PRIMEVIGILANCE
An Ergomed company

Ensuring Patient Safety in Oncology Drug Development

The development and marketing of oncology drugs comes with unique challenges – such as high toxicity, their potential for long-term effects, and their use in vulnerable patient populations. This necessitates the need for rigorous pharmacovigilance measures and implementation of a robust pharmacovigilance system.

The importance of pharmacovigilance in oncology is underscored by the increasing complexity and diversity of oncological drugs on the market.

Targeted therapies, immunotherapies, and combination therapies are prevailing in oncology, with each type of therapy posing unique pharmacovigilance challenges. For instance, targeted therapies may result in specific toxicities, while immunotherapies may lead to immune-related ADRs, and combination therapies may result in synergistic or antagonistic drug interactions. These complexities require tailored pharmacovigilance strategies that take into account for the unique characteristics of each drug.

Choosing the right pharmacovigilance company to partner with can significantly impact a Marketing Authorisation holder's success. With the right services and technology, the implementation of a good pharmacovigilance system can help manufacturers to reduce the risk of adverse drug reactions, to comply with regulations, and to develop safer drugs for patients.

PRIMEVIGILANCE PHARMACOVIGILANCE

"Success is not a secret – it's a system."

PrimeVigilance will help you to achieve your pharmacovigilance goals.

The Indispensable Role of Medical & Scientific Expertise in Oncology Drug Development

What sets us apart from other service providers?

- Pharmacovigilance experts – life science, pharmacology and medical graduates trained on pharmacovigilance processes aligned with worldwide regulatory requirements and guidance.
- Experienced in all areas of the drug development cycle from Phase I to Phase IV.
- Actively involved in proposing new MedDRA terms to the MSSO.
  Contextual understanding leading to high quality medical review of SAEs/AEs.
- Tailored solutions to meet clients' specific needs and challenges.
- Provide ongoing support to our clients, from drug development to post-market surveillance, ensuring that their products are properly supervised for safety and effectiveness.
- Cost-effective solutions, helping manage risks and ensure compliance without breaking the bank.
- Full scope of safety services.

SAE Collection and Medical Review

In oncology, adverse event reporting and management can be challenging due to the complex nature of oncological drugs and the potential for producing long-term effects. In particular, causality assessment requires profound understanding of the underlying conditions, safety profiles of concomitant medication and expected events in the oncologic population. **Our team of medical professionals have a breadth of experience with performing medical review of adverse events occurring in clinical trial setting, ensuring continuous monitoring for potential safety concerns and providing of high quality of case reports.**

Aggregate Reports

Efficient management of spontaneous ADR reports is essential to monitor drug safety in oncology, with further emphasis on analyses provided in U.S. periodic adverse drug experience report (PADER) or in ICH format of Development Safety Update Reports (DSURs) or Periodic Benefit-Risk Evaluation Report (PBRER). While individual case safety reports provide information on adverse events associated with a medicinal product in an individual patient, the analysis of cumulative safety information in form of aggregate reports is necessary not only to understand the safety profile but also to monitor the benefit risk profile of a medicinal product. It is of utmost importance that the presentation of these complex analyses in form of aggregate reports to regulatory authorities is compliant with the legal requirements, consistent with various source documents, and that these documents are produced in a timely and efficient manner. **Our experienced PrimeVigilance medical writing team ensures these goals are achieved, based on their extensive knowledge in the preparation of documentation for complex drugs and biologics with oncology indication.**

REMS

A number of oncology drugs require the setting-up of a complex REMS. REMS must include risk mitigation goals and are comprised of information communicated to and/or required activities to be undertaken by one or more participants (e.g., health care providers, pharmacists, patients) who prescribe, dispense or take the medication. Together, the goals, communications and/or activities make up the safety strategy. **PrimeVigilance provides an expert network with extensive knowledge in identifying challenges across the REMS spectrum, including the areas of standardization and development of REMS programs, with keeping in mind the practical incorporation of REMS into clinical practice.**

Benefit-Risk Assessment

The requirements of the characterisation of the safety profile of anticancer medicinal products have changed with the emergence of molecularly targeted agents (MTAs), immunomodulating drugs and other non-cytotoxic agents as these types of agents may have other types of toxicity and are often dosed differently compared to conventional chemotherapy. Conventional cytotoxic drugs are typically given at weekly or longer intervals and are characterised by major acute but transient toxicity, followed by recuperation before the next treatment cycle. In contrast, targeted drugs and immune modulators are typically administered also continuously/daily, causing a different presentation of toxicities, including toxicities that are delayed. In addition, there are advanced therapies, such as recombinant viral therapies and cell therapies with particular or unique safety profiles. It is often challenging to distinguish symptoms of the disease from the corresponding drug reaction. It may also be impossible to determine the contribution of toxicity from different agents when combination therapy is given. Furthermore, cumulative adverse drug reaction incidences alone do not sufficiently describe a product's safety profile as certain adverse drug reactions are most prominent during the first to second treatment cycle(s), following which tolerance appears to develop, and, on the other hand, there is cumulative toxicity. Therefore, analysis of toxicities in different intervals of treatment is required. The assessment of benefit/risk encompasses all relevant data on efficacy and safety, also taking into account uncertainties as well as relevant data on the disease to be treated. **PrimeVigilance team has medical and scientific expertise required for thorough understanding of different anticancer products and underlying diseases, as well as unique insight into industry best practices. We can support you in safety surveillance activities during the drug development – overseeing the evolving safety profile of the investigational product - including support in preparation of the Safety Surveillance Plan.**

Real-life case examples that demonstrate PrimeVigilance experience in supporting oncological drug development:

Example 1: *A tyrosine kinase inhibitor used in the treatment of chronic myeloid leukemia (CML) and other cancers.*

Post-marketing pharmacovigilance data revealed cases of hepatotoxicity associated with imatinib use. Consequently, the FDA updated the drug's labeling in 2013 to include information on the risk of hepatotoxicity and the need for regular liver function monitoring. Imatinib was originally developed for the treatment of chronic myeloid leukaemia (CML), but accumulating pharmacovigilance data revealed that some patients with gastrointestinal stromal tumors (GIST) experienced significant tumor shrinkage while taking the drug. This finding led clinical trials that evaluated this effectiveness and subsequent approval of imatinib for the treatment of GIST, expanding its indications.

Example 2: *A targeted therapy used in the treatment of HER2-positive breast cancer.*

Pharmacovigilance data identified a potential risk of cardiotoxicity associated with trastuzumab use, including decreased heart function and heart failure. As a result, the drug's labeling was updated to include warnings and recommendations for cardiac monitoring during treatment.

Example 3: *A targeted therapy used in the treatment of BRAF V600 mutation-positive melanoma.*

Pharmacovigilance data showed an increased risk of cutaneous squamous cell carcinoma (cSCC) in patients receiving vemurafenib. This led to the inclusion of warnings about the risk of cSCC and recommendations for regular skin examinations in the drug's labeling.

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