Irish Patients' Association

Tús Áite do Shábháilteacht Othar
Patient Safety First

March 2012

Patient Safety, Patients' Rights and Off-Label Prescribing

Findings of a Europe-wide survey among 150 patient groups

Conducted by PatientView
Supported by an educational grant from Novartis

Introduction from the Irish Patients' Association

Prescription medicines and patients' rights: off-label usage

The Irish Patients' Association has been a strong advocate for patient safety over the past 15 years. On a personal level, I believe that learning in healthcare should not be driven by harm. In other words, reform and change in our healthcare systems should not be preceded by funerals and injury to patients.

An April 2010 Eurobarometer survey, *Patient Safety and Quality of Healthcare*, has shown that 50% of the respondent Europeans feel that they could be harmed when receiving healthcare, while 25% of the respondent citizens say that they (or their family) have experienced an adverse healthcare event. Given ever-increasing levels of patient concern about the safety of medicinal procedures and products, the Irish Patients' Association decided to undertake a pan-European survey of patient groups, to review their understanding of prescribing practices when the safety and efficacy of a medicine for a specific use has not been established (off-label prescribing).

For this project, we defined 'off-label drugs' as drugs that are applied for a use not included as an indication on the drug's label (as approved by regulators). Off-label and unlicensed use is justified when it satisfies an unmet medical need. Such use can literally act as a lifeline to patients for whom no other alternative clinical therapy is available. Off-label drugs are most frequently used to help two categories of patient: children (due to the difficulty in undertaking clinical trials with children), and people with cancer (whenever the terminal nature of the illness means that any potential life-extending benefit is likely to outweigh the chance of risk from the drug being given). Anecdotal reports in the medical literature of the positive therapeutic effects of a drug or medical device may be enough to convince many doctors to prescribe a medicine outside its authorised use. When placed under clinical examination, these anecdotal reports sometimes turn out to have a scientific basis. But, despite its advantages, off-label prescribing remains controversial.

Reasons for doubts about the process include the fact that "the entire EU medicines approval system is based on providing clear, and, to the extent possible, comprehensive descriptions of how each specific medicinal product can be used[1]." Off-label and unlicensed usage is predominately practised by individual physicians, rather than as part of controlled clinical studies, and, therefore, is discretionary. Products that are off-label (and therefore unlicensed) are typically repackaged by pharmacists outside the supervision of the manufacturer. Such re-packaging is discouraged by EU laws. And yet, increasingly, payers of healthcare are encouraging doctors to prescribe cheaper products available off-label, rather than to prescribe the recommended clinically-approved treatment. In April 2011 the UK General Medical Council agreed that it is appropriate for doctors to prescribe cheaper off-label drugs as a substitute for more expensive brands if they feel there is sufficient clinical justification.

At the moment, patients prescribed an off-label or unlicensed product are subject to poor monitoring and surveillance. However, the reform of the EU Pharmacovigilance framework (expected to come into force mid-2012) has extended the EU system for data collection and reporting adverse reactions to off-label use. The doctor must select—with the patient's written consent—the best-possible course of treatment. But every patient has a fundamental right to be informed about the treatments they receive, as well as to participate in the decisions made about their clinical and medical treatment options[2]. Patients should be fully informed and warned of the risks (as well as the benefits) of treatment, be instructed in how to recognise possible side effects—and to know about alternative treatments that comprise an authorised product (if available). In the case of off-label and unlicensed use, we have never really known whether patients are typically being informed that the products they are being prescribed are off-label. Hence this study.

We would like to thank Novartis for the educational grant that helped support this study.

Stephen McMahon
Chairman, Irish Patients' Association

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1. 'The Need for Informed Consent in Off-Label Use in the EU,' *Regulatory Affairs*, November 2010.

