Abstract

The criteria for the registration of new drugs may differ from the criteria for drug reimbursement. In 2000 the French government entrusted the French Medicines Agency with determining the “medical service rendered” (MSR) for each reimbursable drug. The goal was to determine which drugs could be classified with an “insufficient” MSR and therefore should be taken out of the scope of health insurance. We analyze the concepts and methods used for this evaluation and the kind of results that are obtained. We collected data on the result of MSR classification and the criteria used to perform this classification (efficacy-security, severity of the disease, place in the therapeutic strategy, existence of therapeutic alternative, public health value) for a sample of 1453 drugs belonging to five therapeutic areas. We used statistical analysis to determine what were the most influential criteria. Only two criteria – efficacy and disease severity – suffice to very largely explain the MSR classification. The other criteria contribute little added value. Some of these criteria clearly suffer from a lack of clarification, leading to different interpretations according to therapeutic class or even according to drug or drug family. The evaluation procedure differs between therapeutic classes, at least at intermediate MSR levels. Analysis of the French experience with MSR shows that the evaluation procedure has not succeeded in completely breaking away from the traditional logic of the marketing authorization and registration, as witnessed by the importance of the “efficacy/safety” criterion, the absence of an economic criterion, and the vagueness of the “public health value” criterion, which one would have thought would instead be decisive.

Keywords

Postregistration evaluation · Drug evaluation · Economic evaluation · Medical service · Drug utilization review

What criteria for pharmaceuticals reimbursement?

An empirical analysis of the evaluation of “medical service rendered” by reimbursable drugs in France

The criteria for registering new drug may differ from those governing their reimbursement. Registration procedures and criteria have been progressively harmonized across developed countries, especially through the International Conference on Harmonisation (ICH) working groups (www.ich.org), and the EMEA is now responsible for new drug application in the European Union. Conversely, reimbursement decisions remain in the so-called “subsidiarity” domain, and criteria vary from one country to another.

In France the procedure and the criteria for drug reimbursement were defined by a law in the late 1970s. A specialized commission, the Transparency Commission, within the nation’s drug agency (Agence Française de Sécurité Sanitaire des Produits de Santé, AFSSAPS), is charged with evaluating the extent to which new drugs deserve to be listed on the positive list of reimbursable medicinal products. A new criterion for drug reimbursement was added in October 1999. The Transparency Commission of the AFSSAPS was thus entrusted with determining the “medical service rendered” (MSR) for new drugs in each of their indications and deciding for which drugs the MSR was “insufficient” to be listed as a reimbursable. At the same time the French government commissioned the AFSSAPS to reevaluate all medicinal products reimbursed by the AFSSAPS to determine whether maintaining the reimbursable status of these drugs was justified with respect to the new MSR criterion. To assess the level of MSR of a drug the Transparency Commission uses in fact a set of subcriteria (presented below), some of which are related to the traditional efficacy-safety profile and others indicative of the “public health value” of the drug (for instance, the place in the therapeutic strategy and the severity of the treated disease).

We used the results of the reevaluation process to perform a statistical

This research was supported by a grant from “Laboratoires Internationaux de Recherche” (LIR), a group of international research-based pharmaceutical companies in France. The views expressed in the article remain nevertheless under the sole authors’ responsibility.
analysis to examine the logic behind the evaluation of MSR. Our main objective was to determine the extent to which this logic differs from that of the traditional registration procedure, based solely on the efficacy-safety drug profile. A secondary objective was to check the internal consistency of the MSR evaluation procedure.

Such an analysis is important in light of the growing trend in Europe towards “postregistration” evaluation, which is a drug assessment procedure designed for purposes of setting prices, reimbursement status, and conditions of use of medicinal products which have already obtained a product license granted by the drug registration authorities according to the rules in force. In contrast to drug registration procedures, however, the conditions of this postregistration evaluation have not been widely studied and vary considerably from one country to another in terms of objectives, procedures, and participants. The aim of this study was to provide further insight into these issues through analysis of a concrete example which is gaining a following in certain European countries.

