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NAMIBIA MEDICINES REGULATORY COUNCIL

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GUIDANCE ON THE USE OF IVERMECTIN IN THE MANAGEMENT OF COVID-19

About ivermectin

Ivermectin is a broad-spectrum anti-parasitic agent for both human and veterinary use. In humans, it is used to treat a number of tropical diseases such as onchocerciasis and strongyloidiasis as well as in treating lice and scabies. It is widely used to treat and control parasites in animals.

The anti-parasitic agent was found to also inhibit the replication of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) *in vitro*, leading to its emergence as a candidate for repurposing in COVID-19[1]. Several clinical studies have since been undertaken to investigate its efficacy in COVID-19 infection and is therefore an investigational medicinal product (IMP) for this indication.

Various veterinary formulations are registered by the Namibia Medicines Regulatory Council (NMRC). However, no human formulation is currently registered. Access to the human formulation in Namibia is therefore only possible on compassionate use through section 27 of the Medicines and Related Substance Control Act, 2003 (Act No. 13 of 2003).

Current evidence on ivermectin use for the treatment COVID-19 infection

There are several randomised controlled trials and cohort studies on ivermectin use in patients with COVID-19 available as peer reviewed journals, non-peer reviewed reports and preliminary reports.

Some studies have shown benefits such as a shorter time to resolution of disease manifestation[2-5], greater reduction in inflammatory markers[3,4], shorter time to viral clearance[3,6] or lower mortality rates in patients who received ivermectin[3,5,6]. However, other studies showed no benefits or worsening of disease after ivermectin use compared to comparator drugs or placebo[6-9].

The following limitations were noted from the available studies:

- Limited number of randomised controlled trials
- Some studies were open label, introducing potential for investigator bias.

- Small sample sizes
- Varying doses and dosing schedules used
- Various concomitant medication in addition to ivermectin were used, confounding the assessment of the true efficacy or safety of ivermectin
- The severity of COVID-19 infection in the study participants was not always well described
- The study endpoints were not always clearly defined and varied between studies

A recent meta-analysis by Dr. Andrew Hill (not yet published in a peer-reviewed journal), that included randomised controlled trials concluded that the use of ivermectin in the management of COVID-19 infection is associated with faster time to viral clearance, shorter duration of hospitalisation and higher rates of clinical recovery and 75% improvement in survival rates[10].

However, the meta-analysis also concluded that results were based on limited randomised controlled trials thus more clinical trial data is required to confirm the clinical benefits observed. In addition, there is need for an optimised dosing regimen to be defined.

NMRC's view on ivermectin use in the management of COVID-19 infection

No clear conclusion can be drawn from the currently available data on the clinical efficacy and safety of ivermectin in the treatment of COVID-19 infection. To warrant approval for the use of ivermectin in the treatment of COVID-19 infection, robust evidence is required from adequately powered, well designed, and well-conducted clinical trials.

In addition, there are currently no positive recommendations for use of ivermectin in COVID-19 infection by the World Health Organization (WHO) or Stringent Regulatory Authorities (SRAs) that NMRC aligns with.

The NMRC prohibits the compounding of ivermectin as an IMP for COVID-19 infection. In addition, the Council warns against use of veterinary formulations ivermectin in humans as their safety and effectiveness has only been evaluated in the particular animal species for which they are labelled.

As there are still ongoing clinical trials on the use of ivermectin in COVID-19 management, the NMRC will continue to review emerging evidence. The NMRC therefore encourages the Healthcare Practitioners to refer to the Ministry of Health and Social Services, Case Management Standard Operating Procedure for COVID-19.

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