2. Health Care Rights and Responsibilities: A Review of the European Charter of Patients' Rights. O'Mathuna, D, Scott, PA, McAuley, A., Walsh-Daneshmandi, A, Daly, B (*Irish Patients' Association*, Dublin, 2005). http://www.dcu.ie/nursing/downloads/executive_summary.pdf

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Main findings

... from this survey of 150 patient groups throughout Europe

(the groups have different specialities, and represent over 1 million European patients who should be contact with off-label medications)

69% of respondents say off-label prescribing remains an important component of the doctor's repertoire of treatment and care

Particularly true for patients who have only limited treatments available to them, for example in the treatment of rare cancers.

90% of respondent groups say that the patient has a right to informed consent when prescribed off-label medication

Although most patient groups support the practice of off-label prescribing, many also believe that patients should be fully informed about the fact that a prescription is off label. Not all patients are told that they have been prescribed an off-label drug.

Less than half—42%—of respondents say that patients are informed about potential side-effects of off-label medication when prescribed. 23% say that patients prescribed off-label medicines have reported side-effects.

Side-effects do occur among off-label medicines (as with medicines which are authorised for their indicated use). Most patients are not told about the potential for side-effects. In fact, patients only have limited awareness of the issues surrounding the use of off-label prescribing. The majority of patient groups do not believe that off-label prescribing should be undertaken for economic reasons (to save money for healthcare payers).

72% of respondent groups think robust, harmonised regulation of off-label medication is needed in their country; 65% at European level

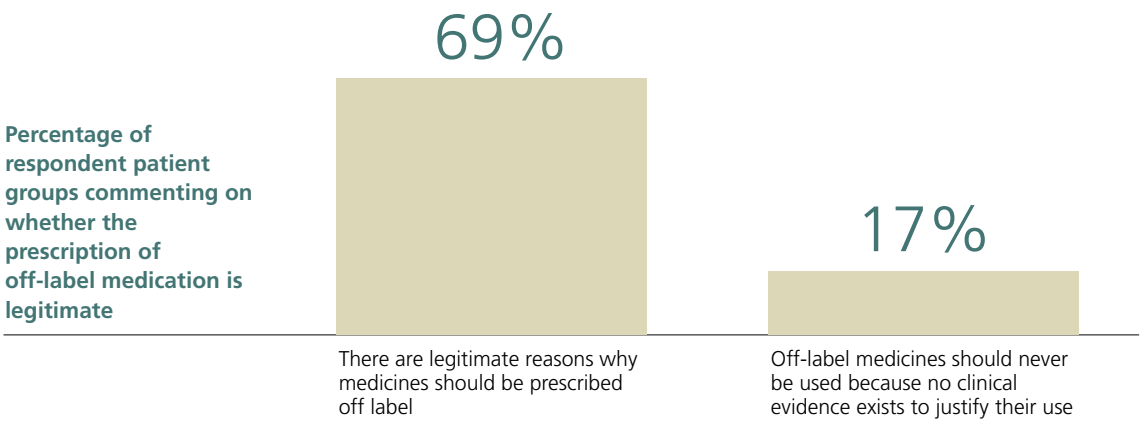
The clarity of standards and guidelines concerning the use of off-label prescribing varies from country to country across Europe. Regulations need to be more harmonious and robust. Patient groups call for healthcare (medical, medicine and pharmacy) regulators in their country (and Europe-wide) to make more effort to monitor the uptake and use of off-label medicines.

Note: for the purposes of this study, an off-label prescription is defined as a discretionary prescription by a doctor of an approved medicine for a use not indicated on the drug's label

