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ANNEXES 1 to 3

ANNEXES

to

Commission Implementing Regulation (EU) .../... of XXX

laying down, pursuant to Regulation (EU) 2021/2282 on health technology assessment, procedural rules for the interaction during, exchange of information on, and participation in, the preparation and update of joint clinical assessments of medicinal products for human use at Union level, as well as templates for those joint clinical assessments

ANNEX I

TEMPLATE FOR THE DOSSIER OF THE JOINT CLINICAL ASSESSMENT OF A MEDICINAL PRODUCT

The provision of information, data, analysis and other evidence in the dossier shall follow standards of evidence-based medicine and take into account, if available, the methodological guidance adopted by the HTACG under Article 3(7), point (d), of the HTAR where applicable. Any deviations shall be described and justified. The information requested in the dossier template shall be provided in a clear format, preferably in tabular format when possible.

Revision history

Unnecessary lines shall be deleted.

Version	**Document**	**Legal reference**	**Submission date**	**Commission's check date**
V0.1	Initial dossier	Article 10(2) HTAR		
V0.2	*(Updated dossier following Commission's second request)*	Article 10(5) HTAR		
V0.3	*(Updated dossier following assessors' request for further specifications, clarifications or additional information)*	Article 11(2) HTAR		N/A
V0.4	*(Updated dossier following changes to the therapeutic indication(s))*	Article 16(4) IR		N/A
V0.5	*(Updated dossier following re-initiation of a JCA)*	Article 10(8) HTAR		N/A
V0.6	*(Dossier with the HTD's indications and justification of confidential information)*	Article 11(5) HTAR		N/A
etc.				

Version	Document	Legal reference	Submission date	Commission's check date
V1.0	Dossier for publication (without confidential information)	Article 20 IR	N/A	
V1.0.1	*(Updated dossier where the joint clinical assessment report specifies the need for an update and additional evidence for further assessment becomes available)*	Article 18(1) IR		N/A
V1.0.2	*(Updated dossier provided on the initiative of the HTD where additional evidence for further assessment becomes available)*	Article 18(2) IR		N/A
V1.0.3	*(Updated dossier following the initiation of an update of a JCA – update of the assessment scope not needed)*	Article 18(5) IR		N/A
V1.0.4	*(Updated dossier following the initiation of an update of a JCA – update of the assessment scope needed)*	Article 18(6) IR		
V1.0.5	*(Updated dossier following the initiation of an update of a JCA with the HTD's indications and justification of confidential information)*	Article 11(5) HTAR		N/A

Version	Document	Legal reference	Submission date	Commission's check date
etc.				
V2.0	*(Dossier for publication following the finalisation of an update of a JCA (without confidential information))*	Article 20 IR	N/A	

List of abbreviations

The following list presents suggestions for abbreviations. It may be adapted to the dossier.

Abbreviation	Meaning
ATC	Anatomical Therapeutic Chemical
ATMP	Advanced Therapy Medicinal Product
CHMP	Committee for Medicinal Products for Human Use
CSR	Clinical Study Report
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
HTA	Health Technology Assessment
HTACG	Member State Coordination Group on Health Technology Assessment
HTAR	Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment and amending Directive 2011/24/EU (OJ L 458, 22.12.2021, p. 1, ELI: http://data.europa.eu/eli/reg/2021/2282/oj)
HTD	Health Technology Developer
IR	Commission Implementing Regulation (EU) …/… of XXX laying down, pursuant to Regulation (EU) 2021/2282 on health technology assessment, procedural rules for the interaction during, exchange of information on, and participation in, the preparation and update of joint clinical assessments of medicinal products for human use at Union level, as well as templates for those joint clinical assessments
JCA	Joint Clinical Assessment
JSC	Joint Scientific Consultation
PICO	A set of parameters for the joint clinical assessment in terms of: Patient Population – Intervention(s) – Comparator(s) – Health Outcomes
PRIME	Priority Medicines scheme by the European Medicines Agency

Abbreviation	Meaning
RCT	Randomised Controlled Trial
RoB	Risk of Bias
SmPC	Summary of Product Characteristics
etc.	

