Committee for Medicinal Products for Human Use (CHMP)

Committee for Advanced Therapies (CAT)

Text in purple: applicable for ATMPs only

Briefing Note and Recommendations on a Request for Accelerated Assessment Pursuant to Article 14 (9) of Regulation (EC) No 726/2004

Active substance(s): <active\_substance>

EMA product number: <product\_number>

REVISION: February 2021

Guidance text is in green italics. You may print a copy of this template with the guidance text, then delete all guidance text except in the comment’s boxes:

Bracketing convention: <text> - Text to be selected or deleted as appropriate.

Do not change or delete the titles and the numbering style. Add “Not applicable” if necessary.

Do not delete the comment boxes, nor its content including the guidance text in green italics as this document will also be used by the Rapporteurs for their assessment.

**General guidance**

**Purpose**

The purpose of this document is for the applicant to request accelerated assessment, and the joint Rapporteur and Co-rapporteur to summarise their comments and recommendations on the request. The joint assessment of the Rapporteurs is to be circulated to CAT/CHMP in preparation of a discussion and recommendation on a request for accelerated assessment.

**Reminder about the legal basis**

Recital 33 of Regulation (EC) No 726/2004 states that “in order to meet, in particular the legitimate expectations of patients and to take account of the increasingly rapid progress of science and therapies, accelerated assessment procedures should be set up, reserved for medicinal products of major therapeutic interest, and procedures for obtaining temporary authorisations subject to certain annually reviewable conditions”.

Article 14 (9) of Regulation (EC) No 726/2004, states that when an application is submitted for a marketing authorisation in respect of medicinal products for human use which are of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may request an accelerated assessment procedure. The request shall be duly substantiated.

**Relevant guidelines**

[Guideline on the scientific application and the practical arrangements necessary to implement the procedure for accelerated assessment pursuant to Article 14(9) of Regulation (EC) No 726/2004.](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/03/WC500202629.pdff)

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Administrative information

For applicants: Please complete relevant sections based on available information at the time of the request.

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| --- | --- |
| Contact information | |
| Applicant Name: | <APPLICANT> |
| Applicant’s contact person: | <name>  Tel.: <telephone>  Email: <email> |
| <CHMP or CAT> Rapporteur: | <name> |
| <CHMP or CAT> Rapporteur’s contact person: | <name>  Tel.: <phone>  Email: <email> |
| CHMP Coordinator of Rapporteur: |  |
| <CHMP or CAT>Co-rapporteur: | <name> |
| <CAT> Co-rapporteur’s contact person: | <name>  Tel.: <phone>  Email: <email> |
| CHMP coordinator of Co-Rapporteur: |  |
| EMA Product Lead: | <name>  Tel.: <phone>  Email: <email> |
| EMA Procedure Assistant: | <name>  Tel.: <phone>  Email: <email> |

Product background information

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| --- | --- |
| Proposed invented name of the medicinal product: | <PRODUCT> |
| INN (or common name) of the active substance: | <common name> or <INN> |
| EMA product number: | <product number> |
| Proposed indication(s): | <therapeutic indication> |
| Strength(s)/pharmaceutical form(s): | <pharmaceutical form> <strength> |
| Intended submission date (the planned submission timing should be respected): | <date> |
| Proposed legal basis of the application according to Directive 2001/83/EC, as amended: | <proposed eligibility> |
| ATMP | Yes/No |
| Under PRIME scheme: | Yes/No |
| Orphan designation: | Yes (<based> / <not based> on claim of significant benefit over existing therapies) / No |
| Waiver for paediatric development granted based on lack of significant therapeutic benefit: | Yes / No  Note: If such waiver covers part of the paediatric population in the target condition, please indicate ‘yes’. |

1. Timetable for the assessment of the accelerated assessment request

*Note: Applicant to select the relevant TT for ATMP vs non-ATMP and delete the other one.*

Timetable for the assessment of the accelerated assessment request for non-ATMPs

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| **Deadline for Submission** | **Start date** | **CHMP Rapporteurs Joint briefing note** | **Comments from CHMP** | **Updated CHMP Rapporteurs Joint briefing note** | **CHMP conclusion** |
|  |  |  |  |  |  |

<https://www.ema.europa.eu/documents/other/timetable-accelerated-assessment-request-initial-marketing-authorisation-applications_en.pdf>

**<Note to the applicant (non-ATMP):**

Accelerated assessment reduces the maximum timeframe for review of an application for marketing authorisation to 150 days. Any procedure lasting longer than 150 days (excluding clock-stops) will not be considered “accelerated assessment”.

