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An inspector's perspective – considerations for patient support and reimbursement programmes

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Views are presented solely to aid the discussion and should not be interpreted as adopted guidance.

GVP Module VI

- A **patient support programme** is an **organised system** where a MAH receives and collects information relating to the use of its medicinal products. Examples are post-authorisation **patient support and disease management programmes**, surveys of patients and healthcare providers, information gathering on patient compliance, or compensation/re-imbursement schemes.

- A **market research programme** refers to the systematic collection, recording and analysis by a MAH of data and findings about its medicinal products, **relevant for marketing and business** development.

ICH E2D

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Step 4 – November 2003

3.2 Solicited Sources

- "Solicited reports are those derived from organized data collection systems, which include clinical trials, registries, post-approval named patient use programs, other patient support and disease management programs, surveys of patients or healthcare providers, or information gathering on efficacy or patient compliance. Adverse event reports obtained from any of these should not be considered spontaneous.
- For the purposes of safety reporting, solicited reports should be classified as study reports, and therefore should have an appropriate causality assessment by a healthcare professional or an MAH."

FDA Guidance

FDA draft 2001 guidance:

"For purposes of safety reporting, reports of suspected adverse experiences obtained from company sponsored patient support programs and disease management programs should be handled as if they were **study reports and not as spontaneous reports**."

FDA 1997 guidance:

"The FDA has determined, for purposes of postmarketing safety reporting under…that information concerning potential adverse experiences derived during **planned contacts and active solicitation** of information from patients (e.g., company sponsored patient support programs, disease management programs) should be handled as safety information obtained from a **postmarketing study**."

Solicited or spontaneous?

- **GVP Module VI** - safety reports originating from those programmes should be considered as **solicited reports**. MAHs should have the same mechanisms in place as for all other solicited reports to manage that information and report valid cases of adverse reactions, which are suspected to be related to the concerned medicinal product. Valid ICSRs should be **reported as solicited**.

- ***What are the implications of a "one size fits all approach?"***

Issues

- Current EU guidance does not take into account the **difference between programmes** where there are **planned contacts and active solicitation** of information i.e. organised data collection, and programmes where there is **no active solicitation**. This may result in **different reporting requirements** for the same reports within and outside EU.

- Current EU guidance does not include **expectations** relating to how programmes should be **managed** in order to promote appropriate collection and reporting of good quality safety data.

- Currently the safety data obtained from such programmes is often of **poor quality** (which affects the value of the data).

Hypothetical scenario 1

- A MAH employs a service provider to run a product-specific enquiry line (called a patient support programme by the MAH) after the launch of a novel product. A significant percentage of patients receiving the product register with the enquiry service (in order to receive educational material).

- Patients contact the enquiry service to report adverse events i.e. reports which were not actively solicited are received via the service. The MAH classifies these reports as solicited, but does not always assess causality in a conservative manner (when no reporter causality is provided).

- This leads to under-reporting of events of special interest which the MAH committed to monitoring as part of the EU RMP for the product.

Hypothetical scenario 2

- A MAH employs a service provider to run a reimbursement programme for a product used in seriously ill patients. During contacts relating to refilling prescriptions, adverse events are sometimes reported to the service provider. Not all of these reports are transmitted to the MAH. Some of the non-transmitted reports relate to patient death (with no other details).

- Once the non-compliance is discovered, the MAH undertakes an exercise to collect and follow-up all of the non-transmitted adverse event reports (very limited follow-up information is obtained).

- Subsequent to this exercise, for all such programmes, when there is limited information in a case to confirm causality (even after follow-up), the MAH adopts a conservative approach. This leads to reporting of events that are probably unrelated to the product (with a potential impact on signal generation).

Inspection Findings

- Failure to collect, collate and, where required, expedite adverse reaction reports from patient support programmes.

- Lack of awareness by Pharmacovigilance and the QPPV of patient support and reimbursement programmes being run by marketing departments or marketing partners.

- Lack of agreements or inadequate agreements for safety data exchange between the MAH and service providers involved in managing patient support and reimbursement programmes.

- Where service providers are utilised to manage programmes, failure to provide adequate training relating to safety reporting requirements and failure to monitor compliance with agreements e.g. lack of reconciliation activity, lack of audits.

Examples of programmes

i. Compliance programmes where consenting patients on a medication are contacted to see how they are **managing with their medication**.

ii. Call centres where patients or patient carers can contact the MAH to obtain further information on medication or a particular disease area as part of a structured programme.

iii. "**Nurse Educator**" programmes where the MAH has hired nurses (company employees or third party) to interact directly with patients to help them properly administer medications and/or manage their disease.

Examples of programmes

iv. Call centres where patients can obtain assistance with health insurance questions and **reimbursement support** as part of a structured programme.

v. Programmes which offer **pure financial support**, including insurance coverage, educational grants, scholarships and medical reimbursement assistance.