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1. Overview

1.1. Information about the medicinal product under assessment and the HTD

This section shall provide:

– *the name of the medicinal product under assessment ('the medicinal product');*

– *the corporate name and permanent address of the HTD. In case the HTD responsible for the submission of the medicinal product for regulatory approval is different from the HTD submitting the dossier for JCA of the medicinal product, the corporate name and address of both HTDs shall be specified.*

1.2. Previous assessments under the HTAR

This section shall indicate whether the medicinal product has been subject to an assessment under the HTAR. If the answer is positive, the section shall provide the therapeutic indication, the date and the reference of the previous JCA report.

1.3. Executive summary

This section shall provide a concise executive summary of the dossier focusing on the assessment scope as set out pursuant to Article 8(6) of the HTAR and shared with the HTD in the Commission's first request referred to in Article 10(1) of the HTAR ('the assessment scope'). The executive summary shall include:

– *the assessment scope, clearly identifying any PICO(s), for which results were not submitted and explaining reasons for their omission;*

– *a summary of the results on relative effectiveness and relative safety of the medicinal product (e.g. effect measures with statistical precision for each outcome) with regard to the assessment scope, indicating whether the results were based on direct or indirect evidence. The results shall be provided for each PICO separately;*

– *the degree of certainty of the relative effectiveness and relative safety with regard to the PICO(s).*

2. Background

2.1. Characterisation of the medical condition to be treated, prevented or diagnosed

2.1.1. Overview of the medical condition

This section shall:

- *describe the medical condition, which the medicinal product intends to treat, prevent or diagnose, including criteria for its diagnosis, if available, using a standardised code such as the International Statistical Classification of Diseases and Related Health Problems ('ICD') code or the Diagnostic and Statistical Manual of Mental Disorders ('DSM') code and the version of the code;*
- *where relevant, describe the main stages and/or subtypes of the medical condition;*
- *include any prognostic factors that may affect the course of the disease or medical condition and the prognosis of the medical condition without the new treatment;*
- *present an estimate of the most recent prevalence and/or incidence for the medical condition in the EEA States in which the HTAR applies and, where relevant, describe any profound differences between these states;*
- *describe the symptoms and burden of the medical condition for patients, including aspects such as pain, disability, psychosocial issues, and other determinants of morbidity and quality of life from a patient perspective;*
- *for medical conditions that result in disability and/or a need for a family caregiver, and for treatments that result in major organisational changes to the healthcare system (e.g., due to manufacturing constraints) or major associated procedures: briefly describe the organisational and societal impact of the medical condition and its treatment, giving some context for interpretation of outcomes.*

References for the statements shall be provided. Full texts of references shall be provided in Appendix D.1.

2.1.2. Characterisation of the target patient population

In case the target population is more specific than the overall medical condition, this section shall:

- *name and describe the default target patient population(s), i.e., the therapeutic indication proposed by the HTD in the application for marketing authorisation or variation to an existing marketing authorisation submitted to the EMA or where applicable, the therapeutic indication wording from the CHMP positive opinion or from the SmPC;*
- *describe and justify the proposed position of the target patient population(s) in the patient pathway of care;*
- *where relevant, take into account sex, age and other specific characteristics;*
- *describe any patient sub-populations, including the criteria for their identification, if specifically defined in the assessment scope, and further patient sub-populations, if appropriate;*
- *describe the natural progression of the medical condition (by patient sub-population, if appropriate).*

References for the statements shall be provided. Full texts of references shall be provided in Appendix D.1.

2.1.3. Clinical management of the medical condition

This section shall:

- *describe the clinical pathway of care for the medical condition, which the medicinal product intends to treat, prevent or diagnose where relevant, for different stages and/or subtypes of the disease or medical condition or patient sub-populations, with diagrams of the care pathway(s) that include comparator(s);*
- *where clinical pathways vary substantially between the EEA States in which the HTAR is applicable, describe these variations in care;*
- *include a list of relevant clinical guidelines at the European level, e.g., by European medical associations or societies, if available.*

References for the statements shall be provided. Full texts of references shall be provided in Appendix D.1.

