How can patients and caregivers contribute to generate data on behavioural changes

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PRO-ACTIVE PHARMACOVIGILANCE

2010

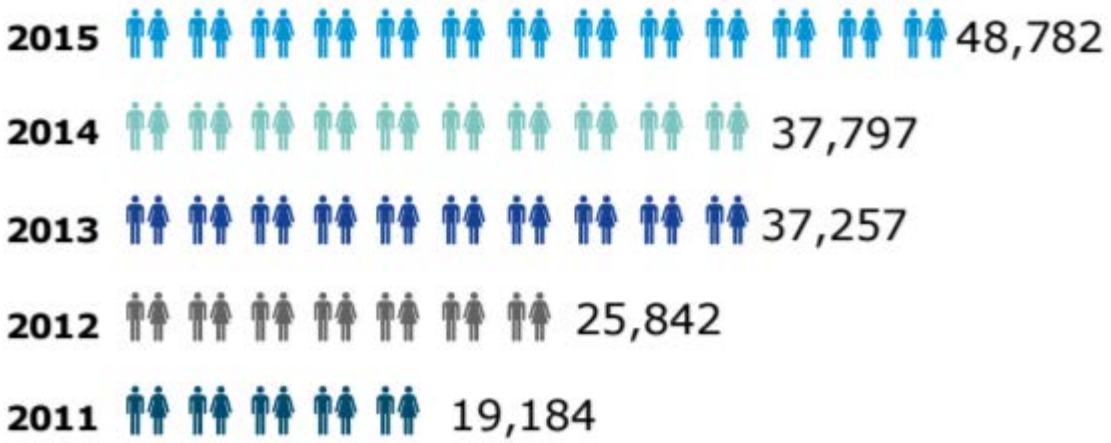
Regulation (EU) 1235/2010

2012

- Risk management plans mandatory for new medicines
- Post-authorisation safety and efficacy studies
- Additional monitoring of medicines
- Pharmacovigilance system master files
- Strengthened signal detection
- Implementation of the PRAC – strengthened referral procedures, public hearings
- Transparency – minutes, agendas, European medicines web portal

Right of patients to report suspected adverse effects

Spontaneous ADR reports from patients (2011-2015)



29% increase from 2014

Higher patient ADR reporting…

Source: EMA Annual report 2015

…with an added value

- Patients identify **new ADRs**
- **More detailed description** of ADRs
- Patients report the **severity and impact of ADRs on daily life**
- Patients **confirm or add new information**, complementing information from HCPs
- Compared to HCPs, patients report ADRs affecting different organ systems, especially **nervous system disorders**
- **Quality issues, medication errors**
- Patients help to identify **new safety signals**

Inácio P. et al. Br J Clin Pharmacol. 2016

Härmark, L. et al. Drug Saf. 2016 Oct;39(10):883-90

Strengthened signal detection

Patient reports have been key in identifying certain signals that would not otherwise have been identified and in the causality analysis of others. Examples include a signal of electric shock-like sensations associated with the use of selective serotonin reuptake inhibitors (SSRIs) and duloxetine [13–16], prolonged sexual dysfunction after discontinuation of SSRIs [17, 18], SSRIs and aggression [19, 20], thyroid dysregulation after packaging change of a levothyroxine preparation from a bottle to a blister [21, 23], vitamin B6 and polyneuropathy [22], amlodipine and interaction with grapefruit juice, donepezil and unusual dreams including nightmares, medroxyprogesterone and infertility, and fentanyl and product adhesion issues [23].

Härmark, L. et al. Drug Saf. 2016 Oct;39(10):883-90

Patients' knowledge of risks and risk minimisation measures

- Is safety information (educational materials, product information) **understandable** by patients?
- **Are patients' organisations aware** of risk minimisation measures/safety information for the products of their disease of interest?
- How to **effectively disseminate** this information?
- How **to ensure that patients follow** these safety recommendations?
- How **to evaluate the final impact** of following these safety recommendations?

Patients want better profiling of safety information, not only severity and frequency, but also:

-how long the ADR lasts
-better description of who is at risk – specific at-risk individuals

Where do patients look for medicines safety information?

Source	Enabler	Barrier
Internet "Dr Google"	Ease of use Fastest way of getting info	Difficulty filtering reliable content Risk of misinformation
Health care professionals	High knowledge on medicines **Physicians most trusted sources of medicines information***	Lack of time** Lack of trust** As a result → poor communication
Patient organisations/ fellow patients	Proximity Peer2peer health education	Lack of resources to make information available Lack of expertise

* Scope joint action WP6 Patients' and Consumers' Organisations Consultation

** Eurobarometer Qualitative Study on Patient Involvement

SCOPE Joint Action work package 6
Risk communication

Workshop in June 2016 - **Patient and Consumer Organisations Consultation**

- **HCPs most trusted source** of medicines information
- **Face to face discussion preferred** – Educational materials should encourage discussion between patient and HCP
- **Familiarity with educational materials is low** – publication in NCA websites
- **Targeted safety information** preferred where possible
- Need for enhanced **awareness of the regulatory system**
- **Transparency**

How can mobile technologies contribute?