The assessment of the MAA under Accelerated assessment is split in 3 phases: 90/30/30 days.

At Day 90 a List of Questions is adopted with 1-month clock-stop for provision of responses set as default. The 2nd & 3rd phase are two consecutives cycles of 30 days giving an opportunity to reach an opinion at Day 120, or to adopt a List of Outstanding Issues (with no clock-stop for provision of responses) in order to reach the opinion at Day 150. The last 30 days cycle should be ideally reserved for non-major objections such as PI and RMP finalisation.

The procedure may not be able to remain under the accelerated assessment (AA) timetable if a longer clock stop is requested. Other reasons for a need to revert back to standard timelines may include the need for GMP or GCP inspection becoming apparent during the assessment or identifications of major objections that cannot be handled in an accelerated timetable.

A decision on accelerated assessment is taken without prejudice to the CHMP opinion (positive or negative) on the granting of a marketing authorisation and any ancillary claims and, where applicable, to the COMP opinion (positive or negative) on the maintenance of the orphan designation.

>Timetable for the assessment of the accelerated assessment request for ATMPs

| Deadline for Submission | Start date | CAT Rapporteurs Joint briefing note | Comments from CAT and CHMP | Updated CHMP Rapporteurs Joint briefing note | CAT conclusion | CHMP conclusion |
| --- | --- | --- | --- | --- | --- | --- |
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<https://www.ema.europa.eu/en/documents/other/timetable-accelerated-assessment-request-initial-marketing-authorisations-atmp_en.pdf>

**<Note to the Applicant (ATMP):**

The request for accelerated assessment will be **reviewed by the CAT** before endorsement by CHMP.

Accelerated assessment reduces the maximum timeframe for review of an application for marketing authorisation to 150 days. Any procedure lasting longer than 150 days (excluding clock-stops) will not be considered “accelerated assessment”.

For Advanced Therapy Medicinal Products, the assessment of the MAA under AA remains as **120 + 30 days** due to:

* + Expected complexity in the scientific and regulatory evaluation of these novel types of products;
  + Evaluation complexity by having three Committees involved (CAT, CHMP and PRAC);
  + Need for additional consultation in some cases (like with GMO competent authorities or notified bodies).

Therefore, at Day 120 a List of Questions is adopted for provision of responses. Due to the complexity of these products, up to 3 months clock-stop after the adoption of the LoQ can be allowed. The procedure will not be able to remain under the accelerated assessment timetable if a longer clock stop is requested. Other reasons for a need to revert back to standard timelines may include the need for GMP or GCP inspection becoming apparent during the assessment or identification of major objections that cannot be handled in an accelerated timetable.

A decision on accelerated assessment is taken without prejudice to the CAT/CHMP opinion (positive or negative) on the granting of a marketing authorisation and any ancillary claims and, where applicable, to the COMP opinion (positive or negative) on the maintenance of the orphan designation.>

1. Tentative timetable for the marketing authorisation evaluation under accelerated assessment

*Note: Applicant to select the relevant TT for ATMP vs non-ATMP and delete the other one.*

Tentative timetable for the MA evaluation under accelerated assessment for non-ATMPs

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| **Deadline for Submission** | **Start date** | **CHMP (Co) Rapporteur ARs** | **PRAC Rapporteur AR** | **Comments from PRAC** | **Comments from CHMP** | **PRAC outcome** | **Early draft LOQ (for Peer review tele-conference)** | **Peer review telecon-ference (TC)** | **Draft LoQ** | **List of Questions (LoQ)** | **Opinion** |
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Tentative timetable for the assessment of the responses to the List of Questions (LoQ) under accelerated assessment

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| **Deadline for Submission** | **Restart** | **CHMP and PRAC Rapporteurs Joint AR (JAR)** | **Comments from PRAC and CHMP** | **Updated CHMP and PRAC Rapporteurs JAR** | **List of Outstanding Issues (LoOI)** | **Opinion** |
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Tentative timetable for the assessment of the responses the to List of Outstanding issues (LoOI) under accelerated assessment

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| **Deadline for Submission** | **Restart** | **CHMP and PRAC Rapporteurs Joint AR (JAR)** | **Comments from PRAC and CHMP** | **Updated CHMP and PRAC Rapporteurs JAR** | **Opinion** |
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<https://www.ema.europa.eu/en/documents/other/timetable-initial-full-marketing-authorisation-application-accelerated-assessment_en.pdf>