Proposal for guidance

Industry has proposed that the following **should not** be included in the definition of a PSP:

- Call centres which **only handle medical information enquiries** unrelated to any structured programme.
- Development and/or distribution of **patient orientated information material** without any direct interaction between the MAH and /or third party acting on behalf of the MAH and patient (e.g. information material provided by post to patients).

It seems appropriate that medical enquiry and product information services which enquirers use to obtain information, but via which safety information is not actively solicited (no outreach contacts), should not fall within the PSP definition. Adverse reactions that are reported via such arrangements would be considered spontaneous.

Implications

If truly spontaneous adverse reaction reports are treated as solicited:

- under-reporting may occur due to non-conservative assessment of causality (in particular, where the reporter has not provided a causality assessment),
- performance of causality assessments has resource implications for MAHs (in particular, where the reporter has not provided a causality assessment).

This may be particularly important for newly launched drugs where, in some cases, the majority of patients receiving treatment may be enrolled in such a programme.

Reimbursement programme issues

- Industry has proposed that if an MAH/vendor contacts a patient/carer/HCP for the purpose of refilling a prescription, then any adverse events reported during the conversation e.g. should be regarded as spontaneous adverse reactions.

- In practice, events reported during such periodic contacts may often be unrelated to the product e.g. death of a patient receiving product for a terminal condition. Treating these reports are spontaneous, often leads to inappropriate reporting of unrelated events. Such reports may distort signal generation results.

Reimbursement programme issues

- On the other hand, at the current time, use of a solicited classification is also leading to inappropriate reporting, because where the reporter does not provide a causality assessment, many MAHs are being conservative and treating the events as possibly related. Often the reports are of poor quality and, therefore, are difficult to evaluate.

- ***Catch 22 - authorities do not wish to miss a signal at an early stage, but also do not wish for spurious "signals" to be generated! How can we prevent this? E.g. classify reimbursement reports as solicited, but attempt to obtain better quality information for causality assessment.***

Possibilities for future guidance

- MAHs should ensure that the **design and execution of patient support/assistance and reimbursement programmes** are fully documented. This should include a description of how adverse event reports will be collected, classified, distributed and managed, in the eventuality that reports are received via the programme.

- The MAH should maintain an **inventory** of such programmes, which should be included in the annex to the MAH's pharmacovigilance system master file.

- The **origin of ICSRs** received from such programmes (e.g. programme code or name) should be clearly identified in the MAH's **safety database** (and should be included in reports sent to NCAs).

Possibilities for future guidance

- If the MAH employs **3rd parties** to assist with the running and management of patient support/assistance and reimbursement programmes e.g. specialist contractors, distributors or pharmacies, the MAH should assess whether the 3rd party has the **capabilities, processes and personnel** in place to enable it to comply with the requirements of programme.

- The responsibilities of each party involved in the running of the programme and the arrangements for safety data collection and exchange should be clearly described in **written agreements**. The MAH should ensure that it has systems in place to **monitor the compliance** of third parties with written agreements (e.g. reconciliation, audits). The right to audit should be included in agreements.

Possibilities for future guidance

- All personnel involved in running and managing such programmes should receive **appropriate training** (and refresher training where required) relating to safety data collection. Training should be documented. For example, personnel should be trained to **seek important information** when adverse events are reported (e.g. minimum criteria for safety reporting, the causality assessment of the reporter), during the initial contact with the reporter.

- Where appropriate, **follow-up** should be performed to ensure that the reports are complete and of good quality, and, where necessary, to attempt to obtain HCP confirmation of the reported events.

Market research

- Industry suggests that if market research is not specifically designed to solicit information about adverse reactions/lack of effect/special situations (e.g. misuse), then any adverse events mentioned during the interaction should be regarded as spontaneous adverse reactions.

- However, market research often involves direct contact with patients/HCPs and provides patients/HCPs with an opportunity to mention events that they may not otherwise have reported. Therefore, a causality assessment may be appropriate.

Classification of reports as HCP confirmed

Proposal: Adverse reactions reported by a non-HCP to a HCP working for a medical enquiry/product information service should be considered as HCP confirmed, if the HCP to whom the report is made has access to sufficient information to confirm the events as described (e.g. access to medical records) or if confirmation is obtained from a HCP involved in the care of the patient e.g. during follow-up.

Final thoughts

- Classifying reports from programmes where safety information is not specifically solicited as part of organised data collection, but where periodic "outreach" contacts are made with patients/HCPs, as spontaneous, may save MAH resource, but may lead to inappropriate reporting and generation of spurious signals.

- Poor quality reports are not very helpful for safety surveillance. Good quality reports may be of benefit for safety surveillance.

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