



SOME IMPORTANT DRUG SAFETY ALERTS DURING 2019-2023: A COMPREHENSIVE PHARMACOVIGILANCE STUDY

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Abstract

Drug safety monitoring is a critical component of healthcare systems to ensure the safe and rational use of medicines. Although drugs undergo extensive pre-clinical and clinical evaluations before approval, some adverse drug reactions (ADRs) may only become evident after widespread use in the general population. Pharmacovigilance plays a key role in detecting, assessing, understanding, and preventing drug-related adverse effects during the post-marketing phase. Regulatory agencies such as the U.S. Food and Drug Administration (FDA), World Health Organization (WHO), and other national regulatory bodies regularly review safety data and issue drug safety alerts when potential risks are identified. Between 2019 and 2023, several important drug safety communications were issued worldwide involving multiple therapeutic classes including antiepileptics, anticancer drugs, immunomodulators, and cardiovascular agents. For example, regulatory authorities warned about serious breathing difficulties associated with gabapentinoids such as gabapentin and pregabalin, particularly when used with central nervous system depressants or in patients with respiratory disorders. In addition, warnings were issued for risks such as blood clots with certain immunomodulatory agents, liver injury associated with antiviral drugs, and rare but serious lung inflammation with some anticancer medicines. These safety alerts often resulted in regulatory actions including boxed warnings, label modifications, prescribing restrictions, and enhanced monitoring. The present study aims to comprehensively review important drug safety alerts reported between 2019 and 2023 and analyze their clinical significance, therapeutic categories, and regulatory outcomes. Understanding these alerts highlights the importance of continuous pharmacovigilance and contributes to improving patient safety, rational prescribing practices, and regulatory decision-making in modern healthcare.

Keywords: Pharmacovigilance; Drug safety alerts; Adverse drug reactions; Post-marketing surveillance; Drug safety communication; Regulatory warnings.

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1. Introduction

Medicines play a crucial role in the prevention, diagnosis, and treatment of various diseases and contribute significantly to improving patient health outcomes. However, despite extensive pre-clinical testing and clinical trials conducted prior to drug approval, certain adverse drug reactions (ADRs) may only become evident after a drug is widely used in the general population. Clinical trials often involve limited sample sizes, controlled conditions, and selected patient groups, which may not fully represent real-world clinical settings. Therefore, continuous monitoring of medicines after marketing approval is essential to identify rare, delayed, or

population-specific adverse effects and ensure patient safety [1].

Pharmacovigilance is defined as the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. Regulatory authorities such as the World Health Organization, U.S. Food and Drug Administration, and European Medicines Agency regularly evaluate safety data and issue drug safety alerts when potential risks are identified. Between 2019 and 2023, several important safety communications were released concerning serious adverse reactions, drug interactions, and quality-related issues affecting various therapeutic classes. Systematic evaluation of these alerts provides valuable insights into emerging drug safety concerns and highlights the importance of effective pharmacovigilance systems in protecting public health [2,3].

OBJECTIVES OF THE STUDY

General Objective

To systematically review and analyze important drug safety alerts reported globally between 2019 and 2023 in order to understand emerging safety concerns and their implications for pharmacovigilance and patient safety.

Specific Objectives

1. To identify significant drug safety alerts issued by major regulatory authorities such as the World Health Organization, U.S. Food and Drug Administration, and European Medicines Agency between 2019 and 2023.
2. To evaluate the types and patterns of adverse drug reactions (ADRs) associated with the reported safety alerts.
3. To classify the drugs involved according to their therapeutic categories and pharmacological classes.
4. To examine the regulatory actions taken in response to these safety alerts, including label changes, boxed warnings, restrictions of use, and drug withdrawals.
5. To assess the clinical significance of drug safety alerts for healthcare professionals and patient care.
6. To highlight the role of pharmacovigilance and post-marketing surveillance in identifying new drug-related risks and improving medication safety.

Methodology

Study Design

The present study was conducted as a descriptive review of drug safety alerts reported globally between January 2019 and December 2023. The study focused on identifying and analyzing significant safety communications issued by regulatory authorities and pharmacovigilance organizations.