2.2. Characterisation of the medicinal product

2.2.1. Characteristics of the medicinal product

This section shall describe the characteristics of the medicinal product and, in particular, report the following information:

- *proprietary name; active substance(s);*
- *pharmaceutical formulation(s);*
- *therapeutic indication;*
- *mechanism of action;*
- *drug class;*
- *ATC code where already assigned;*
- *method of administration;*
- *doses and dosing frequency;*
- *duration of treatment, dose adjustments and combinations with other interventions.*

References for the statements shall be provided. Full texts of references shall be provided in Appendix D.1.

2.2.2. Requirements/instructions for use

This section shall:

- *describe any specifically qualified personnel and equipment required to use the medicinal product, including any specific tests or investigations required. Where such equipment has been fully described in Section 2.2.1, the current section shall refer to the above description and state that there are no additional requirements;*
- *describe any supplies (except generic supplies) required to use the medicinal product, where applicable.*

Where relevant and if appropriate, the characterisation of administration and dosing shall be done by sub-population or patient group.

References for the statements shall be provided. Full texts of references shall be provided in Appendix D.1.

2.2.3. Regulatory status of the medicinal product

This section shall:

- *provide the regulatory status of the medicinal product in the indication considered for this JCA in the EEA States in which the HTAR is applicable, Australia, Canada, China, Japan, United Kingdom, United States of America and other countries if relevant;*
- *provide details of the procedural pathway of the medicinal product in the EU, such as orphan designation, conditional marketing authorisation with any specific obligations of the conditional marketing authorisation, ATMP, PRIME or paediatric investigation plan ('PIP');*
- *detail ongoing or planned early access/compassionate use programs in the EEA;*
- *specify other marketing authorisations in the EEA States in which the HTAR is applicable for other indications except the indication considered for this JCA, as well as additional indication already submitted to the EMA and under review.*

References for the statements shall be provided. Full texts of references shall be provided in Appendix D.1.

2.3. JSC related to the JCA

Where the medicinal product has been subject to a JSC under the HTAR, this section shall explain any deviation from the recommended proposition for evidence generation. The recommendations shall be documented in Appendix D.9.

3. Assessment scope

This section shall:

- *reproduce the assessment scope in the format shared with the HTD in the Commission's first request referred to in Article 10(1) of the HTAR;*
- *clearly identify any PICO(s), for which results were not submitted and explain the reasons for their omission.*

4. Description of methods used in the development of the content of the dossier

This section shall describe the methods used in the development of the content of the dossier, taking into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR. Any deviations shall be described and justified.

4.1. Criteria for selecting studies for JCA

This section shall specify the inclusion and exclusion criteria for studies to be considered for this JCA based on the assessment scope and taking into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR. Any deviations shall be

described and justified. The specification for inclusion and exclusion criteria shall be provided for each PICO, as appropriate.

4.2. Information retrieval and selection of relevant studies

4.2.1. Information retrieval

The HTD shall conduct an information retrieval process with the objective of identifying the evidence to be used for the preparation of the dossier.

The following sources of information shall be systematically considered in the retrieval process:

(1) studies performed or sponsored by the HTD or by third parties in order to include all up-to-date published and unpublished information (data, analyses and any other evidence) from studies on the medicinal product for which the HTD was a sponsor and corresponding information about studies by third parties, if available;

(2) bibliographic databases. The search shall at least be conducted in the National Library of Medicine's bibliographic database (MEDLINE) and the Cochrane Central Registry of Controlled Trials database;

(3) study registries and study results registries (clinical trial databases);

(4) HTA reports on the medicinal product subject to the JCA from EEA States in which the HTAR is applicable and from Australia, Canada, the United Kingdom and the United States of America;

(5) the clinical safety and efficacy data included in the submission file to the EMA;

(6) patient registries.

This section shall:

– *provide a list of the sources that were systematically searched for studies that are relevant for the JCA according to the assessment scope and indicate the date of each search. The cut-off date for the searches shall be a maximum of 3 months before the submission of the dossier;*

– *report whether and when new data with relevance for the assessment scope might become available.*

All search strategies shall be fully documented in Appendix D.2.

4.2.2. Selection of relevant studies

This section shall document the approach for the selection of relevant studies from the results of the information retrieval according to inclusion and exclusion criteria defined in Section 4.1 This specification shall be provided for each PICO, as appropriate. If the selection process differs from what is suggested by the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR, this shall be described and justified.

