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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

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to 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 ([1]), and in particular Article 15(1), points (a) and (c), Article 25(1), point (b), and Article 26(1) thereof,

Whereas:

(1) Regulation (EU) 2021/2282 lays down a support framework and procedures for cooperation between Member States on health technologies at Union level and establishes the Member State Coordination Group on Health Technology Assessment ('the Coordination Group').

(2) Under Article 15 of Regulation (EU) 2021/2282, the Commission is to lay down detailed procedural rules for the implementation of Articles 8 to 14 of that Regulation as regards conducting and updating joint clinical assessments. In particular, under Article 15(1), points (a) and (c), of Regulation (EU) 2021/2282, the Commission is to adopt detailed procedural rules for the cooperation, in particular by exchange of information, with the European Medicines Agency on the preparation and update of joint clinical assessments of medicinal products and for the interaction, including timing thereof, with and between the Coordination Group, its subgroups and the health technology developers, patients, clinical experts and other relevant experts during joint clinical assessments and updates.

(3) In addition, under Article 3(7), points (d), (e) and (g), of that Regulation, the Coordination Group is to adopt further rules on conducting joint clinical assessments, namely methodological guidance on joint work, detailed procedural steps and the timeframe for the conduct of joint clinical assessments and their updates and guidance on the appointment of assessors and co-assessors for joint clinical assessments.

(4) In order to ensure the highest scientific quality of joint clinical assessment reports, Articles 8(6) and 11(4) of Regulation (EU) 2021/2282 provide for the involvement of patients, clinical experts and other relevant experts in joint clinical assessments. Under Article 25(1), point (b), of Regulation (EU) 2021/2282, the Commission is to adopt, after consulting all relevant stakeholders, general procedural rules on the selection and consultation of stakeholder organisations and patients, clinical experts and other relevant experts in joint clinical assessments at Union level. Based on these rules, the Coordination Group, pursuant to Article 3(7), point (j), of Regulation (EU) 2021/2282, is to ensure appropriate involvement of stakeholder organisations and experts in its work.

(5) Under Article 26(1) of Regulation (EU) 2021/2282, the Commission is to adopt the format and templates for the dossiers for information, data, analyses and other evidence to be provided by health technology developers for joint clinical assessments, as well as for joint clinical assessment reports and summary joint clinical assessment reports. This Regulation lays down those formats and templates, to ensure a uniform approach on the presentation of the evidence provided by the health technology developers to the Coordination Group and of the information contained in the joint clinical assessment reports.

([1]) OJ L 458, 22.12.2021, p. 1, ELI: http://data.europa.eu/eli/reg/2021/2282/oj.

(6) In order to allow sufficient time for a high quality joint clinical assessment, that clinical assessment should start at the same time as the centralised procedure provided for under Regulation (EC) No 726/2004 of the European Parliament and of the Council ([2]), that is to say upon the confirmation by the European Medicines Agency of a submission of a valid application for marketing authorisation in accordance with Regulation (EC) No 726/2004 or for a variation to the terms of an existing marketing authorisation in accordance with Commission Regulation (EC) No 1234/2008 ([3]). Therefore, it is appropriate to require the health technology developer to submit information necessary for the development of the assessment scope provided for in Article 8(6) of Regulation (EU) 2021/2282 ('the assessment scope') to the Commission acting as secretariat of the Coordination Group ('the HTA secretariat') at the same time as the health technology developer submits an application for marketing authorisation, or for a variation to the terms of an existing marketing authorisation, to the European Medicines Agency.

(7) The joint clinical assessment of a medicinal product under Regulation (EU) 2021/2282 is carried out in parallel to the centralised procedure provided for in Regulation (EC) No 726/2004, and the Coordination Group is to endorse the joint clinical assessment report no later than 30 days following the adoption of a Commission decision granting a marketing authorisation for that medicinal product. The joint clinical assessment is to be discontinued, for example, where an application for a marketing authorisation or for a variation to the terms of an existing marketing authorisation is withdrawn, or where the outcome of the centralised procedure is negative for the application for a marketing authorisation or for a variation to the terms of an existing marketing authorisation. Therefore, the Coordination Group should be informed of submissions of valid applications for marketing authorisation and for a variation to the terms of existing marketing authorisations of medicinal products falling within the scope of Regulation (EU) 2021/2282 and of updates on steps in the centralised procedure, including changes in the envisaged timelines.

(8) The assessment scope is based on the therapeutic indication(s) of the medicinal product. Therefore, with a view to enabling the subgroup on joint clinical assessments ('the JCA Subgroup') to update the assessment scope where deemed appropriate, while preserving the separation of the respective remits of the Coordination Group and the European Medicines Agency, the European Medicines Agency should inform the HTA secretariat on substantial questions or outstanding issues that might impact the therapeutic indication(s) proposed by the applicant for the medicinal product subject to a joint clinical assessment.

(9) The assessor and co-assessor and the JCA Subgroup should get early access to the draft summary of product characteristics and to the assessment report referred to in Article 9(4), points (a) and (e) respectively, of Regulation (EC) No 726/2004.

