

Patient Support Program in Pharmacovigilance: Foster Patient Confidence and Compliance

Atul Khurana, Rajul Rastogi, Hans-Joachim Gamperl

Abstract—The pharmaceutical companies are getting more inclined towards patient support programs (PSPs) which assist patients and/or healthcare professionals (HCPs) in more desirable disease management and cost-effective treatment. The utmost objective of these programs is patient care. The PSPs may include financial assistance to patients, medicine compliance programs, access to HCPs via phone or online chat centers, etc. The PSP has a crucial role in terms of customer acquisition and retention strategies. During the conduct of these programs, Marketing Authorisation Holder (MAH) may receive information related to concerned medicinal products, which is usually reported by patients or involved HCPs. This information may include suspected adverse reaction(s) during/after administration of medicinal products. Hence, the MAH should design PSP to comply with regulatory reporting requirements and avoid non-compliance during PV inspection. The emergence of wireless health devices is lowering the burden on patients to manually incorporate safety data, and building a significant option for patients to observe major swings in reference to drug safety. Therefore, to enhance the adoption of these programs, MAH not only needs to aware patients about advantages of the program, but also recognizes the importance of time of patients and commitments made in a constructive manner. It is indispensable that strengthening the public health is considered as the topmost priority in such programs, and the MAH is compliant to Pharmacovigilance (PV) requirements along with regulatory obligations.

Keywords—Drug safety, good pharmacovigilance practice, patient support program, pharmacovigilance.

I. INTRODUCTION

THE healthcare domain always remains in evolving state, and patient support vision is becoming progressively supreme. PSPs provide a great opportunity to brief patients about their medical conditions. These productive programs brace patients from disease diagnosis through treatment course and finally to outgrowths that can create a huge difference in patient's health conditions. The common examples include nursing services, call centers and interaction with HCPs. The systematic recording of data can make it feasible to scan drug therapy in a beneficial manner, and various proactive measures can be taken to preclude inappropriate termination of drug therapy. There are numerous elements which need to be considered while designing a PSP. The MAHs face

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obstacles while planning of PSP like encounter global requirements along with harmonisation of national amenities in every country. The recent advancements in PSPs include central and reliable data management system for documentation of safety data worldwide, which is very crucial for a successful PSP.

II. PATIENT SUPPORT PROGRAM

The lack of adherence of patients to prescribed medicines is a huge challenge to pharmaceutical industry worldwide. Therefore, bridging this gap of adherence is utmost necessity for MAHs to preserve their brand value and sale loss. A PSP is assistance for patient or interaction with patient carers outlined to aid in management of medication and disease outcomes. It also involves interaction with HCPs for support to the patients. Over the past few years, more MAHs are maximizing the funds towards PSPs. The concept of PSPs is not new nowadays, and advancement of technology has resulted in budding value of these programs. The various examples of PSPs [1] are described in Table I.

TABLE I
EXAMPLES OF PSPS

Topic	Description
Medication compliance programs	Interaction with patients/carers with respect to managing of medication
Call/Chat centers	Patients contacting the MAH/third part contractors to acquire information pertaining to medication advice or disease management
Nurse Educator programs	Nurses hired by MAH to directly help patients in administration of drug or managing disease outcomes
Financial support programs	Financial support to patients including assistance in medical reimbursement, insurance coverage and discount options
Internet programs	Patients sharing experiences and information material related to medication/disease can be downloaded

III. GUIDANCE AND REGULATIONS

A. European Union

The Good Vigilance Practices (GVP) - Module VI Management and reporting of adverse reactions to medicinal products, includes legal obligations for MAHs for collection, processing, and reporting of suspected adverse reactions linked with medicinal products, which are approved in European Union (EU). The module also includes essential elements for MAHs concerning handling and reporting of safety data arising from PSPs. The serious and non-serious cases of suspected adverse reactions derived from the programs must be reported as solicited reports by MAHs [2].

