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## Pharmaceutical innovations – but how much should we pay for them?

When pharmacy apprentice **Friedrich Wilhelm Adam Sertürner** (1783–1841) was the first person to report in 1806 on the isolation of a water-insoluble crystalline substance from opium, there was no talk at the time about innovation. The isolation of the substance named morphine (consistent with the god of dreams, Morpheus, in Greek mythology) by him in 1817 was nevertheless an innovative proceeding without a doubt. Morphine has maintained the worth of its price ever since.

Assessing the price of a drug is one of the biggest problems in modern pharmaceutical policy-making. How do we distinguish a true innovation in order to find out what could be paid for it? It was suggested recently that “the only correct end result of a successful innovation process is a product or a service that sells like hot cakes”.<sup>1</sup> This is not a suitable way of referring to a drug innovation.

In recent decades the concepts of innovation and innovativeness have been used fairly liberally in the pharmaceutical sector. Among the nearly 50 new active substances introduced on to the world markets every year only a few are considered to be real breakthrough inventions or innovations. As **Anna Karjalainen** in her paper in this journal suggests, the inflation of the concept of drug innovation may be influenced by various viewpoints taken in reviewing the issue. It is, in fact, rather self-evident that the viewpoint of society (often that of the payer) should be dissimilar from that of the pharmaceutical industry (developer), researcher (scientist) or doctor and patient (consumers).

Europe can be seen to have lost to the United States of America some of its standing in the generation of pharmaceutical inventions. Measures to restore the competitiveness of European pharmaceutical research and the European industry have been sought in the EU for about a decade. The legislation covering orphan drugs and paediatric medicines serves as an example. Patent regulations, accelerated authorisation processes, exclusive rights and increasing public research subsidies are some of the measures aimed at speeding up the generation of drug innovations and increasing the competitiveness of the pharmaceutical industry.

The pricing and reimbursement systems of medicines have become special problems in Europe. National health

care systems, their financing and that of social insurance (e.g. the reimbursement system) fall into the domain of national sovereignty. It is therefore difficult to promote competitiveness and innovativeness at the European level unless agreement can be reached on uniform prices and pharmaceutical reimbursement policies. The truth is in fact that in practice a medicinal product is not on the markets and in use until it has gained approval in the reimbursement system.

Before a decision can be made on the refundable cost of a drug, the therapeutic value of the drug should be ascertained in relation to the existing available pharmaceutical therapy. Efforts are at present being made in the European Commission project *Pharmaceutical Forum* to clarify the concepts of relative effectiveness and additional therapeutic value. Measures should be agreed upon which would help the payer and the consumer to find out about the degree of innovativeness associated with a new drug. It is hoped that progress is made in the EU on these issues. This would be for the benefit of society and the patients as well as the pharmaceutical industry.

A common understanding could thereby be reached in order to distinguish the true drug innovations from pharmaceutical novelties of lesser value. More developed societies are prepared to pay for ever more costly therapies as long as their additional therapeutic value for the correct patient group can be adequately ascertained. Plenty of new drugs are being developed and some of them will certainly deserve the distinction of being innovations.

Morphine isolated by Sertürner had the same fate as innovations usually have. Another innovation was required until the road was open for the extensive use of morphine in pain treatment. The innovation involved the introduction of a syringe and a hollow hypodermic needle in the 1850s. Sertürner did not manage to enjoy the success in his lifetime, neither did he in his own opinion receive adequate acknowledgement for his own discovery.

<sup>1</sup> Ruonala J: *Yritykset innovoivat, eivät kansakunnat. Presso 27.10.2006.*

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## Pharmaceutical innovation – what's it all about?

The state of drug development has been a matter for concern for quite some time. Only a couple of pharmaceuticals called breakthrough drugs (1) have been launched on to the market in recent years, while the pharmaceutical industry is blamed for cashing in on it by producing minute modifications of old medicinal products. Paradoxically, the innovativeness of pharmaceutical companies appears to have declined coincidentally with the boom of investments into research and product development. Despite the increased investments in research and product development, the number of drugs defined as innovative has remained relatively stable (about 20 annually) in 1990 to 2004 (2, 3).