We first briefly describe the French system for evaluating reimbursement of both old and new medicinal products. We then review the manner in which the criteria for this evaluation were retrospectively applied to drugs already on the market. Next we present a statistical analysis of these data, particularly using multivariate multinomial logistic regression models.

The evaluation system of reimbursable medicinal products in France

The French system for setting prices and reimbursement rates for medicinal products has been described elsewhere [1, 2, 3]. The “positive list” is established by the Transparency Commission under the aegis of the AFSSAPS. The commission is composed of a chairman, a vice-chairman, and 14 members representing government, public insurance funds and physicians’ representatives. In addition, there are five members “chosen for their qualifications in medical, scientific, and economic issues relating to medicinal products.” The law states that this Commission is responsible for issuing an opinion on the “value” of medicinal products for which reimbursement is being solicited [4, 5, 6]. The Commission’s opinions are made public. Drug companies may request a hearing to appeal the terms of the opinion. It is up to the drug company to apply for reimbursement for their product, knowing that if approved the price will be regulated. Some companies prefer not to seek reimbursement for their prescription drugs in order to circumvent this constraint. This is true particularly for so-called “life-style” drugs such as Viagra and Xenical.

The Commission’s opinion is critical since, in addition to the reimbursement rate, it also determines to a large extent the market price of the drug. Indeed, the government fixes the public selling price largely on the basis of this opinion through a special interministerial authority called the Comité Economique des Produits de Santé.

The procedure for registration on the reimbursement list was recently modified by a decree (27 October 1999) which introduced the new criterion of the MSR. This criterion replaced another, more complex mechanism. In the previous system the Transparency Commission examined not the level of MSR but its improvement relative to reference products. A medicinal product was reimbursable: (a) if it improved MSR, or (b) if it led to savings in drug treatment costs. In the new system it is the absolute level of medical service rendered, and not its degree of improvement which is evaluated. Although this criterion is not directly defined in the decree, there are indications for how it is determined: “This evaluation takes into account the efficacy and safety profile of the medicinal product, its place in the therapeutic strategy, notably with regard to other available treatments, the severity of the disease for which it is indicated, the curative or symptomatic nature of the treatment, and its public health value.”

This text provided the legal basis for the reevaluation procedure of all existing drugs commissioned by the Government in 2000. Concretely, the Transparency Commission in charge of this reevaluation process defined three levels of MSR [7]: “major or important,” “moderate,” and “low.” A fourth level, “no MSR assigned,” is used when the Commission considers that it lacks the scientific data required for the evaluation. To assign an MSR level to each drug the Commission examines the different “dimensions” of MSR according to the criteria set forth in the decree. The dimensions and scoring modalities are listed in the Appendix. The severity of the disease is graded at one of three levels according to the risk of affecting the vital prognosis or causing disability. Efficacy and safety are graded on a four-point scale. The criterion of “place in therapeutic strategy” differentiates between first-line and second-line use, adjuvant or salvage therapy. The classification “no place in therapeutic strategy” is given to drugs whose practical utility is questioned by the Commission. “Public health value” and the existence of alternative treatments are coded yes/no with no further clarification. The same is true for the dimension “conditions of use,” where “yes” is assigned when the drug has several indications.

It may be seen that some of these dimensions, such as “severity of the disease” and “efficacy and safety,” are ordinal variables expressing a gradient of quality or severity, while others are categorical or polytomous variables which do not express a preferential order. The “public health value” dimension is ill-defined and its place as an independent criterion is debatable because, logically, public health value is an artificial notion that should be a product of the other characteristics of the drug. If public health value were truly an independent criterion, it would be possible for a drug with efficacy in a serious disease to have no public health value!

A statistical analysis of the procedure: objectives and methods

The question immediately raised by this procedure is that of the relationship between the MSR level and the Commission’s score for each of the “dimensions.” Do all these dimensions have the same weight? Are some more decisive than others, and if so which ones? Is the weighting system consistent from one therapeutic class to another, or does it vary according to drug families? To answer these questions we have statistically analyzed the data from this reevaluation procedure.