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Guide

For the development of pharmacovigilance in the context SARS CoV (Covid-19)

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This document was prepared within the framework of the Academic Committee of the Colombian Association of Pharmacovigilance.

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Objective

This guide aims to provide technical elements for the development of pharmacovigilance strategies and activities in institutions that care for patients with CoV-2 SARS infection.

Range

This guide was designed by identifying the needs of the medical institutions in the Colombian context; however, it is considered that it could guide the activities of institutions in the Latin American environment, for which the conditions of each territory must be understood.

Introduction

During this health emergency produced by the pandemic caused by SARS CoV-2 infection (COVID-19), the world is facing a challenging array in patient care, mainly due to a lack of robust scientificevidence that allows the presentation of conclusive results to define an adequate clinical and pharmacological treatment based on clinical evidence.

Furthermore, as it is a new virus, it is still unknown which systems it modifies or alters and how these alterations affect the transit of drugs in the body (for example, metabolizing enzymes, modification of excretion or imbalances in coagulation). Thus, on the one hand, drugs with little experience of use are being used, but, on the other hand, common drugs are also being used in an unresearched and unapproved indication, and therefore may have different or unknown adverse effects.

In this sense, pharmacovigilance becomes an even more pressing need to obtain data and information determining the safety and effectiveness of treatments used to manage this disease, in addition to verifying their proper use, knowing and managing interactions (understanding that these may or may not change the safety profile of the molecules being used) and establishing strategies to avoid or mitigate possible medication errors.

Correct development of pharmacovigilance may be affected by too few resources, a limited time to develop this activity on the part of emergency personnel, and the increase in the number of patients received by health care services.

This scenario requires the intervention of a multidisciplinary team trained in the pharmaceutical and pharmacological area to develop strategies and activities that favor patient safety, such as drug reconciliation and therapy safety monitoring, among others, so as to support the detection, analysis and prevention of potential or adverse events derived from drugs.

Such strategies will rely on using available databases for clinical history management and consultation of scientific literature sources to contrast findings and make decisions by the health team. Despite this, as has occurred throughout history, careful observation by health professionals who are in the front line of care will, once again, be the key to detecting and documenting adverse reactions (which may eventually become signals) and other events, such as medication errors.

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, ACFV makes available this guide that aims to generate tools to facilitate the development of pharmacovigilance during the management of the pandemic.

General Considerations for the Development of Pharmacovigilance Strategies

1. Types of pharmacovigilance strategies to be developed

Within pharmacovigilance strategies should be kept in mind, many will be of a routine nature (mainly passive pharmacovigilance), as well as additional strategies such as active, intensive or intensified pharmacovigilance. More information on these topics can be found in PAHO's Good Pharmacovigilance Practices for the Americas. (1)

Routine pharmacovigilance strategies:: These mainly relate to receiving spontaneous reports from health professionals of adverse events associated with the use of drugs, analyzing causal relationship between the patient's drug therapy and the observed event, and managing to prevent further events. It is suggested that institutions maintain the activities of existing pharmacovigilance programs within institutions and under the current regulation, so that the reporting and management of events is kept in communication with the National Regulatory Agency (National Institute of Food and Drug Surveillance - INVIMA) and local entities (Health Secretariats).

Health Care Professionals are expected to report any adverse drug events that occur

in patients at the facility, prioritizing those patients diagnosed with SARS-CoV-2 infection and including all medications in their treatment. Reporting should be encouraged to occur, even if it is suspected, since all information at this point is important for generating evidence. Additionally, institutional procedures could be modified, such as reducing the time of notification of serious events.

When reporting suspected adverse events, at least the following information should be provided, as accurately and completely as possible (2):

- Information about the person who has experienced the adverse effect, including age and sex;
- Whether the infection is confirmed by testing or based on clinical symptoms;
- Description of the adverse events;
- Name of the medicinal product (brand name and active substance) suspected of having caused the adverse events;
- Dosage and duration of treatment with the drug;
- Batch number of the drug (found on the packaging);
- Any other medications taken at approximately the same time (including over-the-counter medications, herbal medicines, or contraceptives);
- Any other health conditions that the person who experienced the side effect may have.

Additional pharmacovigilance strategies: It is suggested that the pharmacovigilance department of the institution should continuously monitor patients who have been diagnosed with COVID-19 and follow up on the effectiveness and safety of therapy. In the absence of a specific pharmacovigilance department, it is suggested that surveillance be carried out by a Health Care Professional group. This document will emphasize intensive pharmacovigilance strategies.