Off-label prescribing is important to patients

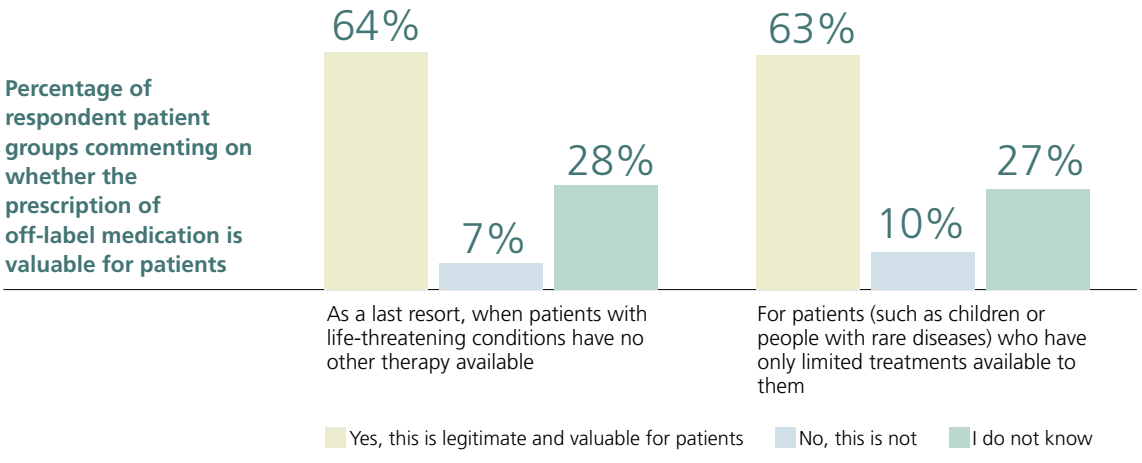
Off-label prescribing remains an important component of the doctor's repertoire of treatment and care

- *Over two thirds of patient groups across Europe believe that legitimate reasons exist for prescribing off label.*



Off-label prescribing remains an important option for patients who have limited treatments available to them

- *64% of patient groups across Europe believe that off-label prescription is valuable and legitimate when patients with life-threatening conditions have no other therapy available to them.*
- *63% of patient groups across Europe believe that off-label prescription is valuable and legitimate for patients (such as children, or people with rare diseases) who have only limited treatments available to them.*



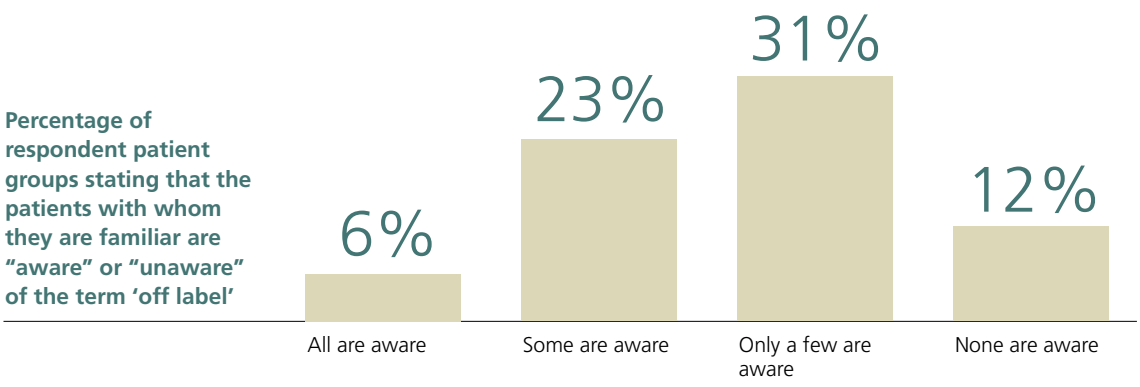
The right to informed consent

Although most patient groups support the practice of off-label prescribing, many also believe that patients should be fully informed when the process applies to them

- *90% of patient groups from across Europe say that patients should be fully informed when prescribed off-label medicines.*

But not all patients are told that they have been prescribed an off-label medicine

- *Only 29% of patient groups from across Europe believe "all, or some, patients are aware" of the term 'off-label' [or its equivalent in their country]; 31% say only "a few patients are aware"; 12% say none are aware.*
- *Only 41% of patient groups from across Europe say that patients are told when they have been prescribed a drug off label.*
- *Only 37% say that patients are told that the doctor is making a deliberate choice to prescribe a medicine off label (acting upon their own discretion).*



