THE HIGH COURT OF SOUTH AFRICA
(GAUTENG DIVISION, PRETORIA)

(x1

CASE NO: 2820/21

On the 1st day of April 2021
Before the Honourable Mister Justice Sardiwalla, J

In the matter between:

DR GEORGE COETZEE First Applicant

GIDEON SAMSON GUMEDE Second Applicant

GEELBOOI MOTSIPA Third Applicant

AFRIFORUM NON-PROFIT COMPANY Fourth Applicant

and

SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY First Respondent

MINISTER OF HEALTH Second Respondent

DIRECTOR-GENERAL OF THE DEPARTMENT OF HEALTH Third Respondent

MEMBER OF THE EXECUTIVE COUNCIL FOR HEALTH: GAUTENG PROVINCE Fourth Respondent

And

CASE NO: 3792/2021

In the matter between:

AFRICAN CHRISTIAN DEMOCRATIC PARTY First Applicant

DOCTORS FOR LIFE Second Applicant

and

SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY (SAHPRA) First Respondent

MINISTER OF HEALTH: ZL MKHIZE Second Respondent

And

CASE NO: 6391/2021

In the matter between:

"I CAN MAKE A DIFFERENCE"

DOCTORS AND MEDICALPRACTITIONERS GROUP Applicant

And

THE SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY (SAHPRA) First Respondent

THE MINISTER OF HEALTH Second Respondent

BOITUMELO SEMETE-MAKOKOTLA Third Respondent

PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA Fourth Respondent

And

CASE NO: 9086/2021

In the matter between:

PHARMA VALU IRENE CC First Applicant

MARX & MARX CC Second Applicant

AW & JA DREYER CC Third Applicant

JJ STRYDOM CC Fourth Applicant

MENLO PARK APTEEK CC Fifth Applicant

JJ STRYDOM APTEEK CC Sixth Applicant

PHARMA VALU NEWLANDS CC Seventh Applicant

STRYDOM & PRETORIUS CC Eighth Applicant

6/4/21

And

THE SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY (SAHPRA) First Respondent

THE MINISTER OF HEALTH Second Respondent

THE DEPARTMENT OF HEALTH Third Respondent

DRAFT ORDER

Having read the documents filed of record, having heard counsel for the applicants and the respondents and having considered the matters the following order is made:

1. SAHPRA is ordered to report back to the Court, by way of affidavit, every three months following the date of the granting of this order, until otherwise ordered on inter alia: –

1.1. adjustments made to the Programme and why such adjustments were necessary, for the prevention and/or treatment of COVID-19;

1.2. newly approved unregistered Ivermectin products;

1.3. newly authorised importers;

1.4. the number of Ivermectin products made available for named patients under the Programme; and

1.5. the particulars of healthcare facilities (including hospitals, pharmacies, compounding pharmacies and licensed dispensing doctors) that have

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been authorised to hold stock of unregistered and/or compounded Ivermectin products.

2. Any party to this application may approach the Court, by way of a Notice of Motion and Supplementary Affidavits, after having given reasonable notice in the circumstances to all relevant parties, for relief, pertaining to:

2.1. the insufficiency or the impracticality of the Programme, or any amendments affected thereto by SAPHRA;

2.2. any party's failure to give effect to the content of the Court order; and

2.3. any further aspects relating to the administration and allowance of the use of Ivermectin as a treatment against COVID-19, which is in the public interest and necessary to be considered by the Court.

3. It is the statutory duty of the South African Health Products Regulatory Authority (SAHPRA) to ensure the efficient, effective and ethical evaluation or assessment and registration of health products that meet defined standards of quality, safety, and efficacy.

4. SAHPRA has and will continue to monitor all scientific data and analysis relating to the potential of ivermectin for use in prevention or treatment of COVID-19 having regard to the requirements of quality, safety and efficacy.

5. SAHPRA has and will continue to consider the recommendations of other relevant international and national organisations including other regulatory authorities, on the use of ivermectin.