4.3. Data analysis and synthesis

This section shall describe the methods used for data analysis and synthesis. The methods used in the preparation of the dossier and their description shall follow international standards of evidence-based medicine and take into account, if available, the methodological guidance adopted by the HTACG

pursuant to Article 3(7), point (d), of the HTAR. Any deviations shall be described and justified.

The underlying documentation for any analysis, i.e., CSR, study protocols and statistical analysis plans (including for evidence syntheses) and details on all software used as well as the respective program code and relevant output shall be provided in the relevant parts of Appendix D.

This section shall cover the following methodological aspects in the following respective sub-sections:

4.3.1. Description of the design and methodology of the included original clinical studies

4.3.2. Description of the results from the original clinical studies

4.3.3. Direct comparisons by pairwise meta-analyses

The protocol for evidence syntheses, including the relevant statistical analysis plan, shall be provided in Appendix D.5.

4.3.4. Indirect comparisons

The protocol for evidence syntheses, including the relevant statistical analysis plan, shall be provided in Appendix D.5.

4.3.5. Sensitivity analyses

This section shall describe and justify the methods of all performed sensitivity analyses. It shall describe the purpose or which methodological parameter the sensitivity analysis addresses, as well as underlying assumptions.

4.3.6. Subgroup analyses and other effect modifiers

4.3.7. Specification of further methods as required

This section shall describe any other methods used in deriving results used in the dossier.

5. Results

The results presented in the dossier shall follow international standards of evidence-based medicine and take into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR. Any deviations shall be described and justified.

The presentation of results shall use text, figures and tables as appropriate.

For relative effectiveness and relative safety, results shall be provided for each clinical study and evidence synthesis, including both direct and indirect comparisons.

5.1. Results from the information retrieval process

Results from the different steps of the information retrieval process shall be presented transparently. For each study, the following information shall be indicated: the study reference ID, the study status, the study duration with data cut-off if applicable, and study arms. For each of the information retrieval steps, the studies not considered in the dossier shall be identified and listed. For each of them, the reason for exclusion shall be specified.

The presentation of the results shall include in the following respective sub-sections:

5.1.1. List of studies conducted or sponsored by the HTD or by third parties

This section shall report information on all the studies, conducted or sponsored by the HTD and third parties, referred to in Annex I, point (b), of the HTAR, including all studies providing clinical safety and efficacy data from the submission file to the EMA. The listing shall be restricted to studies involving patients in the therapeutic indication for which the dossier is prepared. The section shall also report whether and when new data with relevance for the assessment scope might become available during the assessment period.

5.1.2. Studies identified in searches of bibliographic databases

This section shall present results from searches for studies on the medicinal product and its comparator(s) where relevant (e.g. for indirect meta-analyses) in bibliographic databases.

5.1.3. Studies in study registries and study results registries (clinical trial databases)

This section shall present results from searches for studies for the medicinal product and its comparator(s) where relevant in study registries/study results registries.

5.1.4. HTA reports

This section shall list HTA reports available on the medicinal product subject to the JCA from EEA States in which the HTAR is applicable and from Australia, Canada, the United Kingdom and the United States of America. The HTA reports shall be provided in Appendix D.7. Any additional relevant evidence identified in those HTA reports which were not identified in other sources shall be listed.

5.1.5. Studies from submission files to the EMA

This section shall list all studies that were included in the submission file to the EMA. If the main (pivotal) studies were not addressed by any of PICO(s), they shall be presented in Appendix C and be provided in Appendix D.6.

5.1.6. Studies from patient registries

This section shall present results from searches for studies for the medicinal product and its comparator(s), where relevant, in patient registries.

5.1.7. List of studies included overall and by PICO

This section shall define the list of studies included in the description of relative effectiveness and relative safety, informing each PICO.

5.2. Characteristics of included studies

This section shall provide an overview in tabular format of the study design and the study population for all studies included in the description of relative effectiveness and safety in any of PICO(s). Information shall specifically be provided on:

– *the study type and design;*

– *the study date and duration;*

– *enrolled study population including key eligibility criteria and locations;*

– *characteristics of the intervention and comparator(s);*

– *study endpoints;*

– *if applicable, data cut-off;*

– *sample size;*

– *analysis methods.*

The study interventions shall be characterised and information on the course of the study (i.e., planned and actual follow-up times per outcome) shall be provided.