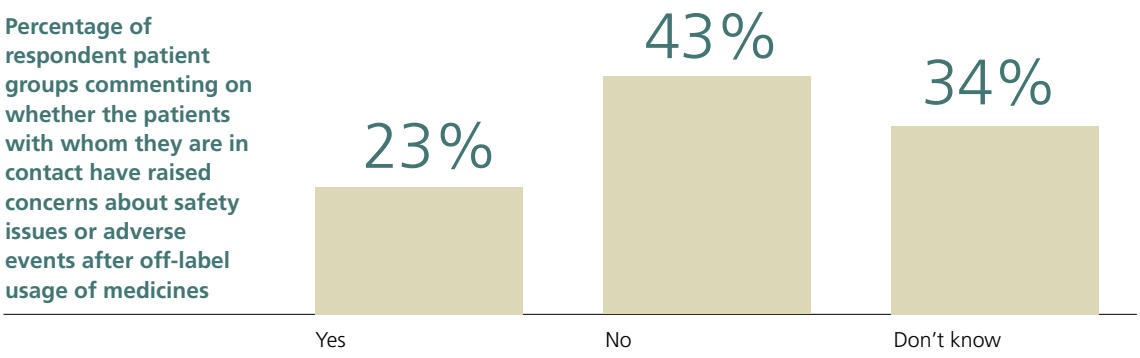
Alzheimer Portugal: *"Usually they [the patients] don't know [that a drug is off label] unless the doctor tells them, or if side effects happen."*

Patient safety must be safeguarded

Side-effects do occur among off-label medicines (as with medicines which have been authorised[1] for their indicated use)

- *23% of patient groups from across Europe say that the patients with whom they are familiar have raised concerns about safety issues or adverse events after taking off-label medicines.*

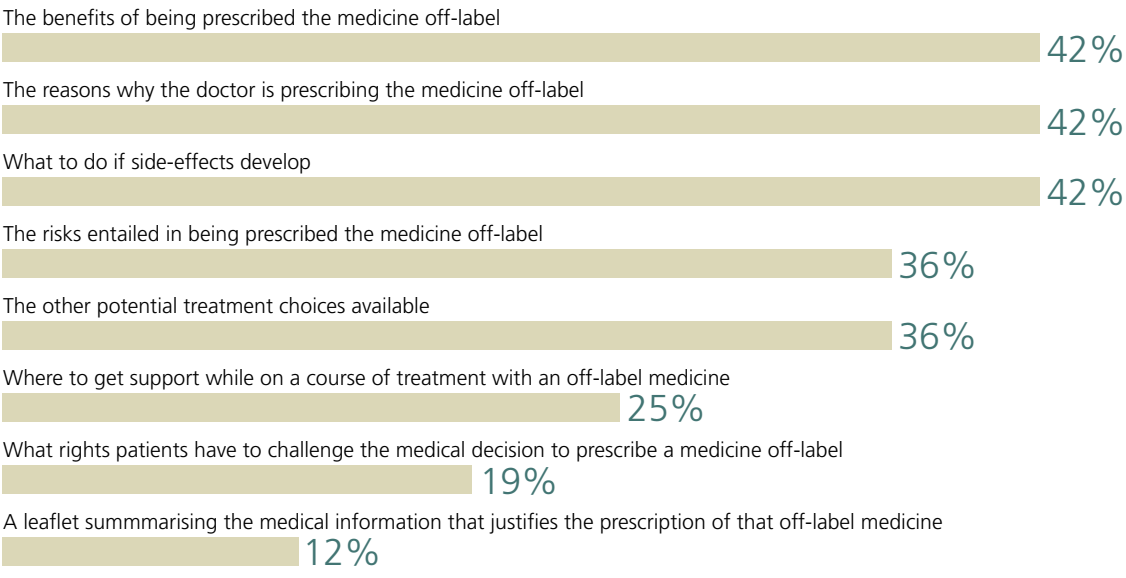
Percentage of respondent patient groups commenting on whether the patients with whom they are in contact have raised concerns about safety issues or adverse events after off-label usage of medicines