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6. On 2 February 2021 SAPHRA, in the matter under case number: 2820/2021 and consequent upon the provisions of Section 21 of the Medicines Act, agreed to a court order incorporating the "Ivermectin Controlled Compassionate Use Program Guideline" ("the Programme"), the relevant portion of the court order as aforesaid reads as follows:

> *"1. In terms of the Notice entitled 'Ivermectin Controlled Compassionate Use Programme Guideline' ("the Programme") issued by SAHPRA on 28 January 2021, a copy of which is annexed hereto marked "A", it is declared that in terms of the Programme:*
>
> *1.1 Ivermectin will be made available in terms of section 21 of the Medicines and Related Substances Control Act 101 of 1965;*
>
> *1.2 Any person, including the second and third applicants, is eligible for access to Ivermectin in terms of the Programme;*
>
> *1.3 The first applicant, and any registered medical practitioner in his position, are entitled to apply for access to Ivermectin on the terms and conditions, including the reporting obligations, specified in the Programme; and*
>
> *1.4 Where urgent access to Ivermectin is required, in the clinical judgment of the first applicant or any attending medical practitioner, and access is available to bulk stock held by an authorised health facility, treatment may be initiated at the same time as an application for the individual, named patient is submitted to SAHPRA, subject to SAHPRA's rights in this regard and the requirements of the Programme".*

7. SAHPRA is enabling the use of ivermectin for the purpose of treating or preventing COVID-19 at the discretion and responsibility of the prescribing clinician. To this end medicines containing ivermectin will be available for this purpose in two ways.

a. First, through the programme SAHPRA has launched, in terms of section 21 of the Medicines Act; and/or

b. Second, through compounding, in accordance with the provisions of section 14(4) of the Medicines Act.

Access through the section 21 Programme:

8. On 28 January 2021, after consultations with the scientific and medical community, SAHPRA adopted a programme under section 21 of the Medicines and Related Substances Act, 101 of 1965 ("the Act") entitled 'Ivermectin Controlled Compassionate Use Programme Guideline' ("the Programme"), annexed as Annexure "A". SAHPRA did so based on the considerations as outlined in its statement dated 28 January 2021 annexed as Annexure B".

9. In essence, the Programme enables access to ivermectin under Section 21 of the Act, until further data becomes available which may or may not support the use of ivermectin in the prevention or treatment of COVID-19. Through this Programme, medical practitioners will be able to apply for approval of access to unregistered ivermectin for the management of COVID-19 in individual, named patients.

10. The Programme follows a tiered mechanism that ensures controlled access, monitored use and stringent reporting. The tiered approach will ensure that quality-assured products are available, that appropriate measures are taken to ensure timely access, and that approval is granted for individual, named patients, with the obligation to report on patient outcomes. The process for this access is, in summary, as follows:

a. Authorisation to registered applicants and holders of a licence to manufacture, import or to act as a wholesaler of or distribute a medicine or Scheduled substance, issued in terms of section 22C(1)(b) of the Act.

b. Authorisation of licensed healthcare facilities to hold bulk stock. The intention of this authorisation is to limit the possible delays between obtaining Section 21 approval for an individual, named patient and accessing the ivermectin product requested.

c. Authorisation of individual named patients:

i. A registered medical practitioner may apply, via the Section 21 online submission portal, for permission to prescribe ivermectin to an individual, named patient.

ii. The medical practitioner authorised to prescribe unregistered ivermectin to an individual, named patient must comply with the reporting requirements stated in the Section 21 approval.

iii. The patient outcomes (both benefits and harms) are to be reported on SAHPRA's COVI-Vig platform, which is accessible on the SAHPRA website homepage: www.sahpra.org.za.

11. Subject to compliance with all reporting requirements of the Programme, where access to ivermectin is required, in the clinical judgment of an attending medical practitioner, treatment may be initiated at the same time as an application for the individual, named patient is submitted to SAHPRA.

12. A list of approved importers of ivermectin and a list of healthcare facilities approved to hold bulk stock will be published on SAHPRA's website and will be updated at regular intervals.

13. SAHPRA will continue to monitor all data and developments locally and internationally and will make adjustments to the Programme as necessary, where such data and/or developments either prove or disprove the safety and efficacy of ivermectin for the prevention and/or treatment of COVID-19.

Compounding with ivermectin

14. Under section 14(4) of the Medicines Act, compounding can only occur with active components of another medicine registered under the Act.

15. SAHPRA has recently registered a topical formulation of a medicine containing ivermectin as an active ingredient, for treatment of moderate to severe inflammatory lesions of papulopustular rosacea in adult patients, in terms of section 15(3)(a) of the Act. The registration was effected on 16 March 2021 upon successful completion by the applicant for registration of the final steps in the registration process.