(10) Pursuant to Article 28, point (h), of Regulation (EU) 2021/2282, the HTA secretariat is to facilitate the cooperation, in particular through the exchange of information, with the European Medicines Agency, on the joint work referred to in Articles 7 to 22 of Regulation (EU) 2021/2282 related to medicinal products, including the sharing of confidential information. The exchange of information relevant to concrete joint clinical assessments and updates of joint clinical assessments should therefore take place through the HTA secretariat. The HTA secretariat should ensure that all the information it receives is communicated to the Coordination Group, its relevant subgroups and/or assessor and co-assessor, as appropriate, upon receipt thereof.

(11) The health technology developer should be informed of the start of a joint clinical assessment, of the steps of that assessment, of its update, as well as of its re-initiation under Article 10(7) of Regulation (EU) 2021/2282. The health technology developer should also be informed of the decision of the Coordination Group to include the update of the joint clinical assessment in its annual work programme, pursuant to Article 14 of Regulation (EU) 2021/2282.

([2]) Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1, ELI: http://data.europa.eu/eli/reg/2004/726/oj).

([3]) Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, p. 7, ELI: http://data.europa.eu/eli/reg/2008/1234/oj).

(12) It is necessary to set out general procedural rules for the selection of patients, clinical experts and other relevant experts to be consulted during the joint clinical assessment. The selection should start as early as possible, whenever the Coordination Group, via the HTA secretariat, receives information about upcoming submissions of applications for marketing authorisations for the medicinal products referred to in Article 7(1) of Regulation (EU) 2021/2282.

(13) The JCA Subgroup should aim to select patients, clinical experts and other relevant experts who have the required expertise in the therapeutic area of the joint clinical assessment, from a European or international perspective. These experts should be consulted during the joint clinical assessment.

(14) In order to ensure that patients, clinical experts and other relevant experts take part in joint clinical assessments in an independent and transparent manner, free from conflict of interest, they should only be selected and involved in joint clinical assessments after the Commission has concluded on their conflicts of interest, in accordance with the rules set out in Article 5 of Regulation (EU) 2021/2282 and with the general procedural rules adopted under Article 25(1), point (a), of that Regulation. Only patients, clinical experts and other relevant experts who have signed a confidentiality agreement should be involved in joint clinical assessments.

(15) The JCA Subgroup should give the opportunity to patient organisations, healthcare professional organisations and clinical and learned societies to provide their input on joint clinical assessments.

(16) To achieve the objective that, during the development of the assessment scope, Member States' needs are translated in the lowest possible number of sets of parameters for the joint clinical assessment in terms of patient population, intervention, comparators and health outcomes, the assessor, with the assistance of the co-assessor, should prepare an assessment scope proposal that will serve as a basis for Member States to express their needs.

(17) In order to ensure that the assessment scope is inclusive and reflects Member States' needs, the assessment scope proposal prepared by the assessor, with the assistance of the co-assessor, should be shared with the members of the JCA Subgroup. These members should consult national authorities and stakeholders in accordance with the procedural rules of the respective Member State.

(18) The Commission should set out procedural rules in order to ensure that the assessment scope is developed respecting the right to good administration and taking into account information provided by the health technology developer and input received from patients, clinical experts and other relevant experts.

(19) Article 10(1) and Article 11(1), point (a), of Regulation (EU) 2021/2282 set the timeframe for joint clinical assessments for medicinal products by reference to the timeframe applicable to the centralised procedure provided for in Regulation (EC) No 726/2004. The Commission should set the deadlines for the finalisation of the assessment scope and of the draft joint clinical assessment reports by the JCA Subgroup. These deadlines should refer to the main steps of the centralised procedure and should comply with the overall deadlines set out in Regulation (EU) 2021/2282. Where Article 11(1), point (a), of Regulation (EU) 2021/2282 does not apply, the Commission should set these deadlines with the aim of improving timely patient access to health technologies.

(20) To contribute to the completeness and high quality of the dossier and the smooth conduct of the joint clinical assessment, the health technology developer should be given the opportunity to request an assessment scope explanation meeting with the JCA Subgroup.

(21) The Commission should set deadlines that should give the health technology developer sufficient time to prepare and submit the dossier for joint clinical assessment of the medicinal product. The Commission should set the rules that provide a possibility to extend the deadline to submit the dossier in justified instances, without however going beyond the deadline specified in Article 10(1) of Regulation (EU) 2021/2282.

(22) Similarly, the Commission should set deadlines that give sufficient time to the health technology developer to take the following actions: (a) provide missing information, data, analysis and other evidence as indicated in the Commission's second request; (b) provide further specifications or additional information, data, analyses, or other evidence; (c) provide updates to previously provided information referred to in Articles 10(8) and 11(2) of Regulation (EU) 2021/2282; (d) signal technical or factual inaccuracies in the draft joint clinical assessment and summary reports and any information the health technology developer considers to be confidential.

(23) The Commission should set deadlines for its assessment on whether the dossier submitted by the health technology developer for joint clinical assessment of the medicinal product meets the requirements laid down in Article 9(2), (3) and (4) of Regulation (EU) 2021/2282. The Commission should consult, as appropriate, the assessor and co-assessor when carrying out this assessment.

(24) The Commission should set procedural rules to ensure that patients, clinical experts and other relevant experts are involved in the assessment process by being given the opportunity to provide input on the draft joint clinical assessment and summary reports.

(25) According to Article 11(2) of Regulation (EU) 2021/2282, the health technology developer is to proactively inform the Coordination Group where new clinical data becomes available during the joint clinical assessment process. The Commission should set the deadline by which the health technology developer is to submit such new clinical data so that these data are considered in the draft joint clinical assessment and summary reports.

