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Guideline

On good pharmacovigilance practices in the context SARS-CoV-2 (Covid-19)

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This document was prepared withing the framework of the
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Content

Objective

This guide is designed to encourage the strengthening of pharmacovigilance processes and activities in the pharmaceutical industry in the context of SARS-CoV-2 disease pandemic (COVID-19)

Scope

This guide is directed to the pharmaceutical industry and proposes activities applicable to the Colombian regulatory environment, taking into account international standards; therefore, it could be applied by the different companies in Latin America according to the regulations established for each country.

Introduction

During the period of the health emergency caused by the COVID-19 pandemic, (SARS-CoV-2), health care workers worldwide face a challenging scene in terms of patient care and safety. In search of an appropriate and beneficial strategy, healthcare workers across the system are working under pressure to make rapid decisions regarding clinical and pharmacological treatment, without the support of robust scientific evidence and with conclusive results, which can favor the use of inappropriate or ineffective therapies that can generate a negative impact on public health.

One of the most complex scientific activities during a health emergency is to determine whether a drug is a candidate to prevent or treat the disease effectively, and in turn, to establish whether the expected benefits outweigh the potential risks when used in patients. For this purpose, the use of the available scientific evidence must be made on pharmacological therapies which, due to the current situation, may change in a short time and may lead to poor quality information.

In order to establish an appropriate drug treatment, the stage of the disease, the approach to the patient's symptomatology according to the needs of the moment and the uncertainty about how the data from clinical trials or test environments are extrapolated to real situations should be taken into account. Therefore, it is necessary to apply specific risk management measures so that known and/or potential risks can be identified and mitigated and to focus on monitoring the safety and efficacy of these new therapies once they are approved for use in the public domain (1).

Although there is currently no specifically authorized and indicated drug treatment for the management of SARS-CoV-2 (COVID-19), newly developed molecules and drugs previously approved for other indications, some of which are used with different administration guidelines from those already authorized, are being used for the treatment of the symptoms associated with this disease; All this, added to the basic characteristics of patients with COVID-19, which may differ from those of the patients for whom these drugs are indicated, may affect the safety profile and the appearance of undescribed adverse reactions, creating a major challenge for

the pharmaceutical industry in terms of analyzing early safety information on the molecules being used.

The overall assessment of all reported cases of a drug-reaction association aims primarily to identify potential unknown risks or changes in the presentation of already known adverse reactions (2).

As the world faces up to this pandemic, which has abruptly changed our daily lives, our work must continue building expertise in drug safety and using this situation as an opportunity to bring pharmacovigilance closer to all the actors in the system that are directly related to the safe use of drugs and patient safety.

The Colombian Association of Pharmacovigilance (ACFV) is a not-for-profit Scientific Society, based on the collaborative work of its members as volunteers and whose Mission is: "*To be a national and international reference for all parties interested in patient safety and in the appropriate and efficient use of medicines, being recognized for its independence, experience and knowledge in research, education, training and for its contribution to the development and learning of Pharmacovigilance in the country*". For this reason, the ACFV makes available this guide that aims to strengthen the pharmacovigilance activities of the pharmaceutical industry during the pandemic period.

General comments

1. Notification of adverse events and special interest events

1.1. Report and description of the event, collection of information

Before addressing the issue of reporting and description of the event, it is relevant to mention that all activities developed within the scope of pharmacovigilance should be included in a regulatory framework and carried out with the best possible practices, in order to ensure the quality and integrity of the information obtained, either spontaneously or through active pharmacovigilance mechanisms. To this end, the veracity and confidentiality of the information should be ensured and appropriate tools for assessment should be used.

This section provides a description of how to process and submits safety information related to medicinal products used for the treatment of SARS-CoV-2 disease (COVID-19). It is clarified that the information must be in accordance with the current legal regulations of each country where the report is submitted and the health registration holder must be responsible for it, in the country.

The following information is considered the "minimum" required for a complete report with which the respective case analysis can be made.

Patient: following the confidentiality clauses according to the country, it is important to:

have initials, age or date of birth and sex. Additionally, if possible, obtain information related to the patient's medical history that includes diseases, clinical procedures, laboratory test results ("Coronavirus test positive"; or "Viral test negative"), among others.

Drug: For this item it is important to obtain: product brand, active ingredient, dose used, frequency, form of administration, indication for use **(which in this case may be used according to MedDRA terminology for: "Coronavirus infection", "COVID-19", "Antiviral prophylaxis" or "Immunization")**, starting and ending date of use of the drug, batch and expiration date. Additionally, if the patient has concomitantly consumed other medications, an attempt should be made to capture the same information from the suspected medication.

Adverse event: it is important to have the starting and ending date of the event, if applicable, and to make a proper selection of the term in MedDRA or the coding that applies according to the regulatory entity. If the patient has an exacerbation of symptoms due to COVID-19, the following two reactions should be coded: **"Coronavirus infection" (LLT code 10051905) and "Condition aggravated" (LLT code 10010264).**

Reporters: Name, contact details, date case is reported. The above, in case more information is required to complete the report or for case follow-up purposes (3). In any case, it is important to remember that reports can be made anonymously.

