Ivermectin exposures reported to the Poisons Information Helpline in South Africa during the COVID-19 pandemic

V Pillay-Fuentes Lorente,[1] MB ChB, MMed (Clin Pharm); **G Voigt,**[1] BPharm; **C E du Plessis,**[1] BSc (Microbiol), MSc (Clin Pharm); **K Balme,**[2] MB ChB, MSc (Paeds); **C J Marks,**[1] MSc (Toxicol), MPhil (HPE); **E H Decloedt,**[1] MMed (Clin Pharm), PhD; **C Stephen,**[2] MB ChB; **H Reuter,**[1] Cert (Rheum), PhD; **R van Rensburg,**[1] MB ChB, MMed (Clin Pharm)

[1] *Division of Clinical Pharmacology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*

[2] *Red Cross War Memorial Children's Hospital and Department of Paediatrics and Child Health, Faculty of Health Sciences, University of Cape Town, South Africa*

Corresponding author: *V Pillay-Fuentes Lorente (14847795@sun.ac.za)*

Background. Ivermectin is an antiparasitic drug that has shown *in vitro* activity against COVID-19. Clinical studies supporting ivermectin for COVID-19 prevention and treatment are conflicting, with important limitations. Public support for ivermectin is significant, with extensive off-label use despite the conflicting views on its efficacy. Ivermectin tablets and injectable formulations are not registered in South Africa for human use by the South African Health Products Regulatory Authority. The National Department of Health does not currently recommend the use of ivermectin for COVID-19.

Objectives. To describe cases of ivermectin exposure reported to the Poisons Information Helpline of the Western Cape (PIHWC) before and after publication of the drug's *in vitro* activity against SARS-CoV-2.

Methods. In a retrospective review, ivermectin-related calls reported to the PIHWC from 1 June 2015 to 30 June 2020 (period 1) were compared with calls received from 1 July 2020 to 31 July 2021 (period 2), dichotomised according to the first publication indicating ivermectin activity against SARS-CoV-2.

Results. Seventy-one cases were screened, and 65 were included for analysis; 19 cases were reported during period 1 and 46 during period 2. During period 2, 25 ivermectin cases (54.3%) were related to COVID-19 use. Of these, 24 cases (52.2%) involved veterinary preparations, 3 (6.5%) human preparations and 19 (41.3%) unknown preparations. Fourteen cases (73.7%) during period 1 and 30 (65.2%) during period 2 were reported to be symptomatic. The most common organ systems involved were the central nervous (*n*=26 cases; 40.0%), gastrointestinal (*n*=18; 27.7%), ocular (*n*=9; 13.8%) and dermatological (*n*=5; 7.7%) systems.

Conclusion. Ivermectin-related exposure calls increased during study period 2, probably as a result of ivermectin being used as preventive and definitive therapy for COVID-19 in the absence of robust evidence on efficacy, dosing recommendations or appropriate formulations.

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COVID-19 is a novel viral infection that has caused a global pandemic leading to millions of deaths.[1] Definitive treatment options for established COVID-19 disease are limited, and the development of effective vaccines has shifted the global focus to preventive strategies.[2] Nevertheless, research into curative strategies for COVID-19 is ongoing, including the repurposing of promising drugs with direct or indirect activity against the SARS-CoV-2 virus.[3]

The anthelmintic drug ivermectin is primarily used in the veterinary sciences, and can also be used in humans for filarial and resistant scabies infections. In June 2020, ivermectin was reported to be effective against SARS-CoV-2 *in vitro*,[4] supporting previous preclinical studies showing that ivermectin has antiviral and anti-inflammatory activity.[5,6] Together these findings sparked global interest in ivermectin as potential prophylaxis and treatment for COVID-19, and led to several randomised controlled trials and subsequent meta-analyses.[7-9] However, the South African (SA) National Department of Health and the World Health Organization (WHO) do not currently recommend the use of ivermectin for COVID-19, citing significant methodological limitations of most trials without clear evidence of benefit.[8,10] Despite this, ivermectin has attracted a great deal of public interest globally.