(26) The Commission should set the deadline for finalising the revised draft joint clinical assessment and summary reports by the JCA Subgroup. This should ensure the delivery of joint clinical assessment reports in a timely manner and allow the Coordination Group to comply with the deadline for the conclusion of the joint clinical assessment set out in Article 11(1), point (a), of Regulation (EU) 2021/2282. The Commission should also set the deadline for the Coordination Group to endorse the revised draft joint clinical assessment and summary reports, with the aim of improving timely patient access to health technologies.

(27) Where, during the centralised procedure, there is a change in the therapeutic indication(s) initially submitted in the application for marketing authorisation or for a variation to the terms of an existing marketing authorisation, the JCA Subgroup should decide whether the joint clinical assessment should continue or be restarted. The Commission should set the procedural rules that apply in case a new assessment scope is to be developed.

(28) Certain specific procedural rules and deadlines should apply where the Coordination Group re-initiates a joint clinical assessment pursuant to Article 10(7) of Regulation (EU) 2021/2282 or where an update of a joint clinical assessment is carried out pursuant to Article 14 of Regulation (EU) 2021/2282.

(29) In order to ensure transparency, traceability and professional secrecy, as well as to contribute to the procedural compliance of joint clinical assessment reports, any correspondence with and between the Coordination Group, the JCA Subgroup, the HTA secretariat, the health technology developer, patients, clinical experts and other relevant experts during joint clinical assessments should be sent in a digital format through the IT platform referred to in Article 30 of Regulation (EU) 2021/2282 ('the HTA IT platform').

(30) This Regulation lays down, in accordance with Article 5(1), point (a), of Regulation (EU) 2018/1725 of the European Parliament and of the Council ([4]), the rules for processing, through the HTA IT platform, personal data for the purposes of conducting joint clinical assessments and their updates. In particular, it specifies the personal data that may be processed through that platform, namely certain personal data relating to the patients, clinical experts and other relevant experts involved in joint clinical assessments and their updates and certain personal data relating to the representatives appointed to the Coordination Group and the JCA Subgroup, the representatives of health technology developers and the representatives of the members of the stakeholder network established pursuant to Article 29 of Regulation (EU) 2021/2282 ('the HTA stakeholder network'). This Regulation also determines that the Commission is to be considered the controller of the processing of personal data through the HTA IT platform in the sense of Article 3, point 8, of Regulation (EU) 2018/1725. Any processing of personal data by the members of the Coordination Group and the JCA Subgroup and their representatives outside of the HTA IT platform is to take place in accordance with Regulation (EU) 2016/679 of the European Parliament and of the Council ([5]).

(31) The identity of the patient may reveal the patient's health status in relation to the subject matter of the joint clinical assessment and therefore should be considered a special category of personal data under Article 10 of Regulation (EU) 2018/1725. Therefore, such data should only be processed where the criteria of Article 10(2), point (i), of that Regulation are met. This Regulation provides for suitable and specific measures to safeguard the rights and freedoms of the data subject. In particular, no personal data of patients shall be made publicly available. Moreover, under Article 5(6) of Regulation (EU) 2021/2282, the representatives appointed to the Coordination Group and the JCA Subgroup, as well as patients, clinical experts and other relevant experts involved in joint clinical assessments and their updates, are subject to a requirement of professional secrecy, even after their duties have ceased. Finally, this Regulation specifies that only patients, clinical experts and other relevant experts who have signed confidentiality agreements be involved in joint clinical assessments.

(32) In order to ensure the possibility to verify whether the joint clinical assessments were conducted in the procedurally compliant manner, notably in the event of complaints or litigation, it is appropriate to provide for a retention period of personal data and for its review at regular intervals.

(33) In order to ensure transparency, on the one hand, and the protection of confidential data for commercial reasons, on the other hand, the Commission should publish the joint clinical assessment and the summary reports, together with the documentation referred to in Article 30(3), points (d) and (i), of Regulation (EU) 2021/2282, after having considered the views of the JCA Subgroup as to the commercially sensitive nature of the information contained in this documentation, which the health technology developer has requested to be treated as confidential.

(34) Joint clinical assessments of medicinal products are to be conducted from the date as of which Regulation (EU) 2021/2282 applies, that is, 12 January 2025. This Regulation should therefore apply from 12 January 2025.

(35) The European Data Protection Supervisor was consulted in accordance with Article 42 of Regulation (EU) 2018/1725 and delivered an opinion on 4 April 2024.

(36) The measures provided for in this Regulation are in accordance with the opinion of the Committee on Health Technology Assessment,

([4]) Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC (OJ L 295, 21.11.2018, p. 39, ELI: http://data.europa.eu/eli/reg/2018/1725/oj).

([5]) Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (OJ L 119, 4.5.2016, p. 1, ELI: http://data.europa.eu/eli/reg/2016/679/oj).

