

R F A S

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A multidisciplinary call for input on the subject of:

‘Regulating pharmaceutical prices: issues, tools, challenges, and future developments’

For the July–September 2018 issue

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This call for input is targeted at researchers in economics and management, political science, law, and sociology, as well as statisticians and those working in the field of social protection.

The articles will need to be submitted by Monday 5 March 2018.

General introduction

For some time, the issue of patients’ accessibility to innovative and sometimes very costly pharmaceuticals has become the focus of public or national debate. It has been the subject of many reports in the media, such as campaigns by the League Against Cancer (Ligue Contre le Cancer) and Médecins du Monde conducted in 2016, a report by the Cour des Comptes in 2017, which was relayed by the media,. It has also highlighted the question of the sustainability of the costs incurred by both public and private payers.

This issue is even more salient when one considers that we are in a phase of epidemiological transition, characterised by an increase in the number of chronic conditions, which is partly imputable to medical and pharmaceutical innovations. The latter are enabling, or will enable, incurable diseases to be transformed into chronic illnesses, requiring specific medicinal treatments.

These issues will also become increasingly sensitive over the coming months, when fresh challenges will emerge as personalised medicine develops, along with treatments resulting from gene therapy. Added to these factors is the phenomenon of globalisation of the activities of pharmaceutical firms, which will lead States to adopt a collective approach, and not only on a national level, ?

In this context, how can the value of health products be assessed? What is France's current contribution (taking into account prices and volumes) to the promotion of research? Can normative criteria be established to determine this contribution?

More than ten years after the publication of an article entitled 'Le Médicament' ('Pharmaceuticals')¹ in the 2007 issue of the *Revue Française des Affaires Sociales*, this dossier will specifically address regulation of pharmaceutical pricing. More precisely, the input will focus on the pricing agreed with the pharmaceutical industry, that is to say the manufacture price, excluding tax, and the contractual provisions that result in a reduction in the actual amount invoiced to the French Health System (Assurance Maladie). Other pricing components may also be included in relation to the latter, such as the prices paid by local authorities (consumer price), the pricing upon which the insurers base their reimbursements,² and so on.

One could also include economic, statistical, sociological, and legal analyses, or those involving political science, and articulate the articles around two main approaches: the first will concentrate on the actors, tools, and forms of pricing regulation in France and abroad; and the second will examine current and future developments in terms of pricing regulation and the issues arising from therapeutic innovations.

¹ Benamouzig, D. Paris, V. 'Le médicament' ('Pharmaceuticals'), in the *Revue Française des Affaires Sociales*, issue no. 3–4, 2007.

² In France, the manufacture price, excluding tax, is established administratively for all pharmaceuticals, except those invoiced by hospitals through the DRG system (Groupe Homogènes de Séjours, GHS). This pricing is published in the *Journal Officiel*. The law does, however, authorise price reductions (discounts).

A review of the relevant literature is attached.

1- Pharmaceutical pricing: an examination of the function, role, and forms of a regulatory tool for the sector in France and abroad

1.1 Why does pricing need to be regulated?

Models for regulating pharmaceutical pricing vary according to the country. How, therefore, can the actors in the sector justify pricing regulation by the public authorities, as is the case in France?

To shed light on this issue, one could focus in particular on the criteria used to regulate pricing: production costs, research and development costs (R&D),³ marketing and promotional expenses, the pharmaceutical drug's therapeutic value; and the various procedures for pricing regulation will be examined (market mechanisms, administered proceedings, etc.), ultimately taking these variables into account. An article could explore this analysis from a historical perspective and attempt to assess the motivations that led to the retention (and development) of the variables used to regulate pricing.

Amongst a great many other possible levers, pricing may also play a central role in limiting the costs of pharmaceuticals. Is it, comparatively, a tool that is more readily 'acceptable' for the public and health professionals? Or is it less 'inconspicuous' than other procedures that target the same objectives—such as a change in the scope of the healthcare supply, reimbursement rates, or mechanisms for regulating pricing and volumes (such as conventional discounts, in France)—or than measures that affect doctors' prescriptions (cash-limited prescription budgets in the United Kingdom, performance-based payments, etc.)?