The information should be recorded in a format that meets the minimum reporting requirements so that it can be evaluated effectively. This information allows the generation of signals and alerts, so it is very important to try to obtain it in full. It is also important to keep an internal record of all the information received and its respective internal codification to facilitate its identification, complying with good documentation practices (4).

Incomplete information should be followed up to complement it, especially in the case of serious and/or unexpected events or reactions.

It is recommended that, if possible, a strict follow-up is carried out until the outcome of the event; this is in the case that the event is reported directly to the pharmacovigilance program of the pharmaceutical laboratory in compliance with the patient's data management and confidentiality policies.

Reporting Sources

Adverse event reporting can be done through the usual channels of institutional pharmacovigilance programs: normal mail, e-mail, telephone contact, web page and other formats.

It is recommended that companies provide communication channels so that patients or health professionals can make any type of report directly to the program (adverse event, adverse reaction, therapeutic failure, etc.)

Recommendations for Reporting

If you receive an Adverse Event (adverse reaction, therapeutic failure, medication error, etc.), it is recommended that you take this into account: (3)

» Do not report an “off-label use”; if it has not occurred or is associated with an Adverse Event (including an unexpected therapeutic benefit report), this should be included in the periodic safety report (IPS) and/or the Risk Management Plan of the product.
» Misuse of non-medicinal products containing substances also present in medicinal products such as pool cleaners containing chloroquine phosphate should not be reported.

1.2. Adverse Reactions

According to the World Health Organization (WHO), adverse reactions are all unintended, unwanted and harmful responses that occur after the administration of a drug, at doses normally used in humans to prevent, diagnose or treat disease and those resulting from dependence, abuse and misuse of medicines (use outside the terms of the marketing authorization and medication errors). These situations require strict monitoring by the pharmacovigilance program given the lack of evidence of the safety and efficacy of drugs used to treat the disease caused by Cov-2 SARS (COVID -19).

It should be noted that, in reports of suspected adverse reactions, it is NOT certain that the suspected drug caused the reported reaction, and the accumulation of reported cases can NOT be used to calculate the incidence or to estimate the probability of occurrence of adverse drug reactions.

The overall assessment of all reported cases of a drug-reaction association aims only at identifying potential unknown risks or changes in the presentation of already known adverse reactions. (2)

1.3. Medication Error

It is any preventable incident that may cause harm to the patient or lead to inappropriate use of medicines, when, these are under the control of health professionals or the patient or consumer. Such incidents may be related to professional practice, products, procedures, or systems, including failures in prescribing, communication, labelling, packaging, designation, preparation, dispensing, distribution, administration, education, monitoring and use. (5)

When receiving a medication error report, it is recommended that you classify according to the source of occurrence into the following categories: (6)

- **Drug procurement**
- **Storage**
- **Prescription**
- **Management of medical records**
- **Validation and transcription**
- **Dispensación**
- **Preparation and/or conditioning**
- **Administration**

Similarly, the classification according to their severity should be kept in mind for the prioritization in the investigation and establishment of the plan of corrective and/or preventive actions as applicable (See Table)

Table 1. Categories of severity in medication errors (7)

CATEGORY		DEFINITION
Potential Error or No Error (1)	Category A	Circumstances or incidents with the potential to cause error
Error without harm	Category B	The error occurred, but did not reach the patient (2)
	Category C	The mistake caught up with the patient, but it did not cause harm to him
	Category D	The error reached the patient and caused no harm, but required monitoring (3) and/or intervention to verify that no harm had been done
Error with damage	Category E	The error contributed to or caused temporary harm to the patient and required intervention (4)
	Category F	The error contributed to or caused temporary harm to the patient and required or prolonged hospitalization
	Category G	The error contributed to or caused temporary harm to the patient and required intervention
	Category H	The mistake compromised the patient's life and intervention was required to maintain his life (5)
Fatal error	Category I	The error contributed to or caused the death of the patient

1. Harm: temporary or permanent alteration of physical, emotional, or psychological structures or functions and/or the resulting pain that requires intervention
2. An "error of omission" reaches the patient
3. Monitoring: observation or recording of relevant physiological or psychological data
4. Intervention: any change made to medical or surgical therapy or treatment
5. Intervention necessary to maintain the patient's life includes cardiovascular and respiratory life support (defibrillation, intubation, etc.).

1.4. Therapeutic Failure

Lack of efficacy or therapeutic failure is an unexpected failure of a drug to produce the intended effect, as previously determined by scientific research. (6)

Therapeutic failures that may be generated with the medicines used in patients who have been diagnosed with COVID-19, should be reported to the Pharmacovigilance programs of the pharmaceutical laboratories that hold the health registration and/or to the manufacturers.

