EVENT REPORT

Virtual workshop on the off-label use of medicines in Sweden and Norway

Striking the right balance between timely access to medicines and maintaining the highest standards of patient safety

24 November 2020

Introduction to the event

The event, hosted by the Swedish Brain Foundation, the Norwegian MS Association and the European Brain Council was held virtually on 24 November 2020. It brought together over 80 **representatives from Norway and Sweden, and a distinguished list of speakers, – including physicians, patient organizations, pharmaceutical industry representatives and the authorities – to discuss the safety of medicines used off-label** as well as the framework regulating their use. The workshop was sponsored by the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), Europe's trade body for small to medium-sized innovative companies working in the field of pharmaceuticals and medical technologies.

A number of questions were considered, notably:

- In what situations is off-label use considered useful, and in what situations should it not occur?
- What are the drivers behind off-label use?
- What are the main consequences of off-label use? How does this affect patient care?

Below we have collected the main observations and areas of potential focus that emerged during the discussion. This could constitute a **basis for interested stakeholders to discuss future initiatives and measures on off-label use**.

Summary of the discussion

<u>Background on off-label use</u>

The use of off-label medicines plays an important role in modern healthcare systems, allowing patients to be treated in cases where an authorized drug is not available for a specific indication. This can be the case across a range of therapeutic areas, including rare diseases, pediatric cancers, palliative care and mental health.

However, off-label use can bring potentially **increased risks** for patients due to lack of clinical investigation or longer-term evaluation for a given indication or patient population, lack of informed consent, and difficulty in monitoring adverse events. Further complicating matters, there is a lack of an aligned strategy among agencies and decision makers regarding off-label use: different regions

have different policy approaches and implementation. **The use of off-label medicines when prescribed under the conditions laid out in the GOLUP Declaration, play an important role in medical practice and do not have a detrimental impact on pharmaceutical innovation. However, the use of off-label medicines for reasons other than a patient's medical need** has the potential to chill pharmaceutical innovation, as newly developed products and indications will not reach the patients they are intended to help.

Background on GOLUP Declaration

To maintain the highest levels of patient safety and minimize any adverse events, while not limiting the access to medications off-label when there is an unmet medical need, a number of organizations have established the **Declaration on Good Off-Label Use Practice (so called GOLUP)** as a series of baseline principles around good off-label use practice. Following a launch event in Brussels, workshops have been held in Rome and Madrid to present the GOLUP and discuss it with local stakeholders and decisionmakers.

The **good practice criteria for off-label use** included in the GOLUP Declaration include:

a) Presence of **a medical therapeutic need** based on a current examination of the patient by a suitably qualified health care professional;
b) **Absence of authorized treatment** and licensed alternatives tolerated by the patient or repeated treatment failure;
c) A **documented review and critical appraisal of available scientific evidence** favors off-label use to respond to the unmet medical need of the individual patient;
d) Patients (or their legal representative) must be given **sufficient information about the medicines** that are prescribed to allow them to make an informed decision;
e) Presence of **established reporting routes** for outcomes and adverse events linked to off-label use.

The drivers behind the off-label use of medicines in Sweden and Norway

In the daily reality of many doctors and patients in both countries, the prescription and use of medicines off-label is common practice. The point was made that **the most common scenario for the use of an off-label medicine, and one generally well established in terms of regulation, should be where an authorized medicinal product is not available.** It was highlighted that in Sweden, off-label use is particularly common in the pediatric space, where 49% of prescriptions are said to be off-label (79% for newborns).

When prescribing drugs to patients, doctors should look at a series of characteristics that are unique to every patient. Information on a therapy's performance in a specific indication or dose, often lacking for off-label medicines, is pivotal to understand whether the treatment is adequate for the patient. For instance, multiple sclerosis is a heterogenous disease, which calls for personalized treatment. While some MS patients may benefit from off-label use, a **one size approach does not work.**

In Norway, physicians are currently incentivized to prescribe off-label for economic reasons, the practice of using off-label products as a means to save on healthcare costs, due to the recent cancellation of tenders for innovative MS products. This not only hinders professional autonomy to

prescribe a different therapy if one is more medically appropriate, but also curtails patient choice in their treatment options.

The patients' perspective

Patients have the right to be protected by a safe regulatory environment, to be fully informed and involved in treatment decisions, and to receive safe and effective treatments, which are backed by robust clinical trial data and regulatory approval. In Norway, healthcare professionals are supportive of the need for patients to play an active role in shared decision-making for their treatment. In Sweden, prescribers are required to discuss a full range of available on and off-label treatment options with the patient, and to choose one in agreement with the patient. However, one participant observed that it is not easy to understand their physician's recommendation or to provide informed input into this decision, as information on off-label therapies is not included in the pamphlets they are provided by their treatment center or hospital. There was agreement in the virtual room that patients must be adequately informed about potential side effects when being prescribed a medicine off-label, preferably in written form to allow for a discussion with their caregivers and families.

A suggested way forward

During the workshop, stakeholders agreed on the fact that **off-label use is beneficial in many cases, but it can be detrimental to patient safety and access to innovative therapies.** Above all else, the **efficacy, safety and preservation of patient consent should be prioritized.**

In conclusion the speakers highlighted areas of potential future focus:

- **More information, that is user-friendly, should be provided to both patients and physicians.** Patients need to be provided with concise, precise and trustworthy information, also in written form, in order for them to be fully informed and involved in treatment decisions;
- **Data should be collected**. Data should be collected and compiled for every treated patients and adverse events reported to the competent pharmacovigilance agency;
- **Patient safety should be the top priority,** and physicians should be given the latitude to prescribe the most appropriate treatments for their medical needs
- **A stable regulatory framework should be maintained, with scientific assessments and patient need clearly separated from economic drivers.**