The studies included in the dossier shall be described briefly. A detailed description of the study methodology shall be provided in Appendix A.

5.3. Study results on relative effectiveness and relative safety

This section shall provide results on relative effectiveness and relative safety according to the assessment scope.

This section shall also provide all information that is required to assess the degree of certainty of the relative effects, taking into account the strengths and limitations of the available evidence. The detailed information, which shall include but is not limited to the assessment of the RoB, required to assess the degree of certainty shall take into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR. Any deviations shall be described and justified.

Details shall be provided in the relevant Appendixes.

5.3.1. Results for the patient population <Z-1>

This section shall discuss to which extent the included patient populations and/or comparator(s) per study cover the relevant patient population/comparator(s) according to the assessment scope.

Within this section, the results for all PICO(s) addressing patient population <Z-1> shall be presented in sub-sections.

A separate section shall be provided for each patient population <Z-1>, <Z-2>, etc. specified in the PICO(s).

Information shall be provided on the type of the analysed comparison (e.g., direct comparison, adjusted indirect comparison) as well as the relevant study arms per study. If a sub-population of a study was analysed for the assessment, the characteristics of the relevant sub-population shall be described and the number of included patients shall be provided.

5.3.1.1. Patient characteristics for <PICO 1>

This section shall present the patient characteristics from all studies covering the relevant patient population included in any of PICO(s). It shall be stated, if the included patient populations differ between studies If only a sub-population of any study represents the relevant population for the JCA, the patient characteristics in this section shall be provided for this appropriate population.

5.3.1.2. Health outcome results for PICO <1> and uncertainties in the results

Within the given patient population, results on health outcomes describing relative effectiveness and relative safety shall be described by PICO in tabular format. The section shall start from describing and justifying the choice of evidence (type of comparison) submitted to address the given PICO <1>.

For any additional PICO question related to a given patient population, a new sub-section presenting the results in terms of health outcomes for this PICO question shall be added.

This section shall provide:

- *an overview of the available outcomes (requested in the assessment scope) per study;*
- *an overview of the course of the included studies, actual treatment duration and observation period for the study intervention and comparator;*
- *a description of the evidence synthesis method used, including the associated strengths and limitations, together with any factors arising from these methods and their application which may affect the certainty of the evidence;*
- *the requested results on relative effectiveness and relative safety (i.e., the relative effects of the medicinal product versus the comparator). It shall include the results from all individual studies, as well as the quantitative syntheses of results, e.g., from meta-analyses. The results of the analyses of each of the presented outcomes shall be described briefly. It shall be clarified whether the evidence comes from direct or indirect comparison. If results are reported for data cut-offs, results for all outcomes shall be provided. Reported data cut-offs shall be justified. Information on the amount of missing data and reasons for missing data as well as results for all sensitivity analyses shall be provided;*
- *a description of any issues affecting the degree of certainty of the relative effects.*

6. List of references

Appendixes

Appendix A. Tabular listing and information on methods of all studies included in the JCA

The appendix shall include a line listing of all studies included in the description of relative effectiveness and relative safety. In addition, information on study methods and a patient flow chart shall be provided for each of the listed studies.

Appendix B. Information to assess the degree of certainty of the relative effects (including, but not limited to, the RoB)

Appendix C. Results of the main study/studies from the clinical development programme of the medicinal product (if not included in the presentation by PICO question(s))

Appendix D. Underlying documentation

D.1. Full texts of references

D.2. Documentation of information retrieval

D.2.1. Documentation of search strategies for each information source

D.2.2. Results of the information retrieval in standard format

D.3. Programming code for programs used for analyses

This appendix shall provide program code and relevant output if the analyses and corresponding calculations cannot be described by a specific standard method.

D.4. Study reports for original clinical studies

This appendix shall provide CSRs, including study protocols and statistical analysis plans, referred to Annex I, point (b), of the HTAR.