The latter must carry out an investigation taking into account the different causes that could lead to failure of therapy and consider other aspects not studied in the context of the new SARS-CoV-2 virus.

In the scenario of off-label use of a drug, the evaluation of a therapeutic failure presents significant challenges since there is no stipulation for the use of the drug for this purpose; therefore, case information must be complete, otherwise additional data will have to be requested from the reporters. In addition, it must be communicated in a timely manner to the regulatory body.

It is important to mention that most investigations of therapeutic failures within the pharmaceutical industry must be accompanied by a review of the batches involved by the quality department, to rule out defects that are related to therapeutic inefficacy in the context of the prescribing information.

1.5. Off-Label Use

The prescription of medicines by the treating physician should be based on adequate knowledge of the pharmacological profile, safety, efficacy, quality, convenience, and costs of the various alternatives approved by the regulatory authorities. However, there are also various clinical circumstances in which a patient may benefit from prescribing a drug outside the conditions of authorization approved by the competent regulatory authority.

For this reason, off-label use or more precisely unlicensed use refers to the use of a medicinal product for an indication other than that for which it is officially registered and authorized, in so far as there are no alternative treatments and the evolution of the condition suffered poses a threat to the health, integrity and/or life of the person suffering from it (8). Some countries even have a list of medicines classified under this use; in Colombia, it is listed under the name of UNIRS (Uses not included in the health register).

This is the case with the off-label use of many medications during the current SARS-CoV-2

(COVID-19) pandemic, which have multiple indications, but none so far with sufficient evidence to be used in the treatment and/or prevention of the many signs and symptoms that can occur during the course of this disease.

In this regard, the regulatory framework of countries should contain laws or policies that allow for the authorization of emergency use of medicines and other health technologies, as well as a preparedness plan, technical procedures that appeal to the decisions of regulatory authorities in other jurisdictions and the recognition of reliable or reference authorities, and a system for monitoring products whose sale has been authorized for emergency use. (9)

Generally, to authorize emergency use, countries require that certain parameters and criteria be met, such as **the presence of a serious or life-threatening disease, evidence that a product "could be effective" in preventing, diagnosing or treating the disease, a positive risk-benefit ratio result, and the absence of other suitable, approved and available alternatives.**

The equivalent WHO procedure is called "emergency use listing" and is often used when WHO declares a public health emergency of international concern. The procedure applies to medicines (including vaccines) and in vitro diagnostic tools. Emergency use listings consider the morbidity and mortality of the disease and the lack of options for treatment or prevention and apply a risk-based decision making approach. Due to the extraordinary nature of emergency situations, countries often shorten the requirements for product use, so risk assessment is critical. (4)

In the event that a country's regulatory agency generates a temporary approval for the off-label use of a drug, it is recommended that its use be subject to the emergence of new scientific information and strict monitoring of patients, that adverse events be properly identified, and that they be timely reported to the regulatory agency's pharmacovigilance system.

Requests for information related to off-label use should be answered by the Medical Department of the laboratory that holds the registration and not by its sales and/or marketing representatives, as well as interactions with the patient or health care professionals who make the inquiries. It is also recommended that all this information be properly recorded and documented.

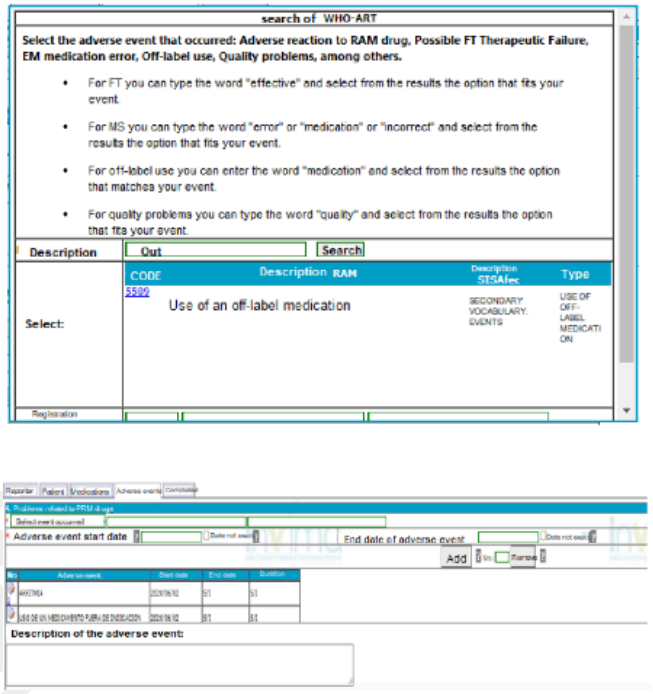
Since off-label prescriptions typically have a lower incidence than on-label use, this practice may be associated with an increase in medication errors (See Chapter). Therefore, the reporting of adverse events related to off-label use plays a crucial role in assessing and adjusting the safety profile of drugs,

particularly with this SARS-CoV-2 infection, for which there is no defined treatment.