16. The effect of the registration referred to in paragraph 13 is that Medicines containing ivermectin may be compounded and is accessible in accordance with the provisions of section 14(4) of the Act.

17. In summary, ivermectin is currently available and accessible as follows:

a. Medicines containing ivermectin may be compounded and accessed in accordance with the provisions of section 14(4) of the Act.

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b. Unregistered ivermectin-containing finished pharmaceutical products remain accessible under the Programme through the authorised suppliers of such products.

Additional matters

18. In light of the demands of the pandemic, SAHPRA will provide the public with accurate information regarding the safety, efficacy and quality of ivermectin and any other potential treatment or preventative medicine for COVID-19.

19. SAHPRA undertakes to consider proposals for exclusion from the application of a section or sections of the Act, in accordance with section 36, read with section 24A, and to engage with the Minister in such circumstances.

The position of the Minister of Health:

20. The Minister of Health who has been cited as a respondent in all the applications and the President of the Republic of South Africa who is cited in one of the applications, place the following on record:

a. That they have complied with and carried out their constitutional and statutory duties in relation to the protection of public health against the COVID-19 pandemic;

b. That the Minister of Health has ensured that SAHPRA is held accountable and provides the necessary reports as required by the relevant legislation;

c. That the Minister places reliance on SAHPRA, its expertise, recommendations and consultations in relation to the medicines and access thereto as governed by the Act; and

d. That the Minister agrees with and approves, in so far as it statutorily reposes upon him, the actions taken and decisions made by SAHPRA in relation to the ivermectin including the issuance of the Programme.

The parties agree to an order in the following terms:

21. A pharmacist, and/or a medical practitioner and/or other persons registered under the Health Professions Act 56 of 1974, who is the holder of a licence contemplated in section 22C(1)(a) of the Act, in the course of carrying on their professional activities, may compound and sell such compounded medicine which contain ivermectin as an active ingredient, for a particular patient, in a quantity not greater than the quantity required for treatment by the medical practitioner, or a quantity not greater than that prescribed by regulation, for the sale in the retail trade, on condition that such medicine is prescribed by a medical practitioner; and

22. Registered medical practitioners, who are entitled to prescribe medicines in schedule 3 of the Act, may in their professional discretion, prescribe ivermectin to be compounded into a medicine that contains ivermectin as an active ingredient for the treatment of their patients, on condition that the medicine is compounded by the holder of a license in terms of section 22C(1)(a) of the Act.

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23. Unregistered ivermectin-containing finished pharmaceutical products remain accessible under the present Programme through the authorised suppliers of such products.

24. Subject to compliance with all prescribing and reporting requirements of the Programme, where in the clinical judgment of an attending medical practitioner access to Ivermectin is required, treatment may be initiated at the same time as an application for the individual named patient is submitted to SAPHRA.

25. Without admission of any liability, the respondents, jointly and severally, the one to pay the others to be absolved, shall make payment in the sum of:

a. R350 000.00 (VAT inclusive) as a contribution towards the Applicants' costs in PHARMA VALU IRENE CC, MARX & MARX CC, AW & JA DREYER CC, JJ STRYDOM CC, MENLO PARK APTEEK CC, PHARMA VALU NEWLANDS CC, STRYDOM & PRETORIUS CC and THE SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHOURITY, THE MINISTER OF HEALTH, CASE NUMBER: 9086/2021.

b. R500 000.00 (five hundred and thousand Rand) plus VAT as a contribution towards the cost of the Applicants in DR GEORGE COETZEE, GIDEON SAMSON GUMEDE, GEELBOOI MOTSIPA, AFRIFORUM NON-PROFIT COMPANY and THE SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY, MINISTER OF HEALTH, DIRECTOR-GENERAL OF THE DEPARTMENT OF

HEALTH, MEMBER OF THE EXECUTIVE COUNCIL FOR HEALTH: GAUTENG PROVINCE, CASE NUMBER 2820/2021.

c. R500 000.00 (five hundred and thousand Rand) plus VAT as a contribution towards the cost of the Applicants in AFRICAN CHRISTIAN DEMOCRATIC PARTY, DOCTORS FOR LIFE and SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY, MINISTER OF HEALTH: ZL MKHIZE, CASE NUMBER: 3792/2021.

d. R450 000.00 (four hundred and fifty thousand Rand) plus VAT as a contribution towards the cost of the Applicants in "I CAN MAKE A DIFFERENCE" DOCTORS AND MEDICAL PRACTITIONERS GROUP and THE SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY (SAHPRA), THE MINISTER OF HEALTH, BOITUMELO SEMETE-MAKOKOTLA, PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA, CASE NUMBER: 6391/2021.