Patients only have limited awareness of the issues surrounding the use of off-label prescribing

- *Less than half of patient groups from across Europe say that patients are provided with valuable information on a range of issues related to the use of off-label medicines.*

Percentage of respondent patient groups saying that patients are provided with the following information when prescribed off-label medication



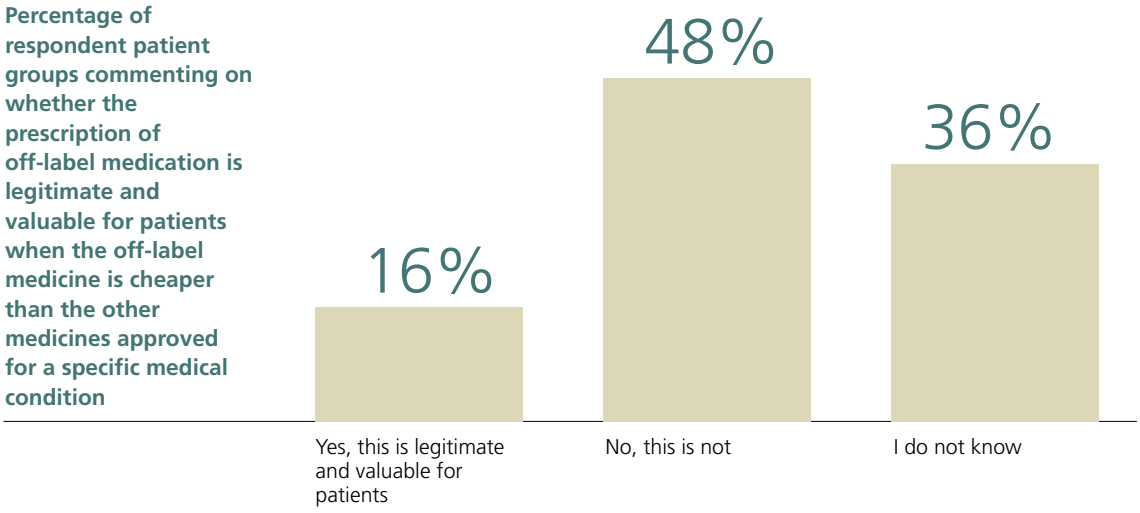
National Vereniging voor Fibromyalgie-Patienten F.E.S. (national fibromyalgia patient group from the Netherlands): *"The side effects of 'off-label' medicines are mentioned very frequently. Often, the patients receive several such medicines before finding one which is suitable."*

1 http://sideeffects.embl.de

Patient safety must be safeguarded

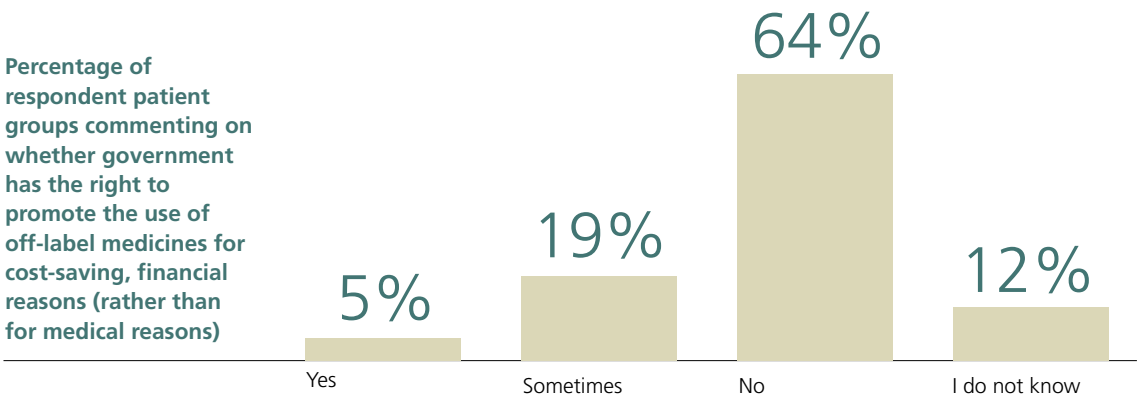
The majority of patient groups do not believe that off-label prescribing should be undertaken for economic reasons (to save money for healthcare payers)

