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Title Companion diagnostic test associated with a targeted therapy: definitions and assessment method

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Aim

Stratified medicine is a therapeutic approach based on drug/diagnostic test associations. The objective of the diagnostic test is to use a marker predictive for the effect of the treatment in order to select the patients to whom it is administered so as to treat only the subpopulation that will benefit from it. In this context, demonstrating the efficacy of the treatment in a limited subpopulation identified by its status for the marker logically leads to the prescription of the treatment being restricted to this subpopulation in its marketing authorisation, making this test a regulatory requirement.

In this guide, HAS defines the precise semantics of the concepts of targeted therapy and companion diagnostic test which thus have to meet strict requirements in terms of evidence.

The fundamental principle for the assessment by HAS of a diagnostic test associated with a stratified therapy lies in the fact that recognition of the designations "companion" test and "targeted" therapy depends on whether or not the clinical utility of the diagnostic test is demonstrated. Demonstrating the clinical utility of the test is necessary because it shows the test's ability to improve patient clinical outcomes and provide added value in terms of optimising patient management. As a consequence, it proves the added value provided by the test compared with a diagnostic test in that it allows a subpopulation to be selected only if a marker is identified.

Since the treatment/test association is an inseparable unit, the assessment of the diagnostic test must be included in that of the treatment. This has direct consequences for study methodologies that may or may not have the ability to provide the evidence needed to meet the level of requirements conferring the added value of a "companion" to a "standard" diagnostic test. In this guide, HAS therefore aimed to present the principles it will use to assess diagnostic tests associated with treatments, with two objectives: firstly to ensure the transparency of its assessments, and secondly to provide the healthcare industry with the specifications needed to conduct clinical studies that are of a quality consistent with the expected requirements.

This guide presents a practical summary of the methodological principles that will guide HAS assessments, the concepts implemented being described in a methodological annex entitled "Companion diagnostic test associated with a targeted therapy: Scientific annex".

Conclusions and results

In order to define its expectations, in this guide HAS describes the evidence that must be provided to prove the clinical utility of a diagnostic test, as well as the level of evidence it attributes to the various development study designs used for the tests considered.

Depending on the evidence provided, two types of conclusions may be envisaged for the assessment of the test:

- If the clinical utility of the test is not demonstrated:
  - the test will be regarded as only a "standard" diagnostic test needed to identify the subpopulation of patients the selection of which is required by the marketing authorisation. Despite the lack of demonstrated clinical utility, conducting this test will be no less essential from a regulatory point of view to allow the use of treatment under its marketing authorisation;
  - the designation "companion test" cannot be claimed, and the treatment cannot be considered a targeted therapy. In fact, since clinical utility is not proven, the possibility of efficacy in all patients cannot be ruled out;
- If the clinical utility of the test is demonstrated:
  - the test will be considered a diagnostic test to identify patients whose selection is required by the marketing authorisation; the test may also be called a "companion test" and the therapy considered to be targeted.

Methods

A methodological review of the literature in the field concerned was conducted. An interim version of the document was submitted for opinion to:

- HAS specialized appraisal committees: Commission d'évaluation économique et santé publique (CEESP), [Economic and Public Health Assessment Committee],

Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé (CNEDiMTS), [National Committee for the Assessment of Medical Devices and Health Technologies], Commission de Transparence [Transparency Committee];

- Stakeholders: INCa (National Cancer Institute), ANSM (French National Agency for Medicines and Health Products Safety), DGOS (General Directorate for Healthcare Provision), DGS (General Directorate for Health), DSS (Directorate for Social Security), SFPT (French Society of Pharmacology and Therapeutics), SNITEM (National Association of Medical Technologies Industry), LEEM (French Pharmaceutical Companies Association), SIDIV (In Vitro Diagnostics Industry Union), CNAM (National Health Insurance Fund), UNCAM (National Union of Health Insurance Funds), CEPS (Economic Committee for the Pricing of Healthcare Products).

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