The role played by pricing regulation in France and in different countries may be examined comparatively, with regard to:

- The influence and progression of pharmaceutical pricing on healthcare costs;
- and the specific effects on the profitability of the pharmaceutical industry and its capacities for innovation (via R&D costs), which may lead us to question whether normative criteria can be established to assess this contribution.

³ With regard to this, an issue that is regularly highlighted underlines the importance of providing industry with enough available R&D funding to ensure that innovation is not penalised.

With regard to France specifically, we could examine what the country's current contribution (taking into account pricing and volumes) is to promoting research. France's contribution is, in any event, limited (given its global market share): should it be reduced or increased? If the monopoly revenue generated on French territory is reduced, will retaliatory measures be taken by the pharmaceutical firms in terms of their choice of location of production or research, with possible adverse consequences on local employment?

These analyses could be based on studies conducted by institutions (National Institute for Health and Care Excellence, NICE) or by university professors, such as Patricia M. Danzon,⁴ which aim to answer the following question: compared with neighbouring countries, is France paying more (too much) for its pharmaceutical products? Like these studies, it would be interesting to see how France fares in comparison with its neighbours and identify the methodological limitations that are inherent to this type of exercise: the need to limit oneself to bilateral or multilateral common fields, and the problems of the reference volumes used for price weighting (Paasche or Laspeyre), without dissociating a country's pricing from its effective consumption volumes.

To adapt to the regulatory and budgetary environment and its developments, laboratories and other private actors are adopting different strategies. Studies will need to analyse those of the pharmaceutical industry as an ensemble or those of specific national or international firms. These strategies can take on extremely varied forms, whether in terms of the orientation of the research conducted or the decision to develop certain products rather than others, the territorial development of their sales, and even the allocation of certain expenses. One could also examine patients' strategies: are the latter obliged to accept the final pricing of the pharmaceuticals or do they adapt their behaviours to these variations, for example by switching to other products or by seeking care abroad?

It will also be interesting to examine the evolution of the criteria used to regulate pricing and the reasons for these choices. Philippe Sauvage's article⁵ cited in the attached review of literature, and the analysis by France Stratégie,⁶ may be used as source material to help reflect on these many parameters (Improvement of

⁴ Patricia M. Danzon is Professor of Healthcare Management at Wharton School in the University of Pennsylvania.

⁵ Sauvage, P. (2008), 'Pharmaceutical pricing in France: a critique', *Eurohealth Pharmaceutical Policy*, issue 2-2008, pp.6-7

⁶ Benamouzig D., Gimbert V. (2014), 'Les médicaments et leurs prix : comment les prix sont-ils déterminés?' ('Pharmaceutical pricing: how is the pricing regulated?'), an analysis by France Stratégie, October 2014.

Medical Benefit assessment (French: ASMR)), comparable pharmaceutical pricing (i.e. pursuing the same therapeutic goals), anticipated or observed sales volumes, anticipated and real conditions of usage, and eventually the results of the medico-economic assessment of the product, etc.). There will be a particular focus on the pricing of patented pharmaceuticals.

1.2 How do other countries regulate pharmaceutical pricing?

An analysis of French and foreign practices relating to the regulation of pharmaceutical pricing may lead to the identification of various economic and institutional reference models, by adopting two types of approach: the first, with economic impacts, will describe the models used to regulate pricing; and the second, which is sociological, will focus on describing the particularities and behaviours of the actors involved in this process and their interactions

The actors responsible for these questions and parameters differ according to the country. France has decided to use a procedure of ‘administered pricing’, which does not appear to be challenged. In the United Kingdom, pricing is not directly set by regulators, but the acceptance criteria for reimbursement are explicitly based on the pricing via a medico-economic evaluation conducted by the National Institute for Health and Care Excellence (NICE). In Germany, pricing is also loosely restrained, but different mechanisms for regulating the expenses define ceilings for reimbursement as an incentive to use the least expensive products in the same therapeutic field (reference price/*Festbetrag* and jumbo groups). An international analysis of this issue could focus on very different national practices, such as those that exist in the United States.

