

Medico-economic Evaluation of Health Products in the Context of the Social Security Financing Act for 2012

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Abstract – The participants in round table 6 of the Giens Workshops 2012 drafted recommendations based on the collective interpretation of important elements of the decree concerning the medico-economic evaluation of health products published a few days earlier (02 October 2012). The medico-economic evaluation (MEE), becomes an additional determinant for fixing the prices of health products by the Health products economic committee (*Comité économique des produits de santé*, CEPS) via the hierarchisation of treatment strategies, and thus modifies the market access conditions.

Limiting the analysis to medicinal products and medical devices for which a major, important or moderate improvement in the medical service rendered (ASMR) or of the expected service (ASA) has been requested and presenting a significant budget impact on the Social Security expenses, excludes health products with ASMR or ASA with a lower level requested which often create complex price fixing problems and often have a major budget impact. This latter concept remains to be defined in detail. The MEE envisaged for the first registration must include the need to confirm or refute the initial hypotheses especially

† Articles, analyzes and proposals from the Giens workshops are those of the authors and do not prejudice the position of their parent organization

efficiency; cost-efficacy ratio; guidelines; acceptability threshold; Economic and Public Health Evaluation Commission; market access

concerning the actual position in the therapeutic strategy at the time of renewal of the registration. For the first registration, the conventional reference to European prices guaranteeing a minimum price to innovative medicinal products, the medico-economic models submitted by the industry to the French Drug Authority (*Haute autorité de santé*, HAS) must be used to guide the compilation of new data to be requested at the time of the registration renewal and to negotiate the level of the discounts in the framework of a price-volume agreement, if applicable. The MEE will allow comparing the result of the analysis to the model hypothesis at the time of the renewal of the registration, which may contribute to the renegotiation (either up or down) of the price of health goods.

The costs related to obtaining new data must be controlled. In order for the MEE to allow confirming the relationship between the price requested and the benefit expected, the group privileges the definition of reference values with an indicative and non-normative value, likely to evolve with time rather than a threshold.

Concerning the evaluation procedure: the time to market access must not be lengthened; while the possibility of regular meetings between the industry and the HAS is recommended to avoid methodological divergences. A transitory period should allow the implementation of the entire evaluation procedure which must also take into account the specificities of health products registered before the 3 October 2013.

Abbreviations: see end of article.

1. Introduction

The decree No. 2012-1116 dated 2 October 2012^[1] concerning the medico-economic missions of the French Health Authority (*Haute autorité de santé* [HAS]) significantly modifies the market access conditions of health goods by demanding a medico-economic evaluation for innovative medicinal products and medical devices with a significant budget impact on the Health Insurance expenses. A year earlier, the Social security financing act for 2012^[2] designated the medico-economic evaluation (besides the clinical added value, comparator price and sales volumes) the fourth determinant of the price of a medicinal product.

The round table N° 6 of the Giens Workshops 2012, entitled “Medico-economic evaluation of health products in the context of the LFSS (Social security financing act) for 2012”, took place shortly after the publication of the decree. While the latter sets the framework of the new missions entrusted to the HAS, certain points of application remain to be specified. As an example, we will cite the absence of clear definition of a significant impact on health insurance expenses or of aspects of the procedure to be stabilised. These questions in suspension open an interpretation window for the participants. In this context, the round table was an opportunity to exchange between representatives on the effective implementation conditions of the reform. This article presents the elements of this debate.

The round table participants tried to answer the following questions: What is the purpose of the medico-economic evaluation? What are the health goods concerned? At what moment in the life cycle of the products should it intervene? According to what procedure(s)? How to interpret the results of this evaluation?

The recommendations from the round table are the result of discussions between participants, representatives of the institutional, industrial (medicinal products and medical devices) and academic worlds, based on presentations about foreign experiences (Sweden, Netherlands, United Kingdom) or on the field of vaccines in France.

2. The medico-economic evaluation: what purpose?

The medico-economic evaluation ranks the treatment strategies. It may be the basis of reimbursement decisions (as for example in the United Kingdom) and/or assist to fix the price of health goods (as it used to be done in Germany before the *Gesetz zur Neuordnung des Arzneimittel Marktes* [AMNOG] law).^[3]

In view of the characteristics of the French health system (social insurance system), the expectations of the population with respect to the healthcare system, societal or even ethical questions and in compliance with the terms of the decree, it seemed to most of the participants in the round table that the medico-economic evaluation may play a useful role in the negotiations between the industry and the Health product economic committee (*Comité économique des produits de santé* [CEPS]) on the price of health goods but should not condition the access to innovative medicinal products or medical devices to the basket of reimbursable goods and services. However, this position was not unanimous. Furthermore, the two decisions are not totally disconnected as if the price attributed is considered to be too low the industry may decide not to market the product in France.