In SA, oral ivermectin for humans is currently unregistered and requires a Section 21 application to the South African Health Products Regulatory Authority.[11] This has led to increased off-label and unmonitored use, increasing the likelihood of toxic ivermectin exposures.[12] Emerging news reports locally and abroad indicate a growing number of poisonings due to ivermectin.[13-15] In SA, the Poisons Information Helpline of the Western Cape (PIHWC) is a national service that receives calls from both the public and medical personnel regarding various toxic exposures, and is therefore well placed to assess toxic ivermectin exposures and any change in trends. Our objective was to describe and compare cases of ivermectin exposure reported to the PIHWC before and during the COVID-19 pandemic.

Methods

A retrospective review of ivermectin exposures reported to the PIHWC from inception of the PIHWC database on 1 June 2015 to 31 July 2021 was conducted. The PIHWC is a combined telephonic service between two poisons information centres situated in two large tertiary academic hospitals in Cape Town: Tygerberg Hospital and Red Cross War Memorial Children's Hospital. The service is a 24-hour helpline available to members of the public and healthcare workers in SA, with occasional international toxicology-related calls. The helpline is supported by 13 specialists in poisons information, comprising 5 clinicians, 7 pharmacists and 1 scientist. All calls

received at the PIHWC are logged onto an electronic database, AfriTox TeleLog, which allows information to be recorded in real time. Quality control of TeleLog data is conducted monthly, when quality assessors screen all calls received at the PIHWC, and errors are detected and corrected.

Ivermectin-related calls were divided into two time periods. The periods were dichotomised according to the publication of the *in vitro* study showing ivermectin activity against SARS-CoV-2 in June 2020,[4] which led to a global increase in off-label use of ivermectin for COVID-19. All calls received between 1 June 2015 and 30 June 2020 (pre-publication period) were regarded as period 1. All calls received between 1 July 2020 and 31 July 2021 (post-publication period) were recorded as period 2. Period 1 included a longer time frame (in months) to increase the probability of detecting rare pre-COVID ivermectin exposures and to limit selection bias.

Calls to the PIHWC were included as cases if the call was about a human exposure at any age, if ivermectin had been ingested within the 24 hours prior to developing symptoms, and if the caller attributed the symptoms to ivermectin use. We excluded repeat calls and calls received exclusively for ivermectin information not related to an exposure. Cases were screened, reviewed, and captured onto an electronic case report form on a secure Research Electronic Data Capture (REDCap) web platform by two study investigators (VP-FL and RvR). Information collected included caller location, whether the caller was a member of the public or a healthcare professional, type of medical facility as applicable, patient demographics (age, caller-identified sex), product type (human or veterinary), dose, route of exposure, circumstances of exposure, clinical presentation and severity of poisoning. Paediatric exposures were defined as exposures occurring in children aged ≤12 years. Poisoning severity was determined at the time of the call using the Poisoning Severity Score (PSS) as recommended by the WHO.[16] The PSS categorises poisoning cases into one of five ordinal categories according to symptoms and signs: none (PSS 0), minor (PSS 1), moderate (PSS 2), severe (PSS 3) and fatal (PSS 4). COVID-19-related cases were defined as exposures when the caller explicitly stated that ivermectin had been used for the prevention or treatment of COVID-19. Data were exported from the REDCap database and imported into Prism 8 (GraphPad Software Inc., USA) for analysis. All binary or categorical data were reported using frequencies and percentages. Medians and interquartile ranges were used to describe continuous data. The study was approved by the Stellenbosch University Health Research and Ethics Committee (ref. no. N21/08/023_COVID-19).

Results

Seventy human-related ivermectin cases were identified, and 65 were included in the analysis (Fig. 1). There were 19 cases in period 1 and 46 in period 2. Caller demographics are described in Table 1. The median (interquartile range) age of paediatric exposures during period 1 was 4 (2.5 - 5.25) years, compared with 2 (1.75 - 4.25) years during period 2.

The trend of ivermectin exposure calls throughout the study period is shown in Fig. 2. Calls increased from an average of 0.3 calls per month during period 1 to 3.5 calls per month during period 2.

