HTA CG | MEMBER STATE COORDINATION GROUP ON HEALTH TECHNOLOGY ASSESSMENT

Scientific specifications of medicinal products subject to joint clinical assessments

This document was agreed upon by the HTACG at its meeting on 10 June 2024.

This document is for information only.

Contents

List of abbreviations

Abbreviation	Definition
ATMP	Advanced Therapy Medicinal Products
EMA	European Medicines Agency
HTACG	HTA Coordination Group
HTAR	Health Technology Assessment Regulation
JCA	Joint Clinical Assessment
NAS	New Active Substance

1 Introduction

Medicinal products subject to joint clinical assessments (JCA) are defined in Article 7 of Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment (Health Technology Assessment Regulation, HTAR).

According to Regulation (EC) 2021/2282, medicinal products subject to JCA are those:

- for which the application for a marketing authorisation is submitted to the European Medicines Agency (EMA),
- for which a variation to an existing marketing authorization corresponds to a new indication and for which a JCA report has been previously published.

Medicinal products are subject to JCA according to the following timeline:

- from 12 January 2025 onwards: medicinal products for which the applicant declares that the application contains a new active substance for which the therapeutic indication is the treatment of cancer and medicinal products which are regulated as advanced therapy medicinal products (ATMP),
- from 13 January 2028 onwards: medicinal products which are designated orphan medicinal products,
- from 13 January 2030 onwards: the remaining medicinal products not previously included.

2 Scope of the document

This document is intended to clarify the scientific specifications of ‘new active substance’ and ‘therapeutic indication of treatment of cancer’ to determine if a medicinal product shall be subject to JCA between 12 January 2025 and 13 January 2030. During this time period also ATMPs and as of 2028, orphan medicinal products shall be subject to JCA . However, there is no need to determine criteria for identifying ATMPs or orphan medicinal products because these criteria are laid down in Regulation (EC) No 1394/2007 and Regulation (EC) No 141/2000. After 13 January 2030, in accordance with Regulation (EC) No 2021/2282, all medicinal products shall be subject to JCA.

3 Scientific specifications of medicinal products subject to JCA

The scientific specifications for determining which medicinal products are subject to the JCA are based on the definitions used by the European Medicines Agency (EMA) to determine which medicinal products are considered new active substances and which are in scope for the centralised procedure for marketing authorisation.

These definitions are as follows are described in the following sections.

3.1 Definition of new active substance

EMA defines a new active substance (NAS) as a new chemical, biological or radiopharmaceutical active substance and includes[1]

- a chemical, biological or radiopharmaceutical substance not previously authorised in a medicinal product for human use in the European Union;
- an isomer, mixture of isomers, a complex or derivative or salt of a chemical substance previously authorised in a medicinal product for human use in the European Union but differing significantly in properties with regard to safety and/or efficacy from that chemical substance previously authorised;
- a biological substance previously authorised in a medicinal product for human use in the European Union, but differing significantly in properties with regard to safety and/or efficacy which is due to differences in one or a combination of the following: in molecular structure, nature of the source material or manufacturing process;
- a radiopharmaceutical substance which is a radionuclide, or a ligand not previously authorised in a medicinal product for human use in the European Union, or the coupling mechanism to link the molecule and the radionuclide has not been authorised previously in the European Union.

The final decision on the new active substance status of a medicinal product is made by EMA during the regulatory assessment procedure.

[1] EMA – Reflection paper on the criteria to be considered for the evaluation of new active substance (NAS) status of biological substances. Available: https://www.ema.europa.eu/en/documents/scientific- guideline/reflection-paper-criteria-be-considered-evaluation-new-active-substance-nas-status-biological- substances_en.pdf

3.2 Definition of cancer

EMA defines cancer as all malignant and borderline malignant neoplasms, following the current International Classification of Diseases for Oncology (ICD-O).[2] [3]

This includes primary or secondary malignant neoplasms, carcinoma in situ, and neoplasms classified as uncertain whether benign or malignant. Thus, those ICD-O behaviour codes that are relevant here are: /1, /2, /3, /6, /9.