26. Should circumstances change such that any of the parties require further relief, they may approach the court for appropriate relief.

BY ORDER OF THE COURT

Registrar of the High Court of South Africa

REGISTRAR OF THE HIGH COURT OF SOUTH AFRICA
GAUTENG DIVISION,
PRETORIA

Private Bag X67, Pretoria 0001

2021 -04- 06

GD-PRET-036

GRIFFIER VAN DIE HOOGGEREGSHOF SUID-AFRIKA,
GAUTENG- AFDELING,
PRETORIA

SAHPRA
South African
Health Products
Regulatory Authority

ANNEXURE A

South African Health Products
Regulatory Authority
Building A
Loftus Park
Arcadia
Pretoria

Section 21 Access to Unregistered Medicines

January 2021

IVERMECTIN CONTROLLED COMPASSIONATE USE PROGRAMME

This document provides guidance on the programme for compassionate use access to unregistered ivermectin for human use through the provisions of Section 21 of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) as amended and clarifies the mandate, intent and scope of the programme. It outlines the process to be followed when requesting compassionate use of ivermectin in the management of COVID-19 by means of Section 21, as well as the information required to comply with the provisions of the Act and Regulations.

SAHPRA reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine and may make amendments to this document in keeping with knowledge which is current at the time of consideration of the data accompanying applications for compassionate use of unregistered medicines. SAHPRA may refuse authorisation if the information supplied does not satisfy regulatory requirements under this programme.

Version 1: First publication for implementation	January 2021

REGISTRAR OF THE HIGH COURT OF SOUTH AFRICA
GAUTENG DIVISION,
PRETORIA
Private Bag X67, Pretoria 0001
2021 -04- 06
GD-PRET-036
GRIFFIER VAN DIE HOOGGEREGSHOF SUID-AFRIKA,
GAUTENG- AFDELING,
PRETORIA

6/4/21

1 INTRODUCTION

1.1 Purpose

The purpose of this guideline is to ensure that requests for compassionate use of unregistered ivermectin are received, processed and decided upon effectively, consistently, timeously and in accordance with the Medicines and Related Substances Act, 1965 (Act 101 of 1965), ["the Act"] and the General Regulations published in terms of the Act ["General Regulations"].

1.2 Scope of the document

The use of ivermectin in the treatment and prevention of COVID-19 infections has received avid interest recently. Ivermectin has been shown to have antiviral and anti-inflammatory properties *in vitro*. Available data to date, mostly from small under-powered studies, show a trend towards some benefit in the management of COVID-19. National and international bodies have reviewed the data; and have concluded that there is unclear evidence of both benefit and harm, in the treatment and prevention of COVID-19.

There are reports of illicit products entering the South African market. Veterinary ivermectin products have also reportedly been used in the treatment and prevention of COVID-19 in South Africa. In response to the demand for access to ivermectin for human use, SAHPRA will enable a controlled compassionate access programme, using Section 21, until further data becomes available. Section 21 allows registered medical practitioners to apply for approval of access to unregistered ivermectin for the management of COVID-19 in individual, named patients. Only quality-assured ivermectin products intended for human use will be made accessible, and these will be controlled as prescription-only Schedule 3 medicines. Importation of ivermectin products for human use will only be allowed in accordance with Section 21, and from sources that meet appropriate quality assurance standards.

1.3 Objectives

This document is intended to clarify the process to follow for controlled compassionate access to ivermectin in terms of Section 21 of the Act.

1.4 Legislative Provisions

Section 1 of the Act defines "sell" as follows:

"sell" *means sell by wholesale or retail and includes import into, advertise, keep, expose, transmit, consign, convey or deliver for sale or authorize, direct or allow a sale or prepare or possess for purposes of sale, and barter or exchange or supply or dispose of to any person whether for a consideration or otherwise; and "sale" and "sold" have corresponding meanings;*

Section 1(3) of the Act states:

*In determining whether or not the registration or **availability** of a medicine is in the public interest, regard shall be had **only** to the safety, quality and therapeutic efficacy thereof in relation to its effect on the health of a person, as the case may be.*

Section 21 of the Act states:

***(1)** The Authority may in writing authorize any person to **sell** during a specified period to any specified person or institution a specified quantity of any particular medicine, medical device or IVD*

which is not registered.