In both types of strategies, it is suggested to implement three subsystems to develop it: 1) information gathering; 2) causality analysis; and 3) intervention for risk minimization. For more information on this topic please consult the Handbook of Good Pharmacovigilance Practices Latin America Edition.

2. Proper selection of the literature

Use of reliable information sources is the main input to favor decision making based on the best evidence existing at the time of the consultation, understanding that reality is changing as new data appear. Several sources of information are suggested in Appendix 1.

3. Pharmacovigilance task force

Ideally, Institutions should have a team with a knowledge of pharmacovigilance and, preferably, experience in the development of this type of activity. However, given the conditions of the emergency, it is suggested that a professional with knowledge of pharmacovigilance or pharmacology in the institution should lead pharmacovigilance strategies, i.e. inform the care team about common adverse events that may be generated by different therapies, including drug interactions, update this information as evidence emerges and coordinate risk minimization and intensive pharmacovigilance strategies. (See Appendix 1)

It is important to remember that, like others in the care group, pharmacovigilance leaders must maintain biosecurity measures to protect their health when interacting with health care professionals and preferably avoid direct contact with the patient.

Risk Minimization Strategies

In order to implement a risk management of the drugs currently used in the treatment of COVID-19, it is necessary that the health care team is trained in the safety profile of the drugs, potential interactions and in the assessment of their severity, as well as in the measures for minimizing these risks and key points for monitoring the patient's clinical parameters and their evolution.

It is suggested, then:

- Reinforcing actions to prevent medication errors and to promote the adequate use of medications, considering the patient's clinical condition, comorbidities and available evidence, as well as to assure that the 10 correct criteria in the safe use of medications are fulfilled:

1. **Verification of the correct patient**
2. **Correct medication**
3. **Correct dosage: According to the existing evidence**
4. **Right route of administration**
5. **Dosage interval and correct treatment duration**
6. **Drug reconciliation**
7. **Identification of allergies**
8. **Proper preparation of medicines and current expiry date**
9. **Proper recording in the medical record**
10. **Patient education on medication issues**

- Reinforcing the identification (with distinctive marks) of LASA drugs (Look Alike, Sound Alike) for those drugs that are similar in their labelling and form, and/or whose names sound very similar, due to these similarities can induce errors in practice and a possible adverse event in the patient (for example, differentiating chloroquine and HYDROXYchloroquine). Caution is recommended, particularly with those drugs recently included in the institution or with those managed for patients with COVID-19.
- Having different health profiles (professionals in nursing, pharmacy, medicine, respiratory therapy, among others) that are part of the committee or area that is managing the pandemic emergency in the institution. They should act together to determine the best therapies for patients when considering the particularities of each knowledge.
- Reconciliation of medication, at least on admission and discharge of the patient, to favor the monitoring of admission and discharge treatments, and the minimization of risks derived from these.
- Identifying within the treatment of patients those drugs with similar mechanisms of action to those used for the treatment of COVID-19 that may potentiate negative effects, in order to monitor their use, and to verify possible interactions that are clinically relevant.
- Encouraging patient education while the patient can participate in their care and/or provide relevant education to their caregivers and family members if they are able to be present or support the care. Special emphasis should be placed on educate patients who are treated on an outpatient basis to ensure compliance with therapy in optimal conditions for them.

- Making health personnel aware of the importance of pharmacovigilance as an indispensable element to promote patient safety and to act as soon as possible at the onset of adverse treatment events for COVID-19 or other therapy drugs and, additionally, to build drug safety profiles under current conditions of use and generate their own records to support decision-making.
- Monitoring frequently evidence and clinical trial information to understand changes in therapies and their safety profiles.

Intensive Pharmacovigilance Strategies

For the development of these strategies it is suggested that the institution::

Define the population to be monitored: prioritize the patients to be monitored, for example, by differentiating groups of patients at higher to lower risk: the intensive care unit group, the inpatient group and, finally, the outpatient group. Define patients to be monitored and the degree of intensity of the monitoring, considering, mainly, the resources available for the institution to carry out this activity.

Characterize the population according to the treatments they are receiving (Hydroxychloroquine/Chloroquine, Lopinavir/Ritonavir, etc.). It is suggested to refer to the Colombian Consensus (3). It is important for the institution to have guidelines for the management of such medicines, such as whether the use is off label or unlicensed by the regulatory authority (INVIMA), and to verify that the informed consent process was carried out, explaining both the risks and the benefits. Also, consider whether the patient is part of any approved protocol, to avoid duplication of information.

