Assessing Drug Effectiveness – Common Opportunities and Challenges for Europe

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TLV
THE DENTAL AND PHARMACEUTICAL BENEFITS AGENCY

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY


Welcome to Stockholm!

Join us to promote European collaboration on follow-up of drug effectiveness in everyday clinical use – along with representatives of European health ministries, medical agencies, payers, healthcare services, patient organisations, researchers and the pharmaceutical industry.

The aim of the Swedish conference is to find ways of cooperating systematically across Europe on the collection and sharing of data on the effectiveness of drugs. A better understanding of how well drug treatments work in everyday clinical use would benefit patients, pharmaceutical companies, government agencies and society as a whole.

Among the potential benefits of European collaboration on the follow-up of drug effectiveness, we envision:

- More rational use of medicinal products and other healthcare resources.
- Spin-off effects from the provision of joint EU information on side-effects, IT support, cross-border healthcare, etc.
- Earlier and safer access by patients to new drugs, and more regular, structured contact with the healthcare professionals responsible for their treatment.
- A stronger position for Europe as an area in which the pharmaceutical industry would be interested in setting up research and development activities.

Examples of cooperation areas of particular interest include biologic agents for chronic inflammatory diseases, cancer drugs, and orphan medicinal products where individual countries often have too few patients to sustain comprehensive assessment programmes.

Among the desired outcomes of the conference is an agreement by the participants to start a pilot project on collective gathering of data on drug effectiveness. We hope to jointly develop a model for systematic and structured follow-up for initial testing on an orphan drug. Following evaluation of the project, other drugs might also be considered.

We look forward to seeing you in Stockholm this summer.

Karin Johansson
State Secretary to the Minister for Health and Social Affairs

A Timely Effort to Advance European Collaboration

Pharmaceutical drugs have greatly contributed to public health in Europe and throughout the world. Yet, there is evidence that drugs may perform differently in everyday clinical practice than in the clinical trials which are the basis for licensing, reimbursement, and prescribing decisions. In its recent report[1], the EU High Level Pharmaceutical Forum has appropriately separated the concepts of *efficacy* (the extent to which an intervention does more good than harm under ideal circumstances) and *effectiveness* (the extent to which an intervention does more good than harm when provided under the usual circumstances of healthcare practice). Factors contributing to the often-quoted "efficacy-effectiveness gap" have been widely discussed, but effectiveness data that could guide policy decisions is sparse.

The initiative from the Swedish presidency to foster the collection and exchange of data on drug effectiveness across Europe is timely – over the past years the pendulum of public opinion on drugs has swung from often unrealistically high hopes to much darker expectations. This development highlights the need for reliable data to support the debate on drugs. On the bright side, increasing availability of drug utilisation and health outcomes data from electronic healthcare databases and other sources provides new opportunities for generating effectiveness information.

[1] http://ec.europa.eu/pharmaforum/

All stakeholders will benefit from more – and more reliable – drug effectiveness data. Patients, healthcare providers, and the general public, deserve the best possible information on a drug's benefits and adverse effects. Drug regulators would greatly benefit from such data to guide their continuous risk-benefit assessment throughout the life span of a drug. Pharmaceutical companies would be able to demonstrate the value of their products for public health, and drug reimbursement bodies could consider, or refine, approaches to value-based drug purchasing.

While the goals of, and potential benefits from, systematic and structured follow-up of drug effectiveness are clear, there remains a plethora of practical challenges. These include the difficulties of initiating effectiveness studies, harnessing the potential of different healthcare databases across the EU, interpreting findings from studies that are outside the concept of the randomised controlled trial, and applying value judgements to heterogeneous clinical outcomes.

These topical and often controversial issues are guaranteed to make the Stockholm conference a stimulating event. I congratulate the organisers of the meeting on putting together an exciting agenda and speaker list and look forward to a number of important results from this initiative.

Prof. Hans-Georg Eichler
Senior Medical Officer of the European Medicines Agency (EMEA)

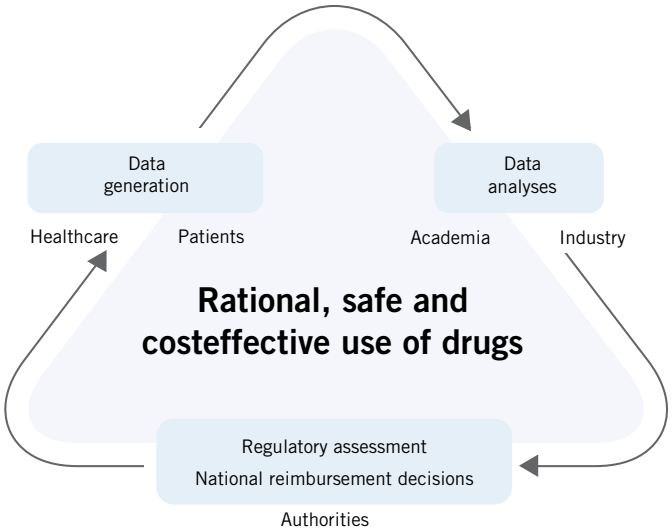
Who benefits from European collaboration on follow-up of drug effectiveness in everyday clinical use?