Twenty-five cases (54.3%) during period 2 were specifically reported as COVID-19 related (Table 1). Of the remaining cases during period 2, 2 callers (4.4%) explicitly stated that ivermectin had not been used for COVID-19 prevention or management, and in 19 cases (41.3%) it was unknown whether ivermectin had been used for COVID-19 prevention or management. Two paediatric cases involved accidental ingestion as a result of ivermectin being accessible in the household secondary to its use for prevention or treatment of COVID-19.

Fourteen cases (73.7%) during period 1 and 30 cases (65.2%) during period 2 were symptomatic. When the periods were combined, the most common organ systems involved were the central nervous (*n*=26 cases; 40%), gastrointestinal (*n*=18; 27.7%), ocular (*n*=9; 13.8%) and dermatological (*n*=5; 7.7%) systems (Table 2). The dominant organ systems involved during period 1 v. period 2 were the central nervous (31.6% v. 43.5%), gastrointestinal (36.8% v. 23.9%), ophthalmological (15.8% v. 13.0%) and dermatological (10.5% v. 6.5%) systems. More cardiovascular symptoms (6.5%) were reported during period 2, but absolute numbers were low. Poisoning severity as measured by the PSS is presented in Table 3. All patients with PSS 3 (*n*=3 cases; 6.5%) in period 2 presented with a depressed level of consciousness. One patient had multiorgan failure and required dialysis.

During period 1, 13 (68.4%) ivermectin exposures were due to oral ingestion, 4 (21.1%) to accidental intramuscular injection and 2 (10.5%) to accidental subcutaneous injection. Oral ingestion (*n*=44 cases; 95.7%) was the most common route of exposure during period 2. All cases during period 1 involved veterinary preparations, compared with 24 cases (52.2%) during period 2. Three cases (6.5%) during period 2 involved preparations for human use, and in 19 cases (41.3%) the preparation was unknown. In 11 cases (16.9%), the dose

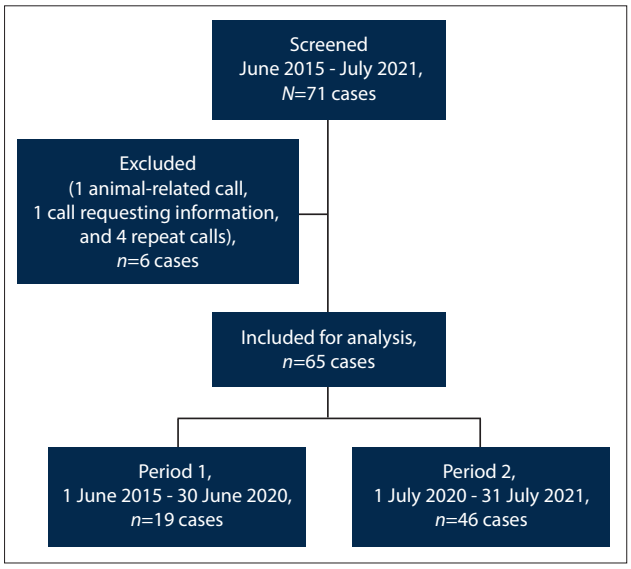

Fig. 1. Flow diagram of the study.

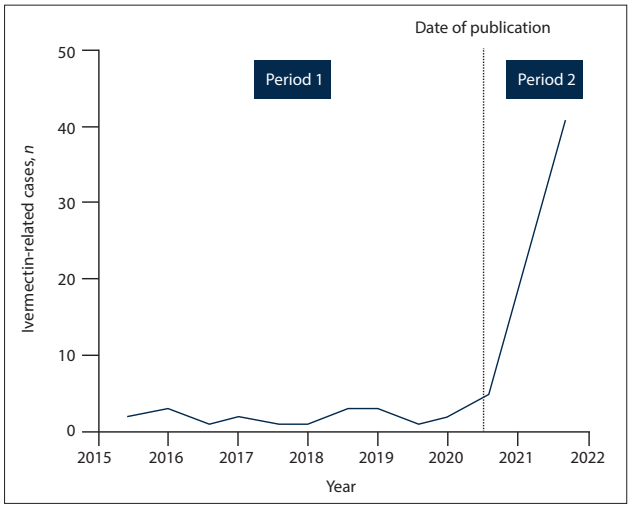

Fig. 2. Ivermectin exposures reported to the Poisons Information Helpline of the Western Cape from 2015 to 2021.