Define the parameters to be monitored pfor each group of patients, understanding the main

adverse events for each molecule, prioritizing those that may put the patient's life at risk and starting with those that are most frequent. (6)

Conduct thorough pharmacotherapy follow-up for patients who will be closely monitored (e.g. high-risk population admitted to ICU) to quickly identify risks or adverse events associated with therapy, including:

1. Recognize the full extent of the therapy the patient is using through medical history records, identify whether there are any high-risk medications and whether they may cause harm under the conditions of use for the specific patient. If possible, make a record of all medications for analysis.
2. Check the doses and possible adjustments required.
3. Review possible drug interactions and whether they are clinically relevant.
4. Define the laboratory results that require monitoring since they allow evidence of a riskto the patient's life.
5. Establish the possible adverse effects according to the therapy and whether the patient has manifested them.
6. Maintain an open and constant dialogue with treating professionals, report your findings and draw attention to potential or actual risks.
7. Suggest actions to the care team, in terms of dose adjustments, concomitant therapies that can be modified, temporary or permanent suspension of a drug.
8. Establish, if possible, the number of units prescribed and taken for each of the drugs under evaluation and compare them with respect to the number of reported adverse events thereby establishing the actual incidence of such events.
9. Consolidate the information so that it becomes the point of communication with the care group if it detects that there are risks or events require intervention. The following table is suggested for this purpose:

Patient	Date	Medica-tion(s) that are related to risk	Risk or event detected	Sugges-ted inter-vention	Interven-tion outcome
Name: ID:	DD/ MM/ AAAA	Medication 1: Medication 2:	Risk: - - Event: -	Suggested action: Responsi-ble:	XXXXXX

In this case, a direct interview with the patient is not suggested, due to the limited availability of the patient to attend and, additionally, due to the risks that the collection of information may imply for the person carrying it out.

Ideally, this review should be performed daily, however, this frequency may vary depending on the resources of the institution. It is suggested that, for example, during each shift the pharmacovigilance manager listens to the observations of the health personnel and in turn communicates his or her findings.

Consolidated information must be analyzed by competent Committees or areas of the institution to make epidemiological decisions (Pharmacy and Therapeutics Committee, Pharmacovigilance Committee, etc.). It is recommended that consolidated information could be shared with the regulatory agency and, if it exists, in collaborative networks of health institutions.

For patients for whom it has been decided to do more routine monitoring, e.g. stable inpatients:

1. Identify high-risk drugs and whether they may cause harm under the conditions of use for the specific patient. Include therapies for COVID-19 whose safety profile is unknown in the circumstances of current use..
2. Check dosages and possible adjustments required.
3. Review possible drug interactions and whether they are clinically relevant..
4. Establish the possible adverse effects according to the therapy and if the patient has manifested them..
5. In case of any relevant finding, notify the treatment group and suggest the intervention.
6. Consolidate the information.

For outpatients::

1. **Educate widely about the therapy he will receive,** the correct form of self-administration of the medication, the importance of therapeutic adherence in terms of dosage, dosage intervals and duration of therapy.
2. **Educate about possible warning signs,** including signs and symptoms of ineffectiveness or lack of safety, highlighting common adverse events of therapy
3. **Give information on how to act,** awhere to go, or who to contact if there are any warning signs.
4. **In the case of events,** the pharmacovigilance leader shall carry out the activities of routine pharmacovigilance.

For all cases, perform reconciliation of the patient's medication: It is recommended that a patient's chronic therapies should be reviewed on admission to the hospital, in particular, the monitoring of possible interactions with the treatment of chronic and often poly-medicated patients. Likewise, it is recommended that the patient could be checked and educated about the medications he or she will be using on an outpatient

basis. Ideally, emphasis should be placed on determining whether there are any latent risks with the medications that the patient will use at home.

Notify the regulatory agency (INVIMA) of the events, according to current regulations.