Data Sources

Data on drug safety alerts were collected from publicly available pharmacovigilance and regulatory databases, including the drug safety communications issued by the U.S. Food and Drug Administration (FDA), safety alerts from the European Medicines Agency (EMA), and reports from the World Health Organization (WHO) pharmacovigilance program (4–6). These sources provide reliable and updated information regarding adverse drug reactions (ADRs), emerging safety signals, and regulatory actions taken to minimize drug-related risks.

Search Strategy

A systematic search was conducted using relevant keywords such as “drug safety alert,” “pharmacovigilance,” “FDA drug safety communication,” “adverse drug reaction warning,” and “post-marketing drug safety”. Safety alerts reported between **2019 and 2023** were screened and evaluated for inclusion in the study.

Inclusion Criteria

- Drug safety alerts issued between **2019 and 2023**.
- Alerts related to **serious or clinically significant adverse drug reactions**.

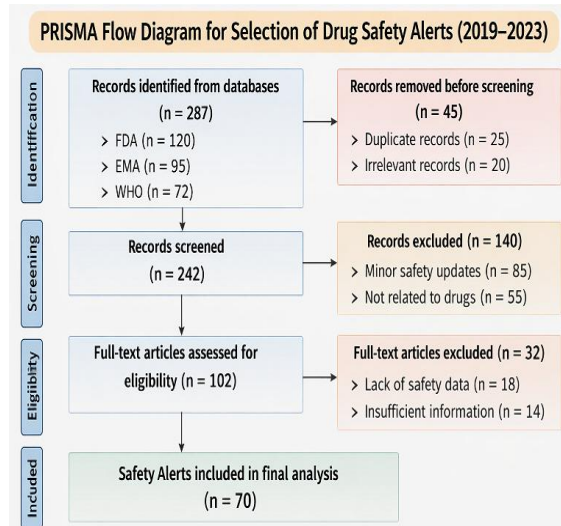
- Safety communications released by recognized **regulatory authorities or pharmacovigilance agencies**.
- Alerts involving **widely used therapeutic agents or major therapeutic classes**.

Exclusion Criteria

- Duplicate safety alerts reported by multiple sources.
- Minor safety updates without significant clinical impact.
- Alerts unrelated to medicinal products.

Data Extraction and Analysis

Relevant information was extracted from each safety alert, including **drug name, therapeutic class, type of adverse reaction, year of safety alert, and regulatory action taken**. The collected data were systematically organized into tables and analyzed descriptively to identify trends in drug safety alerts and associated adverse reactions.



Major Drug Safety Alerts Reported During 2019–2023

Year	Drug	Therapeutic Class	Safety Issue Reported	Regulatory Action	Reference
2019	Gabapentin, Pregabalin	Antiepileptic / Neuropathic analgesic	Serious breathing difficulties when used with CNS depressants or in patients with respiratory risk factors	FDA safety warning and label update	[7]
2019	Febuxostat	Antigout drug	Increased risk of cardiovascular death compared	Boxed warning added	[8]

			d with allopurinol		
2020	Hydroxychloroquine / Chloroquine	Antimalarial / Immunomodulator	Risk of serious heart rhythm problems (QT prolongation)	FDA safety communication	[9]
2020	Metformin	Antidiabetic	Presence of N-nitrosodimethylamine (NDMA) impurity	Product recalls in several countries	[10]
2021	Tofacitinib	JAK inhibitor	Increased risk of serious heart-related events, cancer, and blood clots	FDA boxed warning update	[11]
2021	Remdesivir	Antiviral	Risk of bradycardia and liver enzyme elevation	Safety monitoring recommendations	[12]
2022	JAK inhibitors (Tofacitinib, Baricitinib, Upadacitinib)	Immunomodulators	Increased risk of major cardiovascular events and malignancy	Class-wide safety warning	[13]
2022	Montelukast	Leukotriene receptor antagonist	Neuropsychiatric effects including suicidal thoughts	Boxed warning strengthened	[14]
2023	Semaglutide	Antidiabetic / Anti-obesity	Risk of gastrointestinal adverse effects and possible thyroid tumors	Updated safety information	[15]
2023	Fluoroquinolones	Antibiotics	Risk of disabling and potentially permanent side	Restriction of use recommendations	[16]

			effects including tendon rupture and neuropathy		
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DISCUSSION

Pharmacovigilance plays a crucial role in identifying, assessing, and preventing adverse drug reactions (ADRs) associated with the use of medicines. Although drugs undergo extensive pre-clinical and clinical testing before approval, certain rare, long-term, or population-specific adverse effects may only become evident during post-marketing surveillance. Therefore, drug safety alerts issued by regulatory authorities serve as an important mechanism to inform healthcare professionals and patients about newly identified risks associated with medicinal products [17].