Table 1. Characteristics of ivermectin cases

Characteristics	Period 1, 1 June 2015 - 30 June 2020 (*n*=19), *n* (%)	Period 2, 1 July 2020 - 31 July 2021 (*n*=46), *n* (%)
Sex male	9 (47.4)	24 (52.2)
Paediatric exposures	4 (21.1)	8 (17.4)
Caller category		
Public	4 (21.1)	19 (41.3)
Medical personnel*	15 (78.9)	27 (58.7)
Public healthcare facility*	11 (73.3)	8 (29.6)
Private healthcare facility*	4 (26.7)	19 (70.4)
Circumstances of poisoning		
Accidental	13 (68.4)	5 (10.9)
Intentional self-harm	6 (31.6)	3 (6.5)
Other	0	38 (82.6)
COVID-19-related use of ivermectin†	0	25 (54.3)

*Public facilities refer to government-run hospitals or clinics. Private facilities refer to private hospitals, private general practitioners and pharmacies.
†Cases were considered COVID-19-related use of ivermectin if the callers explicitly stated that ivermectin had been used for either prevention or treatment of COVID-19.

Table 2. Common clinical presentations of ivermectin exposures reported during periods 1 and 2 combined (*N*=65)

Clinical presentation	*n* (%)*
Central nervous system	
Altered level of consciousness	8 (12.3)
Ataxia	6 (9.2)
Dizziness	5 (7.7)
Blurred vision	5 (7.7)
Nystagmus	3 (4.6)
Hallucinations	2 (3.1)
Involuntary movements	1 (1.5)
Gastrointestinal tract	
Abdominal pain	8 (12.3)
Vomiting	6 (9.2)
Diarrhoea	2 (3.1)
Dermatological	
Skin reactions	5 (7.7)
Other	
Respiratory depression	2 (3.1)
Acute renal injury	2 (3.1)
Acute liver injury	1 (1.5)

*Numbers and percentages reflect clinical presentations and not individual cases. Cases may have had more than one organ system involved.

Table 3. PSSs during periods 1 and 2

PSS*	Period 1, 1 June 2015 - 30 June 2020 (*n*=19), *n* (%)	Period 2, 1 July 2020 - 31 July 2021 (*n*=46), *n* (%)
0 (none)	5 (26.3)	16 (34.8)
1 (minor)	12 (63.2)	19 (41.3)
2 (moderate)	2 (10.5)	8 (17.4)
3 (severe)	0	3 (6.5)
4 (fatal)	0	0

PSS = Poisoning Severity Score.
*The PSS was recorded at the time of the call to the Poisons Information Helpline of the Western Cape.

that had been ingested was reported. Two cases were reported for each of the following doses: 12 mg, 24 mg and 48 mg, and 1 case each for 3 mg, 30 mg, 50 mg, 100 mg and 300 mg.

Discussion

Our study describes ivermectin exposures reported to the PIHWC from 2015 to 2021. We found a 12-fold increase in average monthly recorded cases subsequent to the publication of a study reporting *in vitro* activity of ivermectin against SARS-CoV-2.[4] In a recent publication, the Oregon Poison Centre also reported an increase in ivermectin-related calls, from 0.25 calls per month in 2020 to 0.86 calls per month in 2021.[15] The same trend has been seen by other poisons information centres and toxicovigilance reporting authorities across the world.[17,18] It is likely that the increase in ivermectin exposure calls is related to growing pressure by advocacy groups to allow access to ivermectin for use against COVID-19, as well as increasing off-label prescribing of ivermectin by healthcare professionals.[19-21]

