be briefly summarised, where relevant.]

## 3.3. Clinical efficacy

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[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.]

## 3.3. Clinical safety

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[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.]

# 4. List of References

{}

[In general, any potentially relevant publications included in the list of references should be annexed (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.]

# 5. List of Annexes

 [Annexes should include any information potentially relevant to the questions, e.g.

* Investigators’ brochure
* Study protocols (final, draft or outline/synopsis)
* Study reports (final/draft/synopses)
* Previous scientific advice received (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)
* Relevant guidelines (EMA and 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
* Referenced articles in full text versions in English

# 6. Contact point

Any question or comment concerning this document or any other point related to the Early Dialogues conducted in the frame of EUnetHTA JA3 should be sent to early-dialogues@eunethta.eu for EUnetHTA multi-HTA Early Dialogues and to early-dialogues@eunethta.eu and scientificadvice@ema.europa.eufor EUnetHTA EMA multi-stakeholder Early Dialogues.