When new medicinal products are introduced on the market, knowledge of their effectiveness in everyday clinical use is very limited.

The regulations governing the subsidising of medicinal products vary across the EU. However, regardless of the basis on which the subsidy status of a medicinal product is assessed, all countries need to know about the effectiveness of the product in everyday clinical use. This knowledge could be improved significantly if EU Member States were to pool some of the resources they already invest in separately into a collaborative date-gathering effort.

In the longer term, the information assembled in a collaborative European undertaking aimed at improving the collection of data on drug effectiveness could be made accessible to all EU Member States. It could also lead to medicinal products being used in ways better suited to the needs of patients and ensure that the resources invested in subsidies for medicinal products are used more efficiently throughout the EU.

Assessing effectiveness in clinical practice starts at the patient level by collecting relevant and validated data at the right time. These data are initially put together and analysed at individual and group level by health care professionals as a part of their daily work. Moreover, academic research groups, industry and other players have an interest in the collection and analysis of data of relevance to their own needs. Various agencies then make their assessments at national and European level according to their mandate. The conference aims at identifying areas of improvement in the generation, compiling and analyses of data to facilitate the work of all concerned stakeholders.



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Some stakeholder views

On 28–29 July, some of the most influential medicinal stakeholders in Europe will be meeting in Stockholm to address the importance of evaluating drug effectiveness and to explore opportunities for future European collaboration on this issue. A number of key conference participants comment below on the potential benefits – and beneficiaries – of the meeting's objectives.

We are proud to present the views of:

Thomas Lönngren

Executive Director of EMEA (European Medicines Agency)

"If we can coordinate health technology assessments a more harmonised approach could be achieved at EU-level."

Clare McGrath

Senior Director HTA Policy, Pfizer

"Europe needs to invest in improved data systems within health care."

Anders Olauson

Chairman of the Board of Ågrenska AB, President of European Patient Forum and Member of the Board of Eurordis (European Organisation for Rare Diseases)

"The patients will become more involved in the process, which will create a better relation to the medicinal product and to health care."

Bengt Jönsson

Professor of Health Economics, Stockholm School of Economics

"The evaluation of drug effectiveness provides a basis for decisions on how to allocate resources and funds to, and within, the health sector."

How can information on drug effectiveness contribute to society?

"Information on drug effectiveness provides a basis for decisions concerning the allocation of resources and funds to and within the health sector. For example, this information helps us to choose the medicines or other treatment methods that will have the best effects, and reduces the risk of wasting scarce resources," says Bengt Jönsson.

Thomas Lönngren agrees: "When a medicinal product comes on the market we can take its effectiveness into account in our choice of medical treatment, and prioritize within the healthcare sector to give patients the treatment best suited to them." Improved information on the effect of drugs in an everyday clinical setting can enhance medical treatment in a number of respects.

Anders Olauson offers a few examples: "Patients will get the correct dosage at the correct time, which will tend to improve patient safety and compliance, ultimately resulting in the desired treatment outcome. Another benefit is that we can pin-point when a certain treatment should be considered so that it can be prescribed during the correct phase of the illness."

"Structured and systematic follow-up should also generate information about how effective drugs are in the context of the delivery system. This context is important to enable us to develop health care systems that optimise treatment effectiveness," adds Clare McGrath.

How can patients benefit from the systematic follow-up of drug effectiveness?

"Patients will benefit from systematic assessments of drug effectiveness in two principal ways. Firstly, effectiveness will be reported earlier, which will increase the pace of development and treatment improvements. Secondly, the patients will become more involved in the treatment process, which may create better compliance and a better relation to the medicinal product and to health care in general. Cancer treatment has seen a paradigm shift: the disease is now largely a chronic disease that the patient lives with. This opens the way for new treatments, and long-term patient relations become more important," says Anders Olauson.

Clare McGrath adds to the perspective of patient involvement:
"Systematic follow-up of drug effectiveness should help patients to decide which treatment is best for them based on treatment attributes and their willingness to adhere to it. With this information at hand, patients will likely become more engaged in the choice of treatment, together with their doctors. This, among other things, will contribute to giving patients the most effective treatment," says Clare McGrath.