Reports describe not only increasing use of ivermectin, but also inappropriate use of veterinary formulations, adulteration of available products, and prescription of untrialled dose regimens. The Oregon report[15] found an increase in the use of ivermectin veterinary products, in keeping with our study findings, where more than half of the ivermectin exposures during period 2 were secondary to veterinary preparations. This is probably an underestimate, as a further 41.3% of the formulations were unknown. Patients may have been reluctant to divulge information around the acquisition of ivermectin, as the oral formulation is unregistered in SA and only available through Section 21 application or clinical trials.[11,22,23]

An SA study evaluating seven different ivermectin formulations used for COVID-19 from illegal importation or compounding pharmacies found that most were adulterated, with four products containing traces of other drugs such as paracetamol, telmisartan and clopidogrel.[24] The authors further identified the most common ivermectin preparations in SA as 12 mg and 18 mg tablet formulations.[24] This would equate to 171 - 257 µg/kg/tablet for an average 70 kg adult. Although doses of 200 - 400 µg/kg have been recommended for approved antiparasitic indications,[25,26] optimal ivermectin dosage regimens for use against SARS-CoV-2 have not yet been established.[27,28] The consequences of such unregulated dispensing and variable prescribing practices as COVID-19-directed prevention or treatment are that patients may experience unintended ivermectin toxicity.

Our report is one of only a few describing human toxicity due to ivermectin. Limited previous reports have shown that many organ systems may be involved, with clinical presentations including coma, seizures, diarrhoea and vomiting, respiratory failure, hypotension, visual disturbances and metabolic acidosis.[29,30] Our study recorded involvement of certain dominant systems, namely the central nervous, gastrointestinal and dermatological systems, which were aligned with the recent WHO Vigibase pharmacovigilance study reporting on ivermectin adverse drug reactions.[31] Reports[31,32] have commented on the additional effect of homozygous mutations in the *ABCD1* transporter gene, leading to cases of severe neurological toxicity. As this was not assessed in our study, the incidence or impact of such a mutation in the SA population on the presentation of neurotoxicity is not known.

The PSS recorded in our study was at the time the call was received, and no further case follow-up was performed. Despite this, our study found a higher proportion of cases with moderate and severe PSSs during period 2 compared with period 1. This potentially

reflects the use of higher doses of ivermectin for COVID-19 in the absence of appropriate dosing recommendations, as well as inappropriate use of veterinary formulations with limited human safety data. Further factors likely to have contributed to the severity of clinical presentation include the use of formulations with unknown concentrations or other constituents, repeated dosing with short dosing intervals, and the use of routes of administration different to those intended for the specific product.

Study limitations

Our study has several limitations, mainly due to the inherent limitations of poisons information centre data, including that the data used were routine data collected for purposes other than our specific study. Firstly, not all ivermectin exposure cases are reported to the PIHWC. Our study therefore suffers from a reporting bias due to calls being self-reported. Some healthcare professionals may be more comfortable managing ivermectin toxicities and may not call the PIHWC for further advice. Secondly, details around ivermectin formulations and the dose ingested were unknown in some instances, potentially owing to reluctance to divulge information around acquisition of ivermectin for fear of implicating others, or being uninformed regarding the doses administered. Thirdly, the PSS was assigned at the time of the call, but cases may subsequently have become more symptomatic, resulting in under-reporting of the true severity of ivermectin toxicity.

Conclusion

Ivermectin exposures reported to the PIHWC followed worldwide trends, increasing subsequent to the announcement of *in vitro* efficacy of ivermectin against SARS-CoV-2. Our study found a 12-fold increase in the average monthly cases reported to the PIHWC. This has occurred despite widely expressed scientific concerns over the limitations of such research findings.

Off-label use of ivermectin for the management of COVID-19 is not without hazard, and the potential toxic effects of ivermectin may result in serious side-effects requiring hospital admission. It is therefore important that while further evidence is gathered, more stringent processes are implemented to curb the irrational use of ivermectin, thereby protecting against unwanted clinical toxicity.

Declaration. None.

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Author contributions. All authors contributed to the study design, protocol development and manuscript review. GV, CEdP and CJM conducted review of all cases and data capturing. VP-FL and RvR conducted the data analysis and wrote the manuscript.

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Conflicts of interest. None.