B. United States

In accordance with United States Food and Drug Administration (USFDA), as a part of post-marketing safety reporting, information related to adverse experiences originated from planned contracts and solicited source (e.g., company sponsored PSPs, disease management programs) should be managed as safety information derived from a post-marketing safety study. The MAHs are exempted to submit individual case safety reports (ICSRs) originated from these programs except if the adverse event (AE) is serious and unexpected and there is reasonable relationship between drug and adverse experience [3].

IV. ELEMENTS OF PATIENT SUPPORT PROGRAM

The MAHs are extending the focus to improve patient's adherence to prescription medicine with the help of PSPs. In actual fact, investment in PSPs has increased in recent years and it is moved by following factors:

- enhanced involvement of patients in health-related decisions
- prominence on disease outcome
- increased patent expiry of drugs
- growth of targeted drug therapies that needs additional support to patient

The capability of patients to follow the medication course is often deviated because of several reasons. The factors related to patient non-adherence [4] are depicted in Fig. 1.

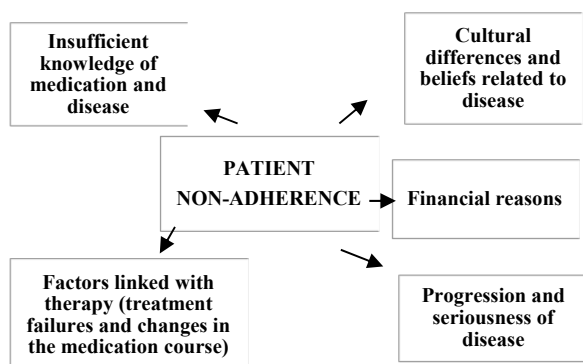


Fig. 1 Factors related to Patient Non-adherence

The PSP should align with the patient's requirements, distinguishing gaps in present competitive environment, and taking into consideration the regulatory obligations. For a PSP to be successful, the MAH should include following factors during designing of PSP [5]:

- The best programs involve direct conversations with patients to reveal personal hindrances like - social, physical, and economic.
- The concerned persons of MAH should use formal language within the regulations of content. The message should be simply understandable during the whole program.
- Make sure that the message delivered is useful and aids every patient complete care throughout the program.

The finest PSPs impart number of services that delivers the needs of patients, carers and concerned HCPs. The MAHs must consider following factors for investing in a PSP for a particular brand [5]:

- Small size of population affected with disease denotes that patients have big discrete value for brand, demanding increased support programs.
- Disease which is asymptomatic is likely to have more patient support, as it is difficult to understand whether medication is effective.
- Disease influence on patient's quality of life is linked with lifestyle, emotional, or social support.

V. PV ASPECTS FOR PSP DOCUMENTATION

The documented procedures for PSP must include the way to achieve all objectives and responsibilities of all stakeholders should be clearly defined. These written documents will play a crucial role in authority inspection as a confirmation that safety data obligations have been suitably achieved.

The MAH should ensure that the recommended design and implementation of a PSP is completely documented and authorized by pharmacovigilance (PV) and other related stakeholders like medical, sales, business strategists and market research. Following are the relevant PV aspects for PSP documentation [1]:

A. Objective

Need for PSP by focusing at potential welfare of every players involved like patients/carers and HCPs.

B. Design of PSP

The PSP should be designed after coordination with concerned stakeholders like medical, sales, business strategists and market research. The design plays a pivotal role in the success of PSP and it is crucial to consider all obstacles that may affect the course of PSP.

C. PSP Details

It should include the workflow of PSP and the factors influencing the same.

- The time duration for PSP operation should be outlined along with schedule for direct interaction with patients like visits to home, call centre service, website help etc.
- The process of registration of patients should be described including the procedure for gathering the follow-up information.
- There should be clear documentation for process of reporting of AEs by patients/carers, HCPs and other safety data like medication error, off label use, pregnancy, overdose, etc.
- It should also include particulars for registration forms, prescribing information, etc. which are to be shared with the patient.

