

28 January 2021

### Update on the use of ivermectin in the prevention or treatment of COVID-19

The second wave of the COVID-19 epidemic in South Africa has put enormous pressure on all aspects of South Africa's health system and on its communities. SAHPRA appreciates the frustration and pain experienced by healthcare practitioners, patients and families given the limited availability of evidence-based options for the prevention and treatment of COVID-19. Against this backdrop many practitioners are prescribing products claiming to contain ivermectin for the treatment and prevention of COVID-19, despite a lack of adequate evidence to support its use. As there is no formulation of ivermectin for human use available in South Africa, the ivermectin being used is either for veterinary use or sourced from illegal importation. This widespread unregulated use of ivermectin has meant that the quality and content of the ivermectin being prescribed cannot be guaranteed. Furthermore, in the absence of approved guidance for use, there is currently no standardisation of dose or indication for use. SAHPRA has also received anecdotal reports of ivermectin replacing other proven therapies as well as reports of falsified and substandard products being sold and used as ivermectin.

In an effort to respond to the urgent appeals of health care practitioners to provide access to this medicine and to curb the current widespread uncontrolled use of ivermectin, SAHPRA has had engagements with the scientific and medical community to explore the options for controlled, monitored access to reliable quality ivermectin-containing products for human use with simple but essential reporting requirements.

In some countries where ivermectin is registered for human use, registered products are being used off-label in the management of COVID-19. In such cases, the clinical responsibility for treatment as well as the monitoring of safety and efficacy lies with the prescriber. There are no ivermectin-containing products registered for human use in South Africa, but SAHPRA occasionally grants Section 21 permits for the use of unregistered ivermectin as a prescription medicine for the treatment of patients with pathogenic parasitic diseases not responding to other medicines. In such cases, applicants (usually prescribers) are required to provide feedback to SAHPRA on any adverse events encountered by the patient/s during the course of this treatment.

SAHPRA has been continually reviewing all new evidence on the safety and efficacy of ivermectin for the treatment and prevention of COVID-19. To date there is insufficient evidence for or against the use of ivermectin in the prevention or treatment of COVID-19. Furthermore, no regulatory authority with which SAHPRA is aligned (such as the US FDA, EMA or MHRA) has recommended the use of ivermectin in the management of COVID-19.

The World Health Organization (WHO) has not made any recommendations for ivermectin use, as indicated in their statement issued last week which states: *"We are closely following the research on ivermectin, which has shown promising results in some trials. With new results from more trials coming in in the following days, we will conduct a systematic review for an independent panel of experts - the guideline development group - to consider the full evidence available. All changes to WHO recommended treatments follow this expedited but comprehensive review, and are shared with the public at the earliest possible"*.

The status of availability of robust scientific information has not changed since SAHPRA issued a statement on 6 January 2021. However, some additional information has become available since then.

On 11 January 2021 the Ministerial Advisory Committee on COVID-19 released an advisory in which they concluded that “there is insufficient evidence at this stage to support the routine use of ivermectin for either the prevention or treatment of COVID-19”.

On 20 January 2021, a pre-print of a systematic review and meta-analysis on ivermectin, by Hill *et al.*, concluded that while there were some promising trends in smaller studies that there is “not yet sufficiently robust evidence base to justify the use or regulatory approval of ivermectin” and that “current randomised clinical trials of ivermectin need to be continued until ready for rigorous review by regulatory agencies.”

On 25 January 2021 the National Essential Medicines Committee COVID-19 sub-committee released the results of a rapid review of ivermectin for the prevention of COVID-19 in which they concluded that *“Overall, the benefits and the harms of ivermectin for prophylaxis of COVID-19 remains uncertain. The committee further suggests that ivermectin not be used routinely for COVID-19 except in the context of a clinical trial”*. The subcommittee also released the results of a rapid review of ivermectin for the treatment of COVID-19 in which they concluded that *“There is currently insufficient evidence to recommend ivermectin for the treatment of patients with COVID-19.”*

SAHPRA has also conducted a review of the new data and has arrived at the same conclusion as these esteemed, independent review groups. SAHPRA has a team of expert reviewers on standby to review any new data on the use of ivermectin for the prevention and treatment of COVID-19 infections which are expected to become available in the forthcoming weeks and months.

In the interim, as communicated at the press briefing of the 27 January 2021, SAHPRA will implement a compassionate use access program via the legal framework of Section 21 of the Medicines and Related Substances Control Act (101 of 1965 as amended). Clear guidance on how this access programme will work will be published separately. This access programme will utilise the opportunity to collect much-needed data on the performance of ivermectin in South African patients through its COVI-VIG reporting platform.

In addition, SAHPRA has had discussions with clinical researchers who are proposing clinical trials of ivermectin targeting different prevention and treatment scenarios. SAHPRA continues to encourage the submission of clinical trial applications designed to establish the safety and efficacy of ivermectin in the prevention and treatment of COVID-19 infection, and commits to expediting the review of any such applications received.

SAHPRA will update its position as needed, after careful and critical appraisal of such data as soon as it becomes available. SAHPRA reiterates its commitment to remaining responsive to public health needs by ensuring rapid review of any potentially valuable health products for COVID-19 while supporting prescribers and the public with up to date, reliable information on products being promoted or used for the management and prevention of COVID-19 infections.