Ivermectin Interest Group

Email: dr@ymedii.com/aldousc@ukzn.ac.za

Phone No: +27828091182/+27844077603

2nd January 2021

To:

The Honourable Minister of Health – Dr Zweli Mkhize

The Honourable Deputy Minister of Health – Dr Joseph Phaahla

The Director General of Health – Dr Sandile Buthelezi

The Ministerial Advisory Committee (MAC)

The South African Health Regulatory Authority (SAHPRA)

The National Institute of Communicable Diseases (NICD)

South Africa Medical Research Council (SAMRC)

The Academy of Science of South Africa (ASSAF)

INTRODUCTION

The COVID-19 epidemic in South African has worsened. The current second wave is potentially compounded by the SARS-COV-2 variant N501Y that is just as lethal as the wild type but more readily transmitted, as well as human behavioural changes at a traditional time of celebration. Movement across provincial borders to be with families during the holidays has compounded the risk of transmission. Our resources, specifically healthcare resources in coping and dealing with the onslaught that the pandemic has brought, have been stretched beyond capacity across all sectors. .

The logistics of dealing with COVID-19 are proving difficult, with the government attempting to balance attempts to lower morbidity and mortality, with protecting the economy. While the vaccine rollout has been initiated in a number of countries, the pace of vaccination has been slower than anticipated. For example, in the United States by 28 December 2020, against a projected 20-million vaccinations by year-end, only 11-million doses have been distributed and 2.1 million vaccinations implemented. The rollout in the European Union

has only recently been initiated. The actual costs of logistical and human resource requirements, as well as timely and efficient implementation, are yet to be clarified. A critical issue to consider is that we need to roll the vaccine out to over 60% of the population before herd immunity snuffles the disease out. This could take several months, not enough time to prevent a third wave.

Lower and middle-income countries ("LMIC"), including South Africa, lag behind high-income countries in their ability to access the COVID-19 vaccines and enormous numbers of new infections can be anticipated prior to large-scale implementation of vaccination efforts. As a country, we need to keep an open mind to various immediately accessible options for prevention and treatment of COVID-19, to mitigate the impact of the pandemic until such time as we can roll out a comprehensive vaccination program.

Across the globe, and more especially many LMIC nations, have realised that the vaccine cannot be the only solution in the immediate future.

The impact of the second wave is felt largely at the frontline, namely at the general practitioner, clinic and hospital level. Therefore, the Country must explore every possible healthcare solution for COVID-19 prophylaxis and treatment to minimise morbidity and mortality, reduce the risks to health care workers, and reduce immense stress on our health system.

The search for preventative and curative solutions has presented a possible opportunity with the use of a well-established medicine listed on the WHO essential drug list. The latter is the antiparasitic drug, Ivermectin. It has changed the landscape of the scourge of parasite infections in many third world countries. The developers were recognised for their achievement by being awarded the Nobel Prize for Medicine in 2015.

Please note that a full list of references is available for this missive upon request. Extensive referencing is excluded for ease of reading this document.

WHO WE ARE AND WHAT ARE OUR INTERESTS

We are a group who are advocating for the principles of good critical science and flexibility of thought to be applied in looking at potential treatments in a pandemic, where our resources are exhausted and/or under considerable strain. We are not dismissive of any treatment that has shown benefit in treating COVID-19 but examine evidence to inform evidence-based medicine.

The Ivermectin Interest Group ("IIG") is a grouping of clinicians, public health specialists, community health workers and scientists that have an interest in exploring the potential of the medicine Ivermectin to both prevent and treat COVID-19. While we fully endorse the pursuit and implementation of all available evidence-based vaccines, as they are essential to ending the pandemic, we wish to ensure that the potential of promising preventive and therapeutic measures, including drugs, be fully and urgently investigated.

As the world's attention is focused on the rollout of vaccines, South Africa appears to be lagging behind in securing a stockpile, especially for the most vulnerable of our population. There is not much optimism that we can have any reasonable form of protection from a possible third wave in the forthcoming winter. The inability and lack of capacity in securing the vaccine and the uncertainty of its protection to new strains and variants demands a search for and implementation of alternative preventative measures in addition to the current benefit of physical distancing, masks and sanitiser.

This submission relates to the potential for Ivermectin as a prophylactic and therapeutic drug for COVID-19. The IIG does not endorse or endeavour to breach any laws or professional and ethical rules and regulations and distances itself from individuals who have made inflammatory and misleading statements about our local regulators and experts. As a group, we are aware of the information being presented from those advocating it's use without research evidence. However, we strongly believe that an objective, unbiased and scientific approach is necessary.

IVERMECTIN

Currently, the use of Ivermectin is controversial for sound scientific reasons. We acknowledge that the drug has not been indicated for use in COVID-19 prophylaxis or treatment, either locally or by the major regulatory bodies globally. However, we must note that Ivermectin has been the subject of a number of studies and reviews, including a review funded by the World Health Organisation (WHO) as part of the ACT Accelerator and UNITAID programmes (Hill et al., 2020) that concluded that urgent further trials are required and that results anticipated from clinical trials currently underway will be available in January 2021 and could provide the numbers required for a meta-analysis to provide a reliable outcome.