HAS ADOPTED THIS REGULATION:

Article 1

Subject matter

This Regulation lays down detailed procedural rules for joint clinical assessments of medicinal products at Union level, as regards:

(a) cooperation, in particular by exchange of information, with the European Medicines Agency on the preparation and update of joint clinical assessments of medicinal products;

(b) interaction, including the timing thereof, with and between the Coordination Group established under Article 3 of Regulation (EU) 2021/2282, its subgroups and health technology developers, patients, clinical experts and other relevant experts during joint clinical assessments of medicinal products and their updates;

(c) general procedural rules on the selection and consultation of stakeholder organisations and patients, clinical experts, and other relevant experts in joint clinical assessments at Union level;

(d) the format and templates for dossiers with information, data, analyses and other evidence to be provided by health technology developers for joint clinical assessments;

(e) the format and templates for joint clinical assessment reports and summary joint clinical assessment reports.

Article 2

Relevant information for the development of the assessment scope

1. Health technology developers shall, at the same time as they submit to the European Medicines Agency an application for marketing authorisation for medicinal products referred to in Article 7(1), point (a), of Regulation (EU) 2021/2282, provide the HTA secretariat with relevant information for developing the assessment scope of a joint clinical assessment of those medicinal products. That information shall consist of:

(a) the summary of the product characteristics proposed by the applicant;

(b) the clinical overview section of the submission file to the European Medicines Agency.

2. Health technology developers shall, at the same time as they submit to the European Medicines Agency an application for a variation to the terms of an existing marketing authorisation for medicinal products referred to in Article 7(1), point (b), of Regulation (EU) 2021/2282, provide the HTA secretariat with relevant information on the development of the assessment scope of a joint clinical assessment of those medicinal products. That information shall consist of the new therapeutic indication proposed by the applicant and the clinical overview section of the submission file to the European Medicines Agency.

3. If the JCA Subgroup considers it necessary, the HTA secretariat shall invite the health technology developer to provide further information relevant for the development of the assessment scope in a meeting with the JCA Subgroup or in writing.

Article 3

Exchange of information with the European Medicines Agency

1. The European Medicines Agency shall notify the HTA secretariat of the submission of an application for a marketing authorisation or for a variation to the terms of an existing marketing authorisation referred to in Article 2 of this Regulation upon receipt thereof.

2. With regard to the medicinal products referred to in Article 7(1), points (a) and (b), of Regulation (EU) 2021/2282, the European Medicines Agency shall inform the HTA secretariat of the following:

(a) submission of a valid application for marketing authorisation in accordance with Article 3(1) and Article 3(2), point (a), of Regulation (EC) No 726/2004, including the date on which the application for marketing authorisation was validated and the timetable for the initial evaluation during the centralised procedure;

(b) submission of a valid application for a variation to the terms of an existing marketing authorisation which corresponds to a new therapeutic indication in accordance with Regulation (EC) No 1234/2008, including the date on which the application for a variation to an existing marketing authorisation was validated and the timetable for the initial evaluation during the centralised procedure.

3. The European Medicines Agency shall provide the HTA secretariat with the information referred to in paragraph 2 on the day it issues the health technology developer the receipt of a valid application.

4. During the centralised procedure for medicinal products subject to a joint clinical assessment, the European Medicines Agency shall inform the HTA secretariat of the following:

(a) updates on steps in the centralised procedure, including changes in the envisaged timelines;

(b) substantial questions or outstanding issues that might impact the therapeutic indication(s) of the medicinal products proposed by the applicant.

Point (a) also applies to medicinal products of which the joint clinical assessment was discontinued pursuant to Article 10(6) of Regulation (EU) 2021/2282.

The main steps for the exchange of the information referred to in the first subparagraph, as well as the exact content of the information to be communicated at those steps, shall be agreed upon by the European Medicines Agency, the HTA secretariat and the JCA Subgroup.

5. The European Medicines Agency shall send the draft summary of product characteristics and the assessment report referred to in Article 9(4), points (a) and (e) respectively, of Regulation (EC) No 726/2004 to the HTA secretariat at the latest within 7 days from the adoption by the Committee for Medicinal Products for Human Use of its final opinion.

Article 4

Information to the Coordination Group

The HTA secretariat shall ensure that all the information received from the health technology developer, the European Medicines Agency, patients, clinical experts and other relevant experts and Member States related to joint clinical assessments and updates of joint clinical assessments is communicated to the Coordination Group, to its relevant subgroups and/or to the assessor and co-assessor, as appropriate, upon receipt of that information.

Article 5

Information to the health technology developer about the start of a joint clinical assessment

Upon the appointment by the JCA Subgroup of an assessor and a co-assessor to conduct the joint clinical assessment, the HTA secretariat shall inform the health technology developer of the start of the joint clinical assessment.

Article 6

Selection of patients, clinical experts and other relevant experts

1. The JCA subgroup shall specify, for each particular joint clinical assessment, the disease, the therapeutic area concerned and other specific expertise, based on which the HTA secretariat shall identify patients, clinical experts and other relevant experts to be consulted during that joint clinical assessment.

2. The HTA secretariat shall compile a list of relevant patients, clinical experts and, where necessary, other relevant experts, in consultation with the JCA Subgroup and the appointed assessor and co-assessor. When compiling the list, the HTA secretariat may consult:

(a) the members of the HTA stakeholder network;

(b) the European reference networks for rare and complex diseases and their respective European patient advocacy groups;

(c) the portal for rare diseases and orphan drugs ('Orphanet');

(d) the national contact points designated in accordance with Article 83 of Regulation (EU) No 536/2014 of the European Parliament and of the Council ([6]);

(e) the European Medicines Agency.

