LEO Pharma's position on Health Technology Assessment

October 2016

Executive Summary

In Europe, budgets for public healthcare are severely constrained . In view of limited financial resources, it is important to make socially responsible decisions about innovative pharmaceuticals and services by means of an assessment process which is transparent, open, fair and consistent.

The application of health technologies should always lead to optimal health outcomes for patients. In the field of dermatology where skin diseases are often chronic or recurrent, evaluation should be continuous since the severity of a disease can fluctuate over time. Health Technology Assessment (HTA) plays a role in systematic evaluation, the summarising of evidence, presenting the value of new technologies and, consequently, in supporting decisions regarding the optimal use of new technologies in routine care, including those in the specific field of dermatology.

When conducting an HTA, one of the most important objectives is to determine the added value of this new technology. However, it is also crucial to identify what is real additional value for people affected by skin disease.

LEO Pharma A/S, a patient-focused pharmaceutical company, aims to help people achieve healthy skin and our goal is to be a constructive partner, committed to entering into dialogue with national payers, HTA agencies, regulators, healthcare providers and patients, in order to:

- Support the development of processes and methods used in assessing and appraising the value of new pharmaceuticals, where the ultimate goal is the **sustainable management of health systems which continue to ensure affordable access to innovative care for people with skin diseases**.
- **Engage directly and indirectly with patients during the entire clinical development process** in order to identify patients' unmet needs and capture the burden of disease and quality of life for people living with skin disease. Primarily, LEO Pharma considers Patient-Reported Outcome Measures (PROMs) a valuable instrument for capturing patient inputs correctly by means of its clinical development cycle.
- **Collaborate with HTA bodies and payers in developing methods and processes that will incorporate patients' views** and the understanding of skin disease.
- Contribute to the development and implementation of a system for **European Relative Efficacy Assessment (REA)[4]** as proposed by several stakeholders, e.g. the European Federation of Pharmaceutical Industries and Associations (EFPIA).

The role of HTAs in a sustainable healthcare system which continues to ensure affordable access to innovative care for people with skin disease

Background

Public healthcare budgets are severely constrained in today's challenging financial environment. In view of limited financial resources, it is vital to make socially responsible decisions about innovative pharmaceuticals and services by means of an assessment process which is transparent, open, fair and consistent.

Health Technology Assessments (HTAs) are the result of a multidisciplinary, scientifically-rooted process of systematically evaluating and summarising information about the medical, social, economic and ethical issues related to the use of a new treatment option. This process is aimed at informing decisions about the use of the technology to achieve optimal health outcomes through access to best value, safe and effective technologies.

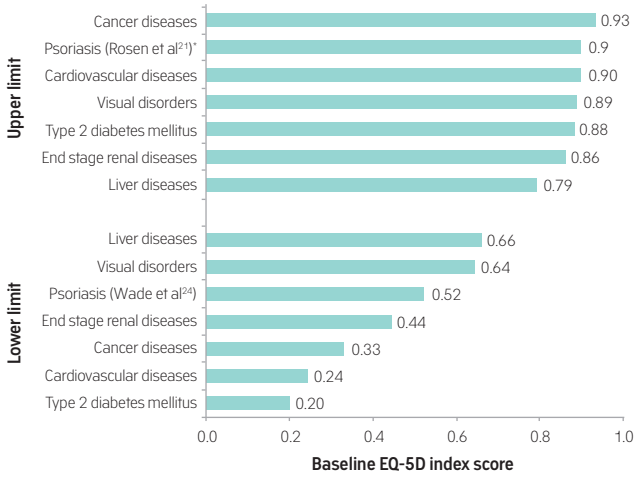
The burden of skin disease

Skin disease is a heterogeneous group of conditions. Many of them are chronic and some develop as early as during childhood, whereas others only develop later in life. In the case of psoriasis, it is a chronic, painful, disfiguring and debilitating disease which is a substantial burden, not only on patients, but also on society and healthcare systems[5]. However, **the consequences of skin disease go beyond the patient's clinical burden, and patients currently have many unmet needs, leading to non-optimal health outcomes**.

For example, psoriasis can adversely affect people's social lives because people suffering from this skin disease are frequently stigmatised[6]. The main focus of the industry, HTA organisations and payers in the future should therefore be to increase the evidence-based awareness of skin disease. For this reason, LEO Pharma is firmly committed to the development and implementation of solutions to alleviate the burden of the disease, seen from the perspective of various stakeholders.