D.5. Study reports for evidence synthesis studies

This appendix shall provide all up-to-date published and unpublished information and data-analyses, including study protocols and statistical analysis plans, referred to in Annex I, point (b), of the HTAR required for evidence synthesis studies.

D.6. Clinical safety and efficacy data included in the submission file to the EMA

This appendix shall provide Modules 2.5, 2.7.3 and 2.7.4 of the CTD (format of submission to the EMA) and CSRs (see Section C.4 Study reports). For each study, the CSR shall be provided only once.

D.7. HTA reports of the medicinal product subject to the JCA

D.8. Information on studies based on registries

This appendix shall include studies with the medicinal product from patient registries, if available.

D.9. Information on JSCs

ANNEX II
TEMPLATE FOR THE JOINT CLINICAL ASSESSMENT REPORT

The report shall follow standards of evidence-based medicine and take into account, if available, the methodological guidance, adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR.

List of abbreviations

The following list presents suggestions for abbreviations. It may be adapted to the report.

Abbreviation	**Meaning**
ATC	Anatomical Therapeutic Chemical
ATMP	Advanced Therapy Medicinal Product
CSR	Clinical Study Report
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
HTA	Health Technology Assessment
HTACG	Member State Coordination Group on Health Technology Assessment
HTAR	Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment amending Directive 2011/24/EU
HTD	Health Technology Developer
JCA	Joint Clinical Assessment
JSC	Joint Scientific Consultation
PICO	A set of parameters for the joint clinical assessment in terms of: Patient Population – Intervention(s) – Comparator(s) – Health Outcomes
PRIME	Priority Medicines scheme by the European Medicines Agency
RCT	Randomised Controlled Trial
RoB	Risk of Bias
SmPC	Summary of Product Characteristics
etc.	

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1. General information on the JCA

   This section shall provide:

   – *information on the assessor and co-assessor;*

   – *an overview of the procedural steps and their dates;*

– *information on the involvement of patients, clinical experts and other relevant experts, as well as on the input received from patient organisations, healthcare professional organisations and clinical and learned societies. The input from experts and stakeholders shall be provided in Appendix A;*

– *information on previous JSC under the HTAR.*

2. Background

2.1. Overview of the medical condition

This section shall provide:

– *a summary of the medical condition, including the symptoms, the burden and natural progression of the medical condition, its prevalence or incidence in the EEA States in which the HTAR is applicable, as available;*

– *a brief description of the target patient population and its characteristics reflected in the assessment scope as set out pursuant to Article 8(6) of the HTAR;*

– *a brief description of the clinical pathway of care for the medical condition, whether they vary substantially between the EEA States in which the HTAR is applicable, as well as, if relevant, for different stages and/or subtypes or sub-populations of the medical condition.*

2.2. Characterisation of the medicinal product

2.2.1. Characteristics of the medicinal product

This section shall describe characteristics of the medicinal product under assessment ('the medicinal product') and report the following information:

– *proprietary name;*

– *active substance(s);*

– *pharmaceutical formulation(s);*

– *therapeutic indication;*

– *marketing authorisation holder;*

– *mechanism of action;*

– *ATC code where already assigned.*

2.2.2. Requirements/instructions for use

This section shall include a description of the methods of administration, dosing of the medicinal product and duration of treatment.

2.2.3. Regulatory status of the medicinal product

This section shall describe the regulatory information on the medicinal product and provide details of the procedural pathway of the medicinal product in the EU, such as orphan drug designation, conditional marketing authorisation with any specific obligations of the conditional marketing authorisation, ATMP or PRIME. It shall also provide details of ongoing or planned early access/compassionate use programs in the EEA.

When appropriate links to SmPC shall be inserted for details of other licensed therapeutic indications and to the dossier for further regulatory information.

3. Assessment scope

This section shall reproduce the assessment scope as set out pursuant to Article 8(6) of the HTAR.

4. Results

The results presented in this section shall follow international standards of evidence-based medicine and take into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR. Any deviations shall be described and justified.