While the medico-economic evaluation can help fix the price of a health good, it is imperative that this determination continues to be the subject of a negotiation between the CEPS and the industry within the convention framework. The French Drug Companies (*Les entreprises du médicament* [LEEM]) -CEPS framework agreement^[4] guarantees for medicinal products that have obtained a level 1 to 3 to improvement of medical service rendered (*amélioration du service médical rendu* [ASMR]), that the price level will not be less than the lowest price given in the main four European markets. Under these conditions, the medico-economic evaluation may be used to negotiate the level of discounts within the framework of a price-volume agreement.

The publication of the results of this evaluation, envisaged in the decree, partially lifts the confidentiality of the negotiations between the CEPS and the industry. If applicable, the CEPS could

justify the price negotiated via the comparison to the cost/efficacy ratios estimated by the HAS for a price range. All the round table participants recognise that the medico-economic evaluation is only an element in the negotiation of the price of a health good.

3. The medico-economic evaluation: what health goods?

The scope of application of the decree is wide. It concerns all the prevention, care, prescription or management strategies. The discussions in the round table only concerned health goods, medicinal products and medical devices, given how important the stakes are for the industry. However, it is important to remember the medico-economic evaluation only concerns health goods as elements of a management strategy (preventive, diagnostic or therapeutic).

The obligation to produce a medico-economic analysis only concerns products for which a major, important or moderate improvement in the service expected (medical devices) or rendered (medicinal products) has been claimed by the pharmaceutical company and having a significant impact on the Health Insurance expenses.

The improvement of service expected (*amélioration du service attendu* [ASA]) or ASMR criterion does not give rise to debates.

The second criterion is less clear. What limit should be retained to consider that the impact on the Health Insurance expenses is significant? Who should determine it? The significant impact concept seems to exclude from the start orphan drugs and a number of medical devices for which the target population is small. Different values were mentioned during the discussion. For example, the value of 30 million Euros corresponding to the exoneration threshold of discounts by pharmaceutical conglomerates^[4] for orphan or paediatric medicinal products was mentioned. In order to progress, statistical work on data from national health insurance cross-schemes Information system (*système national d'informations inter régions d'Assurance maladie* [SNIIRAM]) should be performed especially since the sole amount of sales cannot summarise the impact on the health system. From a pragmatic point of view, the participants proposed to transpose the discussions in a convention framework between the CEPS and the pharmaceutical industry associating the HAS (Economic and public health evaluation commission [*Commission d'évaluation économique et de santé publique*, CEESP]).

Certain representatives of the round table regretted that the requisite association of two conditions (ASMR/ASR 1-3 and significant budget impact) excludes the case of ASMR/ASR 4 health goods with a strong budget impact for which the medico-economic evaluation could represent a useful assistance in the often difficult determination of the price.

Performing a medico-economic evaluation mobilises resources. In the eyes of the participants in the round table it seems to take into account the income generated by the product evaluated to calibrate the study requests. This precaution applies especially to medical devices.

It would seem important to progressively increase the requirements in medico-economic evaluation matters to give the actors time to adapt to the new regulatory context.

4. The medico-economic evaluation: when?

The decree dated 2 October 2012 envisages the performance of a medico-economic evaluation during the procedures for the registration or renewal of registration of products of lists.

In the framework of a first registration, the medico-economic evaluation should help the CEPS in the negotiation of the price and therefore takes place prior to its determination. The evaluation performed by the HAS should start, from modelisations fed by clinical studies results, incremental cost/efficacy ratios (with respect to the reference strategy) with respect to a price range.

The performance of a medico-economic analysis in the first registration should also allow the quantification of the degree of uncertainty with respect to the impact of the medicinal product and/or medical device on the healthcare system and identify the parameters that affect the most the estimate of incremental cost/efficacy ratios. This procedure will guide the collection of new data and post-registration studies requests. By nature it would ensure a better connection between the first registration and future reassessment.

The medico-economic evaluation during the renewal of the registration (5 years after registration) should allow the confirmation or refutation of the hypotheses taken into account in the determination of the initial price and place the product within the treatment strategy. New data must be generated for this purpose. They come from risk management plans (pharmacovigilance) for the frequency and nature of the undesirable effects or post-registration studies, included in the contract linking the CEPS and the pharmaceutical industry, for the compliance and persistence, the population touched (with respect to the target population), the proper usage (prescription outside marketing authorization [MA] in particular), or even efficacy. The medico-economic evaluation by integrating these data can contribute to redefine the price of the health good up or down. It can also be useful to enact good professional practice recommendations.

Some participants of the round table considered the possibility of medico-economic re-evaluation prior to the re-registration deadline (in case of arrival of a new product that significantly modifies the management or appearance of generics of a major medicinal product, etc.) in the framework of a class evaluation.

5. The medico-economic evaluation: what interpretation?

How should the incremental cost/efficacy ratios be interpreted? The question of the choice of an acceptability threshold is crucial. Should a threshold be defined? How? The participants in the round table unanimously reject the idea of an absolute and unique threshold. A threshold would not be useful in the French context. Once

we admit that the economic evaluation does not condition the access to the reimbursable goods and services basket, it is not a matter of issuing a binary decision (such as in the English National Health Service [NHS]) but to detect any deviation between the price claimed by the company and the benefit expected or provided by the product to patients and/or to the community (in the presence of externalities). Conversely, fixing a threshold *a priori* could have negative effects, especially generating an anchoring bias.