D. Data Management

PSP should include the provisions like database for safety data management.

E. Data Security

As the data originating from PSPs are probably sensitive, so there should be suitable provisions for data security.

VI. HANDLING OF SAFETY DATA

In order to safeguard patient safety, the MAH should ensure that the safety data from PSP must be in line with the PV obligations. As there is a direct interaction with patients/carers, it is most likely that AEs or product quality complaints may be obtained, and it is compulsory to collect AEs while conducting PSP.

In accordance with the GVP Module VI, management and reporting of adverse reactions to medicinal products [2]:

- Safety reports arising from the PSPs should be handled as solicited reports.
- Serious, non-serious cases of suspected adverse reactions emerging in these programs should be reported as solicited reports by MAHs.

In case of safety data from PSPs, the MAHs should have the similar procedures to assess and evaluate this safety data, as it is performed for other solicited reports. For valid ICSRs, there should be proper medical assessment and reporting [5].

Both solicited and spontaneous reports may be originated during PSPs. The MAH should have internal procedures to ensure proper collection and classification of safety data, in order to comply with regulatory obligations.

The reported AEs must be directed to the PV department of MAH within the defined timelines. For obtaining the follow-up information of safety reports, the MAH should employ attentiveness and they should also ensure the causal relationship between drug and reported AE. In case of no causality information available from patients or HCPs, the MAH should perform its judgement as per the available information to decide the validity and reportability of ICSR. All the conventions should be included in company's documented procedures [6].

VII. RESPONSIBILITIES OF MAH

The PSPs are often endowed with both proactive and reactive aspects. A PSP may comprise of proactive aspects if the MAH begins communication with patient, and there may be reactive aspects in case of patients communicating with MAH. The responsibilities of MAH include training, collaboration with vendor, etc. Fig. 2 represents the conventional Program Workflow.

A. Training

The concerned persons involved in a PSP must be trained on product information and AE collection to make sure that AE reporting is performed within the defined timelines to MAH. There should be proper training records for the same to avoid non-compliance during authority inspection [1].

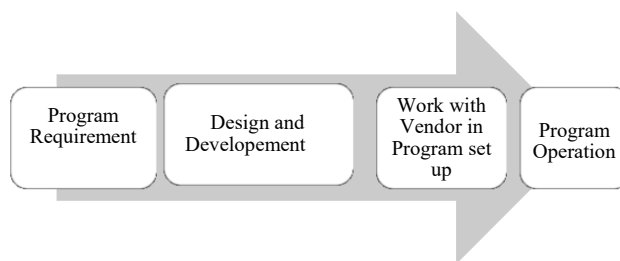


Fig. 2 Conventional Program Workflow

B. Third Party Contractors

In the case where the MAH hires third party contractors for running the PSP, there should be vendor evaluation (for e.g. questionnaire) to determine whether it is endowed with required potential, procedures and capable personnel for conducting the program. The MAH should make certain that patient safety is not compromised, PV obligations are met, and vendor staff is appropriately trained before and throughout the running of PSP [5].

After successful evaluation of vendor, a service agreement should be finalized with the MAH, which must include the objective of PSP, duration, data management, data security and business continuity plans. The agreements must include [1]:

- process for forwarding AE reports, including company's internal timelines;
- procedure for data reconciliation to make sure that all AE reports were identified at vendor's end and were reported to MAH;
- rights for MAH to monitor and conduct audit (risk based) throughout program;
- necessity of training of AE reporting before conduct of PSP and training of vendor personnel;
- provisions of communication channel with the contact persons of MAH and vendor along with procedure for issue escalation.

During AE reporting, it is significant to note Day 0, as it is critical for expedited reporting, which is the date when vendor personnel becomes aware of AE and not the date when it is reported to MAH.

