www.sciformix.com

sciformix
Trusted Services. Built on Science.

Patient Centricity In Pharmacovigilance:

New Directions, New Horizons

Background

The importance of Pharmacovigilance (PV) as a science and its role in effective patient care in clinical practice and public health is growing. Patient-centeredness and patient safety have emerged as core elements in today's interactive and responsive healthcare systems. As patients are taking more interest in their health and healthcare, they support the maxim of ''Nothing about me, without me'' and expect caregivers to engage in shared decision making, so that the patient voice is always included.

Patients usually report adverse drug reactions (ADRs) to their doctors which enables reporting to PV centers, however, since only 5% of doctors are estimated to participate in PV, traditional reporting mechanisms may not be sufficient in ensuring adequate safety reporting. Studies indicate that systems for direct recording of patient concerns may identify new drug safety signals earlier than the professional reporting systems alone[1]. This underlines the fact that the patients' role in actively reporting ADRs is key to building a better PV system.

Public health programs and responsible media coverage aimed at increasing access to drug information has led patients in many countries to take greater responsibility for their own health. This is reflected in the creation of patient charters, patients' bills of rights and patient advocacy groups. For e.g., patients with HIV/AIDS have been instrumental in creating international awareness of disease impact, improving access to therapies and communication of associated medication risks[2].

Patient centric innovation will be at the heart of the transformation of PV over the next couple of decades and this will likely forever change PV as we know it today. But are we really prepared to implement patient-centric approaches in PV? What steps are required to bring safety to patients, as opposed to bringing patient to safety?

This whitepaper examines the advantage of applying patient-centric approaches across the PV spectrum and how such approaches coupled with the recent advances in social media, internet and technology, herald the advent of a new era in safety reporting, analysis and risk communication with the "**Patient**" at the epicenter of all PV activities.

The Path To Implementing Patient-Centered PV

In Europe, the EU Directive 2010/84/EU (amending Directive 2001/83/EC on the community code relating to medicinal products for human use) and EU Regulation No. 1235/2010, provide recommendations for patient-centered implementation for PV. These recommendations developed by the European Patients' Forum (EPF) are intended to lead to a strong, open and transparent PV system that ensures the confidence of patients, health care professionals (HCPs) and regulators alike and represents a step forward for safety, high quality and patient-centered healthcare[3,4].

The Directive 2010/84/EU amends the definition of Adverse Drug Reaction to include medication errors and misuse as part of ADR reporting to help collect more information on the real life working of medicines, when used in different circumstances by different people.

Products, subject to additional monitoring (e.g. products with new active substances, biologics) need to be identified by a black symbol with a standard explanatory sentence on the packaging indicating that the medicine is under additional monitoring, what such monitoring means, the reasons behind it, without creating unwarranted alarm so patients do not stop their treatment unnecessarily. This transparency is paramount to ensure patients' trust in the functioning of the PV system.

The shift from pure safety analysis to benefit-risk evaluation and thereby the overall implementation approach for an effective patient-centric PV model is entrenched in four main steps; namely to educate, encourage, engage and enable patients, as outlined in figure 1.

Figure 1: Implementation Model for Patient-Centric Pharmacovigilance

Educate Seamlessly and Encourage Closely

One of the key approaches in patient-centric PV is raising patient awareness regarding the importance of reporting ADRs and continuously highlighting the critical role they can play in PV from AE reporting through risk communication.

Targeted educational initiatives include training programs that directly train consumers and patients regarding AE reporting systems, as well as train investigator site teams, patient organizations and HCPs. Dissemination of product safety summaries, benefit-risk data and risk management plan summaries for public consumption on a real-time basis through company websites, national web portals and patient information centers is important in spreading awareness. This would go a long way to educate and encourage "direct patient reporting" and maximize involvement of patients and patient organizations in the PV process.

Medical concepts need to be comprehensively communicated in an understandable and accessible format to patients. Involvement of patient organizations as experts for the development of safety information as well as for the set-up and development of national web-portals on medicines is critical.

The growing commercial relevance of emerging markets coupled with lower levels of patient awareness in these regions poses a specific challenge and would likely limit the success of patient-centric measures in a global PV environment. In this context, involving HCPs like pharmacists, nurses or physicians builds upon existing relationships between providers and patients and helps activate their patients to participate in safety reporting activities. Reported information can be acted upon by the HCP or reported to other HCPs, as appropriate and it provides a mechanism for providers to report complementary clinical information or enable linkage to a medical record.

Measures like direct appreciation and recognition of contributions of clinical trial subjects and patients to report AEs both online and through other face-to-face channels would be useful, including the provision of incentives (non-monetary) to patients and consumers to encourage ADR reporting.