Bengt Jönsson brings in another aspect of the benefit to patients of systematic assessments of drug effectiveness, in the context of orphan medicinal products:
"Orphan medicinal products target very few patients in each member state. It is expensive to develop these drugs, so collaboration aimed at including more patients in – and sharing data from – the systematic follow-up of the effectiveness of these drugs will increase the value of investments and improve the development process," says Bengt Jönsson.

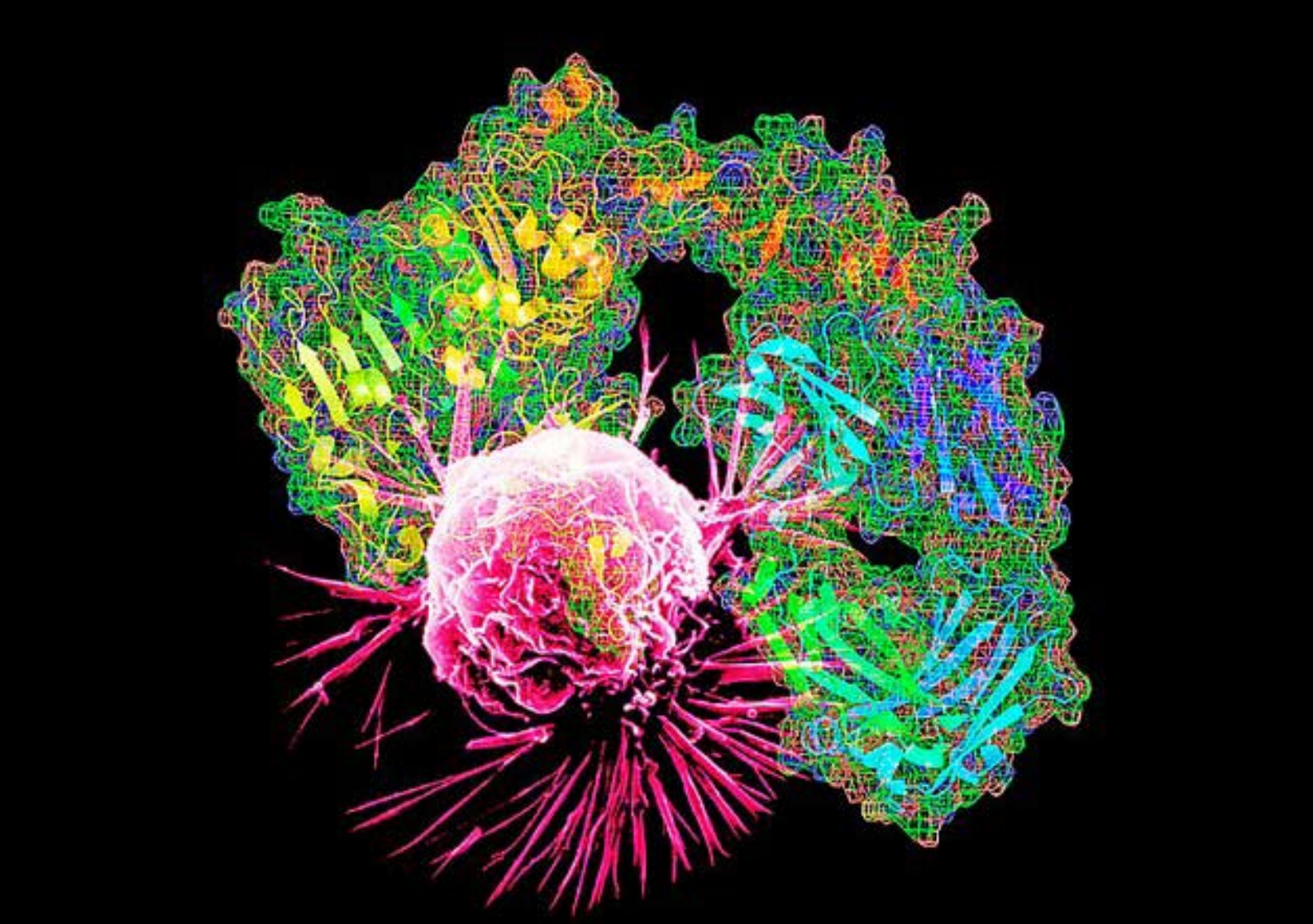
Can systematic follow-up of drug effectiveness increase Europe's competitiveness in pharmaceutical research and development?

"In order to be a player, Europe needs to invest in improved data systems in healthcare. Future requirements for follow-up of drug effectiveness might drive investment, but investment is crucial. We also need a very effective dialogue among all stakeholders to determine what questions can be answered within a reasonable time frame. This conference is a very important venue, where we start the dialogue with all the stakeholders, and none are excluded," says Clare McGrath.