3. Where the consultation of the sources referred to in paragraph 2 has not allowed to identify a sufficient number of relevant patients, clinical experts and other relevant experts, the HTA secretariat may consult other existing databases or directories or contact members of the Coordination Group, its subgroups and relevant European Union and international agencies and organisations.

4. The HTA secretariat shall provide the JCA Subgroup with a list of available patients, clinical experts and, where necessary, other relevant experts, after the Commission has concluded on their conflicts of interest, in accordance with the rules set out in Article 5 of Regulation (EU) 2021/2282 and with the general procedural rules adopted under Article 25(1), point (a), of that Regulation.

5. The JCA Subgroup shall make the final selection of patients, clinical experts and, where necessary, other relevant experts to be consulted during the joint clinical assessment. In making the final selection, the JCA Subgroup shall give priority to patients, clinical experts and other relevant experts who have expertise, covering several Member States, in the therapeutic area of the joint clinical assessment.

Article 7

Professional secrecy obligations of patients, clinical experts and other relevant experts

The HTA secretariat shall ensure that only patients, clinical experts and other relevant experts who have signed a confidentiality agreement are involved in joint clinical assessments.

Article 8

Consultation of stakeholder organisations during joint clinical assessments

At any time during the joint clinical assessment, the JCA Subgroup may seek input on the disease and therapeutic area from patient organisations, healthcare professional organisations or clinical and learned societies via the members of the HTA stakeholder network.

([6]) Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (OJ L 158, 27.5.2014, p. 1, ELI: http://data.europa.eu/eli/reg/2014/536/oj).

Article 9

Assessment scope proposal

1. The assessor, with the assistance of the co-assessor, shall prepare an assessment scope proposal with a set of the parameters for the joint clinical assessment in terms of patient population, intervention, comparators and health outcomes, taking into account the information provided by the health technology developer under Article 2. At any time during the preparation of the assessment scope proposal, the assessor and/or co-assessor may seek, via the HTA secretariat, input on the assessment scope from the patients, clinical experts and/or other relevant experts selected in accordance with Article 6. The HTA secretariat shall make this input available to the entire JCA Subgroup.

2. The HTA secretariat shall share the assessment scope proposal with the members of the JCA Subgroup. Based on the input received from the Member States, the assessor, with the assistance of the co-assessor, shall prepare a consolidated assessment scope proposal reflecting the Member States' needs.

3. The HTA secretariat shall share the consolidated assessment scope proposal with the patients, clinical experts and other relevant experts selected in accordance with Article 6 and give them the opportunity to provide input.

Article 10

Finalisation of the assessment scope

1. The JCA Subgroup shall discuss the consolidated assessment scope proposal referred to in Article 9(2), as well as the input of patients, clinical experts and other relevant experts during an assessment scope consolidation meeting. The JCA Subgroup, via the HTA secretariat, may invite patients, clinical experts and other relevant experts to provide their input during a dedicated part of the assessment scope consolidation meeting.

2. The JCA Subgroup shall finalise the assessment scope at the latest 10 days after the Committee for Medicinal Products for Human Use adopts its list of questions.

The JCA Subgroup shall finalise the assessment scope within 75 days from the day on which the European Medicines Agency validates the application for a marketing authorisation or a variation to the terms of an existing marketing authorisation, where:

(a) the application for a marketing authorisation for a medicinal product is assessed under the accelerated procedure referred to in Article 14(9) of Regulation (EC) No 726/2004; or

(b) the joint clinical assessment is conducted for a medicinal product referred to in Article 7(1), point (b), of Regulation (EU) 2021/2282, for which a variation to the terms of an existing marketing authorisation is of the type referred to in point 2(a) of Annex II to Regulation (EC) No 1234/2008 and corresponds to a new therapeutic indication.

3. The HTA secretariat shall share the assessment scope finalised by the JCA Subgroup with the health technology developer in the Commission's first request referred to in Article 10(1) of Regulation (EU) 2021/2282.

Article 11

Assessment scope explanation meeting

Upon request of the health technology developer, the HTA secretariat shall invite the health technology developer to an assessment scope explanation meeting with the JCA Subgroup. The meeting shall take place no later than 20 days from the day on which the JCA Subgroup finalises the assessment scope.

Article 12

Dossier and further data for joint clinical assessment provided by the health technology developer

1. The health technology developer shall submit the dossier for joint clinical assessment of the medicinal product, requested by the Commission in its first request referred to in Article 10(1) of Regulation (EU) 2021/2282, to the HTA secretariat in a digital format. The dossier, as well as any additional information, data, analyses and other evidence submitted by the health technology developer for joint clinical assessment of the medicinal product, or its update, shall be presented in accordance with the template set out in Annex I to this Regulation.

2. The deadline to submit the dossier referred to in paragraph 1 shall be 100 days from the date of the notification of the first request to the health technology developer. However, that deadline shall be 60 days where:

(a) the application for a marketing authorisation for a medicinal product is assessed under the accelerated procedure referred to in Article 14(9) of Regulation (EC) No 726/2004; or

(b) the joint clinical assessment is conducted for a medicinal product referred to in Article 7(1), point (b), of Regulation (EU) 2021/2282, for which a variation to the terms of an existing marketing authorisation is of the type referred to in point 2(a) of Annex II to Regulation (EC) No 1234/2008 and corresponds to a new therapeutic indication.

