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

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, 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;*

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

(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

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

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