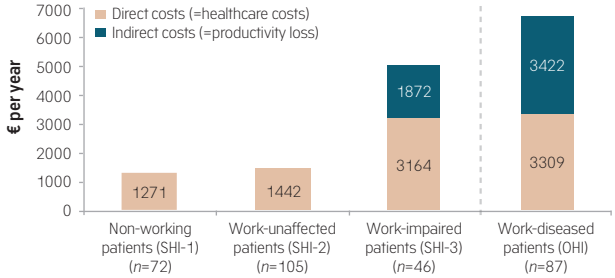
The direct and indirect costs of skin disease place a significant burden on national healthcare budgets. For example, when it comes to indirect costs, patients with chronic hand eczema are negatively impacted in their level of productivity at work as well as normal activity[7,8] (see Figure 2). Therefore, it is important, within the context of increased financial pressure, to develop sustainable models to ensure that people with skin disease have affordable access to new treatment options that could minimise the burden of their disease.

Figure 1: The burden of skin disease negatively impacts patients' quality of life



Psoriasis patients undergo the same deterioration in Health-Related Quality of Life as patients with other serious chronic diseases, including cancer and cardiovascular diseases. The mean baseline EQ-5D utility index scores for patients with psoriasis ranged from 0.52 (standard deviation: 0.39) to 0.9 (standard deviation: 0.1) for all disease severities. All baseline EQ-5D scores in psoriasis patients were within the range reported for other chronic diseases (0.20–0.93).

Figure 2: Annual costs per patient with chronic hand eczema (CHE) by impact of CHE on work (according to insurance-specific tariffs) in Germany.



Defining value in HTAs for skin disease

A definition of value which can cover the above-mentioned aspects when assessing new treatment options would lead to better health outcomes and, consequently, to the sustainable management of healthcare resources.

We encourage member states of the European Union to adopt a wider definition of value in which the assessment of costs and benefits should be presented in accordance with international best practice guidelines for economic evaluation.

At LEO Pharma, we acknowledge these existing challenges. Therefore, we would like to be a constructive partner for payers, HTA agencies, regulators and patients, and we are willing to engage in dialogue from the early stages of the life cycle of technologies, in order to develop processes and methods to be applied when assessing and appraising the value of new pharmaceuticals. The ultimate goal should be the sustainable management of health budgets which continue to ensure affordable access to innovative care for people with various skin diseases.

The role of Patient-Reported Outcome Measures in HTA decision-making processes

Patient-reported outcome measures (PROMs) are tools used for collecting and measuring the outcomes obtained from patients directly[10]. The most common PROMs measure Health-Related Quality of Life (HRQoL)[11,12] via questionnaires, such as EQ-5D[13], SF-36[14], and, more specifically in the field of dermatology, DLQI[15] or Skindex[16,17,18]. Traditionally, researchers in the field of dermatology have used non-standardised outcome measures or combined those used in several other studies to prove the efficacy of a particular intervention as a defined "gold standard" does not exist. This can lead to difficulties when comparing treatment options.

Obtaining authorisation from a global regulator for marketing is only the first step towards patient access, and regulators require different kinds of evidence than HTA bodies and payers. In the field of skin disease specifically, it is a challenge to determine what exactly the value, is based on the various perspectives, e.g. those of HTA advisers, payers and patients.

Clinical trials are not always a sufficient reflection of the therapeutic benefits for people with chronic skin diseases since it is only possible to focus on a few primary and secondary endpoints. **At LEO Pharma, we aim to expand our research to include patient-relevant benefits so as to better reflect the patient's perspective. Therefore, we have taken a decision to always include patient-reported outcomes (PROs)[19] in our future clinical trials.**

> **WHO Global Report on Psoriasis, 2016 :26-27**
> *"It is evident that the results of clinical studies do not sufficiently reflect the therapeutic benefits from psoriasis treatment since they mostly focus on a few primary and secondary endpoints. Instead,* ***extended outcomes research based on patient-relevant benefit endpoints of psoriasis would better reflect the patients' perspective – that is, patient reported outcomes.****"*

In addition, in order to gain a better understanding of the situation from the patient's perspective, real-life studies are needed as well. These could help to identify factors such as unmet needs, the performance of the various treatment options as well as the effect of the burden of disease on the patient, and better link clinical studies to real-life settings.

In most skin diseases, survival is not the ultimate goal of the treatment. Quality of life plays a crucial role in the treatment process as most skin diseases are chronic, and patients may suffer from depression and be stigmatised owing to the visibility of their disease[20]. Consequently, in the field of dermatology it is crucial to involve and listen to the patient, and for regulatory bodies and payers to acknowledge the relevance of these patient-reported outcomes.

Patients' involvement in HTA

As one of the goals of HTA is to improve patient care through informed policy making, HTA processes should include participation by patients and formally incorporate their views when assessing the value of a pharmaceutical.