Engage Purposefully and Enable Proactively

ADRs are estimated as the fifth largest cause of deaths in hospital[4], yet only around 10% to 25% of all ADRs are reported. Underreporting of ADRs is a serious issue, which undermines the evaluation of safety of medicines. Direct patient participation in reporting drug related problems can increase the efficiency of the PV system and compensate for some of the shortcomings of systems based on reports from HCPs only[5].

The Directive 2010/84/EU [Article 102] proposes guidance encouraging direct patient reporting, via appropriate measures including web based formats and alternative formats [Article 102(b)], to encourage patients and HCPs to report suspected ADRs to the national competent authorities (NCA).

Studies show that patient reports are more valuable compared to HCP reports as patients often give more detailed descriptions, including specific circumstances in which the reaction occurred. Patients often report earlier and perceive the impact and severity of reactions differently[6]. The patient-HCP relationship would remain central, yet patients may have difficulty in reporting through HCPs in certain situations e.g. if ADR is of intimate nature, or if it results from an error. In certain situations, like ADRs resulting from prescribing errors or off-label use of medications and ADRs of intimate nature, HCPs may be reluctant to report. Direct reporting would enable the collection of these crucial safety data to ensure better medication safety.

Patient-reported outcomes (PROs) are data elements directly reported by patients or their surrogates about experiences with care, including symptoms, functional status, or quality of life[7]. The Patient-Reported Outcomes Safety Event Reporting (PROSPER) Consortium has put forth guidance for improved safety reporting by better incorporation of the patient's perspective. This consortium comprises of industry, regulatory authority, academic, private sector and patient representatives interested in the area of patient reported outcomes of adverse events (PRO-AEs). The guidance aims to ensure that the patient 'voice' and perspective feed appropriately into collection of safety data, so that the safety profile and hence benefit-risk balance of new and existing medicines is better defined[8].

Active involvement of patients and the public in AE reporting is possible by the use of effective and patient-friendly reporting systems, channels and processes (both technology independent and driven). This can be achieved by designing and deploying simple and easy-to-use ADR reporting tools and processes e.g. simpler and easy to access ADR reporting forms for patients (online and through local chemists/pharmacies), mobile applications, designating a simple, common 3-digit call-in number for reporting ADRs, etc.

Further, patient involvement in set-up and user-testing of the reporting systems ensures the system is fit-for-purpose and user-friendly. Developing guidelines for the follow-up procedure for reports in consultation with patients' and HCP organizations enables collection of high-quality data, conveys feedback to patients on how the information will be used and provides patients with further information or where information is available (e.g. the publicly-accessible part of the EudraVigilance database[3]).

Engaging patients as partners in the data collection enterprise would enable systematic collection of information and provide a more comprehensive picture within a population. This can be achieved in limited populations via patient registries, or in a wider population using existing infrastructure to engage patients e.g. community pharmacies and pharmacists[9].

Additional patient-centred PV initiatives include real-time monitoring of clinical trial safety data with targeted back-up data collection methods to reduce missing data for non-compliant patients (e.g. electronic reminders, email, telephone or a human call). Collection of patient reports via approaches linked to electronic health records, clinical practice records and pharmacy registries within national health systems (containing confirmed patient-level health and treatment information) would provide the ability to link validated patient information (around diagnosis, co-morbidities, allergies and other treatments) for analysis of aggregated safety data, and help better understand the etiology of rare reactions and possible correlation of patient-related genomic data with specific safety issues[10].