If you have any questions about this guide, please contact the Colombian Association of Pharmacovigilance at asocolombianafarmacovigilancia@gmail com

Sources of information

Free sources of information useful in pharmacovigilance, specific to COVID-19:

PubMed (Website dedicated to COVID-19 clinical data available for real-time information check) https://www.ncbi.nlm.nih.gov/research/coronavirus/

Johns Hopkins University (follow-up of global cases of COVID-19) https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6

National Institutes of Health (NIH) https://www.nih.gov/coronavirus

Centers for Disease Control (CDC) https://www.coronavirus.gov

World Health Organization https://www.who.int/emergencies/diseases/novel-coronavirus-2019

OPS/PAHO: with protocols, guides, infographics. https://www.paho.org/es/tag/enfermedad-por-coronavirus-covid-19

Medscape https://www.medscape.com/today

Clinical Trials (ongoing clinical trials) www.clinicaltrials.gov

FDA www.fda.gov

DIME project www.proyectodime.info

COCHRANE ENT (ear, nose, and throat): COVID-19 (coronavirus disease) - ENT, Hearing & Balance: https://ent.cochrane.org/news/covid-19-coronavirus-disease-ent-hearing-balance

OMS/WHO: Global Research on Coronavirus Disease https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov con base de datos con artículos publicados (más de 9.000) sobre COVID-19 y facilitados desde la biblioteca BIREME: https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/

Sources of medication information:

Safety data sheets: It is suggested to have documents analyzing the safety profile of the drugs (target population, dosage, dose adjustment, adequate administration, risks of adverse reactions and medication errors). For this point, it is recommended to consult the

safety data sheets prepared by the Colombian Association of Hospital Pharmaceutical Chemists.

Institutional Therapeutic Form: It is important to have the updated form, which means a quick inclusion of products that were not previously available. Having this information supports the prescription decisions of treating physicians.

About interactions in the field of COVID-19, additional information can be obtained in:
https://www.hiv-druginteractions.org/checker
https://www.covid19-druginteractions.org

It is suggested to use databases of specialized journals that have granted free access, including

Dotlib (JAMA, BMJ, NEJM)
http://mkt.dotlib.com/covid-19/

Google Scholar (CDC, Lancet, Cell, Nature, Science, Elsevier, Oxford, Wiley, medRxiv)
https://scholar.google.com/

Available treatments for the management of SARS-CoV-2 respiratory infection:
https://www.aemps.gob.es/la-aemps/ultima-informacion-de-la-aemps-acerca-del-covid%e2%80%9119/tratamientos-disponibles-para-el-manejo-de-la-infeccion-respiratoria-por-sars-cov-2/

https://www.minsalud.gov.co/salud/publica/PET/Documents/MEDICAMENTOS%20ESCENCIALES-UCI-COVID-19%20final-25-marzo.pdf

Handbook of COVID-19 Prevention and Treatment (5) https://gmcc.alibabadoctor.com/prevention-manual/reader?cdnorigin=video-intl&pdf=Read%20Online-Handbook%20of%20COVID-19%20Prevention%20and%20Treatment.pdf

List of essential drugs for the management of patients admitted to intensive care units with suspected or confirmed diagnosis of covid-19 (lmeuci-covid-19) (6)
https://www.minsalud.gov.co/salud/publica/PET/Documents/MEDICAMENTOS%20ESCENCIALES-UCI-COVID-19%20final-25-marzo.pdf

NIH, FDA (EE.UU.): Coronavirus (COVID-19):
https://www.nih.gov/health-information/coronavirus

COVID-19 Treatment Guidelines (21-04-20):
https://www.covid19treatmentguidelines.nih.gov/overview/

World Health Organization. Off-label use of medicines for COVID-19; 2020. https://www.who.int/news-room/commentaries/detail/offlabel-use-of-medicines-for-covid-19

It is recommended that all reviewed and approved information could be available and easily accessible to decision makers and that the care staff not be guided by information without a verifiable source. This can be done by making it available in common areas of care services for nurses, doctors, pharmacists, and other members of the health care team.

Consult the web page of the Colombian Association of Pharmacovigilance for the updating of this or other related documents at: www.asofarmacovigilancia.org