- WEB-RADR – Recognising adverse drug reactions (IMI project)
- Mobile app for **HCP and patients to report ADRs**
- And to **receive targeted information** on medicines of interest for the user – watch list of medicines
- **Two-way communication**
- Recently a survey to HCPs and patients has been launched - Results will allow to improve mobile apps, to increase knowledge on this two-way communication and ADR reporting/reception of news and safety alerts
- 3 pilot apps launched in UK, Netherlands and Croatia

It will change the current behaviour on ADR reporting and obtaining safety information

How can patients generate data?

Rare Barometer Voices
A EURORDIS INITIATIVE

EURORDIS RARE BAROMETER PROGRAMME

How can patients change behaviours?

Engagement within their own patient organisations

- Survey the knowledge of their members regarding the use of their treatments (including off-label)
- Explain the importance and encourage ADR reporting – explain that safety data from CTs is limited and the importance of having real world data
- Explain the meaning of the black triangle
- Gather information on real use of medicines – **collaboration with regulators** to organise data collection on relevant safety issues

Ex: French regulatory authority call to patients' organisations for projects related with safe use of medicines, information and adverse drug reaction reporting

Engagement with regulators

National Competent Authorities	EMA
• Test online reporting tool in the country and feedback to NCA • Review useful ADR reports with NCA experts • Review and discuss risk communication channels in the country – do they work?	• As **members of the PRAC** • Participating in **public hearings** at the PRAC • Reviewing **Risk Management Plan summaries** for medicines of interest • Getting involved in **scientific advice** for **post-authorisation studies** – patient-relevant study designs • **Pre-authorisation advice on RMPs**

EUPATI European Patients' Academy

EURORDIS SUMMER SCHOOL ExPRESS Yourself!

- Capacity-building programmes for patient experts (and researchers - ExPRESS)
- Online training modules + face-to-face training courses
- Covering medicines R&D (drug discovery, pre-clinical and clinical development), Regulatory EU environment (scientific advice, benefit-risk assessment, marketing authorisation), Pharmacovigilance and Health Technology Assessment
- Benefit/risk and pharmacovigilance topics covered:
  - ✓ Benefit risk assessment and patient involvement in benefit-risk at EMA
  - ✓ The role of patient organisations in pharmacovigilance/role of all relevant stakeholders
  - ✓ Pharmacovigilance Risk Assessment Committee and public hearings
  - ✓ Risk communication
  - ✓ Signal detection and management

Patient engagement during valproate referral

1967 Epilepsy

Migraine prophylaxis in some EU member states

1995 Bipolar disorder

2009

Restricted indication BD manic episodes contraindication or intolerant to Li

Product information updated to reflect the risks of birth defects and developmental delay associated with valproate use during pregnancy.

2013

New risk identified

MHRA triggered a referral

Literature evidence of developmental disorders after in utero exposure

2014

Consultation with POs epilepsy, BD, migraine and representatives of patients and families affected by valproate

PRAC recommendation

CHMP/CMDh position

Consultation with patients organisations identifies risk communication problems

- ✓ **Information** about the risk of valproate use during pregnancy both in package leaflet and provided by HCPs was **limited and inconsistent** across the countries and across different products (e.g. reference and generics)
- ✓ There was a need for **targeted and appropriate information** to HCPs and patients
- ✓ Information for patients and parents should be **harmonised at European level** and should be the same regardless of the age of the patient, given from the first prescription, and **written in an age appropriate language.**
- ✓ **Use of different communication tools** – not only package leaflet
- ✓ Written **statement** highlighting the risks should be **signed off** by the female patients

PRAC recommendation

- PI amended
- DHCP issued
- RMMs – **A guide for prescribers, a patient booklet and acknowledgement of risk information form**
- Case-control study
- Drug utilisation study

Celecoxib and familial adenomatous polyposis

- FAP is characterised by the development of hundreds to thousands of colon polyps leading to colorectal cancer by age 40
- Onsenal (celecoxib) was granted **marketing authorisation under exceptional circumstances** in 2003 for polyp reduction in addition to surgery and endoscopic monitoring
- In 2011, the MAH decided to withdraw marketing authorisation due to inability to fulfil post-authorisation data requirements
- Since it was withdrawn from the market, no treatment was available for FAP – **potential off-label use** of other celecoxib-containing products
- **CHMP** reviewed the available evidence and concluded that **clinical efficacy not confirmed** in this indication and **additionally new cardiovascular risks identified** for cox-2 inhibitors
- FAP patients consulted during this review regarding the use of celecoxib who **confirmed that the use of celecoxib in this indication had declined due to perception of uncertain clinical benefit**

Conclusions

- Pharmacovigilance legislation – milestone for patients
- Spontaneous reporting by patients gives additional information on the impact of adverse drug reactions and leads to strengthened signal detection
- Mobile technologies are changing current behaviours - two way communication
- Patients' organisations can generate relevant data to measure impact
- Patient engagement can influence regulatory decisions regarding the safety of medicines