Medicines Control Authority of Zimbabwe

MONITORING AND DATA COLLECTION FRAMEWORK FOR LIMITED OFF-LABEL USE OF PRESCRIPTION PREPARATION IVERMECTIN IN COVID-19 AUTHORISED IN TERMS OF SECTION 75 OF THE MEDICINES AND ALLIED SUBSTANCES CONTROL ACT (CHAPTER 15:03)

Background

Ivermectin is an anti-parasitic drug approved for the treatment of parasitic infections, including Strongyloidiasis and Onchocerciasis in humans. There is a reported increase in the use of ivermectin for the prevention and treatment of COVID-19 by the public. Please note however that there is limited evidence on its effectiveness and that it is prescription preparation (PP) off label use under prescription and supervision in line with conditions authorised in terms of section 75 of the Medicines and Allied Substances Control Act(*Chapter 15:03*) (*hereinafter referred to as the Act*).

Currently, there is:

1. No scientific evidence from pre-clinical studies on the therapeutic effect of ivermectin for the management of COVID-19;
2. No evidence of its clinical efficacy for the management of patients with asymptomatic, mild, moderate or severe COVID-19; and
3. No safety data regarding the use of ivermectin for COVID-19 in the majority of the published studies.

While there are some studies that suggest potential effectiveness of ivermectin in the prevention and management of COVID-19, existing data has the following limitations:

1. Most of the studies had small numbers of participants.
2. The doses and schedules of ivermectin administration varied.
3. Some patients taking ivermectin were also on other medications during the study.
4. Many of the studies did not clearly describe the severity of COVID-19.
5. Some of the randomized controlled trials were open-label studies.

Although ivermectin inhibits the replication of SARS-CoV-2 in laboratory studies, the doses used in the laboratory to produce those results are 100-fold higher than those approved for use in humans. Therefore, data from well-designed, randomized, controlled clinical trials are needed to provide evidence for decision on the efficacy of ivermectin for preventing and treating COVID-19.

Scope

This document is intended to provide guidance on the operationalization of the authorisation for use of ivermectin for prophylaxis and/or treatment of COVID-19 disease in terms of Section 75 of the Act. The use shall be under the supervision and guidance of the MCAZ on condition that the prescribers and users get quality human ivermectin preparations manufactured under current Good

Manufacturing Practice (GMP) and imported in terms of Section 75 of the Act. The procedures outlined in this document are not intended to replace the procedure for clinical trials therefore any researchers intending to do research should use the existing clinical trial application guidelines. The MCAZ is also in compliance with the current World Health Organization (WHO) COVID-19 Disease Treatment Living Guideline that recommends use of ivermectin for treatment of COVID-19 disease under clinical trials setting only. This is due to the limited evidence and goal to generate evidence-based practice at country level, and promote patient safety.

Objectives

The objectives of this document is to:

1. Authorise Section 75 procurement of quality assured human formulations of ivermectin for use in COVID-19 disease cases.
2. Ensure that qualified and suitably experienced healthcare providers have access to human formulations of ivermectin for prophylaxis and/ or treatment of minor to moderate COVID-19 cases.
3. Gather information on the quality, safety and efficacy of human formulations of ivermectin in treatment of COVID-19 minor to moderate cases.

Protect the public and provide a systematic way for the use of human ivermectin for of COVID-19 cases through the Section 75 procedure, and current WHO COVID-19 Disease Treatment Living Guideline.

MoHCC Secretary for Health Authorisation

The Secretary for Health and Child Care has authorised the MCAZ to authorise the importation and use of ivermectin for treatment and prophylaxis of COVID-19 disease in terms of Section 75 of the Act, Prescription Preparation (PP) "off label use" under strict monitoring conditions for ivermectin treatment outcomes for effectiveness and safety for each patient.