(2) *Any medicine, medical device or IVD sold in pursuance of any authority granted under subsection (1) may be used for such purposes and in such manner and during such period as the Authority may in writing determine.*

(3) *The Authority may at any time by notice in writing withdraw any authority granted in terms of subsection (1) if effect is not given to any determination made in terms of subsection (2).*

Regulation 29 of the General Regulations made in terms of the Act (Government Notice 859, 25 August 2017) states:

29. Authorisation of sale of an unregistered medicine for certain purposes

(1) Subject to the provision of information, requirements and conditions as determined by the Authority, a person desiring to sell an unregistered medicine subject to registration in terms of section 14 of the Act, for purposes other than a clinical trial, shall apply to the Authority, on an application form obtainable from the office of the Chief Executive Officer, for authorisation in terms of Section 21 of the Act to sell such a medicine.

(2) An application referred to in sub-regulation (1) must be accompanied by the prescribed fee and must contain at least the following information-

(a) duly completed application form,

(b) product brochure containing relevant chemical, pharmaceutical, pre-clinical pharmacological and toxicological data and where applicable, human or animal pharmacological and clinical data with the medicine concerned;

(c) witnessed informed consent document, where applicable;

(d) details of registration or pending registration of the medicine with any other regulatory authority, if available;

(e) evidence of compliance of the manufacturer of the medicine with Good Manufacturing Practice standards as determined by the Authority;

(f) reasons why a South African registered medicine cannot be used; and

(g) any other information as may be required by the Authority.

(3) The person under whose supervision the unregistered medicine or substance is prescribed shall submit to the Authority-

(a) any adverse event report;

(b) progress reports after every six months from the date following commencement of the use of the unregistered medicine; and

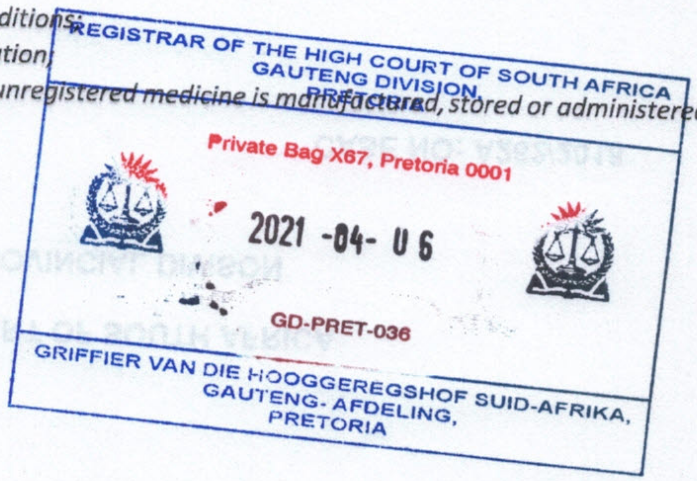
(c) progress report 30 days after the completion or termination of the use of the medicine.

(4) The Authority may-

(a) impose any additional conditions;

(b) request additional information;

(c) inspect the site where the unregistered medicine is manufactured, stored or administered; or



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(d) withdraw the authorisation to treat the patient, if the Authority is of the opinion that the safety of any patient is compromised, that the scientific reasons for administering the unregistered medicine have changed or for any other reason as determined by the Authority.

(5) A medicine referred to in sub-regulation (1) shall be properly labelled and the package shall sufficiently identify the information.

1.5 Definitions

For the purposes of this guideline any word or expression to which a meaning has been assigned in the Act or Regulations shall have the meaning so assigned and, unless the context otherwise indicates-

"adverse drug reaction" means a noxious and unintended response to a medicine;

"Authority" means the South African Health Products Regulatory Authority established by section 2;

"health care provider" means a health care provider as defined in section 1 of the National Health Act, 2003 (Act No. 61 of 2003);

"healthcare facility" means any organisation that wishes to sell an unregistered medicine and includes a health establishment as defined in section 1 of the National Health Act, 2003 (Act No. 61 of 2003), other than the holder/s of a licence to manufacture, import or to act as a wholesaler of or distribute a medicine or Scheduled substance, issued in terms of section 22C (1) (b) of the Act;

"medicine" means a medicine as defined in terms of the Act.