Benign neoplasms (i.e. ICD-O behaviour code /0) are not considered as cancer.

This definition of cancer will be used by the HTA Coordination Group (HTACG) for the confirmation if a medicinal product submitted to EMA is subject to a JCA under the HTAR.

3.3 Definition of treatment of cancer

EMA defines treatment for cancer as including anti-neoplastic agents (including modulators and enhancers of anti-neoplastic activity) and adjuvant treatments.[2]

EMA notes that medicinal products intended for the following interventions are not included in the mandatory scope of the centralised procedure (unless they belong to other categories within the mandatory scope of the Annex to Regulation (EC) No 726/2004):

- Agents developed to prevent or treat side-effects of cancer treatment (e.g., neutropenia, nausea and vomiting, tumour lysis syndrome);
- Diagnostic agents aimed at diagnosing, staging or monitoring of the disease;
- Agents intended to reduce the risk or prevent cancer or to treat pre-cancerous lesions;
- Agents intended to treat cancer associated symptoms (e. g. cancer pain).

Anti-neoplastic treatment includes chemotherapy, biologic therapies and hormonal agents that produce antitumour cytotoxic or cytostatic effects, or therapies that increase sensitivity of malignant cells to other anti-neoplastic treatments (including radiosensitizers).

Traditionally, chemotherapy has a role in four different clinical settings:

1) Induction treatment for advanced disease (induction chemotherapy): therapy given as the primary treatment for patients who present with advanced cancer for which no alternative treatment exists.

[2] https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/scientific-aspects-and-working- definitions-mandatory-scope-centralised-procedure_en.pdf

[3] https://www.who.int/standards/classifications/other-classifications/international-classification-of-diseases- for-oncology

2) As an adjunct to local treatment (adjuvant chemotherapy): use of systemic treatment after the primary tumour has been controlled by an alternative modality, such as surgery and radiation therapy.

3) Primary treatment (primary chemotherapy, or neoadjuvant chemotherapy): chemotherapy as the initial treatment for patients who present localized cancer for which there is an alternative but less than completely effective local treatment.

4) Local treatment by direct instillation into sanctuary sites or by site-directed perfusion of specific regions directly affected by the cancer.

Medicinal products given without curative intent but with the aim of achieving pain or other symptom palliation (palliative care) via anti-tumour effects are considered anti-neoplastic treatment. Hormonal agents used in hormonally responsive cancers such as breast, prostate or endometrial carcinomas are considered anti-neoplastic treatment.

However […] the following are not considered products for cancer treatment: hormonal agents used to treat symptoms caused by cancer without anti-tumour effect as well as other agents intended to treat cancer associated symptoms e.g. supportive and palliative care treatments (without curative intent of the cancer), such as analgesic drug therapy (opioids, non-opioid drugs), local anaesthetics, corticosteroids for the management of pain, bone resorption inhibitors used as adjuvants for bone pain, antidepressants, anticonvulsants.

This definition of treatment of cancer will be used by the HTACG for the confirmation if a medicinal product submitted to EMA is subject to a JCA under the HTAR.

3.4 Definition of ATMPs

Article 7 (2a) of the HTAR defines ATMPs according to Regulation (EC) No 1394/2007. Therefore, the HTACG will use this regulation to confirm if a medicinal product submitted to EMA is subject to a JCA as an ATMP.

3.5 Definition of orphan medicinal products

Article 7 (2b) stipulates that orphan medicinal products designated pursuant to Regulation (EC) No 141/2000 of the European Parliament and of the Council are within scope from 13 January 2028 and includes those products. Therefore, the HTACG will use this regulation to confirm if a medicinal product submitted to EMA is subject to a JCA as an orphan medicinal product.