3. In justified cases, with the consent of the assessor and co-assessor and considering the timetable for the evaluation during the centralised procedure, the HTA secretariat may extend the deadline referred to in paragraph 2. However, that extension shall not exceed the deadline specified in Article 10(1) of Regulation (EU) 2021/2282.

4. The health technology developer shall submit the missing information, data, analyses and other evidence indicated in the Commission's second request referred to in Article 10(5) of Regulation (EU) 2021/2282 within 15 days from the date of notification of the Commission's second request to the health technology developer. However, that deadline shall be 10 days where:

(a) the application for a marketing authorisation for a medicinal product is assessed under the accelerated procedure referred to in Article 14(9) of Regulation (EC) No 726/2004; or

(b) the joint clinical assessment is conducted for a medicinal product referred to in Article 7(1), point (b), of Regulation (EU) 2021/2282, for which a variation to the terms of an existing marketing authorisation is of the type referred to in point 2(a) of Annex II to Regulation (EC) No 1234/2008 and corresponds to a new therapeutic indication.

The deadlines referred to in the first subparagraph shall be 7 days for cases where only minor information is missing.

5. Where the assessor, with the assistance of the co-assessor, at any time during the preparation of the draft joint clinical assessment and summary reports, considers, under Article 11(2) of Regulation (EU) 2021/2282, that further specifications or clarifications or additional information, data, analyses, or other evidence are necessary, the HTA secretariat shall request the health technology developer to provide such information, data, analyses or other evidence within the deadline set by the assessor and co-assessor depending on the nature of the information requested. That deadline shall be set at minimum 7 days and maximum 30 days counting from the date of notification of the request to the health technology developer.

6. Where the Coordination Group decides to re-initiate a joint clinical assessment pursuant to Article 10(7) of Regulation (EU) 2021/2282, the health technology developer shall submit, upon request of the HTA secretariat, updates of previously provided information, data, analyses and other evidence pursuant to Article 10(8) of Regulation (EU) 2021/2282 within the deadline set by the assessor and co-assessor depending on the nature of the information, data, analyses or other evidence requested. That deadline shall be set at a minimum 7 days and maximum 30 days counting from the date of notification of the request to the health technology developer.

7. If during the joint clinical assessment, the health technology developer submits new data from clinical studies to the European Medicines Agency, it shall notify the HTA secretariat thereof and provide this data upon request of the assessor, with the assistance of the co-assessor. The deadlines referred to in paragraph 5 apply to that request.

8. Once the HTA secretariat receives the dossier and further data submitted by the health technology developer pursuant to paragraphs 1, 4, 5, 6 and 7, it shall make the dossier and these data available to the assessor, co-assessor and the JCA Subgroup at the same time.

Article 13

Commission's confirmation of the dossier for a joint clinical assessment

Within 15 working days from the date on which the health technology developer submitted the dossier, and as appropriate in consultation with the assessor and co-assessor, the Commission shall confirm whether, based on the information available at the time, the dossier for a joint clinical assessment of the medicinal product meets the requirements laid down in Article 9(2), (3) and (4) of Regulation (EU) 2021/2282. However, that deadline shall be 10 working days where:

(a) the application for a marketing authorisation for a medicinal product is assessed under the accelerated procedure referred to in Article 14(9) of Regulation (EC) No 726/2004; or

(b) the joint clinical assessment is conducted for a medicinal product referred to in Article 7(1), point (b), of Regulation (EU) 2021/2282, for which a variation to the terms of an existing marketing authorisation is of the type referred to in point 2(a) of Annex II to Regulation (EC) No 1234/2008 and corresponds to a new therapeutic indication.

Article 14

Draft joint clinical assessment and summary reports

1. The assessor, with the assistance of the co-assessor, shall prepare the draft joint clinical assessment and summary reports using the templates set out in Annex II and Annex III. At any time during the preparation of the draft joint clinical assessment and summary reports, the assessor and/or co-assessor, via the HTA secretariat, may seek input from the patients, clinical experts and/or other relevant experts selected in accordance with Article 6. The HTA secretariat shall make that input available to the entire JCA Subgroup.

2. The HTA secretariat shall share the draft joint clinical assessment and summary reports prepared by the assessor, with the assistance of the co-assessor, for comments with the JCA Subgroup. After having considered the comments from the members of the JCA Subgroup, the assessor, with the assistance of the co-assessor, shall prepare the revised draft joint clinical assessment and summary reports.

3. The HTA secretariat shall share the revised draft joint clinical assessment and summary reports with the patients, clinical experts and other relevant experts selected in accordance with Article 6 and give them the opportunity to provide input on the revised draft joint clinical assessment and summary reports.

4. The HTA secretariat shall provide the revised draft joint clinical assessment and summary reports to the health technology developer. The health technology developer shall signal any purely technical or factual inaccuracies and any information it considers to be confidential within 7 days from the date on which it received the revised draft joint clinical assessment and summary reports. The health technology developer shall demonstrate the commercially sensitive nature of the information it considers to be confidential.

The deadline referred to in the first subparagraph shall be 5 days from the date on which the health technology developer received the revised draft joint clinical assessment and summary reports where:

(a) the application for a marketing authorisation for a medicinal product is assessed under the accelerated procedure referred to in Article 14(9) of Regulation (EC) No 726/2004;

(b) the joint clinical assessment is conducted for a medicinal product referred to in Article 7(1), point (b), of Regulation (EU) 2021/2282, for which a variation to the terms of an existing marketing authorisation is of the type referred to in point 2(a) of Annex II to Regulation (EC) No 1234/2008 and corresponds to a new therapeutic indication; or

(c) a new assessment scope was developed during the joint clinical assessment, pursuant to Article 16 of this Regulation.