C. Other Responsibilities

- The PV department of MAH plays a crucial role in approval of PSP initiative, beyond all local regions and countries, to ensure that identification of AEs is appropriately handled.
- Other departments like marketing, medical affairs and market research should be watchful regarding the risks, PV costs and authority expectations emerging from these programs.
- There should be audits from Quality Assurance (QA) to ensure compliance of procedures related to PSP.
- The reported AEs from PSPs must be included under process of signal detection with specific set of data and preferably assessed as different group instead of inclusion with bulk of AEs reported from other sources during routine PV activities. The non-serious solicited reports

can also include relevant safety information and hence during signal detection, both serious and non-serious reports must be assessed by MAH.

- There should be provisions from end of MAH for vendor personnel to receive significant updates on safety profile of product like changes in risk management plan, and the concerned vendor personnel should be appropriately trained on the same.
- The way how MAH is in compliance to the activities of PSP must be a section of inspection readiness program

VIII. INSPECTION FINDINGS

The Medicines and Healthcare products Regulatory Agency (MHRA) identified large number of uninvestigated AE reports in early 2012 through a PV inspection of a big pharmaceutical company. These reports were collected from a company sponsored PSP. The succeeding examination by the European Medicines Agency (EMA) observed that the said AEs had no impact on the benefit-risk assessment of the concerned products [7].

However, in similar situations, there can be penalties up to 5% of MAHs revenue of preceding year and in cases of further non-compliance, a continuing recurrent fine up to 2.5% of daily earnings until the MAH ensures compliance [8].

Following are some common findings during authority inspection concerning PSPs [9]:

- Lack of collection and reporting of AEs from PSP;
- Unawareness of PV department and Qualified Person for Pharmacovigilance (QPPV) in reference to PSPs conducted by business partners;
- Absence or inappropriate agreements with third party contractors concerning collection of all AEs including reports from special situation (pregnancy, medication error, etc.);
- Lack of training to third party contractors conducting the PSPs;
- Deficit of reconciliation process;
- MAH failure of monitoring and audit of vendor running the PSP.

IX. CONCLUSION

Due to advancements in healthcare industry, nowadays, the patients have approached to more information, which can be profuse and also empowering. If patients are aware of the processes to steer healthcare services, understanding of the rationale behind specific treatment, adherence to treatment course and disease management, then it can make a big difference to patient's expedition. The patients require persistent inspiration and support for adherence to supervision plan, especially in cases of management of chronic disease.

The designing and implementing of a cost-effective PSP can be demanding, especially in complex healthcare systems which may be self-funded or financially supported by insurance, taxation and multiple similar perspectives. Besides the dissimilarities beyond markets, the endmost objective should be healthier patient outcomes with the help of

productive patient support. The PSP is an indispensable characteristic of brand strategy and sometimes these programs are outsourced to third party contractors. So, the contractors should be involved in marketing strategy and safeguard that information gathered by both parties is interchanged. This information must be used to maximize advantage for well being of involved stakeholders in PSPs. The MAH can also use PSPs to expand market ingress efforts.

The most important PV aspect in a PSP is collecting all identified AEs, which should be expeditiously recorded, assessed, and reported in order to ensure authority obligations. It is very crucial to include process of identifying any safety signal from PSPs, which is somehow demanding but should be definitely present in the process of signal detection. Therefore, PV department has an influential role in analyzing all PSP initiatives to make certain that authority expectations are persistently met.

It is very crucial to regularly assess the performance metrics of PSP along with continuing adaptation of its design in accordance with feedback or requirements of the involved stakeholders. The MAH should evaluate if a specific PSP meets the ever-changing needs to concerned stakeholders in comparison to the changing orientation of company's brand in the market. For successful PSPs, the MAHs can employ automated systems including the analytic reporting for optimizing the performance of every PSP. However, the main objectives of PSP should always be improvement of quality of life of patients with best possible care and strengthen product confidence.

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