Regulation (EU) 2021/2282 on health technology assessment (the HTA Regulation):

Frequently Asked Questions (FAQ)

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Version 1

List of acronyms

EC	European Commission
EMA	European Medicines Agency
HTA	Health Technology Assessment
HTD	Health Technology Developer
HTACG	Member State Coordination Group on Health Technology Assessment
JCA	Joint Clinical Assessment

Regulation (EU) 2021/2282 on health technology assessment: Frequently Asked Questions (FAQ)

This document provides answers to questions frequently asked by stakeholders related 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 ('the HTA Regulation')**. Any views expressed in this document are the preliminary views of the European Commission (EC) services and may not under any circumstances be regarded as stating an official position of the EC. The information transmitted intends to clarify the provisions of the HTA Regulation. Only the Court of Justice of the European Union is competent to authoritatively interpret EU law.

These FAQ are based on enquiries received and will be regularly updated.

The HTA Regulation is available at:

https://eur-lex.europa.eu/eli/reg/2021/2282/oj

Joint Clinical Assessments (JCA)

Medicinal products subject to JCA

General conditions

1. What medicinal products are subject to JCA?

Medicinal products subject to JCA are defined in Article 7(1), points (a) and (b), of the HTA Regulation.

Under Article 7(1), point (a), of the HTA Regulation, a medicinal product is subject to JCA if it fulfils **all of the following conditions**:

1) The medicinal product either falls within the mandatory scope of **Annex I of Regulation (EC) 726/2004** or the applicant claims that the medicinal product contains **an active substance which, on 20 May 2004, was not authorized in the Union**;
2) The application for a marketing authorisation for that medicinal product is submitted in accordance with **Regulation (EC) No 726/2004**;
3) That application is in compliance with Article 8(3) of **Directive 2001/83/EC** ('**full application**');
4) The application is submitted **after the relevant dates** set out in Article 7(2) of the HTA Regulation ('**stepwise approach**').

Moreover, under Article 7(1), point (b), of the HTA Regulation, if a medicinal product that is authorised in the Union has **a JCA report published**, it is subject to JCA when an application is submitted for **a variation to an existing marketing authorisation** which corresponds to **a new indication**.

2. What does "*stepwise approach*" mean?

As regards the medicinal products subject to JCA, the HTA Regulation follows in Article 7(2) a stepwise approach that means that the HTACG will start with a small number of jointly assessed medicinal products to progress only at a later stage to assess all the other medicinal products within the scope of the HTA Regulation.

In this respect, there are three relevant dates:

a) **After 12 January 2025** the HTACG starts with two categories of medicinal products falling within the scope of the HTA Regulation: (1) medicinal products with a new active substance for the treatment of cancer and (2) advanced therapy medicinal products;
b) **After 13 January 2028**, the HTACG will in addition jointly assess orphan medicinal products;
c) **After 13 January 2030**, the HTACG will jointly assess all medicinal products falling within the scope of the HTA Regulation.

Moreover, where a JCA report has been published for a medicinal product, a JCA will also be carried out where that medicinal product is **subsequently authorised for a new therapeutic indication**.

3. As of the dates referred to in Article 7(2), points (b) and (c), of the HTA Regulation, would any new marketing authorisation application meeting these conditions be in scope regardless of whether they include new active substances or not?

As of 14 January 2028, all medicinal products that **comply with the conditions defined in Article 7(1), point (a), of the HTA Regulation** and that are designated as orphan medicinal products, and, as of 14 January 2030, all other medicinal products that comply with the conditions defined in Article 7(1), point (a), of the HTA Regulation are subject to JCA. Compared to Article 7(2), point (a), of the HTA Regulation as regards medicinal products for the treatment of cancer, there is no requirement in Article 7(2), points (b) and (c), of the applicant's declaration that the medicinal product contains a new active substance.

4. Do applications under Article 10a ('well-established medicinal use'), Article 10b ('fixed combination application'), Article 10c ('informed consent'), Article 10(1) ('generic'), Article 10(3) ('hybrid') and Article 10(4) ('biosimiliar') of Directive 2001/83/EC fall under the scope of Article 7(1), point (a), of the HTA Regulation?

Pursuant to Article 7(1), point (a), of the HTA Regulation, the marketing authorisation application must be "*in compliance with Article 8(3) of Directive 2001/83/EC*" ('**full application**'). Applications under Articles 10(1), 10(3), 10(4), 10a, 10b and 10c of Directive 2001/83/EC thus fall outside scope of that provision.

Medicinal products subject to JCA as of 2025

5. What medicinal products are subject to JCA as of 13 January 2025?

Medicinal products subject to JCA as of 13 January 2025 are medicinal products that comply with the conditions defined in Article 7(1), point (a), of the HTA Regulation (please refer to our answer to Question 1 above). In addition, as per Article 7(2), point (a), of the HTA Regulation, they must belong to one of the following categories of medicinal products:

1) They are medicinal products for which the applicant declares in its application for marketing authorisation that it contains **a new active substance for the treatment of cancer**;

2) They are regulated as **advanced therapy medicinal products**.

6. When will an orphan medicinal product indicated for the treatment of a rare cancer fall under the scope of a JCA?

Any medicinal products, **including orphan medicinal products**, that comply with the conditions defined in Article 7(1), point (a), of the HTA Regulation and that belong to one of the two categories defined in Article 7(2), point (a), of the HTA Regulation (please refer to our answer to Question 5 above) are subject to JCA as of 13 January 2025.

7. What happens in case of a potential regulatory finding that the medicinal product for which the therapeutic indication is the treatment of cancer and for which a JCA has been initiated does not contain a new active substance?