Apendix 2

Público	Medicamento: Hidroxicloroquina	Cloroquina	Lopinavir/Ritonavir	Remdesivir	Interferón (IFN-B)	Interferón (IFN-B)	Inhibidores de neuroaminidasa (Ejm: Oseltamivir)	Combinación: Cloroquina e hidroxicloroquina lopinavir/ritonavir	Terapia antibiótica (Ejm :Azitromicina)
Paciente adulto estándar	Débil a favor	Débil a favor	Débil a favor Condiciones de admón: Los comprimidos de lopinavir/ritonavir no se pueden triturar o machacar pues disminuye el área bajo la curva (biodisponibilidad) del 45-47% respectivamente de lopinavir y de ritonavir (Best el al. JAIDS 2011; 58: 385-91). (3) Los comprimidos se deben tragar enteros, sin masticar, ni romper ni triturar, por riesgo de rotura de la estructura. Los comprimidos están recubiertos por un film y formulados con Meltrex (Melt Extrusion Technology) para mejorar la escasa solubilidad del lopinavir/ritonavir, mediante dispersión del medicamento en el polímero (Klein et al. JAIDS 2007; 44: 401-410). (3) La solución oral se reservará para pacientes intubados en UCI. Debido a que la solución oral tiene alcohol, no se recomienda su uso con sondas de alimentación de poliuretano, debido a su incompatibilidad potencial, debiendo utilizarse sondas de silicona o polivinilo. (3)	Fuerte en contra	Fuerte en contra	Fuerte en contra	Fuerte en contra Punto de buena práctica: Si se sospecha infección por Influenza, o se tiene evidencia de la existencia de la misma está indicado el uso de Oseltamivir.	Débil a favor Se sugiere terapia combinada con cloroquina o hidroxicloroquina y lopinavir/ritonavir para pacientes con formas severas de la enfermedad	Se recomienda terapia antibiótica empírica en los pacientes con sospecha de coinfección SARS CoV-2 /COVID-19 y neumonía bacteriana leve o moderada acorde a guías nacionales o guías institucionales. Se recomienda terapia antibiótica empírica en los pacientes con sospecha de coinfección SARS CoV-2 /COVID-19 y neumonía bacteriana grave acorde a guías nacionales o institucionales para esta enfermedad, cuando no estén disponibles pruebas diagnósticas de alta precisión (PCR múltiple)
Paciente con enf. cardiovascular	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/-COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/-COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/-COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/-COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/-COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos	Débil a Favor Se sugiere no suspender y continuar el tratamiento con IECA/ARA2 (en ausencia de contraindicaciones especificas) en pacientes a riesgo o con infección confirmada por SARS CoV-2/COVID 19. Considerando los beneficios demostrados en el control de la presión arterial, hipertrofia ventricular izquierda, disfunción diastólica, proteinuria, falla cardiaca e incluso mortalidad en escenarios específicos
Mujeres gestantes	Fuerte a favor * Se recomienda que el uso de corticoides para maduración pulmonar fetal debe hacerse de forma interdisciplinaria. Débil a favor *Tratamiento y abordaje debe hacerse de forma interdisciplinaria.	Fuerte a favor * Se recomienda que el uso de corticoides para maduración pulmonar fetal debe hacerse de forma interdisciplinaria. Débil a favor *Tratamiento y abordaje debe hacerse de forma interdisciplinaria.	Fuerte a favor * Se recomienda que el uso de corticoides para maduración pulmonar fetal debe hacerse de forma interdisciplinaria. Débil a favor *Tratamiento y abordaje debe hacerse de forma interdisciplinaria.	Fuerte a favor * Se recomienda que el uso de corticoides para maduración pulmonar fetal debe hacerse de forma interdisciplinaria. Débil a favor *Tratamiento y abordaje debe hacerse de forma interdisciplinaria.	Fuerte a favor * Se recomienda que el uso de corticoides para maduración pulmonar fetal debe hacerse de forma interdisciplinaria. Débil a favor *Tratamiento y abordaje debe hacerse de forma interdisciplinaria.	Fuerte a favor * Se recomienda que el uso de corticoides para maduración pulmonar fetal debe hacerse de forma interdisciplinaria. Débil a favor *Tratamiento y abordaje debe hacerse de forma interdisciplinaria.	Fuerte a favor * Se recomienda que el uso de corticoides para maduración pulmonar fetal debe hacerse de forma interdisciplinaria. Débil a favor *Tratamiento y abordaje debe hacerse de forma interdisciplinaria.		
Neonatos		Débil a favor. Se sugiere considerar tratamiento con cloroquina en los casos clasificados como severos	Débil a favor Se sugiere considerar tratamiento antiviral con lopinavir/ritonavir en los casosclasificados como severos						Débil en contra. Se recomienda NO usar de forma rutinaria el tratamiento antibiótico.