During the reporting of cases of adverse events on the INVIMA website, specifically when it comes to events associated with off-label use, it is recommended that this is done individually and in the shortest time possible, because this information is important for identifying the use of unauthorized drugs in the context of the pandemic and corresponding safety data, as well as taking regulatory measures based on the continuous evaluation of the risk-benefit profile.

The individual report allows for the inclusion of associated adverse event(s) (in the event of patient harm) and clarification of off-label use, which does not occur when cases are reported through mass upload at the end of the reporting period (see image).

Image 1. Adverse Event Reporting and Off-Label Use of INVIMA virtual platform



1.6. Review of minutes and administrative measures issued by regulatory bodies

The minutes issued by the Revision Commission of the Specialized Medicine Room of INVIMA, as well as the regulations established by the Ministry of Health and Social Protection of Colombia in the context of the new SARS-CoV-2 virus, provide information on the approvals of off-label uses, temporary approvals of health records, modifications in registration requirements for essential medicines during the pandemic, guidelines for the surveillance of these products, among others.

Therefore, it is recommended that information related to active ingredients used during

the pandemic that is of interest to the pharmaceutical company be continuously reviewed and recorded in a tracking format.

Likewise, it is recommended to continuously review the information published by all the reference regulatory agencies such as; the European Medicines Agency EMA and its Member States, the United States Food and Drug Administration (FDA), the Federal Department of Health Canada, among others, as well as those, regulatory entities that govern the countries where the pharmaceutical company markets its products..

1.7. Literature Review

It is important to keep in mind that in the context of the new SARS-CoV-2 virus, much medical- scientific information has been generated associated with possible treatments for the management of COVID-19, therefore, care should be taken during the review of the published literature, in order not to generate duplication of individual safety cases.

To perform an adequate literature review, it is recommended to select all relevant publications from databases such as PubMed, Embase, Scielo, Lilac (among others). We recommend carrying out systematic and periodic searches, following the procedure available to each company to carry out this review and record and document the information found. (4)

Recommendations

For individual case reporting, it is recommended to follow the time frame established, according to the seriousness classification, by the regulatory body from the day the event is identified within a literature review. It should be noted that some regulations detail exclusion criteria such as (3)

» Cases from publicly available databases (e.g., poison control centers) where cases are presented in aggregate tables or line lists. **The submission requirement remains for valid cases described individually.**

» When results of post-authorization studies, meta-analyses or literature reviews are presented.

» When suspected adverse reactions are described in a group of patients with a designated drug **and the patients cannot be identified individually.**

It is recommended that when safety information is found it should be considered in the elaboration of the periodic safety reports and the continuous evaluation of the risk-benefit ratio of the medicines.

1.8. Review of Signals and Alerts

Signals are defined as reported information about a possible causal relationship between an adverse event or reaction and a drug when this relationship was previously unknown or incompletely documented.

Usually more than one report is required to generate a signal, depending on the severity of the event and the quality of information. (9)

It is recommended that the information contained in pharmacovigilance program databases be analyzed for signals, with the aim of defining its relevance for referral to the regulatory authority in cases where it applies.

If the signal is considered an imminent public health problem, it should be immediately reported to the INVIMA National Pharmacovigilance Program. This review applies not only to the territory of Colombia but should be evaluated in all countries where the pharmaceutical companies markets its products, for those companies that require it under local legislation.

It is recommended that signal management be carried out as follows: (10)

1.8.1. Signal Detection

Review of adverse event reports, citizen complaints or information from reference health agencies or the National Pharmacovigilance Network, which seeks to identify terms corresponding to the event according to the following criteria:

» **Seriousness:** terms referring to serious adverse events

» **Population:** terms that refer to events affecting vulnerable populations (pregnant women, newborns, pediatric population, the elderly, among others).

» **International reference:** terms associated with signals issued from international reference centers (Uppsala Monitoring Centre, EMA, Health Canada, AEMPS and FDA), including their health alerts.

1.8.2. Signal Validation

Verification of the technical sheets of each product, to confirm the knowledge of the event being studied. Both the information available in INVIMA and that available in reference regulatory agencies is used, to initially rule out those events that are already documented for the different active ingredients.

1.8.3. Signal Priorization

For high-risk events to be investigated as a matter of priority, the potential signals detected are classified according to their impact on public health, considering the following criteria:

- **The seriousness of the adverse event**
- **The affected population**
- **The characteristics of the adverse event**
- **The novelty of the suspected adverse reaction or drug**
- **The feasibility of preventive meeasures**

1.8.4. Signal Evaluation

The potential resulting signals should be evaluated through the clinical information available in each of the related adverse event reports and through verification of the information in the scientific literature. In some cases, the primary sources of information may be investigated to complement data or the person responsible for the product in the market may be cited so that their investigations can strengthen the analysis initiated or so that commitments can be generated in the light of new safety information detected.