- *Only 16% of patient groups from across Europe believe that off-label prescribing should be undertaken because the off-label medicine is cheaper than other medicines; 48% say that off-label prescribing for economic reasons should not happen (the rest do not know).*



Werk Groep Hersentumoren vzw (national brain cancer patient group from Belgium): *"C'est evident. C'est la raison pour laquelle l'information donne par le medecin doit etre complete. La decision ultime reside chez le patient bien informe." ["It's obvious. It is the reason why the information given by the doctor must be complete. The ultimate decision lies in the well-informed patient."]*

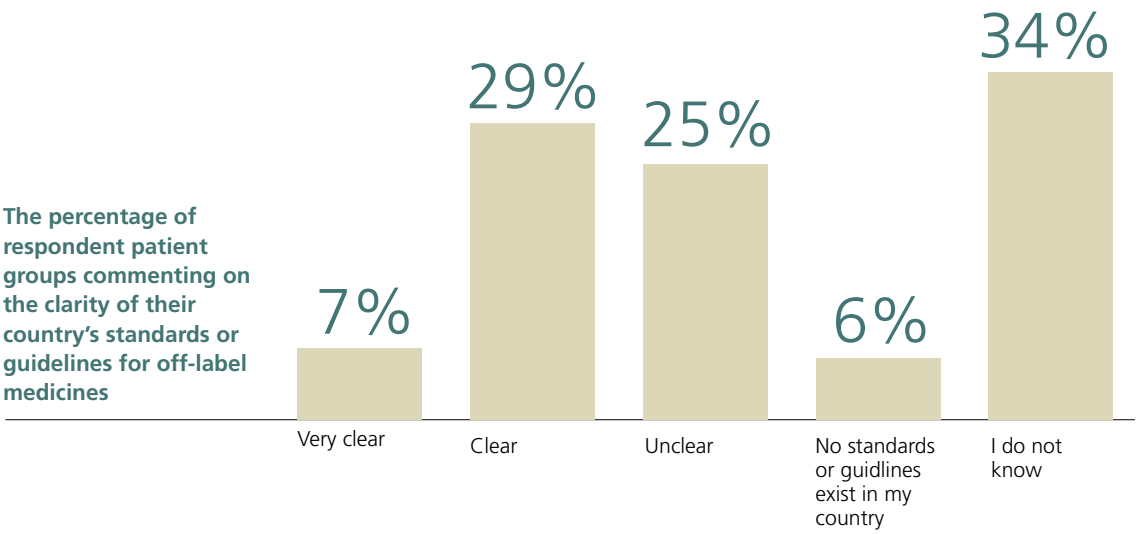
- *64% of patient groups from across Europe believe that governments should not advocate the use of off-label medicines for cost-saving, financial reasons (rather than for medical reasons).*



The need for robust regulation

Policing of the use of off-label prescribing varies from country to country in Europe