The present review highlights several significant drug safety alerts reported globally between 2019 and 2023. These alerts involved multiple therapeutic classes including antiepileptics, cardiovascular agents, immunomodulators, antibiotics, and antidiabetic drugs. The diversity of therapeutic classes involved indicates that drug safety concerns are not restricted to a specific category of medicines but may arise across a wide range of pharmacological agents.

One of the notable safety alerts during the study period involved gabapentinoids such as gabapentin and pregabalin, which were associated with serious breathing difficulties when used in patients with respiratory disorders or in combination with central nervous system depressants. This finding emphasized the importance of careful patient selection and monitoring when prescribing these medications [18]. Similarly, the addition of a boxed warning for febuxostat due to an increased risk of cardiovascular mortality compared with allopurinol highlighted the need for cautious use of this medication in patients with pre-existing cardiovascular disease [19].

During the COVID-19 pandemic, drugs such as hydroxychloroquine and chloroquine received considerable attention due to reports of serious cardiac adverse events including QT prolongation and ventricular arrhythmias. Regulatory authorities issued safety warnings to limit their inappropriate use outside controlled clinical settings [20]. In addition, several safety alerts were associated with immunomodulatory agents such as Janus kinase (JAK) inhibitors, which were linked to an increased risk of major cardiovascular events, malignancy, and thromboembolic complications [21].

Another important observation was the increasing concern about **drug impurities and quality-related issues**, such as the presence of N-nitrosodimethylamine (NDMA) impurities in certain formulations of metformin. These findings highlighted the importance of stringent

manufacturing standards and regulatory oversight to ensure drug safety and quality [22].

Overall, the safety alerts reported between 2019 and 2023 demonstrate the dynamic nature of pharmacovigilance systems and the need for continuous monitoring of medicines after their approval. Timely identification of safety signals and effective risk communication can significantly reduce the incidence of drug-related harm. Healthcare professionals should remain vigilant regarding updated drug safety information and integrate these warnings into clinical practice to enhance patient safety.

Conclusion

Drug safety monitoring is a fundamental component of modern healthcare systems to ensure the safe and effective use of medicines. The present study reviewed important drug safety alerts reported globally between **2019 and 2023** and highlighted several significant safety concerns associated with commonly prescribed drugs. These alerts involved multiple therapeutic classes including antiepileptics, immunomodulators, cardiovascular drugs, antibiotics, and antidiabetic agents. Many of these safety communications were related to serious adverse drug reactions such as respiratory depression, cardiovascular complications, thromboembolic events, neuropsychiatric effects, and drug impurities.

The findings of this review emphasize the importance of **post-marketing surveillance and pharmacovigilance systems** in identifying previously unrecognized risks associated with medications. Regulatory authorities play a critical role in issuing timely safety communications, updating prescribing information, and implementing regulatory actions to minimize drug-related harm. Continuous monitoring of adverse drug reactions and effective dissemination of safety information can significantly improve patient safety and rational drug use. Therefore, healthcare professionals must remain aware of updated drug safety alerts and integrate this information into clinical decision-making to optimize therapeutic outcomes and reduce medication-related risks.

Future Perspectives

1. Strengthening pharmacovigilance systems is essential for early detection of emerging drug safety signals.
2. Healthcare professionals should be encouraged to actively report adverse drug reactions to national pharmacovigilance programs.
3. Regulatory agencies should continue to improve transparency and accessibility of drug safety communications.
4. Greater emphasis should be placed on real-world evidence and post-marketing studies to evaluate long-term drug safety.
5. Integration of digital pharmacovigilance tools, artificial intelligence, and big-data analytics may

enhance signal detection and safety monitoring in the future.

6. Continuous education and awareness programs for healthcare professionals are necessary to promote rational drug use and improve patient safety.

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