Context and challenges

TAVI devices are listed by brand name in Section II of the list of products and services qualifying for reimbursement in France (LPPR list). This inclusion procedure involves the submission of a medico-technical file to the National Committee for the Evaluation of Medical Devices and Health Technologies (CNEDiMTS) for assessment of their expected or actual clinical benefit with a view to funding by the French national health insurance system.

In addition, the CNEDiMTS must “specify the procedures and principles it uses to apply assessment criteria for health products with a view to their funding by the French national health insurance system” (art. L 161-37 of the French Social Security Code).

The purpose of this document is therefore to explain the requirements of the CNEDiMTS in terms of the minimum clinical data to be supplied in France for:

► a new TAVI device;
► the acceptance of a new indication for a TAVI device already listed in the LPPR list;
► the renewal of inclusion of a TAVI device in the LPPR list.

Method

This document was developed by cardiologists and methodologists from the CNEDiMTS and the dedicated department of the HAS:

► taking into account all assessments issued by the CNEDiMTS since 2011 regarding TAVI devices;
► consulting the TAVI manufacturers identified, as well as the French National Medical Technologies Industry Union (SNITEM) in order to gather information concerning the methodologies of ongoing studies on TAVI devices (both as concerns new devices and indication extensions for devices already eligible for reimbursement).

At the end of this phase, the draft was submitted to the identified TAVI device manufacturers and to the SNITEM to obtain their feedback.

In view of these documents, the clinical data requirements were examined and then adopted by the CNEDiMTS on 29 January 2019 for application as soon as possible.

Minimum clinical data

The introduction of a TAVI device in the management of aortic stenosis or aortic regurgitation must be accompanied by demonstration of the efficacy and safety of this approach compared to the gold standard strategy (surgery, standard TAVI device, etc.) depending on the indication, the symptoms and the risks to the patient of the surgical procedure (surgical risk scores). The implantation of a TAVI device inside a native aortic valve or inside a previously implanted bioprosthetic aortic valve which failed are two quite different clinical situations that must be the subject of separate studies or pre-planned subgroup analyses.

The CNEDiMTS requests that a prospective, comparative, randomised superiority or non-inferiority study aimed at comparing the TAVI device with the gold standard in the indications claimed be systematically provided. The primary endpoint must be a relevant clinical outcome measure enabling assessment of mortality (relevant composite endpoint...
possible) with a follow-up duration of at least 1 year. If the design used is a non-inferiority study, the non-inferiority of the TAVI device compared to the comparator must be demonstrated, with an acceptable and justified loss of efficacy accepted for the primary endpoint (non-inferiority margin required to represent the greatest clinically negligible loss of efficacy given the other advantages presented by the TAVI device studied).

The studies must report procedure-related complications after 30 days in accordance with current VARC guidelines (mortality, disabling stroke, major, disabling or life-threatening bleeding i.e. BARC ≥ 3, major vascular complication, central and paravalvular aortic regurgitation of grade ≥ 2, permanent pacemaker implantation) and adverse events after 1 year of follow-up. In patients undergoing transcatheter aortic valve implantation for a bioprosthetic aortic valve failure, the risk of prosthesis-patient mismatch must be indicated.

For renewal(s) of inclusion, the following must be supplied:
► observational data in routine practice. These follow-up data must concern a significant number of patients, representative of the target population concerned. They must describe the symptoms and quality of life of patients (using validated scales), the durability (valve thrombosis, endocarditis, non-structural valve dysfunction, moderate to severe structural valve dysfunction, prosthetic valve failure in accordance with the standardised definitions of the current EAPCI-ESC-EACTS consensus) in the long term (5 years then 10 and 15 years), late assessment of effective orifice area and accessibility for percutaneous coronary artery revascularisation following TAVI.
► The long-term results of the randomised controlled study having led to reimbursement of the TAVI device.

Furthermore, it is recalled that the French decree of 3 July 2012 and instruction No. DGOS/PF4/2013/91 of 7 March 2013 schedule the collection by healthcare institutions of pre- and perioperative data for all French patients undergoing TAVI. Consequently, the CNEDiMTS will consult the clinical data from the FRANCE-TAVI registry, which also incorporates postsurgical data concerning patients.

**Specific case of incremental range upgrades**

In this particular case and on condition that justification of the equivalence between the different generations of TAVI devices is provided, a study specific to the previous generation and meeting the abovementioned requirements may be extrapolated to the prosthesis generation that is the subject of the application.

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For medical devices in the clinical development phase, the company or developer of the medical device may request early dialogue concerning questions related to the clinical development of the health product. The objective of this early dialogue is to obtain answers to questions posed by companies or developers with respect to how they may conduct clinical studies in order to be able to supply data meeting health technology assessment requirements. The answers supplied by the Medical Devices Assessment Department (SED) to companies or developers during an early dialogue process in no way constitute an assessment and are not an indicator of the conclusions that may be reached in the National Committee for the Evaluation of Medical Devices and Health Technologies (CNEDiMTS) assessment following submission of the application. The early dialogue processes organised by the French National Authority for Health (HAS) are optional, non-binding, confidential and free of charge. To find out more about early dialogue procedures, consult the following link [link].

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