Despite an increase in positive patient involvement during the HTA process, as reported by HTA organisations like the Canadian Agency for Drugs and Technologies in Health (CADTH) in Canada[21] and the Scottish Medicines Consortium (SMC) in Scotland[22], many countries are still not incorporating patients' views into their HTA decision making[23]. Moreover, even if these views were incorporated, it is not always clear what impact the patients' views have had on national payer decisions.

LEO Pharma believes that the incorporation of patients' voices into HTA models will increase understanding of the burden of a disease as well as its social, physical and psychological impact – specifically for patients with skin disease.

Ultimately, a greater understanding will assist in assessing the value of new pharmaceuticals.

In order to gain a deeper understanding of the effect of skin disease on peoples' lives, LEO Pharma consistently supports and conveys patients' views to national payers and HTA agencies, and firmly believes that a transparent process should be established to incorporate patients' input in HTA models.

The development of a system for a European Relative Efficacy Assessment

Discussions are ongoing about greater collaboration on HTAs at a European level. Decisions regarding funding and the adoption of new technologies should remain vested in the member states so that they can be adapted to different local needs. Accordingly, HTAs should be conducted in such a manner that local decision makers will receive the information they require, as this will lead to quicker access to innovative care solutions.

LEO Pharma has encountered various approaches to assessing the value of pharmaceutical products across Europe, leading to different requirements for evidence in the assessment processes and different decisions about access to the same product[24]. When information is not shared, it could result in the duplication of assessments across countries as well as delayed access to new pharmaceuticals for patients.

In order to improve patient access across Europe, LEO Pharma is committed to the development of a system for European Relative Efficacy Assessment (REA) at the time of launch, in line with the extent proposed by the European Federation of Pharmaceutical Industries and Associations (EFPIA).

The ultimate goal of a system for scientific European REAs should be to accelerate the assessment process by harmonising the clinical data requirements related to relative clinical performance only, while the economic assessments should be conducted locally so that it reflects the diversity of the various healthcare systems.

GLOSSARY

Terms	Definitions
DLQI (Dermatology life quality index)	10-question tool that measures the impact of skin conditions on various aspects of a patient's life (including symptoms, social life, work and the impact of treatment)
EQ-5D	Standardised instrument for use as a generic measure of the quality of health-related life and of health outcome in aspects of mobility, self-care, usual activity, pain/discomfort and anxiety/depression.
HT (Health Technology)	Any intervention that may be used to promote health, to prevent, diagnose or treat disease, or for rehabilitation or long-term care. This includes the pharmaceuticals, devices, procedures and organisational systems used in healthcare.
HTA (Health Technology Assessment)	A multidisciplinary process which summarises information about the medical, social, economic and ethical issues related to the use of a specific health technology in a systematic, transparent, unbiased and robust manner. Its aim is to inform the formulation of safe, effective health policies which focus on the patient and seek to achieve the best possible value. Despite its policy goals, an HTA must always be firmly rooted in research and scientific methods.
HRQoL (Health-Related Quality of Life)	A patient's general subjective perception of the effects of illness and intervention on the physical, psychological and social aspects of daily life.
PRO (Patient-Reported Outcome)	A measurement based on a report made directly by the patient (i.e. study subject/research participant) about the status of that patient's health condition, without any amendment or interpretation of the patient's response by a clinician or anyone else. A PRO can be measured by means of self-report or interview, provided that the interviewer records only the patient's responses.
PROMs (Patient-Reported Outcome Measures)	PROMs are the tools or instruments used for measuring PROs. These tools are often self-completed (patient) questionnaires and may include instruments or tools that measure functional status, health-related quality of life, symptoms as well as the burden of symptoms, personal experience of care and health-related behaviour such as anxiety and depression.
Relative Efficacy	Extent to which an intervention does more good than harm under ideal circumstances, when compared with one or more alternative interventions.
Relative Effectiveness	Extent to which an intervention does more good than harm when compared with one or more alternative interventions for achieving the desired results, when provided under the usual circumstances of healthcare practice.
SF-36 (Short Form 36)	Multipurpose, short-form health survey with 36 questions. It yields an 8-scale profile of scores for functional health and wellbeing as well as summarised psychometrically-based physical and mental health measures and a preference-based health utility index.
Skindex	61-item self-administered survey instrument to measure the effects of skin diseases on patients' quality of life. It includes eight scales, each of which addresses a construct, or an abstract component, in a comprehensive conceptual framework: cognitive effects, social effects, depression, fear, embarrassment, anger, physical discomfort and physical limitations.

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