Tentative timetable for the MA evaluation under accelerated assessment for ATMPs

| **Deadline for Submission** | **Start date** | **CAT (Co) Rapporteur ARs** | **PRAC Rapporteur AR** | **Comments from PRAC, CAT, CHMP** | **Early draft LOQ (for Peer review tele-conference)** | **PRAC outcome** | **Updated PRAC Rapporteur AR** | **Peer review telecon-ference (TC)** | **Draft LoQ** | **CAT List of Questions (LoQ)\* or draft Opinion** | **CHMP Opinion\*** |
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Tentative timetable for the assessment of the responses to the List of Questions (LoQ) under accelerated assessment

| **Deadline for Submission** | **Restart** | **CAT and PRAC Rapporteurs Joint AR (JAR)** | **Comments from CAT, PRAC and CHMP** | **Updated CAT and PRAC Rapporteurs JAR** | **CAT List of Outstanding Issues (LoOI)/Draft opinion** | **CHMP LoOI/Opinion** |
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<https://www.ema.europa.eu/en/documents/other/timetable-initial-full-marketing-authorisation-application-accelerated-assessment-timetables_en.pdf>

1. Submission of the request

The applicant <APPLICANT NAME> submitted on <date> a request for accelerated assessment pursuant to Article 14 (9) of Regulation (EC) No 726/2004, for an application for marketing authorisation to the Agency for <PRODUCT>, for <therapeutic\_indication>.

1. Background information concerning the medicinal product

Summary of applicant’s position:

Description of the medicinal product

Provide a brief description of the medicinal product, and include the regulatory status of the product.

Rationale for use in proposed indication(s)

Outline the main features of the disease/target condition and the rationale for the use of the medicinal product in the proposed indication(s), based on the mechanism(s) of action of the product.

Note:

Applicants are reminded that in the case where more than one indication is applied for in a single application, the likelihood that accelerated assessment can be granted and/or maintained are reduced if not all indications fulfil the AA criteria. In such case, it is particularly important that the dossier for all indications is sufficiently mature and suitable for an accelerated assessment and this should be discussed in Section 7.

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| *Note: Section for Rapporteurs. Applicants should not modify/delete guidance text.*  **Comments on the applicant’s position, if applicable:** |

1. Description of unmet medical need

Unmet medical needs mean a condition for which there exists no satisfactory method of diagnosis, prevention or treatment in the Union or, even if such a method exists, in relation to which, the medicinal product concerned will be of major therapeutic advantage to those affected.

Summary of applicant’s position:

Describe the unmet medical need for each proposed indication using as much as possible epidemiological data about the disease and outcomes (e.g. life expectancy, symptoms and duration, health-related quality of life). The claims should be substantiated with data from published literature, registries or healthcare databases. If relevant, the unmet need should be described separately for different indications or subpopulations.

Summary of applicant’s position:

Epidemiology

The purpose of this section is to describe the disease burden, which is related to the unmet medical need. Summarise the epidemiology of the disease (e.g. incidence, life expectancy, symptoms and duration, health-related quality of life). The description should be as specific as possible to the therapeutic indication proposed above rather than the entire condition.

Note: High-level textbook introductions to a therapeutic area should be avoided. For instance, if the therapeutic indication is for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, there is no need to describe the epidemiology of multiple myeloma in great detail, but the discussion should mainly focus on the specific clinical setting.

Existing methods

*Describe all available diagnostic (if applicable), prevention and treatment options/standard of care (SOC) for each indication, including all relevant treatment modalities, e.g. medicinal products used in clinical practice (whether approved or not), devices, surgery, and radiotherapy should be included, as relevant in this discussion.*

*The most important effects and limitations of available treatments should be described. Consider unmet need in different subgroups of the target population, if relevant based on the intended patient population(s).*

Conclusions on unmet medical needs

*Discuss how the unmet medical need highlighted above is fulfilled or not by the available methods (if any). This should include a discussion on the limitations of the current options/standard of care discussed under existing methods that the proposed product aims to address. Quantify the unmet medical needs based on medical or epidemiological data.*