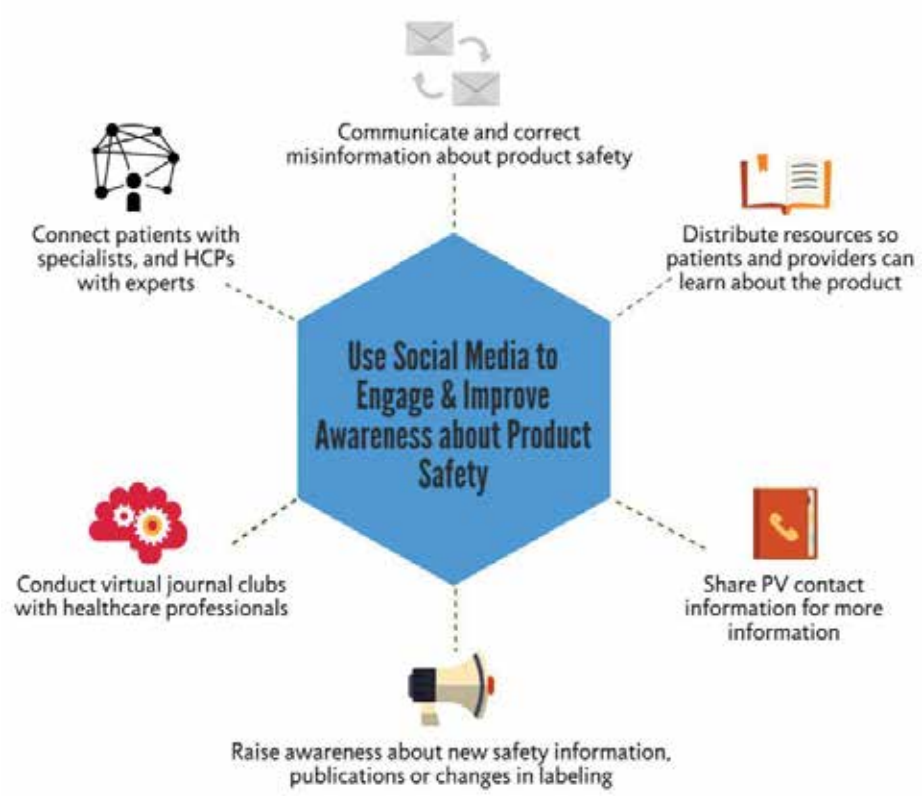
Social media offers another novel channel for driving patient-centric PV. Most social media activities for PV by companies are focused on screening of social media sites to ensure adequate safety reporting. Easy, convenient reporting of AEs via simple patient-friendly mobile applications (deployed on mobiles, smartphones), monitoring of company-managed websites, health forums and monitoring of safety data reported on social media sites like Facebook, Twitter are useful in this context[11].

High-quality information empowers patients to play their role in the PV system, for better patient safety and high quality of care[5, 6]. EU Directive 2010/84/EU [Chapter 2 of title IX] contains crucial provisions from the patients' perspective concerning transparency and communication regarding medicines and PV via established national medicines web-portals. Article 21 and 106, 2010/84/EU lists information that NCAs should make publicly available through national web portals. This includes marketing authorization, package leaflet, summary of product characteristics and additional information like assessment reports for marketing authorization, summaries of risk management plans, list of medicinal products subject to additional monitoring and information on different ways of reporting ADRs to the NCA by HCPs and patients.

Patient engagement in the PV process can be considered truly complete only when the patients and the public are involved in the risk management and

communication process. The industry, regulators and HCPs must build public trust through effective risk communication by proactively publishing required safety information per EU guidance. Involvement of patients and patient organizations in testing of patient information leaflets and other safety information prior to release per mandatory (readability) user testing of Patient Information Leaflets in the EU and use of US FDA's new Physician' Labeling Rule (PLR) format for display of important risk information for patients would help. Social media can also serve as an effective digital tool for risk management and communication for PV teams within companies to directly connect and engage with patients, consumers and HCPs to improve awareness about product safety, leading to improved health literacy amongst consumers and patients[12].

Figure 2: Using social media to engage patients and improve awareness about product safety



Another recommendation [Section 4, Chapter 3 of the Pharmacovigilance title [Article 107i to k] requires Member States to involve and consult patient organizations and HCPs as appropriate to provide the right messages, advice in case of urgent safety measures such as suspensions or recalls and employ appropriate temporary measures[3, 4].

Today, patients in the US depend on prescription and over-the-counter (OTC) medications to sustain their health, with 3 billion prescriptions written annually. The Institute of Medicine (IOM) estimates that at least 1.5 million preventable ADRs, including medication misuse occur within the healthcare system each year[12, 13]. The goal of the US FDA Safe Use Initiative is to create and

facilitate public and private collaborations within the health care community to reduce preventable harm by identifying specific, preventable medication risks and developing, implementing and evaluating cross-sector interventions with partners who are committed to safe medication use[15].

The label is the patient's best and often only, source of information. It is the safety net to prevent medication errors. While written information and oral consultations may sometimes be available, the Rx container label must be able to fulfill the professional obligations of physicians and pharmacists to give the patient all the information needed to understand how to safely use the medication. The recommendations made by the U.S. Pharmacopeia Health Literacy and Prescription Container Labeling Advisory Panel in November 2009[14] outline multiple patient-centric labeling measures to reduce preventable adverse events, including to organize the prescription label in a patient-centered manner, simplify label language, use explicit text to describe dosage/interval instructions, include purpose for use on label, improve label readability, provide labeling in patient's preferred language, include supplemental information on label and standardize directions to patients on label.

Future Outlook

The patient perspective is an essential component of the drug safety monitoring and risk communication process. PV organizations that incorporate the patients' "voice" in PV systems and processes would be better positioned over the long term to ensure patient safety and add real value back to the patients by enhancing product benefit-risk profiles. Overall, adopting a patient-centric approach and partnering with patients and public for reporting, analysis and communication of safety data seems to be the way forward.