Many actors—both public and private—are mobilised in these various processes; it is worth analysing their attributions, the tools they apply, and their the way they operate. Hence, in France, the functions are shared between the Transparency Committee (Commission de la Transparence), which assesses the medical added value and the therapeutic progress provided by the pharmaceutical drug, the Economic and Public Health Evaluation Committee (Commission d’Évaluation Économique et de Santé Publique, CEESP), which issues an efficiency statement, and the Economic Committee for Health Products (Comité Économique des Produits de Santé, CEPS), which is responsible for pricing negotiations. Sociological and political science studies will need to focus on the dynamic interplay between these institutional actors,

and likewise study the institutions that use a different model in other countries. Studies conducted by a sociologist specialising in public organisations may provide a valuable introduction to this analysis. Procedures and tools may be addressed with regard to their dynamics, by examining, for example, the system for the revision of pricing in France and abroad, or the regulatory role of risk-sharing agreements, periodic reviews, patent expiry situations, and jumbo groups.

2- In the current context, the development of innovative products raises new questions about the regulation of pharmaceutical pricing

This second analysis will shed light on current and future developments and the question of the relation between innovative products and the regulation of pharmaceutical pricing.

2.1 What role does medico-economic evaluation play in pricing regulation?

Particular attention should be paid to medico-economic evaluation. Medico-economic evaluation highlights the clinical benefits of a healthcare strategy and its costs, with an overall objective of optimal allocation of public resources. It was introduced to France in 2012 in the system of pharmaceutical regulation, in the framework of registration procedures for reimbursement, as outlined by Marine Jeantet and Alain Lopez (IGAS report). The input relating to medico-economic evaluation could focus on these practices, which are necessarily variable depending on the country in question, and the resulting pricing.

These observations may, in particular, lead to a study of the future uses of medico-economic evaluation in France and abroad. There is a widespread interest in the quest to find new pricing regulation mechanisms. There are two main approaches that could be adopted:

- Using medico-economic evaluation to decide on the access to reimbursement and also to regulate pricing. In this case, it is particularly important, on the one hand, to determine the theoretical bases for this decision (is the use of medico-economic evaluation based on utilitarian or egalitarian principles?) and, on the other hand, to distinguish the practical difficulties of such a practice.
- Defining new ways in which medico-economic evaluation can be used: the use of a trigger point according to the cost/efficiency ratio, and assessing the

budgetary impact. An article that presents these new instruments would be an important contribution to the issue.

2.2 How is benchmarking used for pricing regulation by the authorities?

This subsection sets out to assess the role of European and international comparisons in each country and the new contractual tools used by the authorities to regulate pricing.

Faced with the difficulty of regulating pharmaceutical pricing in the fairest possible manner, given that the concept of justice is a valid concept in this context, States often use benchmarking (in particular, to ensure that they are not spending more than their neighbours). This practice raises various questions:

- What are the theoretical justifications of the benchmarking? Why, for example, would the willingness to pay, and therefore collective preferences in France, be similar to that of the English?
- What strategies are firms adopting to benefit from this? Some of them may choose to market their pharmaceutical products initially in countries where they can expect to obtain the highest price or accept occasional confidential discounts to obtain the highest possible face value.

To respond to these questions, the authors may base their articles on the literature review proposed by B. Parkinson.⁷ The latter examines the reasons why public decision-makers have decided to stop reimbursing or only partly reimburse certain pharmaceuticals. Also available for consultation is the research brief⁸ published by the National Institute for Healthcare Reform, which focuses on ‘reference pricing’ and *Point de Repère*, published by the French National Fund of Health Insurance for Employees (Caisse Nationale d’Assurance Maladie pour les Travailleurs Salariés, CNAMTS),⁹ which compares French mechanisms for regulating the prices of generic pharmaceuticals with those of three European countries: Germany, England, and

⁷ Parkinson, B. et al. (2015). ‘Disinvestment and value-based purchasing strategies for pharmaceuticals: an international review’, in *Pharmacoeconomics*, 2015.

