The implications of administrating ivermectin to Covid-19 patients

Being a new virus, Covid-19 has evoked a great deal of uncertainty around which treatments will be beneficial to patients. Medical practitioners also worry about the medicolegal implications of clinical decisions they take in the face of rapidly evolving clinical knowledge and shifting regulations.

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One of the drugs causing a dilemma for practitioners is ivermectin – the anti-parasitic drug that has been punted in the media for its abilities to suppress coronavirus infections and its complications.

“Other than still undergoing clinical trials to understand potential benefits and risks at various doses, there are concerns about the availability of illegal products that are by-passing standard regulatory processes aimed at preventing distribution of sub-standard medications,” says Dr Bettina Taylor, head of clinical risk management at EthiQal. “

The rapid clinical deterioration of some patients who have contracted Covid-19, doctors may nevertheless feel compelled to provide the medication, especially if pressurised by patients or their loved ones, she says.

Legal considerations

Given that no ivermectin formulations for human use are registered in South Africa, the drug can only be administered legally in South Africa, if authorised on a named patient basis by the South African Health Products Regulatory Authority (Sahpra), which is enabled to do so by Section 21 of the Medicines and Related Substances Control Act (Act no. 1010 of 1965). According to Sahpra , license to use ivermectin will only be granted if the following requirements are met:

- The relevant Sahpra application form has been completed and submitted. As part of this process, the doctor must also agree to provide feedback to Sahpra on any adverse events encountered by any patient during treatment.
- The source of ivermectin product to be used meets appropriate quality assurance standards. This includes that the product must have been supplied by a duly authorised importer that is compliant with the set requirements for authorisation, and where the product has a product validation report, a certificate of analysis, and outcomes of post-importation testing.
- When access is required on an urgent basis, Sahpra guidelines make provision for treatment to be initiated at the same time as an application for use for an individual patient. There is also a court order to this effect. There is no

need to await approval by Sahpra in these instances.
- Licensed healthcare facilities or medical practitioners with a dispensing licence, may apply for authorisation to hold emergency stock of an ivermectin product obtained from an authorised importer, to ensure availability of certified products when prescribed.
- Where ivermectin is prescribed as part of Sahpra's compassionate use programme, the prescriber must ensure that the patient, or legal representative, has provided signed informed consent to the use of the drug.

Clinical considerations

Unless a product is obtained from an authorised source that complies with Sahpra standards, its quality is unknown. A recent study that analysed seven ivermectin formulations being sold in South Africa for human use, demonstrated that four of five formulations tested had at least one additional undeclared active pharmaceutical ingredient (API), while another product had seven.

These active ingredients ranged from non-steroidal anti-inflammatories to anti-depressants, and from anti-platelet to antiemetic drugs amongst others. Other than not knowing the quantity of ivermectin in any product purchased illegally, there are safety concerns with regards to these unknown additional ingredients that can cause unexpected allergic reactions, drug interactions and side-effects specific to any undeclared ingredient.

Various local and international authorities like Sahpra, the US Food and Drug Administration (FDA) and the European Medicines Agency have highlighted that the benefit risk ratio of ivermectin in Covid-19 patients remains unknown. Based on published studies, no recommendations in terms of whether treatment works and adverse events justify any potential benefit, can be made.

Given clinical equipoise with regards to use of ivermectin in Covid-19, patients for whom treatment is considered should, wherever possible, be enrolled in relevant therapeutic trials.

Taking the above into consideration, the policyholder was advised that, unless ivermectin is attained via an acceptable source, and in accordance with the Section 21 processes, their actions would be deemed unlawful and unethical according to the Health Professions Council of South Africa's ethical and professional rules.

“Merely accepting the fact that the family is in possession of ivermectin, without anything else, could have onerous unintended effects for the doctor, including being charged for unprofessional conduct by the HPCSA, tried criminally or being civilly pursued,” says Dr Hlombe Makuluma, EthiQal’s medicolegal advisor.

“The doctor could also lose his admission privileges at the hospital where he or she works, should the hospital become aware that they had unlawfully administered ivermectin to the patient, and breached hospital protocols in the process by not obtaining the drug through the hospital's pharmaceutical channels. The patient should be enrolled in a clinical trial if possible,” says Makuluma.

Ivermectin has traditionally been used for river blindness and intestinal strongyloidiasis in humans in other parts of the world. It has also shown in vitro activity against SARS-Cov-2 and early signs of potential clinical benefit in patients infected with Covid-19. However, in South Africa only formulations for animal consumption are currently registered.