The outcome of a new active substance (NAS) assessment by the EMA has **no retrospective impact** on the decision on starting and finalising a JCA.

As of 13 January 2025, all medicinal products that comply with the conditions in Article 7(1), point (a), of the HTA Regulation and that belong to one of the two categories defined in Article 7(2), point (a), of the HTA Regulation are subject to JCA.

One of those two categories is medicinal products for which **the applicant declares** in its application for marketing authorisation that it contains a new active substance for the treatment

of cancer. The triggering criteria to undertake a JCA is thus the applicant's declaration in its application for marketing authorisation.

8. Are coformulations/combinations of an authorised and a new active substance falling under the scope of a JCA?

The medicinal products subject to JCA must fulfill the requirements in Article 7(1), point (a), of the HTA Regulation (please refer to our answer to Question 1 above).

Where these requirements are met, the medicinal products will be subject to JCA even if the claimed new active substance is used in combination with another authorised active substance.

For further guidance on the criteria for an active substance to be considered as "new" please refer to **Notice to Applicants Volume 2A, Chapter 1**.

9. What is the definition of the terms "*medicinal product with a new active substance for which the therapeutic indication is the treatment of cancer*" used in Article 7(2), point (a), of the HTA Regulation?

The HTA Regulation does not provide a definition of those terms. Neither such a definition is provided in point 3 of Annex I to Regulation (EC) No 726/2004.

In its document "**Scientific specifications of medicinal products subject to joint clinical assessments**" (see Chapter 3.3), the HTACG referred to the the EMA's guidance on the mandatory scope that provides the working definition of what constitutes a medicinal product, for which the therapeutic indication is the treatment of cancer. The EMA guidance can be found here: **Scientific Aspects and Working Definitions for the Mandatory Scope of the Centralised Procedure (europa.eu)** (see Chapter 3.2).

Medicinal products subject to JCA as of 2028

10. Will a JCA be continued in cases where a designated orphan medicinal product is removed from the Community Register of Orphan Medicinal Products at the request of the sponsor during the centralised procedure provided for under Regulation (EC) No 726/2004, but is still granted a marketing authorisation?

Pursuant to Article 7(1), point (a), and Article 7(2), point (b), of the HTA Regulation, as of 14 January 2028, all medicinal products that comply with the conditions defined in Article 7(1), point (a), of that Regulation and are designated as orphan medicinal products pursuant to **Regulation (EC) No 141/2000** are subject to JCA.

Where a JCA is initiated on such a designated orphan medicinal product, the removal of that medicinal product from the Community Register of Orphan Medicinal Products at the request of the sponsor during the centralised marketing authorisation procedure provided for under Regulation (EC) No 726/2004 has **no retrospective impact** on the decision on starting and finalising a JCA.

Variations to an existing marketing authorisation

11. For the purposes of the application of Article 7(1), point (b), of the HTA Regulation, is there a difference between the specific type of a variation?

Article 7(1), point (b), of the HTA Regulation concerns a variation to an existing marketing authorisation which corresponds to a new therapeutic indication. This applies independently of the specific type of variation procedure under **Commission Regulation (EC) No 1234/2008** (e.g. Type II variation or extension of a marketing authorisation) that is used to add the new therapeutic indication in the particular case.

12. Would a medicinal product that was granted a marketing authorisation for an oncology indication with orphan medicinal product status before 13 January 2025 be subject to JCA, if a new oncology indication with orphan medicinal product status is submitted to the EMA?

As of 13 January 2025, all medicinal products, including orphan medicinal products, that comply with the conditions in Article 7(1), point (a), of the HTA Regulation and that belong to one of the two categories defined in Article 7(2), point (a), of the HTA Regulation are subject to JCA (please refer to our answer to Question 6 above).

Variations to an existing marketing authorisation which correspond to a new therapeutic indication (see **Commission Regulation (EC) No 1234/2008**) will be subject to JCA only where a JCA report for that medicinal product has been published, in accordance with Article 7(1), point (b), of the HTA Regulation.

13. Where a JCA report has been published for a medicinal product, is an application for a Type II variation to the existing marketing authorisation for that medicinal product which corresponds to a new therapeutic indication, subject to JCA only after 13 January 2030?

No. Medicinal products authorised in the Union for which a JCA report has been published are subject to JCA in cases where an application is submitted for a variation to an existing marketing authorisation which corresponds to a new therapeutic indication, pursuant to Article 7(1), point (b), of the HTA Regulation (please refer to our answer to Question 11 above).

Conditional marketing authorisation

14. What happens in case a conditional marketing authorisation is issued to a medicinal product subject to JCA?

The HTA Regulation does not distinguish between conditional and standard marketing authorisations. Thus, where a conditional marketing authorisation is issued for the medicinal product undergoing a JCA, that JCA will be conducted and finalised.

Any medicinal product might be subject to an update of JCA, if the initial JCA report specified the need for an update when additional evidence for further assessment becomes available.

Diagnostic products

15. Many new medicinal products for the treatment of cancer are conditioned to the presence or absence of molecular alteration. Since the HTACG is starting with the evaluation of new medicinal products for the treatment of cancer, why not to include in this first wave starting from 13 January 2025 the assessment of diagnostic tests that allow to detect these molecular alterations?

As regards *in vitro* diagnostic medical devices (IVDs), Article 7(1), point (d), of the HTA Regulation limits the scope of JCA to the higher-risk class IVDs, *i.e.* class D referred to in Article 47 of **Regulation (EU) 2017/746**. The companion diagnostics are therefore out of scope of the HTA Regulation since they are classified as class C devices.