With regard to the European economical policy the pharmaceutical industry is an important operator and its decline in relation to the United States of America and the rising Asian states has not gone unnoticed by the political media. As a result of the Lisbon strategy (4), support for European innovativeness and competitiveness has taken over the centre stage in EU politics. Despite the political will to do so, prioritising the promotion of innovativeness is difficult in member states engaged in crises involving health care costs. To support innovativeness without becoming involved in insurmountable economical problems appears in fact to require the ability to distinguish the true innovations from the multitude of minor modifications. It is, however, difficult to define the grade of innovativeness of medicinal products.

### Drug innovation

The definition of drug innovation often varies according to the point of view of the definer (5). A breakthrough drug developed for the treatment of a severe disease can be consid-

ered an innovation, but equally so can an improvement in a product which has been on the market for a long time. According to one definition, innovation can be seen as a technological progress as a result of which either a totally new product is generated, or production costs can be reduced, or the therapeutic value of an existing drug is increased (6). In principle, the difficulty of defining drug innovation is in fact at the core of the whole problem: classifying a new drug as an innovation guarantees a high price and increases the profit margin of the pharmaceutical industry. Accuracy in definition is nonetheless recommended, since this is the only way to exert control on drug costs while investments can be focused on treatments and thereby generate true added value for the patients.

### Drug innovation and EU

The aim set by the EU in the Lisbon strategy was to make an effort to become by the end of the decade the most competitive and dynamic economy based on information (4). The concept of innovation may be considered to have been elevated to the centre stage of common European politics. The G10 recommendations (2002) also focused on the public health standpoints (8). The EU pharmaceutical policy has in fact always represented a tug of war between the interests of business and those of public health (8). Innovation at the EU level may in fact be seen as the synthesis of European competitiveness and supportive employment measures with public health advancement.

Efforts are being made to support the European innovativeness and competitiveness through a variety of initiatives. However, the national decision-maker's attention is easily focused on the costs instead of the support that

competitiveness requires. The payers react to drug innovations from the standpoint of cost control (5). The European Union approach to the problematic relationship between drug innovations and costs is, for instance, via the concepts of additional therapeutic value and relative effectiveness. A drug which has additional therapeutic value is hoped to rapidly be included in the member state national reimbursement systems (9). The European Commission also aims to create uniform assessment systems of relative effectiveness which, it is hoped, will lead to standard requirements and increased competitiveness (10).

The discussions on innovation also influence the work of the drug regulatory authorities. EMEA aims to facilitate innovation and stimulate research (11) by means, for example, of increased scientific consultation, accelerated marketing authorisation processes relating to innovative drugs, and innovative drug development guidelines. The regulatory authorities are balancing between ensuring drug safety for patients and applying the most recent achievements in science and technology. Foolhardiness may lead to safety risks, whereas excessive caution slows down development and the introduction of new therapies on to the market (12). From the viewpoint of the regulatory authority, drug innovation can in fact be seen as the combination of all these features: a significant innovation creating additional therapeutic value, good patient safety and maintenance of competitiveness in the pharmaceutical industry.

### Drug innovation and the patient

According to the definition by the World Health Organisation (WHO), innovation in the public health sector implies the introduction of such new

ideas, practices and programmes as will improve the health of the population (13). From the patient's point of view a drug to treat a disease for which there has formerly been no effective treatment available is an innovation. A new indication of a product already available on the market may also convey additional value for the patient (6).

Issues relating to the safety of new medicinal products, i.e. the acceptable level of risk, are constantly being discussed. Each patient defines the acceptable level of risk and cost on his or her own premises. A seriously ill patient is readier to take a higher risk and pay a higher price for the treatment than a patient who is less seriously ill. The proportion of the cost for which the patient is responsible is in fact likely to grow along with the drug cost crisis in society. The number of treatment alternatives also affects the level of acceptable risk: with no alternatives available, even a high risk associated with the only drug available will find acceptance (5). A rapid introduction of a breakthrough drug on to the market can therefore be considered an advantage to the patient, despite the fact that possible adverse effects may have gone unnoticed if it has happened that the extent and duration of clinical trials have had to be compromised due to a fast-track procedure in the marketing authorisation approval.