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int/ (accessed 6 August 2021).
2. World Health Organization. Clinical management of COVID-19 patients: Living guidance. 25 January 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2 (accessed 6 August 2021).
3. De P, Chakraborty I, Karna B, Mazumder N. Brief review on repurposed drugs and vaccines for possible treatment of COVID-19. Eur J Pharmacol 2021;898:173977. https://doi.org/10.1016/j.ejphar.2021.173977
4. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*. Antiviral Res 2020;178:104787. https://doi.org/10.1016/j.antiviral.2020.104787
5. Heidary F, Gharebaghi R. Ivermectin: A systematic review from antiviral effects to COVID-19 complementary regimen. J Antibiotics 2020;73(9):593-602. https://doi.org/10.1038/s41429-020-0336-z
6. Zhang X, Song Y, Ci X, et al. Ivermectin inhibits LPS-induced production of inflammatory cytokines and improves LPS-induced survival in mice. Inflamm Res 2008;57(11):524-529. https://doi.org/10.1007/s00011-008-8007-8
7. Hill A, Abdulamir AS, Ahmed S, et al. Meta-analysis of randomised trials of ivermectin to treat SARS-CoV-2 infection. Open Forum Infect Dis 2021;8(11):ofab358. https://doi.org/10.1093/ofid/ofab358
8. National Department of Health, South Africa. Rapid Review Report Component: COVID-19. Ivermectin for treatment of COVID-19: Evidence review of clinical benefits and harms. 18 June 2021. https://www.health.gov.za/wp-content/uploads/2021/06/Rapid-review-of-Ivermectin-for-COVID-19-Update_18June2021.pdf (accessed 6 August 2021).
9. Krolewiecki A, Lifschitz A, Moragas M, et al. Antiviral effect of high-dose ivermectin in adults with COVID-19: A proof-of-concept randomised trial. EClinicalMedicine 2021;37:100959. https://doi.org/10.1016/j.eclinm.2021.100959
10. World Health Organization. WHO advises that ivermectin only be used to treat COVID-19 within clinical trials. 31 March 2021. https://www.who.int/news-room/feature-stories/detail/who-advises-that-ivermectin-only-be-used-to-treat-covid-19-within-clinical-trials (accessed 30 December 2021).
11. South African Health Products Regulatory Authority (SAHPRA). Registration of Medicines Section 21 Application Form. Section 21 Application. South African Health Products Regulatory Authority's responsibilities and liability when performing its function in terms of Section 21 of Act 101 of 1965. January 2013. https://www.sahpra.org.za/wp-content/uploads/2020/04/CM-Section-21-Application-Form.pdf (accessed 2 November 2021).
12. South African Health Products Regulatory Authority (SAHPRA). Media release. SAHPRA clarifies its stance on ivermectin. 3 February 2021. https://www.sahpra.org.za/wp-content/uploads/2021/02/SAHPRA-clarifies-its-stance-on-Ivermectin-Afriforum.pdf (accessed 6 August 2021).
13. Sinkins E. UPDATED | Two people end up in ICU after ivermectin overdose in Pietermaritzburg last year. The Witness, 16 January 2021. https://www.news24.com/witness/news/pietermaritzburg/two-people-end-up-in-icu-after-ivermectin-overdose-in-pietermaritzburg-20210116 (accessed 6 August 2021).
14. Widmer S. Do-it-yourself COVID treatments an evolving threat. ABC News, 26 February 2021. https://abcnews.go.com/Health/covid-treatments-evolving-threat/story?id=75946569 (accessed 6 August 2021).
15. Temple C, Hoang R, Hendrickson RG. Toxic effects from ivermectin use associated with prevention and treatment of Covid-19. N Engl J Med 2021;385(23):2197-2198. https://10.1056/nejmc2114907
16. World Health Organization. Poisoning Severity Score. Technical document. 20 October 2007. https://www.who.int/publications/m/item/poisoning-severity-score (accessed 2 November 2021).