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| *Section for Rapporteurs. Applicants should not modify/delete guidance text.*  **Assessment of applicant’s justification:**  Note: ‘unmet medical needs’ should be understood as a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the EU or, even if such a method exists, in relation to which, the medicinal product concerned will be of major therapeutic advantage to those affected.  Points to address and comment for each indication:  Evaluate the applicant’s description of available methods; is the description of available methods accurate? Does it include all available methods (not just medicinal products)?  Evaluate the epidemiological data and justifications provided to quantify the unmet medical need in the claimed indication. Has the unmet need been adequately described in epidemiological terms in the target patient population? Are important differences in the subpopulations (if claimed by the applicant) well described?  Conclude and quantify the unmet need (e.g., expected 5-year survival of 50%, compared to 90% for a comparable healthy population, despite available treatments), as much as possible. In principle however, if there is an identifiable population or subpopulation for whom an unmet need can be described, then this would be sufficient to establish an unmet need.  If there are available methods, identify the limitations that the proposed product aims to address. |

1. Fulfilment of unmet medical need

Summary of applicant’s position:

*In this section, the applicant should discuss how the medicinal product addresses to a significant extent the unmet medical need.*

*Describe for each indication how and to what extent the product is expected or assumed to fulfil the unmet need. This should be based on available data that should be summarised here using data from the main studies focusing on the observed effects and their clinical relevance in terms of primary endpoint, key secondary endpoints together with a summary of the safety profile. Importance of the observed effects of the product should be discussed, as well as the expected added value of the product and impact on medical practice in comparison to existing treatments (if any). Added value over existing methods would normally be based on meaningful improvement of efficacy and/or safety and/or in exceptional cases, major improvements to patient care (e.g. allows ambulatory vs. hospital treatment only) using robust evidence. Discuss also how the overall B/R balance compares with that of current methods.*

*Consider in the argumentation any previous COMP conclusions on (expected) significant benefit or absence thereof, and PDCO conclusions on (expected) absence of significant therapeutic benefit if that has been the basis for a paediatric development waiver.*

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| **Assessment of applicant’s justification:**  Evaluate the claims made by the applicant for each indication.  Assess how the product is expected or assumed to fulfil the unmet needs identified in section 5. This should be based on the observed effects of the product and how robust and important these are judged to be (e.g., effect on overall survival, undisputed clinical relevance of the endpoint) as well as methodological considerations. Claims on benefits and risks can be based on traditional efficacy and safety endpoints or other health outcomes (e.g., patient-reported outcomes). Consider if the chosen endpoints are adequate to support the claim in the proposed condition. Consider if the magnitude of the effects brings a substantial improvement compared to available methods. Consider also whether the effect size and follow-up are sufficient to support robustness of data and duration of the effect.  At this stage, the effects will be based on reasonable assumptions and high-level summary results, taking into account plausible applicant’s claims or abridged reports pending in-depth analysis of benefits and risks based on assessment of clinical study reports.  Note that a new mechanism of action does not per se constitute a major therapeutic advantage.  The major therapeutic advantage over existing methods could be based on improved efficacy and/or safety and/or a major improvement to patient care, but in any case, should not be at the expense of an unfavourable overall B/R balance versus other existing therapies. |

1. Strength of evidence to support accelerated assessment

Summary of applicant’s position:

*Describe the strength of evidence to be included in the planned application, to substantiate that available data will allow conducting and maintaining accelerated assessment (potentially leading to an earlier marketing authorisation and addressing of the unmet needs). While the main evidence on the potential of the product to address unmet medical need is presented in section 6. , this section should focus on general suitability of the planned data package for an accelerated assessment. Specifically discuss robustness and completeness of data package on quality, non-clinical and clinical aspects (where applicable for each indication), taking into account the planned authorisation type (standard MA vs. conditional MA vs. MA under exceptional circumstances). Describe the number and types of main clinical studies, sample size, design and key results. Discuss any identified limitations of the dossier, covering quality, non-clinical and clinical aspects. Serious/treatment emerging adverse events should be summarised.*

*For conditional MA or MA under exceptional circumstances where the benefit of immediate availability of the medicine outweighs the risk of less comprehensive data than normally required, please discuss how the benefit-risk balance can be established based on available data. Reflect whether additional data may become available for submission during the review and discuss the importance of those data with regard to the assessment of B/R; to that end, applicants are reminded that at the time of the initial filing, the dossier needs to be mature including all relevant data that is needed to support an assessment of benefit: risk in the connect of a marketing authorisation, including any justification for extrapolation beyond the population studied in clinical trials.*

