Module 13: Pharmacovigilance Agreements

Introduction

- Recently, there has been a significant increase in the collaborations, partnerships, in-licensing and out-licensing.
- While some companies specialize in compliance with GMP for manufacturing, many others have well-developed marketing networks in one or several countries. Such companies often collaborate so as to synergize on their specific expertise.
- it may happen that the active ingredient is supplied by one company and the finished formulation manufactured by another company. This finished formulation may be the procured by several companies for marketing in different countries.
- Pharmacovigilance and continuous assessment of the benefit risk analysis may either be overlooked duplicated.

Introduction: Contd.

- A well-drafted pharmacovigilance agreement ensures regulatory compliance and prevents the duplication of pharmacovigilance activities by various partners.
- PV agreements are written contracts between two or more companies, to define the responsibilities of each party for and for the sharing of data with each other in the context of
  - Receipt of adverse reactions,
  - Processing of Individual Case Safety Reports (ICSRs), literature searching, submission of periodic reports,
  - Signal detection, single evaluation, development and
  - Implementation of risk management plans.

Contents of PV Agreements

Pharmacovigilance agreements should be drafted to clearly define who will be responsible for the following activities.

- Maintenance of Global safety database.
- Maintenance / updating company core safety information (CCSI)
- Call receipt
- Case processing including medical assessment and follow-up.
- Regulatory reporting for expedited reporting as well as significant follow-up.
- Preparation of (PSURs) and submission to various regulatory authorities
- Literature review
- Signal evaluation, Signal detection
- Updating SmPC/ Package Inserts (PI), Patient info leaflets
- Archiving of PV documents.
- Development, review, evaluation and implementation of RMP
- Continuous benefit-risk assessment.

Various types of PV agreements

- A company may be executing a pharmacovigilance agreement as a manufacturer, Marketing Authorization Holder (MAH), co-licensor, supplier for clinical trials on its own marketing authorization (MA) or for the transfer of MA.
- The approach and the roles and responsibilities of pharmacovigilance team members will differ under each condition.
- As PV is the responsibility of MAH, MAH takes the initiative to draft a pharmacovigilance agreement.

Various types of PV agreements

MAH should take care that following are included in the PV agreement with manufacturer:

- Manufacturers are responsible for notifying the MAH of adverse reactions associated with products complaints.
- Since the manufacturer's name and contract details may appear on form for reporting of ARs or product complaints, The PV agreement should outline the responsibility of manufacturer to appropriately direct such reports to the MAH.
- Manufacturers are also responsible for notifying the MAH of, product recalls, withdrawals, regulatory actions associated with safety in other countries.

When to draft PV Agreements?

- Since collaborations are usually driven by business companies focus on the commercial agreements and financial aspects. Thus, PV agreements may not get adequate attention in the beginning and are usually rushed up and completed at the last moment.
- Therefore, it is advisable to prepare a draft acceptable to both parties at the earliest possible while the business negotiations are still ongoing.
- This will give PV teams from various partners enough time to understand each other's structure, processes, expectations and regulatory requirements.
- Such an approach will facilitate realistic commitments by pharmacovigilance teams.

Review of PV Agreements

- PV agreements are reviewed periodically, whenever there in change in the legislation or regulatory requirements or change in the business agreements.
- The scope of PV agreements also changes with the increase in the number of products and may also cover new territories. It may happen that, business development terms miss to inform pharmacovigilance teams about such change in scope.
- As a consequence, PV agreements may not be updated to reflect the change
- Therefore, regular communication and reconciliation between PV and business groups is a must to ensure that PV agreements are current and updated as per the business agreements.

Agreements with Service Providers

- Appropriate and legally binding agreement should be developed with third parties to whom one or more pharmacovigilance activities have been outsourced.
- These agreements should describe details of the services that have been outsourced.
- Sponsors/ MAHs should develop elaborate procedures for auditing and monitoring of third parties to ensure compliance with MAHs obligations relevant to pharmacovigilance.
- One must remember that even when outsourced, MAH remains responsible for pharmacovigilance function.

Indexing of PV agreements- Readiness for Inspections

- During inspections, inspector usually request for the list of pharmacovigilance agreements and thereafter, they may request for the copies of those executed.
- Therefore, maintaining a ready list/index of pharmacovigilance agreements comes quite handy. Such a list may include the following
  - The name of the partner
  - Date of Agreement
  - Date of next review
  - Type of agreements explaining the responsibility (MAH / manufacturer / clinical trial supply / transfer of MA / co-licensor / co-developer

PV agreements: Inspections

- Inspectors also expect that companies should have SOPs and templates for PV agreements. Large companies that have hundreds of such agreements should maintain a database of PV agreements along with reminders for periodic revision dates and alerts to revised when there is a change in the local regulations.
- This database of PV agreements can also be linked with business groups to ensure updation with changes in business agreement
- This database of PV agreements can also be linked to regulatory database to enable the sharing of updates of approved package inserts and other regulatory actions with the partners.
- In large companies, the exchange of ICSRs and reconciliation can be carried out by suitably configuring the distribution servers of the global safety database

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