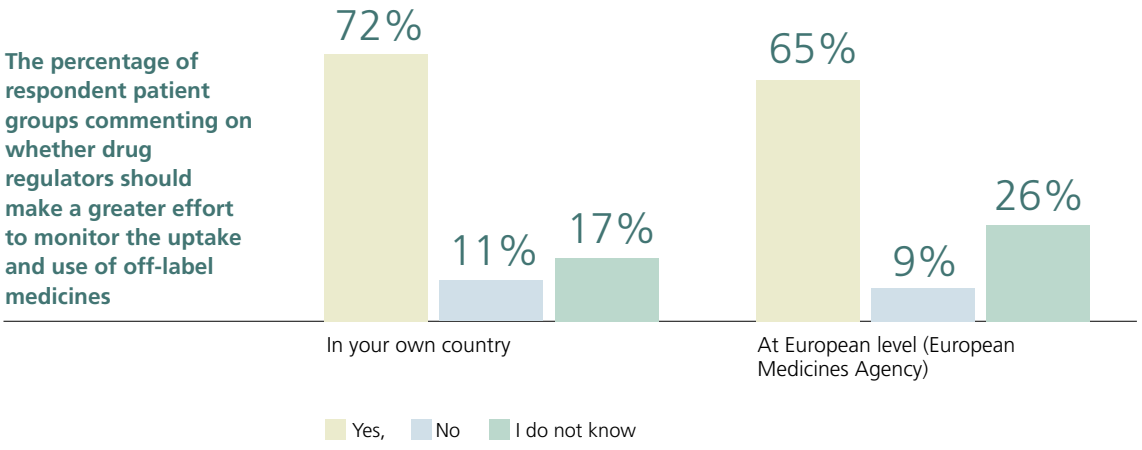
- *Only 36% of patient groups from across Europe think that standards or guidelines in their country governing the use of off-label medicines are "very clear" or "clear".*



Volwassenen, Kinderen en fwisselingsziekten *(VKS) (Dutch Society for Metabolic Diseases, a national patient group from the Netherlands focusing on inborn errors of metabolism): "Much off-label use will be under the radar to any authority. As long as the drug is paid back by the insurance, no authority has insight into the scale of off-label use, because prescriptions are not linked to diagnosis."*

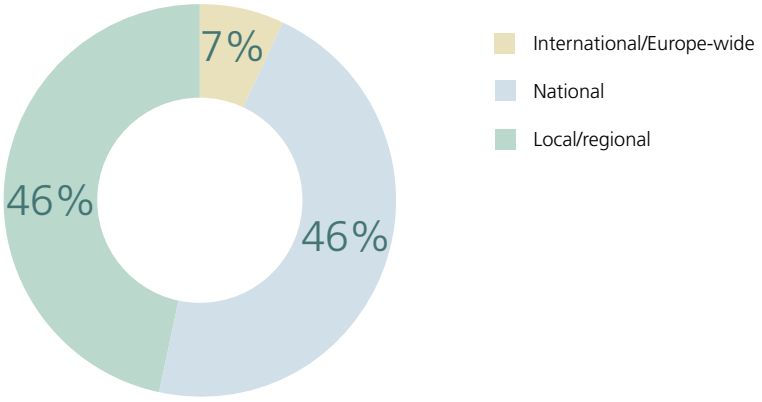
Patient groups call for drug regulators in their country (and Europe-wide) to make more effort to monitor the uptake and use of off-label medicines

- *72% of patient groups from across Europe think that drug regulators should make a greater effort to monitor the uptake and use of off-label medicines in their country.*
- *65% of the groups think that drug regulators should make a greater effort to monitor the uptake and use of off-label medicines at European level.*



Appendix: Profiles of the patient groups participating in this study

What is your organisation's main geographic remit?



In which country is your organisation based or headquartered?