*If the development programme has been previously agreed via CHMP Scientific Advice/Protocol Assistance, this should be summarised here, in particular when the extent of the data required for a particular claim/indication has been discussed. Discuss any deviations from scientific advice and other advice received (e.g. in PRIME discussions or pre-submission meetings).*

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| *Note: Section for Rapporteurs. Applicants should not modify/delete guidance text.*  **Assessment of applicant’s justification:**  Assess the completeness of the planned dossier, taking into account the intended authorisation type. The suitability of the dossier for accelerated assessment needs to be estimated. Are the data planned to be submitted (e.g., number and types of studies) sufficient, in principle, for conducting the assessment or are there obvious gaps in the dossier that would make several rounds of assessment likely? Have any important gaps been identified in the quality data of the planned submission that may impact eligibility to accelerated assessment?  Would the planned data package (including sample size, design of studies) in general allow drawing conclusions on safety and efficacy of the product in the proposed indication(s)?  For example, if the only data presented are in terms of non-parallel controlled studies (e.g., single-arm study with historical controls), can the effects of the product be determined compared with the current standard of care? Do the studies appear in principle large enough for a convincing quantification of efficacy and safety? If not, are the claimed effects so compelling that potential methodological issues can be overcome?  Any issues identified with the proposed dossier can be flagged; however, it is not expected to conduct a pre-assessment of the benefit-risk balance or other outcomes of the MAA assessment (e.g. pre-assessment of fulfilment of CMA criteria).  Note that the need to do an in-depth assessment of the clinical trial data should not in principle constitute a reason for rejection but concerns should be flagged in this section. |

1. Conclusion on major public health interest and major therapeutic innovation

The assessment should conclude on whether the request for an accelerated assessment has been duly substantiated, and if the medicinal product is of major interest from the point of view of public health.

*Note: Section for Rapporteurs. Applicants should not modify/delete guidance text.*

**Assessment of applicant’s justification:**

Main reasons for the conclusion should be re-summarised in this section. In principle, if an unmet need does not exist or cannot be adequately quantified ((Section 5. ), if the potential to address the unmet need is not supported (Section 6. ), or if the claimed effects are minor or not plausible based on the data available, this would lead to a rejection of the request.

* Has the request been duly substantiated?
* Be explicit as much as possible as of why or why not this product constitutes a “major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation”; useful concepts include the expected impact on medical practice, change in the natural history of the disease, therapeutic advantage compared to available treatments, survival benefit or other important benefit, improvement in safety, clinical relevance of the effect, very convincingly positive balance of benefits and risks. A new mechanism of action or a technical innovation per se may not necessarily represent a valid argument for justifying major interest from the point of view of public health. Justify this based on the conclusions from the previous sections.
* Ability to review the data within the procedural time (e.g. due to complexity of the data) alone should not be a reason for rejection. However, a premature or incomplete application without sufficient quality, safety and efficacy data at the time of submission or for which there are concerns about the strength of evidence can be a reason for rejection if it is clear from the information available than an accelerated assessment cannot be conducted unless a specific plan for a conditional marketing authorisation has been laid out.
* In case of several indications, if at least one indication is considered to fulfil the criteria for major interest from the point of view of public health, the entire application is to be considered to fulfil the criteria, unless for any other indication(s) the application is incompatible with accelerated assessment and unlikely to lead to an earlier authorisation (e.g. due to incomplete available data).
* Is the assessment consistent with PRIME eligibility?   
  To be granted PRIME, a medicine has to show its potential to benefit patients with unmet medical need. Developers of a medicine that benefitted from PRIME can expect to be eligible for accelerated assessment at the time of application for a marketing authorisation. Should the AA be denied for a product eligible to PRIME, the change in its potential to benefit patients with unmet medical need since granting of the PRIME eligibility should be explained using relevant information from previous sections (e.g. availability of new treatment options, limitations in the strength of evidence).
* When provided by the applicant, ensure that the assessment is consistent with previous COMP conclusions on (expected) significant benefit or absence thereof, and PDCO conclusions on (expected) absence of significant therapeutic benefit if that has been the basis for a paediatric development waiver or justify the rationale for any deviation.

1. Committee Recommendation

*Note: for Rapporteurs use. Not for applicants to complete.*

Based on the assessment of the request provided by the applicant and the CHMP guideline on the procedure for accelerated assessment pursuant to Article 14 (9) of Regulation (EC) no 726/2004, **it is <not>** recommended to grant the accelerated assessment procedure pursuant to Article 14 (9) of Regulation (EC) No 726/2004 for <PRODUCT>.