The proposal of the group is to define reference values, with an indicative and not a normative function, likely to evolve with time. These reference values could vary from a therapeutic domain to another, from a context to another (for example, depending on the gravity/severity of the disease, whether there are therapeutic alternatives or not), depending on the ASA/ASMR level (in as much as the ASA/ASMR is indicative of the social desirability of a new product with respect to the existing product and takes into account the previous criteria), etc.

They could be defined on a historical based with respect to previous decisions (with a bias risk) or referring to collective values, external to the healthcare world (with the question of the transferability).

According to the participants in the round table, empirical work need to be performed rapidly to define these reference values. Otherwise, being optimistic, the creation of a public database that reports the values the incremental cost/efficacy ratios of the products evaluated could lead to the start of a collective learning process which will bring up these reference values.

Taking into account non-economic dimensions that come under the competence of the CEESP (sociological, legal, ethical, public health, etc.) raises questions. The publication of methodological guides as for the economic evaluation,^[5] could dissipate a certain number of uncertainties.

The evaluation of the burden of the disease, if used as a guideline for the determination of efficiency values, could involve the participation of citizen juries.

Finally, it should be remembered that the medico-economic evaluation is only an element in the determination of the price and that the function of the CEPS is to integrate all the pertinent dimensions evaluated (ASA/ASMR, medico-economic evaluation, equity, industrial policy elements).

6. The medico-economic evaluation: how?

The addition of a medico-economic section should not lengthen the time to market access. The entire procedure must remain constrained to 180 days. As much as the HAS is in charge of the medico-technical evaluation (Transparency commission [*Commission de la transparence*, CT] or National commission for the evaluation of medical devices and health technologies (*Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé*, CNEDIMTS)) and the economic evaluation (CEESP), it is important that the role of the different commissions

is clarified. The industry representatives present called for the independence of the two evaluation procedures. In this “parallel” configuration, the coordination of the evaluation work will fall to the College of the HAS.

The risk of contradiction between the expectations and the opinions of the two commissions and the complexity of the decision making concerning the price was discussed at length.

The round table recommends holding early meetings (ideally before the phase 3 clinical trials decision) between the pharmaceutical company and the CEESP that will allow anticipating the expectations of the CEESP in particular concerning the comparators and pertinent populations. In most cases, the opinion of the CEESP will complete that of the CT or of the CNEDIMTS from the estimate of the cost/efficacy ratio (operationalisation of the opportunity cost concept).

From a procedural point of view, the discussions concerned the form of the CEESP opinion which must be motivated, intelligible (for all players) and useful in decision-making (from the point of view of the CEPS).

The possibility of regular meetings (“as many as necessary” between the pharmaceutical industry and the HAS is deemed useful especially in the transition phase of the device. These meetings should allow the validation of methodological choices throughout the medico-economic evaluation (choice of comparator(s), valuation of costs and calculation of quality-adjusted life year [QALY], modelling options, etc.).

The round table representatives recommend to associate together the parties involved (CEESP, CEPS, pharmaceutical industry) in the elaboration of practical evaluation procedure methods.

In view of the time delay related to the production of data and the management of the stock of products marketed, a pragmatic “transition” period of the medico-economic evaluation rules should be envisaged.

At the end of the round table, the medico-economic evaluation appeared as a pertinent tool to assist in decision making in terms of medicinal product price fixing. The participants in the round table tried to situate the position of the medico-economic evaluation with respect to current regulation processes involving the specialised commissions of the HAS and CEPS in their respective role. According to the participants in the round table, the interpretation of the incremental cost/efficacy ratios bring us back to the definition of reference values, likely to change depending on the context and evolve with time, with an indicative and non-normative function, and not to a single efficiency threshold.

Certain questions remain in suspension at this stage. These questions mainly refer to procedure aspects which are not addressed in the decree or in the methodological guide for the medico-economic evaluation of the HAS.

Empirical work must be undertaken on two important questions: 1) What is a significant impact on the Health Insurance expenses? and 2) What are the reference values to be used for the interpretation of incremental cost/efficacy ratios?

Conflicts of interests. None.

Abbreviations. AMNOG: *Gesetz zur Neuordnung des Arzneimittel Marktes*; ASA: expected service (*amélioration du service médical attendu*); ASMR: medical service rendered (*service médical rendu*); CEEPS: Economic and public health evaluation commission (*Commission d'évaluation économique et de santé publique*); CEPS: Health product economic committee (*Comité économique des produits de santé*); CNEDIMTS: National commission for the evaluation of medical devices and health technologies (*Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé*); CT: Transparency commission (*Commission de la transparence*); HAS: French Drug Authority (*Haute autorité de santé*); LEEM: French drug companies (*Les entreprises du médicament*); LFSS: social security financy act; MA: marketing authorization; MEE: medico economic evaluation; NHS: English national health service; QALY: quality-adjusted life year; SNIIRAM: National

health insurance cross-schemes information system (*système national d'informations inter régions d'Assurance maladie*)

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