Product Requirements:

1. MCAZ will allow only authorised licensed pharmaceutical wholesale dealers to import and supply ivermectin to authorised institutions.
2. MCAZ will issue bulk Section 75 approval for importation of human formulations of oral ivermectin manufactured by GMP compliant facilities.
3. Approved pharmaceutical wholesale dealers shall keep records of all stocks of ivermectin procured and supplied to facilities in Form LEF 18 (Appendix I).
4. The approved wholesaler dealers shall only supply to licenced pharmacies, hospitals and dispensing doctors.
5. MCAZ will require monthly returns (reconciliations of products imported, sold, dispensed, product in hand) from authorised wholesale dealers, pharmacies (hospital, DCP), dispensing medical practitioners. Form LEF 18 - Record of Bulk Importation of Unregistered Medicines (Appendix I) shall be used for this purpose.

Monitoring and Reporting

The prescribing doctors shall submit monthly stimulated reporting surveillance forms (Appendix II and Appendix III) to the MCAZ, as part of the conditions for authorisation to use ivermectin for COVID-19.

1. The stimulated reporting surveillance forms shall be completed for every patient that is prescribed ivermectin, for treatment of COVID-19(Appendix II) or prophylaxis (Appendix III).
2. The stimulated reporting surveillance forms are intended to capture basic information on the efficacy and safety of ivermectin in the treatment of COVID-19.
3. The stimulated reporting surveillance forms shall be kept by the prescribing doctor who is supposed to complete all the required information.
4. The dispensing pharmacy shall contact the prescribing doctor and provide details of the product to be completed on the monitoring forms, upon dispensing of a prescription.
5. The forms must capture ALL adverse events experienced by the patients, including those deemed to be coincidental.
6. Continued authorisation to access the product is dependent on compliance to this framework, and submission of the required monthly reports and monitoring forms.
7. The MCAZ electronic reporting details below are available for use in reporting any adverse drug reactions, including by the patients themselves.
8. Please note that it is the primary responsibility of the prescribing doctor, dispensing pharmacist, administering healthcare worker and patient to complete the ivermectin treatment outcome form for effectiveness and safety and submit it to MCAZ.

MCAZ electronic reporting tools

Web-based platform

Healthcare professionals shall report adverse reactions at https://e-pv.mcaz.co.zw

Patients/consumers who intend to report any adverse reactions shall report at https://www.mcaz.co.zw/index.php/online-services/pv-reporting/e-reporting

Mobile apps

Mobile phone applications are available for two major operating systems listed below:

1. Android – search "MCAZ Pharmacovigilance" on the Google Play Store
2. iOs (iPhone and iPad) – search "MCAZ Pharmacovigilance" on the Apple App Store

The mobile applications can be downloaded from the respective app stores.

Desktop apps

Desktop applications for three major operating systems listed below can be downloaded from the MCAZ website:

Windows desktop application

MacOS desktop application (MacBook)

Linux based operating systems

N.B.

- ***Facilities and practitioners are required to submit written requests to the Authority if they intend to get authorisation to use ivermectin for COVID-19 in line with this framework.***
- ***Facilities and practitioners intending to use ivermectin for research purposes are required to comply with the existing provisions for clinical trials - processing of such applications will be expedited, in line with the emergency use guidelines and provisions.***

Definitions

1. Stimulated reporting operational research – A method used to encourage and facilitate reporting by healthcare professionals, either for new products or for a limited period of time.
2. Adverse event - any undesirable experience associated with the use of a medical product in a patient and which does not necessarily have a causal relationship with the product.

Disclaimer:

1. Please note that since there is limited evidence on the use of ivermectin for treatment of COVID-19 disease, the prescriber, dispenser, healthcare worker administrator and patient will be using it at their own risk.
2. Further note that only ivermectin preparations that have been authorised for use in terms of section 75 of the Act should be used.

Enquiries and submission of forms are to be directed to the Director-General, Medicines Control Authority of Zimbabwe. 106, Baines Avenue, Harare. Mobile phone: 0772145191/3

Email address: mcaz@mcaz.co.zw, website: www.mcaz.co.zw