4.1. Information retrieval

This section shall include:

– *a description of the information retrieval performed by the HTD;*

– *an assessment of the appropriateness of the sources and the search strategies of the HTD.*

It shall provide the date of the list of the studies, performed or sponsored by the HTD or by third parties, referred to in Annex I, point (b), of the HTAR, as well as the date of the last searches for the medicinal product and the comparator(s) in bibliographic databases and in study registries and study results registries (clinical trial databases).

Detailed information shall be provided in Appendix B.

4.1.1. Resulting list of included studies overall and by PICO

This section shall provide in tabular format:

– *an overview of all included studies and the associated references for these studies overall and by PICO;*

– *the list of studies included by the HTD which were excluded within the assessment, with a justification for their exclusion.*

4.2. Characteristics of included studies and RoB

4.2.1. Included studies

This section shall provide for the studies included in the assessment:

– *information on the study design (e.g., on randomisation, blinding, or parallel observation, and the key inclusion and exclusion criteria);*

– *information on enrolled study populations (e.g., diagnosis, general severity of medical condition, and line of therapy);*

– *characteristics of the study interventions;*

– *information on the course of the study (e.g., planned and actual follow-up times per outcome);*

– *information on the study duration.*

4.2.2. RoB

This section shall describe the assessment of RoB at the study level taking into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR.

4.3. Study results on relative effectiveness and relative safety

The results on relative effectiveness and relative safety shall be presented according to the assessment scope as set out pursuant to Article 8(6) of the HTAR, per PICO.

An assessment of the degree of certainty of the relative effectiveness and relative safety, considering the strengths and limitations of the available evidence shall be performed taking into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR.

4.3.1. Results for patient population <Z-1>

This section shall discuss to which extent the included patient populations and/or comparator(s) per study cover the relevant patient population/comparator(s) according to the assessment scope as set out pursuant to Article 8(6) of the HTAR.

For each patient population specified in PICO(s), a separate section shall be provided. Within this section, the results for all PICO(s) addressing this patient population shall be presented in sub-sections.

4.3.1.1. Patient characteristics

This section shall present patient characteristics from all studies covering the relevant patient population included in any of PICO(s) addressing this patient population.

4.3.1.2. Evidence synthesis methods

This section shall briefly describe, when applicable, the evidence synthesis methods used by the HTD, including the associated strengths and limitations, and any factors arising from these methods and their application which may affect the certainty of the evidence taking into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR.

4.3.1.3. Health outcome results for PICO <1> and uncertainties in the results

Within the given patient population, results on health outcomes describing relative effectiveness and relative safety shall be described by PICO. The section shall start from describing and justifying the choice of evidence (type of comparison) submitted to address the given PICO <1>.

The section shall present an overview of the available outcomes requested in the assessment scope per study.

Results on relative effectiveness and relative safety (i.e., the relative effects of the medicinal product versus the comparator) shall include the results from all individual studies, as well as any quantitative syntheses of results, e.g., from meta-analyses.

The results of the analyses of each of the presented outcomes shall be described briefly.

The description shall address any issues affecting the degree of uncertainty of the relative effects taking into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR.

For any additional PICO question for a given patient population required according to the assessment scope, a new subsection presenting the results for outcomes for this PICO question shall be added.

4.3.2. Results of the main study from the clinical development programme of the medicinal product (if not addressed by any of PICO(s))

4.3.2.1. Characteristics of the pivotal study

4.3.2.2. Patient characteristics

4.3.2.3. Health outcome results of the pivotal study and uncertainties in the results

5. References

Appendixes

Appendix A. Input from experts and stakeholders

Appendix B. Assessment of information retrieval

Appendix C. Additional study information and data, including uncertainties in the results

ANNEX III
TEMPLATE FOR THE JOINT CLINICAL ASSESSMENT SUMMARY REPORT

The summary report shall be concise and an independently readable overview of the assessment. It shall take into account, if available, the methodological guidance adopted by the HTACG pursuant to Article 3(7), point (d), of the HTAR.

The summary report shall include, at least:

– *background information with at least a description of the intervention and medical condition to be treated;*

– *the assessment scope provided for in Article 8(6) of the HTAR;*

– *information on the involvement of patients, clinical experts and other relevant experts, as well as on the input received from patient organisations, healthcare professional organisations and clinical and learned societies;*

– *summary tables including uncertainties of the evidence for each PICO with short description of the results.*