17. Cook MA, Brooke N. Event-based surveillance of poisonings and potentially hazardous exposures over 12 months of the COVID-19 pandemic. Int J Environ Res Public Health 2021;18(21):11133. https://www.mdpi.com/1660-4601/18/21/11133/htm
18. Romo V. Coronavirus updates: Poison control centers are fielding a surge of ivermectin overdose calls. NPR, 4 September 2021. https://www.npr.org/sections/coronavirus-live-updates/2021/09/04/1034217306/ivermectin-overdose-exposure-cases-poison-control-centers (accessed 30 December 2021).
19. BBC News. Ivermectin: South African medics using unproven worm drug to treat Covid-19. 27 March 2021. https://www.bbc.com/news/world-africa-56526632 (accessed 23 November 2021).
20. Stokel-Walker C. Ivermectin buyers clubs. New Sci 2021;251(3355):8-9. https://doi.org/10.1016/S0262-4079(21)01767-X
21. SAHARI. South Africa has a right to ivermectin. https://www.quicket.co.za/events/130424-sahari-south-africa-has-a-right-to-ivermectin/?ref=event-page (accessed 23 November 2021).
22. South African Health Products Regulatory Authority (SAHPRA). Section 21 access to unregistered medicines: Ivermectin controlled compassionate use programme. 28 January 2021. https://www.sahpra.org.za/wp-content/uploads/2021/01/Section_21_Ivermectin_Controlled_Compassionate-Use-Programme_Jan21_FINAL.docx.pdf (accessed 6 August 2021).
23. South African Health Products Regulatory Authority (SAHPRA). Update on the use of ivermectin in the prevention or treatment of COVID-19. 28 January 2021. https://www.sahpra.org.za/wp-content/uploads/2021/01/Statement-from-SAHPRA-on-Ivermectin-use-for-treatment-of-COVID-19_28-JAN-2021.pdf (accessed 23 November 2021).
24. Bhorat QE, Bhorat AE. A qualitative analysis of seven ivermectin formulations in South Africa. S Afr Med J 2021;111(4):288-290. https://doi.org/10.7196/SAMJ.2021.v111i4.15630
25. Canga AG, Prieto AMS, Diez Liébana MJ, Martínez NF, Sierra Vega M, García Vieitez JJ. The pharmacokinetics and interactions of ivermectin in humans – a mini-review. AAPS J 2008;10(1):42-46. https://doi.org/10.1208/s12248-007-9000-9
26. Batiha GES, Alqahtani A, Ilesanmi OB, et al. Avermectin derivatives, pharmacokinetics, therapeutic and toxic dosages, mechanism of action, and their biological effects. Pharmaceuticals (Basel) 2020;13(8):196. https://doi.org/10.3390/ph13080196
27. Schmith VD, Zhou J, Lohmer LRL. The approved dose of ivermectin alone is not the ideal dose for the treatment of COVID-19. Clin Pharmacol Ther 2020;108(4):762-765. https://doi.org/10.1002/cpt.1889
28. Momekov G, Momekova D. Ivermectin as a potential COVID-19 treatment from the pharmacokinetic point of view: Antiviral levels are not likely attainable with known dosing regimens. Biotechnol Biotechnol Equip 2020;34(1):469-474. https://doi.org/10.1080/13102818.2020.1775118
29. Ivermectin. In: In Depth Answers [database on the Internet]. Greenwood Village, Colo.: IBM Corporation, 2017. www.micromedexsolutions.com (accessed 6 August 2021, subscription required to view).
30. Yang C-C. Acute human toxicity of macrocyclic lactones. Curr Pharmaceut Biotechnol 2012;13(6):999-1003. https://doi.org/10.2174/138920112800399059
31. Campillo JT, Boussinesq M, Bertout S, Faillie JL, Chesnais CB. Serious adverse reactions associated with ivermectin: A systematic pharmacovigilance study in sub-Saharan Africa and in the rest of the world. PLoS Negl Trop Dis 2021;15(4):e0009354. https://doi.org/10.1371/journal.pntd.0009354
32. Baudou E, Lespine A, Durrieu G, et al. Serious ivermectin toxicity and human *ABCB1* nonsense mutations. N Engl J Med 2020;383(8):787-789. http://www.nejm.org/doi/10.1056/NEJMc1917344

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