Concern has been expressed about the emphasis given to the business point of view. The developed countries should shoulder the responsibility for the development of medical treatment for a number of diseases afflicting the developing countries, because the profit-focusing pharmaceutical industry cannot be expected to show an interest in the needs for medical treatment in the developing countries (14). The support shown by the public sector is also of great importance for the development of orphan and paediatric drugs.

### **Drug innovation and the pharmaceutical industry**

The pharmaceutical industry aims to generate a profit for its shareholders. However, it appears to have become ever more difficult to increase sales and profits (15). Pharmaceutical companies can be considered to be responsible, not only to their various owners, but also to the general public using its

products. Pressures are generated by authorities' demands and reimbursement system practices. These internal and external pressures may exhaust the innovative ability of the industry (5). The continuously growing need for resources in drug development is also undermining its possibilities, as the increased costs will lead to a situation where the drug companies will invest in development projects with the highest profits possible (5). From the standpoint of the pharmaceutical industry, therefore, innovation shows itself to be a complicated aggregation of the investment/product relationship, patient satisfaction and safety, the additional therapeutic value expected by national drug reimbursement systems, and a moderate price.

The implications for the pharmaceutical industry from the multitude of public sector practices and decisions, such as the uncertainty factors associated with drug reimbursement decisions, can involve reduced innovativeness (16). The problem is most salient in Europe, where the reimbursement decisions are made independently by each member state. Many of the regulations are considered to inhibit development and to be costly to implement. Several public sector adopted practices are also considered outdated and are not found to offer adequate incentives for innovation, whereas the uncertainty created by quick practical changes again will take its toll on the capacity for innovation (16).

### **Discussion**

Relatively few medicinal substances classified as innovative have been introduced on to the market in recent years. Besides Europe, concern for the declining innovativeness also affects Japan and the United States of America. Common to the projects dedicated to improving the effectivity of innovativeness appears to be the increasing collaboration between various operators, both private and public.

In Europe, efforts are being made to solve the member states' drug cost crisis by introducing uniform definition criteria for the relative effectiveness and added therapeutic value of the drugs. Even though some type of hierarchy can be built on the strength of therapeutic progress, classification of

medical treatment is nevertheless often complicated and ethically questionable: how should we define, on the one hand, society's responsibility for the individual, and the individual's responsibility for himself/herself on the other? Drug costs continue to grow and will eventually lead to prioritising among treatment costs.

Innovativeness and competitiveness continue to remain the key topics in EU politics while there is a wide selection of measures for supporting innovativeness. The danger is, however, that too many various operators are focusing on too many issues at the same time, which may lead to a lack of co-ordination, diffusion of plans and wastage of the European tax resources.

Among the various concepts of drug innovation, is it possible to reach a universally fruitful synthesis? This is probably feasible, and also preferable by all parties. Nor is there any doubt that all involved will have to compromise. Societies should accept the rising drug costs, in which case correct targeting of the funds available is of the utmost importance. Primary care especially is often forced to give preference to less costly generic drugs to make it possible to compensate for true innovations at a rate which is adequate also from the industry's viewpoint. Patients should accept a higher excess and a possibly increased safety risk associated with drugs granted a fast-track marketing authorisation, which the authorities will take into consideration in the process of granting marketing authorisations. The pharmaceutical industry will have to accept the growing generic competition, together with profits lower than before. These compromises would clarify the meaning of the term 'drug innovation', which has become vague. A successful drug innovation can consequently be regarded as a synthesis of a significant reform which generates additional therapeutic value, a high patient safety profile and the safeguarding of pharmaceutical industry competition and jobs. In that way it would also benefit all the parties involved.

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Translation Mervi Moisander