Likewise, it is essential to constantly review the health alerts and safety reports issued by the regulatory bodies in a constant and systematic manner, as they are distributed in the countries in which the medicines are marketed by a pharmaceutical company so as to identify regulatory changes or updates in the risk-benefit balance of the medicines used in the context of the new SARS-CoV-2 virus. It is also recommended that these searches be recorded and tracked.

General comments

2. Valuable information to enrich the safety profile

Considering that pharmacovigilance activities should be carried out based on continuous monitoring of the risk-benefit balance of marketed drugs, the next step is to enrich the safety profile of such drugs, taking into account globally published information on the molecule, as well as the result of the analysis of information collected through adverse events reported by pharmaceutical laboratories.

2.1. Periodic Safety Report

The Periodic Safety Update Report (PSUR) is a compilation of national and international drug safety information, which represents the worldwide experience of the product at specific times after the marketing authorization of a drug, for the purpose of:

- **Reporting any new security information from appropriate sources.**
- **Relating this data to the patient's exposure.**
- **Summarizing the authorization status in different countries and any safety-related variations.**
- **Periodically creating the opportunity for a global reassessment of safety.**

» **Indicating whether changes should be made to the product information to optimize its use. (12)**

These publications, together with the health alerts and reporting adverse events, seek to promote the protection of the population's health, in the hope that recommendations for the use of the drug will be accepted within the National Pharmacovigilance Program.

In order to carry out a continuous analysis on the risk-benefit relation of the medicines marketed in times of pandemics, taking into account the high demand for them, their inclusion as vital unavailable, off-label uses, compassionate uses and even medication errors associated with their inadequate administration, it is recommended to monitor more closely the safety performance of medicines and to update the Periodic Safety Reports (IPS) according to the Pharmacovigilance Guide for Periodic Safety Reporting of INVIMA and the guidelines established by the ICH E2C (International Conference on Harmonization, ICH Harmonized Tripartite Guideline, Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs E2C).

These reports must be submitted at the request of the regulatory agency INVIMA or to the regulatory agency where the products are marketed, in accordance with the regulations in force in each country, or when the company has detected problems concerning drug safety, taking into account, as mentioned above, local regulations.

2.2. Risk Management Plan

Risk Management is a process of evaluating the benefits and risks of a drug; it is the development and implementation of tools to minimize its risks while preserving its benefits; it also evaluates the effectiveness of these tools and makes adjustments as appropriate through continuous analysis to further improve the risk-benefit balance. (13)

Risk minimization measures are an essential part of the process of monitoring the behavior of medicines on the market and a tool for continuous assessment that makes it possible to anticipate the known risks described for the medicines and the potential risks. Similarly, risk minimization measures make it possible to consider those populations in which the drug could be used, but for which little pre-marketing information is available.

Within the Risk Management Plans (RMP), routine pharmacovigilance activities and additional pharmacovigilance activities are contemplated, which allow for the adequate monitoring of the behavior of the medicines marketed, within which they are contemplated:

a. Characterization of the drug safety profile through preclinical, clinical, and post-marketing information obtained through the pharmacovigilance program.

b. Monitoring of global safety information, signals, and alerts.

c. Analysis of relevant cases obtained from the review of the world literature.

d. Passive pharmacovigilance: Reporting of adverse events through the attention channels of institutional pharmacovigilance programs: physical mail, e-mail, telephone contact, website, among others.

e. Active pharmacovigilance: Considerations for this expanded surveillance role should include appropriate evidence-generation or adverse-reaction-monitoring strategies, such as phase IV clinical trial studies; observational studies; patient registries and/or manufacturer- administered patient support programs; patient focus groups; and implementation of proactive adverse-reaction-monitoring strategies. (1)

f. Signal detection: Through the monitoring and analysis of cases reported through the pharmacovigilance program, the aim is to identify signs of adverse effects associated with the administration of the drug, as well as relevant unexpected events.

g. Analysis of individual cases and databases: The analysis of the information collected will allow for updated information to be reported in a timely manner to the regulatory authorities and manufacturers.

h. Continuous evaluation of risk-benefit profile

i. IPS: All drug-related safety information collected in post-marketing use should be included in periodic safety reports, and, depending on their relevance, in updates to the drug risk management plan.

j. Training: It is recommended that health professionals in charge of prescribing the drug receive educational material with complete and timely information on the indications, contraindications, posology, precautions, warnings, interactions and side effects of the drug, as well as updated information related to efficacy and safety under the regulatory entity's guidelines, by the National Pharmacovigilance Program according to the Global Safety Information Tracking.

k. Evaluation of medication errors: Considering that medication errors are a major cause of adverse events, complications and mortality, it is recommended that the company evaluate all conditions

associated with the manufacture, transport, storage, prescription and administration of the product, in order to identify risks and establish actions to minimize them.

