Off-label use

Introduction

Off-label use of a medicine is the use of an authorised medicine by a healthcare professional to treat a patient in a way not covered by the Marketing Authorisation (MA) and detailed in the Summary of Product Characteristics (SmPC) of the medicine.

Off-label use of medicines is not regulated by EU legislation and no uniform definition is available. Advertising the off-label use of an authorised medicinal product is prohibited. All advertising must comply with the SmPC.

Unlicensed medicines versus off-label use

A medicine is ‘unlicensed’ when it does not have a marketing authorisation (MA). An unlicensed medicine is not available on the market and it can only be used in clinical studies or in a compassionate use/expanded access setting.

Off-label use, by contrast, involves a medicine that is licensed (has an MA) and which is available on the market. In off-label use, a healthcare professional uses an authorised medicine to treat a patient in a different way than the medicine is authorised to be used in. This could involve:

- Using a different dosing regimen
- Use for a different indication/disease
- Use for a different population, for instance paediatric (children) use when the medicine is only intended for use in adults.

When is off-label use appropriate?

In certain circumstances, off-label use can be medically appropriate and an important element of high-quality patient care, but only in the context of existing, stringent legal requirements. This includes discussing with the patient/parents/carer:

- Whether the medicine is approved for treatment of the particular condition or is off-label;
- Whether there is an approved alternative;
- Whether the off-label treatment has advantages compared to approved alternatives; **or**
- Whether credible research supports the off-label use.

Requiring disclosure protects patient autonomy and educates patients about alternatives and risks, leading to improved healthcare decisions. As the medicine is being used off-label, additional information about any uncertainties associated with such use should be given. Patients should ask for additional information to address specific concerns. A doctor’s decision whether to prescribe a medicine off-label should be guided by evidence-based medicine and the best interest and medical needs of patients.

Documentation of the consent process is recommended and, in some cases, obtaining written consent may be appropriate.

When prescribing a medicine off-label, doctors are liable for any problem arising from the off-label use of the medicine. Even when an off-label treatment is successful and, in comparison with other possible treatments in the best interest of the patient, the treatment may not be reimbursed because it is not in-line with standard practice. However, in many cases, off-label prescriptions may be part of best practice or standard-of-care.

Examples

HIV therapies

One example of an off-label prescription is an HIV combination therapy often used off-label for HIV prevention. The medicine is only indicated for the treatment of HIV-positive patients, but numerous patients take it for prevention purposes. Patient organisations are playing a key role in requesting an extension of the indication to include prevention in addition to treatment.

Another example is an HIV medicine that has been proven to work in lower doses than those that are licensed for adults. However, a lower dosage pill is not available for adult patients. A different formulation (a sprinkle granule) has been introduced for paediatric use, which allows reduced dosing of the same compound. Adult HIV patients opt to use the paediatric formulation off-label to reduce side effects and over-exposure to the medicine.

Oncology

The off-label situation is more extensive in oncology than in other medical areas for several reasons, but the principal reason is the large number of different cancer types. An anti-cancer medicine may be useful in several types of cancer. Many widely used anti-cancer medicines are not licensed for all the indications under which they can be effectively employed.

Paediatrics

Paediatric prescriptions are frequently off-label, as many medicines were not tested for use in paediatric populations and are therefore not licensed for use in children. The most common examples for off-label use in children are medicines prescribed at a different dose or frequency than indicated.

There are also cases where children received the medicine for a different indication or by an alternative route.

The Paediatric Regulation came into force in the European Union in to address the problem of off-label use in paediatrics. This regulation aims to improve the health of children in Europe by facilitating the development and availability of medicines for children between 0 to 17 years. The regulation ensures that the medicines are of high quality, ethically researched, and appropriately authorised.

Pharmacovigilance and off-label use

The Marketing Authorisation Holder (MAH) is required to report to the Competent Authorities 'any other new information which might influence the evaluation of the benefits and risks of the medicinal product concerned', including 'data on the use of the medicinal product where such use is outside the terms of the MA.'[2] If important safety information relating to off-label use becomes available, this should be introduced into the SmPC. Further guidance is given by the EMA guideline on Good Pharmacovigilance Practices.

With the recent emergence of the use of social media and direct interaction across patient communities, patient organisations can play an instrumental role in extending and deepening the reach and effectiveness of pharmacovigilance. This is especially important in the case of off-label use. Pharmaceutical companies are increasingly monitoring social media sites, and establishing formal interactions with patient organisations to follow up on the life cycle of their products in other forms than post-marketing trials.

[glossary_exclude]Further Resources

- European Parliament (2003). *Directive 2001/83/EC on the Community code relating to medicinal products for human*

use. Retrieved 11 July, 2021, from https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32001L0083&qid=1626030967311
- European Commission (2015). *Medicinal products for human use: Medicines for children*. Retrieved 4 July, 2021, from https://ec.europa.eu/health/human-use/paediatric-medicines_en[/glossary_exclude]

[glossary_exclude]References

1. Centers for Disease Control and Prevention (2015). *CDC Statement on IPERGAY trial of pre-exposure prophylaxis (PrEP) for HIV prevention among men who have sex with men*. Retrieved 11 July, 2021, from https://www.cdc.gov/nchhstp/newsroom/2015/croi-media-statement.html
2. European Medicines Agency (2014). *EMA/873138/2011 Rev 1 Guideline on good pharmacovigilance practices (GVP): Module VI – Management and reporting of adverse reactions to medicinal products (Rev 1)*. Retrieved 14 September, 2015, from http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/09/WC500172402.pdf[/glossary_exclude]

[glossary_exclude]Attachments

- Off-label-use-v1_EN
  Size: 393,601 bytes, Format: .pptx
  A presentation describing the off-label use of medicine, which can be adapted for own use.

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