⁸ White C. Eguchi M. (2014), ‘Reference Pricing: A Small Piece of the Health Care Price and Quality Puzzle’, National Institute for Healthcare Reform, *Research Brief*, issue 18, October 2014.

⁹ Delcroix-Lopes S., Van Der Erf (2012). ‘Coût des génériques en Europe et mécanismes de régulation des prix en Allemagne, en Angleterre et aux Pays-Bas’ (‘The cost of generic pharmaceuticals in Europe and pricing regulation mechanisms in Germany, England, and the Netherlands’), CNAMTS, *Point de Repère*, issue 39, 2012.

Holland. These foreign examples are a good illustration of the impact of the competitive mechanisms of the manufacturers, whether with regard to pharmacists or insurers, with the aim of decreasing the costs of generic pharmaceuticals.

2.3 To what extent are risk-sharing agreements used?

New contractual arrangements have emerged over the last ten years, grouped under the expression ‘results-based risk sharing agreements’. These agreements create a link between attaining predefined results and the modifications of the financial conditions for access to the reimbursed market, particularly in terms of pricing. This development is not unique to France. According to the Pharmaceutical Outcomes and Research Program in Washington State University, more than 100 agreements have been concluded between laboratories, reimbursement access authorities, and healthcare payers over the last twenty years on an international level; their purpose has been to make the reimbursement of pharmaceuticals conditional on the production of new data about their therapeutic affects and on achieving results. It may be beneficial to analyse these new contractual tools, which are used in France and abroad. The analysis could adopt a comparative approach because these agreements are given different names according to the country or region in question: ‘Managed Entry Agreements’ in Europe, ‘Risk-Sharing Agreements’ in the United States, ‘Patient Access Scheme’ in the United Kingdom, ‘Deeds of Agreement’ in Australia, and ‘Access With Evidence Development’ (‘Accessibilité par la Production de Preuves’) in Canada. It could also focus on the usefulness of these agreements in regulating innovative molecules and identifying implementation problems.

2.4 Future developments: what challenges does pricing regulation face with regard to future innovations?

The characteristics of various developments in knowledge and highly innovative pharmaceutical techniques will probably bring new challenges to pricing regulation, such as products associated with complementary technologies,¹⁰ and gene therapy, for example. These products and techniques raise a number of

¹⁰ The latter associate a pharmaceutical drug with all or part of a diagnosis, a medical device, information systems, or services

questions. Some of them are both economic and ethical in nature: for example, what prices (and volumes) can be collectively agreed with laboratories? Other questions relate to the most common practices today: how can one establish the pricing of pharmaceuticals resulting from gene therapy? Is it necessary to use new (innovative?) contractual solutions to finance health products? And other questions are related to technical problems: how can data be used in real life?¹¹ What are the effects of issuing launch permits on the basis of phase-2 clinical trials on the pricing regulation of these pharmaceutical products (and their medico-economic evaluation)?

These issues will need to be examined in order to open up avenues for reflection on the pricing schemes for gene therapy and other medical innovations. Some of these have already been outlined by the Section des Affaires Sociales et de la Santé du Conseil Économique, Social et Environnemental (CESE),¹² whose studies provide an initial source of reference. It would also be important to examine further issues relating to the scale of implementation of the pricing regulation and policy. Would it be worthwhile to have an international, or at least a European mechanism for assessing and regulating prices? Would it be possible to create a ‘joint buying association’, based on the union of the Benelux countries and Austria or Mediterranean countries, but at a European level? The CESE report sets out such a development, whose implementational advantages and difficulties will need to be identified.

¹¹ The term ‘real-life data’ designates data that does not affect the usual procedures in the treatment of patients and that are not collected for experimental purposes, but rather generated by routine treatments undergone by a patient. Hence, they reflect, a priori, standard practices and can have many sources (computerised patient records, the Internet, social networks, connected objects, etc.).

¹² Saout C., Pajares y Sanchez C. (2017), ‘Prix et accès aux médicaments innovants’ (‘The pricing of and access to innovative pharmaceuticals’); a report issued by the Section des Affaires Sociales et de la Santé, Conseil Économique, Social, et Environmental.

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