At the same time, it is critical to remember that patient centricity is more about listening, communicating and disseminating to the patients, to ultimately empower them to participate in the decision-making process and not about putting the decision-making solely in their hands. The public has increasingly influenced HCP prescribing and patterns of drug use in recent years due to increased reach of the media and internet. Further, direct advertising to consumers of prescription medicines has become commonplace in many countries. With this information, patients feel more empowered to make their own therapeutic decisions, without assistance from HCPs, resulting in increasing self-medication, over-prescribing by doctors on patients' demand and misuse of medications[15, 16].

Variations in the way medicines are used can potentially alter their safety profiles and this needs to be investigated further. Further, it needs to be determined how access to drug information can influence patient safety, including patients' perception of safety and the level of harm patients are prepared to accept for different medicines. The outcome of such research would make possible a better formulation of policies within the evolving patient-centric models with a view to reducing patient risk[17].

References

1. Egberts GPG, Smulderes M, De Konig FHP et al. Can adverse drug reactions be detected earlier?: a comparison of reports by patients and professionals. British Medical Journal 1996; 313: 530- 31.
2. De Vries CS, Duggan CA, Tromp TFJ, de Jong-van den Berg LTW. Changing prescribing in the light of tolerability concerns: How is this best achieved? Drug Safety 1999 Sep; 21(3): 153-160.
3. EPF Guidance on Pharmacovigilance. April 2012. http://www.eu-patient.eu/globalassets/policy/pharmaceuticalpackage/pharmacovigilance-recommendations-for-patient-centred-implementation.pdf. Accessed Jun 28, 2015.
4. Source: European Commission.
5. http://ec.europa.eu/health/files/pharmacovigilance/qa_pharmacovigilance_2011_en.pdf 3
6. Becomes 5 Consumer reporting of ADRs. WHO Drug Information 2000; 14: 211-215.
   Lloyd AJ. The extent of patients' understanding of the risk of treatments. Quality in Health Care 2001; 10 Supplement
7. 1:14-8. 37.
   Basch E. New frontiers in patient-reported outcomes: adverse event reporting, comparative effectiveness and quality
8. assessment. Annual Review of Medicine. Nov 20, 2014; 65:307-17.
   Anjan K. Banerjee, Sally Okun, I. Ralph Edwards et al. Drug Safety (2013) 36:1129–114. Patient-Reported Outcome
9. Measures in Safety Event Reporting: PROSPER Consortium Guidance.
   Leone R, Moretti U, D'Incau P, et al. Effect of pharmacist involvement on patient reporting of adverse drug reactions:
10. first Italian study. Drug Safety 2013 Apr; 36(4):267-76.
    Ethan Basch. Systematic Collection of Patient-Reported Adverse Drug Reactions: A Path to Patient-Centred
11. Pharmacovigilance. Drug Safety 2013 April; 36(4): 277–278.
    Supriya Desai. Social Media for Drug Safety: Navigating the Evolving, Complex Global Regulatory Ecosystem. PharmaAsia. 14 August 2015.
    http://www.pharmaasia.com/article/social-media-for-drug-safety-navigating-the-evolving-complex-global-regulatory-ec
12. osystem/11921
13. Institute of Medicine of the National Academies, Preventing Medication Errors, National Academies Press, 2007, p 124.
14. http://www.fda.gov/Drugs/DrugSafety/ucm188760.htm
15. http://www.iom.edu/Reports/2010/The-Safe-Use-Initiative-and-Health-Literacy-A-Workshop.aspx
    Schwartz RK, Soumerai SB, Avorn J. Physician motivation for non-scientific drug prescribing. Social Science and
16. Medicine 1997; 44(4): 541-8.
    Sachs L, Tomson G. Medicines and culture- a double perspective on drug utilization in a developing country. Social
17. Science and Medicine 1992; 34 (3): 307-315.
    De Vries CS, Duggan CA, Tromp TFJ, de Jong-van den Berg LTW. Changing prescribing in the light of tolerability concerns: How is this best achieved? Drug Safety 1999 Sep; 21(3): 153-160.

Sciformix Corporation
1500 West Park Drive, Suite 210
Westborough, MA 01581 USA
Phone : 1 (877) 576-5005
Fax : 1 (508) 302-6520
Email : bizteam@sciformix.com

www.sciformix.com

USA | UK | India | Philippines

Sciformix Corporation is a global scientific process organization (SPO) that partners with life science companies to develop, launch and sustain medical products that aim to improve the quality of healthcare worldwide.

We collaborate with our clients through the entire product development lifecycle to provide a full range of services from study design to post marketing surveillance and commercialization support.