Pacientes inmunosuprimidos	Fuerte a favor Se recomienda que los pacientes que reciben medicamentos como infliximab, adalimumab, etanercept, vedolizumab o ustekinumab y presentan CUADROS LEVES sugestivos o confirmados de infección por SARS-CoV-2 / COVID-19, de común acuerdo con su médico tratante, aplacen la aplicación de la siguiente dosis de medicación hasta que se considere que la infección este controlada sin riesgo de complicaciones. Este periodo puede oscilar entre 30 y 45 días después de adquirir la infección por SARS CoV-2/COVID 19. - Se recomienda que en los pacientes que reciben medicamentos como infliximab, adalimumab, etanercept, vedolizumab o ustekinumab y presenten cuadros graves sugestivos o confirmados de infección por SARS-CoV-2 / COVID-19, se suspenda inmediatamente la medicación y no se debe reiniciar hasta que se considere controlada la infección y no haya riesgo de recaída por SARS CoV-2/COVID 19 u otras infecciones. La valoración del riesgo-beneficio debe ser realizada por su médico tratante	Fuerte a favor Se recomienda que los pacientes que reciben medicamentos como infliximab, adalimumab, etanercept, vedolizumab o ustekinumab y presentan CUADROS LEVES sugestivos o confirmados de infección por SARS-CoV-2 / COVID-19, de común acuerdo con su médico tratante, aplacen la aplicación de la siguiente dosis de medicación hasta que se considere que la infección este controlada sin riesgo de complicaciones. 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Reacciones adversas	Cardiovascular: intervalo QT prolongado, taquicardia ventricular polimorfa en entorchado (Torsades de Pointes). endocrino: hipoglucemia (grave). Hematológico: agranulocitosis, anemia aplásica, trombocitopenia. Musculoesquelético: trastorno del músculo. Oftálmico: trastorno de la retina (7,5%). Otic: pérdida de audición. Otros: angioedema.	Cardiovascular: bloqueo auriculoventricular, miocardiopatía, insuficiencia cardíaca, intervalo QT prolongado, taquicardia ventricular polimorfa en entorchado (Torsades de Pointes), fibrilación ventricular, taquicardia ventricular. endocrino: hipoglucemia. Hematológico: anemia hemolítica. Inmunológico: anafilaxia. Neurológico: enfermedad extrapiramidal (aguda), convulsiones. Oftálmico: trastorno de la mácula de la retina, trastorno de la retina.	Cardiovascular: bloqueo auriculoventricular (0.1%), cardiotoxicidad, intervalo PR prolongado, intervalo QT prolongado, torsades de pointes Dermatológico: eritema multiforme, síndrome de Stevens-Johnson, necrólisis epidérmica tóxica Metabólico endocrino: glucosa en sangre anormal, hipercolesterolemia, Hipertrigliceridemia. Gastrointestinales: pancreatitis (1.7%) Hematológico: disminución de la hemoglobina, disminución del recuento de plaquetas, hemorragia, aumento en pacientes con hemofilia, recuento de neutrófilos anormal. Hepático: nivel de ALT / SGPT elevado, nivel de AST / SGOT elevado, Gamma-glutamil transferasa elevada, hepatotoxicidad. Inmunológico: síndrome de reconstitución inmune (0.1%) Neurológico: depresión del sistema nervioso central Respiratorio: depresión respiratoria		Cardiovascular: miocardiopatía, insuficiencia cardíaca congestiva. Dermatológico: necrosis en el sitio de inyección (1% a 3%). Hematológico: anemia (3% a 5%), leucopenia (hasta 36%), pancitopenia, trombocitopenia (2% a 8%). Hepático: hepatotoxicidad, lesión del hígado (raro), insuficiencia hepática (raro). Inmunológico: anafilaxia (poco frecuente), reacción de hipersensibilidad, lupus eritematoso sistémico. Neurológico: convulsiones (4% a 5%). Oftálmico: trastorno vascular retiniano Psiquiátrico: pensamientos suicidas		Cardiovascular: disritmia cardíaca. Dermatológico: eritema multiforme (raro), hinchazón facial, síndrome de Stevens-Johnson (raro), necrólisis epidérmica tóxica (raro). Gastrointestinales: hemorragia gastrointestinal, colitis hemorrágica. Hepático: hepatitis. Inmunológico: anafilaxia (rara). Neurológico: convulsiones. Psiquiátrico: comportamiento anormal, delirio.		Cardiovascular: intervalo QT prolongado, Torsades de pointes. Dermatológico: pustulosis exantemática generalizada, aguda, síndrome de Stevens-Johnson, necrólisis epidérmica tóxica. Gastrointestinales: estenosis pilórica hipertrófica congénita. Hepático: necrosis hepática, hepatitis (menos del 1%), insuficiencia hepática. Inmunológico: reacción farmacológica con eosinofilia y síntomas sistémicos, reacción de hipersensibilidad. Musculoesquelético: síndrome de Eaton-Lambert, miastenia gravis, exacerbación de, crisis miasténica. Oftálmico: erosión corneal (menos del 1%).

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