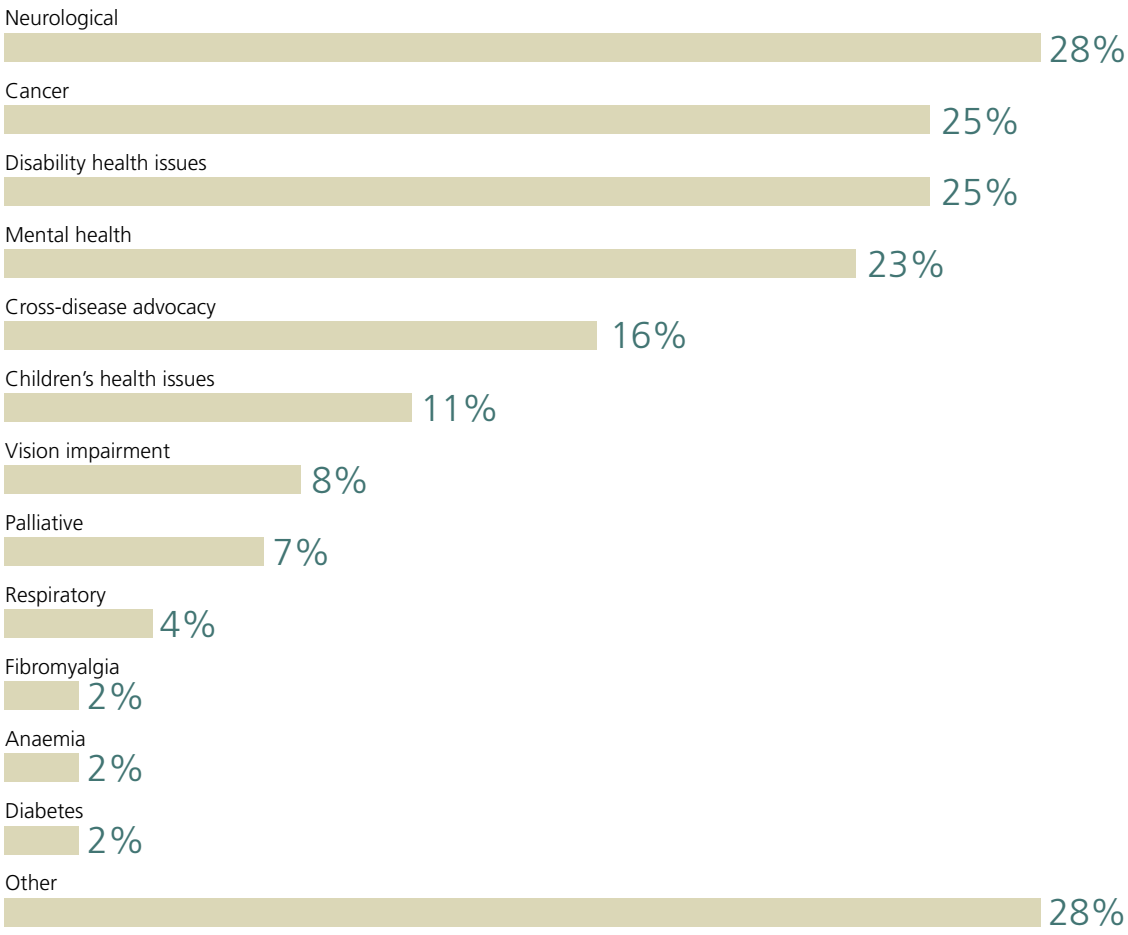
Respondent groups were headquartered in the following countries:

Austria. Belgium. Croatia. Denmark. Estonia. Finland. France. Germany. Greece. Hungary. Ireland. Italy. Lithuania. Malta. Netherlands. Norway. Poland. Portugal. Romania. Russia. Slovenia. Spain. Sweden. Switzerland. United Kingdom.

Volwassenen, Kinderen en fwisselingsziekten *(VKS) (Dutch Society for Metabolic Diseases, a national patient group from the Netherlands focusing on inborn errors of metabolism): "Much off-label use will be under the radar to any authority. As long as the drug is paid back by the insurance, no authority has insight into the scale of off-label use, because prescriptions are not linked to diagnosis."*

Appendix: Profiles of the patient groups participating in this study

What is the main specialty of your organisation?



Minimum number of patients represented by the respondent patient groups: 1,382, 820

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