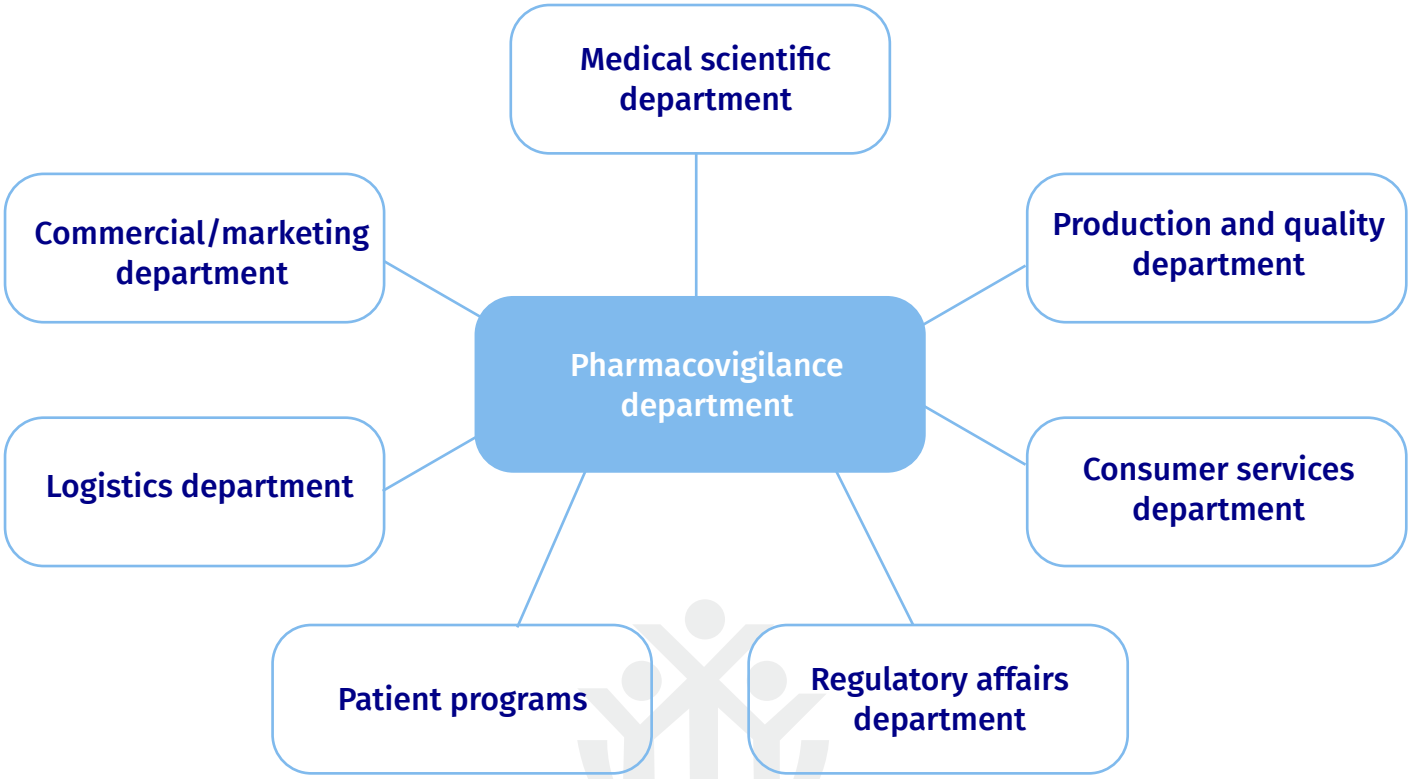
All the activities mentioned here, as well as all those that pharmaceutical companies can implement and/or have already implemented, should strengthen a companies' pharmacovigilance system to make it more possible to anticipate expected and unexpected adverse situations during treatment, analyze the causal relationship with the use of the drugs and provide information on the real behavior of the drugs, especially where there is no solid scientific evidence to support their recommendation in the context of the new SARS-CoV-2 virus.

General comments

3. Interaction between areas

Interaction between areas is vital in the daily operation of the pharmaceutical industry and even more so in this period of emergency. Therefore, the Pharmacovigilance Department must be supported by other areas of compliance, such as the Medical-Scientific Department, Regulatory Affairs, Production and Quality. Likewise, the interaction with commercial areas, patient programs, administrative, logistic and customer service services is very important since they are areas that can receive valuable information in terms of adverse event reports.

Interaction



To achieve an adequate interaction between the areas, it is very important to define the activities that directly and indirectly impact the Pharmacovigilance Program:

» **The training of employees, especially those who interact with patients or health professionals, should be reinforced,** in order to raise awareness of the impact that reporting on the evaluation of the risk-benefit ratio of medicines and their safety profile over time can have in times of pandemics. For this training, it is advisable to address basic concepts on pharmacovigilance, the reporting process to be followed, reporting times, minimum information to be collected and means by which it is done.

» Communication between consumer services or customer service areas should be fundamental, since, in the case of receiving a report through this channel, the information should reach the pharmacovigilance program in an integrated manner so that it can be followed up and managed appropriately, achieving timely handling of the case.

» The approach in conjunction with the medical-scientific area for the management of the answers to the questions related to the off-label use of drugs used in the context of SARS CoV-2 for the treatment of COVID-19.