Follow-up of drug effectiveness should be an important part of the industrial development process. Better information on drug effectiveness may help pharmaceutical companies to prioritise their research and development activities. Bengt Jönsson explains:

"An efficient health care sector is a necessary condition for a competitive industry which can develop and produce new drugs, devices and methods. The production and development by a competitive industry of new drugs, devices and methods. Information on the effect of a drug in an everyday clinical setting may provide valuable feedback for R&D companies, which in turn will help them direct their research efforts so as to compete more effectively in the market," says Bengt Jönsson.

These and more views from the key speakers and other participants promise a constructive debate in Stockholm. Join the discussion and shape the future of assessing drug effectiveness in Europe for the benefit of patients, the pharmaceutical industry, governmental agencies and society.



Therapeutic antibody neutralizing a cell.

Follow-up on drug effectiveness – an example from real life

Taking chronic inflammatory diseases as their example, Nils Feltelius of the Swedish Medical Products Agency and Johan Askling of the Karolinska Institutet share below their experience of the ARTIS register – a Swedish register on anti-rheumatic biologic medicinal products. The register has been developed in cooperation with corresponding registries in Germany and Great Britain.

Ten years of clinical experience of biologics in rheumatoid arthritis in Sweden

In Scandinavia, population-based registers and healthcare databases provide excellent opportunities for drug assessments in everyday clinical practice. The ARTIS register (Anti-Rheumatic Therapies In Sweden) documents outcome of treatment with biologic pharmaceuticals, so called *biologics*. These are potent compounds for the treatment of rheumatoid arthritis, other arthritic conditions, inflammatory bowel disease and psoriasis. Data from the ARTIS register has clearly shown the benefits and risks correlated with a certain class of biologic drugs – the TNF-alpha antagonists.

By blocking tumour necrosis factor alpha, a substance essential to the inflammatory response, the TNF-alpha antagonists inhibit inflammatory processes and prevent damage to joints and the mucous membrane in the intestine, for example. Back in 1998, when the TNF-alpha antagonists were introduced, their targeted mechanism of action represented a new therapeutic approach. Their subsequent long-term effectiveness were essentially unknown.

The TNF-alpha antagonists were approved by the European Medicines Agency, EMEA, on condition that the manufacturers would follow-up on their long term safety. The ARTIS clinical network, population-based outcome registers and regulatory support were the key factors contributing to success. Over time, the scope of the ARTIS register has broadened to include all biologics with rheumatological indications.

Everyone's a winner

The ARTIS register currently comprises 14,000 patients, corresponding to 22,000 treatments. The model for assessing the long-term effectiveness of the pharmaceuticals in the register has yielded benefits for all stakeholders:

- *Patients* have early and safe access to unique and innovative pharmaceuticals.
- *Health Care Professionals* have better information as a basis for open comparisons and control of prescriptions in terms of effect, safety and indication trends.
- *Regulatory agencies* have access to new safety and efficacy information. This holds true for the Swedish Medical Products Agency, the EMEA and for the FDA in the USA.
- *Industry* can improve compliance with legislative demands during the introduction of a new medicinal product on the market. Moreover, the companies will have also fulfilled their assessment obligations through the ARTIS register.
- *Clinical researchers* have the opportunity to access state-of-the-art pharmaceutical and epidemiological safety data.

Register writes the roadmap

The ARTIS register has laid the basis for an assessment of the risks – in for example lymphoma and other cancer forms, infections and cardiovascular diseases – associated with different treatments, correlated to different patient groups. Manufacturers can subscribe for access to data on their own specific products, which helps them fulfil their assessment obligations. Data for a whole range of products has, however, been made available for publication by the register.

In Sweden the ARTIS register serves as a role model for the development of other national registries for the assessment of medicinal products. There is a register already in place for new multiple sclerosis (MS) medicinal products. Another is being set up for inflammatory bowel diseases.

The ARTIS register has been developed in cooperation with corresponding registries in Germany and Great Britain, thus promoting a common development of registry data quality and research methodology of benefit to manufacturers and regulatory agencies. Several other rheumatology registries have published important data and are collaborating under the auspices of EULAR (European League Against Rheumatism).

Assoc. Prof Nils Feltelius,
Swedish Medical Products Agency, Chairman ARTIS Steering Committee

Assoc. Prof Johan Askling,
Karolinska Institutet, Co-chairman of EULAR Task Force on Requirements for Observational Treatment Registers

A dinner for all conference delegates will be held at Stallmästaregården in the evening of July 28.