"sell" means sell by wholesale or retail and includes import, offer, advertise, keep, expose, transmit, consign, convey or deliver for sale or authorize, direct or allow a sale or prepare or possess for purposes of sale, and barter or exchange or supply or dispose of to any person whether for a consideration or otherwise; and "sale" and "sold" have corresponding meanings;

2. TIERED AUTHORISATION

The compassionate access programme will follow a tiered mechanism that ensures controlled access, monitored use and stringent reporting. The tiered approach will ensure that quality-assured products are available, that appropriate measures are taken to ensure timely access, and that approval is granted for individual, named patients, with the obligation to report on patient outcomes.

2.1 Authorisation to registered applicants and holders of a license to manufacture, import or to act as a wholesaler of or distribute a medicine or Scheduled substance, issued in terms of section 22C(1)(b) of the Act :

Authorisation will only be issued to registered applicant(s) and holder(s) of a license to manufacture, import or to act as a wholesaler of or distribute a medicine or Scheduled substance, issued in terms of section 22C (1) (b) of the Act to import, hold in bulk and distribute an authorised product to healthcare facilities that have received Section 21 authorisation to hold emergency stock of the

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unregistered medicine (see Authorisation 2.2).

Applications for authorisation must identify the ivermectin product(s) to be imported, the manufacturer of such products, the registration status in the country of origin and any other countries, whether the product(s) is/are registered by any national medicines regulatory authority with which SAHPRA is aligned, or whether the product(s) is/are prequalified by the World Health Organization (WHO).

If importation is authorised, the authorised pharmaceutical company must provide SAHPRA with a product validation report, a Certificate of Analysis (CoA) and the outcomes of post-importation testing (identification, assay and dissolution testing) for all imported ivermectin product(s) when that product/products is/are received in South Africa. These documents are to be emailed to **section21@sahpra.org.za.**

2.2 Authorisation of healthcare facilities to hold bulk stock:

A licensed healthcare facility (hospital or pharmacy) or a medical practitioner who holds a section 22C(1)(a) dispensing licence may apply for authorisation via the Section 21 **online submission portal** facility to hold emergency stock of an ivermectin product obtained from an authorised importer (as described in 2.1). The intention if this authorisation is to limit the possible delays between obtaining Section 21 approval for an individual, named patient and accessing the ivermectin product requested. Applicants for authorisation are also required to notify SAHPRA of the submission of applications for individual named patients by sending a short message service (SMS) to 072 134 4546 and 063 771 8906.

2.3 Authorisation of individual named patients:

A registered medical practitioner may apply, via the Section 21 online submission portal, for permission to prescribe ivermectin to an individual, named patient. In addition, the applicant must notify SAHPRA of the submission of applications for individual named patients by sending a short message service (SMS) to 072 134 4546 and 063 771 8906.

The medical practitioner authorised to prescribe unregistered ivermectin to an individual, named patient must comply with the reporting requirements stated in the Section 21 approval. The patient outcomes (both benefits and harms) are to be reported on SAHPRA's COVI-Vig programme. The reporting portal can be accessed by clicking on ONLINE SERVICES and navigating to COVI-Vig reporting system on the SAHPRA website homepage, www.sahpra.org.za

Where urgent access to ivermectin is required, in the clinical judgment of the attending medical practitioner, and access is available to bulk stock held by an authorised health facility, treatment may be initiated at the same time as an application for the individual, named patient is submitted to SAHPRA. Nonetheless, authorisation is not guaranteed, and SAHPRA retains the right to refuse permission for access, as required by the Act and Regulations. A full justification is required for each individual patient, as stipulated in the Regulations and enabled on the Section 21 online submission portal. Each application must identify the specific ivermectin product requested and the authorised supplier of that product (see 2.1).

SAHPRA undertakes to respond to all applications for individual, named patient access within 24 hours

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of submission. Where additional information is requested, responses will be dealt with accordingly.

3. UPDATE HISTORY

Version 1: First publication released for implementation	January 2021

6/4/21

SAHPRA
South African Health Products Regulatory Authority

ANNEXURE B

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

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".*

REGISTRAR OF THE HIGH COURT OF SOUTH AFRICA
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PRETORIA

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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 COVDI-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.

6/4/21