» The recall process that can be activated by the quality area when faced with the notification of the health authority in the event of a quality and/or safety impact of

a pharmaceutical product. This consists of the collection of information on the market of the product that has been released, from the quality area, as well as the collection of information on adverse events related to the use of the impacted products. This process must be approached jointly by the company's Quality, Regulatory Affairs and Pharmacovigilance or Patient Safety areas, as it involves several logistical aspects. (if applicable)

» The handling of the report to the health authority against alerts of falsification and adulteration, which may occur with certain lots of product. This process must be coordinated with the quality and logistics areas.

» Updating of safety or labeling information that may require modification of the registration to update indications, safety information, contraindications, warnings, among others, after the results obtained through clinical studies and regulatory follow-up at the global level, in conjunction with the regulatory affairs area.

» The inclusion of molecules in the UNIRS list must be shared by the regulatory affairs area.

3.1. Special Cases

Vitals Not Available

Considering the current situation of the pandemic and the management of some of the pharmaceutical products, we cannot stop talking about the management of vital unavailable products, which is led by the area of regulatory affairs and which several aspects will be taken into account and will have to be reviewed jointly.

The National Government and INVIMA have made an effort to prioritize those elements that have had an increase in consumption or even a shortage, in order to declare them as vital and unavailable, and accordingly accelerate those procedures and flexibly adapt technical and administrative measures to facilitate the import or manufacture of these without compromising the quality of the products and the safety of users to ensure their availability in the country.

A vital medicine that is not available, is an indispensable and irreplaceable medicine to safeguard the life or alleviate the suffering of a patient or group of patients and that, due to conditions of low profitability in its marketing, is not available in the country or the quantities are not sufficient. (14)

INVIMA declared as vital and unavailable those drugs, medical devices and biomedical equipment related to the prevention, diagnosis and treatment of COVID-19, as well as those that have been affected by the cancellation or suspension of the production and commercialization chain at a global level. (15)

Given the special characteristics of the supply chain of these unavailable vital products, it is very important that surveillance programs (Pharmacovigilance - Technovigilance - Reactivevigilance) are strengthened, seeking to safely promote the use of these products.

It is recommended to consider the information provided by the regulatory body, or other official entities in order to keep surveillance programs updated.

Glossary

Regulatory Agency: A government entity, usually incorporated in the ministry of health or its equivalent, whose purpose is to enforce laws regulating the manufacture and use of medicines used by humans (diagnostic agents, biological products, medical devices, radiopharmaceuticals). (16)

Alert or signal: Information reported about a possible causal relationship between an adverse event or reaction and a drug when this relationship was previously unknown or incompletely documented. Usually more than one report is required to generate a signal, depending on the severity of the event and the quality of information. (9)

Health Alert: is any suspicion of a situation of potential risk to the health of the population and/or of social importance, in the face of which it is necessary to develop urgent and effective Public Health actions. (11)

Pharmacovigilance database: A computer system that allows the recording of reports of suspected adverse events, once they have been evaluated and coded, and the generation of alerts or signals. (9)

Benefit/risk ratio: Reflects the relationship between the benefit and risk presented using a drug. It allows a judgement to be made about the role of the drug in medical practice, based on data about its efficacy and safety and on considerations of possible misuse, disease severity and prognosis, and so on. The concept can be applied to a single medicinal product or to comparisons between two or more medicinal products used for the same indication. (9)

Good pharmacovigilance practice: A set of rules or recommendations aimed at ensuring: the authenticity and quality of data collected for the ongoing assessment of risks associated with medicines; the confidentiality of information concerning the identity of persons who have reported or presented adverse reactions; and the use of uniform criteria in the assessment of reports and in the generation of warning signals. (17)

Causality: The result of the accountability analysis and the individual evaluation of the relationship between the administration of a drug and the occurrence of an adverse reaction allows the determination of a category of causality. (9)

Medication error or medical mistake: An avoidable incident caused by the improper use of a medication. It can cause injury to a patient, while the medication is under the control of health care personnel, the patient, or the consumer. (18)

Adverse event: Any unfortunate medical occurrence that may occur during treatment with a drug but does not necessarily have a causal relationship with the drug. (9).

According to the Colombian Ministry of Health's Patient Safety Policy, it is the result of health care that unintentionally caused harm. (18)

Serious adverse event: An unintentional event that could have led to the death or serious deterioration of the health of the patient, operator or anyone else directly or indirectly involved, as a result of the use of a drug or medical device.

Considered to be a serious deterioration of health:

1. Life-threatening illness or injury.
2. Damage to a body function or structure.
3. A condition that requires medical or surgical intervention to prevent permanent damage to a body structure or function.
4. An event that leads to a permanent partial disability.
5. An event that requires a hospitalization or an extended hospitalization.
6. Event that is the origin of a congenital malformation. (9)

Non-serious adverse event: An unintentional event, other than one that could have led to the death or serious deterioration of the health of the patient, operator or anyone else directly or indirectly involved, as a result of the use of a medical device or appliance. (9)

Manufacturer: Company that carries out at least one of the stages of manufacture (23)

Manufacturing: All operations involving the procurement of materials and products, production, quality control, licensing of transport, storage, shipment of finished products, andcontrols related to these operations (23).