5. Where the health technology developer submits new clinical data on its own initiative under Article 11(2), third sentence, of Regulation (EU) 2021/2282, the JCA Subgroup shall ensure that the new clinical data is considered in the joint clinical assessment report, if received no later than 7 days after the adoption by the Committee for Medicinal Products for Human Use of its final opinion.

Article 15

Finalisation of the revised draft joint clinical assessment and summary reports

1. The JCA Subgroup shall discuss the revised draft joint clinical assessment and summary reports, as well as the input provided pursuant to Article 14(3) and (4), in a meeting. The JCA Subgroup, via the HTA secretariat, may invite patients, clinical experts and/or other relevant experts in a dedicated part of the meeting discussing the relevant revised draft reports.

2. The JCA Subgroup shall finalise the revised draft joint clinical assessment and summary reports at the latest on the date of the adoption of the Commission decision granting the marketing authorisation and submit them to the Coordination Group for endorsement.

3. Where the Coordination Group re-initiates a joint clinical assessment pursuant to Article 10(7) of Regulation (EU) 2021/2282 or initiates an update of a joint clinical assessment pursuant to Article 14 of Regulation (EU) 2021/2282, and no update of the assessment scope is necessary, the JCA Subgroup shall finalise the revised draft joint clinical assessment and summary reports within 180 days from the date of re-initiation of the joint clinical assessment or of the initiation of the update of the joint clinical assessment and submit them to the Coordination Group for endorsement.

4. Where the Coordination Group initiates an update of a joint clinical assessment pursuant to Article 14 of Regulation (EU) 2021/2282 and an update of the assessment scope is necessary, the JCA Subgroup shall validate the revised updated draft joint clinical assessment and summary reports within 330 days from the date on which the Coordination Group initiated the update of the joint clinical assessment. The JCA Subgroup shall submit the revised updated draft joint clinical assessment and summary reports to the Coordination Group for endorsement.

5. If the deadline specified in Article 11(1), point (a), of Regulation (EU) 2021/2282 does not apply, the Coordination Group shall endorse the revised draft joint clinical assessment and summary reports within 30 days from their receipt.

Article 16

Changes to the therapeutic indication(s)

1. Where during the centralised procedure, there is a change of the therapeutic indication(s) initially submitted to the European Medicines Agency, the assessor, with the assistance of the co-assessor, shall assess whether that change affects the assessment scope and inform the JCA Subgroup.

2. The JCA Subgroup shall decide whether the joint clinical assessment shall continue, or whether the assessor, with the assistance of the co-assessor, shall prepare a new assessment scope proposal. The HTA secretariat shall inform the health technology developer of the JCA Subgroup's decision.

3. If a new assessment scope proposal is prepared, Articles 9 and 10(1) of this Regulation shall apply with the necessary modifications.

4. The HTA secretariat shall inform the health technology developer of the new assessment scope finalised by the JCA Subgroup and shall request the health technology developer to submit an updated dossier. The deadlines referred to in Article 12(5) shall apply to that request. Articles 14 and 15(1) of this Regulation shall apply with the necessary modifications.

Article 17

Re-initiation of joint clinical assessments

1. Where the joint clinical assessment has been discontinued pursuant to Article 10(6) of Regulation (EU) 2021/2282, and where, at least 30 days before the end of the deadline referred to in Article 10(7) thereof, the Member State shares through the HTA IT platform the information, data, analyses and other evidence that formed part of the Commission's first request, the Commission shall confirm whether, based on the information available at the time, the requirements laid down in Articles 9(2), (3) and (4) of Regulation (EU) 2021/2282 have been met.

2. The Commission shall provide the confirmation referred to in paragraph 1 within 10 working days from the date on which the Member State shared these data and as appropriate in consultation with the assessor and co-assessor. The HTA secretariat shall inform the Coordination Group and the health technology developer of the results of the Commission's assessment.

3. Where the Coordination Group decides to re-initiate a joint clinical assessment pursuant to Article 10(7) of Regulation (EU) 2021/2282, Article 14 and Article 15(1), (3) and (5) of this Regulation shall apply.

4. The HTA secretariat shall inform the health technology developer of the re-initiation of a joint clinical assessment.

Article 18

Updates of joint clinical assessments

1. Where the joint clinical assessment report specifies the need for an update and additional evidence for further assessment becomes available, the health technology developer concerned shall inform the Coordination Group thereof.

2. The health technology developer may also provide, on their own initiative, new relevant information, data, analyses and other evidence to the Coordination Group in cases where the joint clinical assessment report did not specify the need for an update. Based on this information, data, analyses and evidence, the Coordination Group may decide to include an update in its annual work programme.

3. The HTA secretariat shall inform the health technology developer of the decision of the Coordination Group on the inclusion of the update of the joint clinical assessment in the annual work programme of the Coordination Group.

4. Where possible, the JCA Subgroup shall appoint the same assessor and co-assessor to conduct the update of the joint clinical assessment as the assessors in the initial joint clinical assessment and involve in the update the same patients, clinical experts and/or other relevant experts. Upon the appointment by the JCA Subgroup of the assessor and the co-assessor to conduct the update, the HTA Secretariat shall inform the health technology developer about the initiation of an update of the joint clinical assessment.

5. The JCA Subgroup shall decide whether an update of the assessment scope is necessary. If the JCA Subgroup concludes that an update of the assessment scope is not necessary, the HTA secretariat shall inform the health technology developer of the maintained assessment scope and request the submission of the updated dossier for a joint clinical assessment of the medicinal product. The deadlines referred to in Article 12(6) shall apply to that request. Article 14 and Article 15(1), (3) and (5) of this Regulation shall apply to the preparation and finalisation of the updated draft joint clinical assessment and summary reports.

6. If the JCA Subgroup concludes that an update of the assessment scope is necessary, the HTA secretariat shall share the initial assessment scope for the purposes of collecting Member States' needs. Based on the input received from the Member States, the assessor, with the assistance of the co-assessor, shall prepare an updated assessment scope proposal reflecting the Member States' needs. Article 9(2) and (3) and Article 10(1) of this Regulation shall apply with the necessary modifications. The JCA Subgroup shall finalise the updated assessment scope within 90 days from the initiation of the update.

7. If the assessment scope is updated, the HTA secretariat shall inform the health technology developer of the updated assessment scope and request the submission of the updated dossier for joint clinical assessment of the medicinal product. Article 12(1) and Article 13 of this Regulation shall apply with the necessary modifications. The deadlines referred to in Article 12(2) first sentence, Article 12(4) first sentence and Article 12(5) apply.

8. If the Commission confirms that the requirements laid down in Article 9(2), (3) and (4) of Regulation (EU) 2021/2282 are met, the assessor, with the assistance of the co-assessor, shall prepare an updated draft joint clinical assessment and updated draft summary reports. Article 14 and Article 15(1), (4) and (5) of this Regulation shall apply to the preparation and finalisation of the updated draft joint clinical assessment and summary reports.

Article 19

Correspondence during joint clinical assessments

Any correspondence with and between the Coordination Group, the JCA Subgroup, the HTA secretariat, the health technology developer, patients, clinical experts and other relevant experts during joint clinical assessments and updates of joint clinical assessments shall be sent in a digital format through the HTA IT platform.

Article 20

Confidentiality requests

1. The Commission shall publish the joint clinical assessment and summary reports as referred to in Article 12(4) of Regulation (EU) 2021/2282, together with other documentation listed in Article 30(3), points (d) and (i), thereof, after having considered the views of the JCA Subgroup as to the commercially sensitive nature of the information contained in that documentation, which the health technology developer has requested to be treated as confidential.

2. Before publishing the documentation referred to in paragraph 1, the Commission shall provide the health technology developer with the list of information that it does not consider as confidential, having assessed the justification provided by the health technology developer and considered the views of the JCA Subgroup. It shall inform the health technology developer of the right to appeal the refusal to redact this information.

Article 21

Personal data processing

1. The Commission shall be the controller of the processing, through the HTA IT platform, of personal data collected for the purpose of conducting joint clinical assessments and their updates under this Regulation.

2. The categories of personal data necessary for the purpose referred to in paragraph 1 shall be:

(a) the identity, email address and affiliation of the representatives appointed to the Coordination Group and the JCA Subgroup;

(b) the identity and email address of patients, clinical experts and other relevant experts that were identified to be selected for, and consulted in, joint clinical assessments and their updates;

(c) the identity, email address and affiliation of the representatives of health technology developers;

(d) the identity, email address and affiliation of the representatives of the members of the HTA stakeholder network.

3. The representatives appointed to the Coordination Group and the JCA Subgroup shall have access only to the parts of the secure system of the HTA IT platform relevant for the performance of their tasks and may collaborate, through the HTA IT platform, with other representatives appointed to the Coordination Group, or the JCA Subgroup to which they belong, for the purpose of conducting joint clinical assessments and their updates.

4. The personal data of patients involved in joint clinical assessments and their updates shall not be published.

5. The Commission shall keep the personal data listed in paragraph 2 only for as long as necessary for the purpose referred to in paragraph 1 and no longer than 15 years after the date on which the data subject no longer participates in joint work. The Commission shall review the necessity of storing the personal data every 2 years.

Article 22

Entry into force and date of application

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 12 January 2025.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels, 23 May 2024.

For the Commission
The President
Ursula VON DER LEYEN

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 international 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.				
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

Version	Document	Legal reference	Submission date	Commission's check date
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
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

Abbreviation	Meaning
IR	Commission Implementing Regulation (EU) 2024/1381 of 23 May 2024 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 (OJ L, 2024/1381, 24.5.2024, ELI: http://data.europa.eu/eli/reg_impl/2024/1381/oj)
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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List of tables

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.

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.

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 EEA 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 care pathway 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 care 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,

— therapeutic 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(s) 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) clinical efficacy and safety studies and where relevant, other applicable 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 Register 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 clinical efficacy and safety studies and where relevant, other applicable 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 included studies 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 population(s) and/or comparator(s) per study cover the relevant patient population(s)/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 in the CSR). 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 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.

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.	

Table of contents

List of tables

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 and 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 care pathway for the medical condition and whether it varies 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 medicinal product 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 studies, 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 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.

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.