Therapeutic failure: Unexpected failure of a drug to produce the intended effect, as previously determined by scientific research. (9)

Pharmacovigilance: Science and activities related to the detection, assessment, understanding and prevention of adverse reactions or any other drug-related problems. (9)

ICH: International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) which brings together regulatory authorities and the pharmaceutical industry from Europe, Japan, and the USA to discuss the scientific and technical aspects of drug registration chat. Since its inception in 1990, the ICH has gradually evolved to respond to the global increase in drug development, so that the benefits of international harmonization to improve global health can be extended to the entire world. (12)

Indication: The uses for which a product (medicine, medical device, food supplement, etc.) is intended after it has been scientifically proven that its use for a particular purpose is effective and safe. That is, that such use is justified in terms of the risk-benefit ratio that the product provides in the prevention, diagnosis, treatment, relief or cure of a disease or condition. The indications are included in the labeling of the product when they have been approved by the health authority. (9)

Safety Report: Information aimed at preventing the occurrence of an adverse event associated with the use of a Drug, Phytotherapeutic, Medical Device, Biomedical Equipment, In Vitro Diagnostic Reagent or supplement. This information does not imply a high risk for health and can be generated or defined from the warnings, recommendations, indications or insert of the use or consumption of an active ingredient or product. (11)

Periodic Safety Report: The Periodic Safety Reports (IPS) are a compilation of the drug safety information at the national and international level, representing the worldwide experience of the product at specific times after the authorization of the medicinal marketing. (12)

Drug-drug interaction: Any interaction between one or more drugs, between a drug and a food, and between a drug and a laboratory test. The first two categories of interactions are important because of their effect on the drug's pharmacological activity: they increase or decrease desirable or adverse effects. The importance of the third category of interaction lies in the alteration that a certain drug may cause in the results of the laboratory tests affecting their reliability. (16)

Medicine: Is a pharmaceutical preparation obtained from active ingredients, with or without auxiliary substances, presented in a pharmaceutical form, used for the prevention, relief, diagnosis, treatment, cure, or rehabilitation of the disease. The containers, labels and packaging are an integral part of the medicine, since they guarantee its quality, stability, and proper use (22).

Concomitant medication: Additional medication that a patient receives during a clinical trial or medical treatment but is not the one being evaluated. It may be prescription or over the counter. (16)

Vital Medicine Not Available: A medicine that is indispensable and irreplaceable for safeguarding the life or alleviating the suffering of a patient or group of patients and which, due to conditions of low profitability in its marketing, is not available in the country or the quantities are not sufficient. (26).

Notification: The reporting of a suspected adverse drug reaction to a pharmacovigilance center. Usually these reports are made using the adverse reaction reporting forms (yellow card), providing the necessary means in each case to maintain the confidentiality of the data. (9)

Risk Management Plan (RMP): A document prepared by the pharmaceutical laboratory that holds the Health Registration, based on the planning of pharmacovigilance that aims to collect all the information of the safety profile of the drug for the registration of a new product or every time new information becomes available, in particular with the Periodic Safety Reports. (13)

Active principle: Compound or mixture of compounds that has a pharmacological action. (19)

Adverse Drug Reaction (ADR): According to WHO, ";a harmful and unintended reaction that occurs after the administration of a drug, at doses normally used in humans, to prevent, diagnose or treat disease, or to modify any biological function. This definition implies a causal relationship between the administration of the drug and the appearance of the reaction, excluding intoxication or overdose." (9)

Unexpected adverse reaction: Reaction that has not been described in the product labeling or that has not been communicated to the health authority by the laboratory that obtained the registration of the product at the time of application. (9)

Report: Healthcare professional who comes into direct contact with the patient, identifies a Drug-Related Problem or Adverse Event and reports it to the Health Registration Holder and/or the manufacturer, a pharmacovigilance system or INVIMA (24)

Reporting: The means by which a reporter notifies a pharmacovigilance system of an adverse event that has occurred to a patient (24)

Safety: A characteristic of a drug that can be used with a very small chance of causing unjustifiable toxic effects. The safety of a drug is therefore a relative characteristic, and in clinical pharmacology its measurement is problematic because of the lack of operational definitions and for ethical and legal reasons. (9)

Spontaneous reporting system: A method of pharmacovigilance based on the reporting, collection, and assessment of reports of suspected adverse reactions by a health care professional; it also includes the adverse clinical consequences of dependence and misuse and abuse of medicines. (9)

Proper use of medication. This is the continuous process, structured and designed by the State, which will be developed and implemented by each institution, and which seeks to ensure that the medicines are used appropriately, safely, and effectively (25).

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