Dr Andrew Hill Sr, a respected academic and World Health Organisation (WHO) researcher who has been tasked, as part of the Unitaid ACT Accelerator initiative to improve access to COVID-19 treatments and diagnostics, recently reported at an international ivermectin conference a meta-analysis of data from the first 11 randomised controlled trials that have been identified. This meta-analysis, while still ongoing, points towards the significant promise of Ivermectin as a low cost, widely available therapy potentially useful in COVID-19. His finding thus far, in the trials totalling 1452 patients, is that ivermectin treatment is associated with faster time to viral clearance, shorter duration of hospitalisation, 43% higher rates in clinical recovery (95% CI 21-67%), and a profound 83% improvement in survival (95% C.I. 65-92%). Other reviews that draw similar conclusions (Appendix 1) and national health authorities are also looking at Ivermectin (Appendix 2). The ivermectin studies stand out because there are virtually no studies showing a negative outcome.

There is a plethora of clinical research trial results supporting the efficacy of Ivermectin for COVID-19 prophylaxis and treatment, including both small and large randomised controlled trials and observational studies reported in peer-reviewed journals and pre-publication websites. A living systematic review of all papers is required in South Africa, to monitor this literature and further support meta-analysis data to gain a clearer picture of the effect of Ivermectin on COVID-19.

THE SCIENCE BEHIND IVERMECTIN

Properties of Ivermectin

Many existing drugs have been investigated for their potential to be re-purposed, Ivermectin is one such drug. However, Ivermectin is unique in that it possesses both anti-viral and anti-inflammatory properties. For example, since 2012, a growing number of cellular studies have demonstrated that Ivermectin has anti-viral properties against an increasing number of RNA viruses, including influenza, Zika, HIV, Dengue, and most importantly, SARS-CoV-2. Insights into the mechanisms of action by which Ivermectin both interferes with the entrance and replication of SARS-CoV-2 within human cells are mounting.

Caly et al. first reported that Ivermectin significantly inhibits SARS-CoV-2 replication in a cell culture model, observing the near absence of all viral material 48h after exposure to Ivermectin. However, some questioned whether

this observation is generalisable clinically given the inability to achieve similar tissue concentrations employed in their experimental model using standard or even massive doses of Ivermectin. It should be noted that the concentrations required for effect in cell culture models bear little resemblance to human physiology given the absence of an active immune system working synergistically with a therapeutic agent such as Ivermectin. Further, prolonged durations of exposure to a drug likely would require a fraction of the dosing in short term cell model exposure. Most importantly, the belief that 100 fold concentration would be required for clinical effects has been disproven by the rapidly increasing numbers of studies showing efficacy at standard dosing. This is reassuring in light of safety concerns.

Furthermore, it is also possible that co-existing or alternate mechanisms of action explain the clinical effects observed, such as the competitive binding of Ivermectin with the host receptor-binding region of SARS-CoV-2 spike protein, as proposed in six molecular modelling studies. In four of the studies, Ivermectin was identified as having the highest or among the highest of binding affinities to spike protein S1 binding domains of SARS-CoV-2 among hundreds of molecules collectively examined, with Ivermectin not being the particular focus of study in four of these studies. This is the same mechanism by which viral antibodies, in particular, those generated by the Pfizer and Moderna vaccines, contain the SARS-CoV-2 virus. The high binding activity of Ivermectin to the SARS-CoV-2 spike protein could limit binding to either the ACE-2 receptor or sialic acid receptors, respectively either preventing cellular entry of the virus or preventing hemagglutination, a recently proposed pathologic mechanism in COVID-19.

Ivermectin has also been shown to bind to or interfere with multiple essential structural and non-structural proteins required by the virus in order to replicate. Finally, Ivermectin also binds to the SARS-CoV-2 RNA-dependent RNA polymerase (RdRp), thereby inhibiting viral replication.

Safety of Ivermectin

The discovery of Ivermectin in 1975 was awarded the 2015 Nobel Prize in Medicine given its global impact in reducing onchocerciasis (river blindness), lymphatic filiariasis, and scabies in endemic areas. It has since been included on the WHO's List of Essential Medicines. Beyond the massive, global reductions in morbidity and mortality achieved in many low-and middle-income populations, the knowledge base establishing its high margin of safety and low rate of adverse effects are nearly unparalleled given it is based on the experience of

billions of doses dispensed. Numerous studies report low rates of adverse events, with the majority mild, transient, and largely attributed to the body's inflammatory response to the death of the parasites and include itching, rash, swollen lymph nodes, joint pains, fever and headache. In a study which combined results from trials including over 50,000 patients, serious events occurred in less than 1% and largely associated with the administration in Loa.

Further, according to the pharmaceutical reference standard Lexicomp, the only medications contraindicated for use with Ivermectin are the concurrent administration of anti-tuberculosis and cholera vaccines while the anticoagulant warfarin would require dose monitoring. A longer list of drug interactions can be found on the drugs.com database, with nearly all interactions leading to a possibility of either increased or decreased blood levels of Ivermectin. Another special caution is that immunosuppressed or organ transplant patients who are on calcineurin inhibitors such as tacrolimus or cyclosporine or the immunosuppressant sirolimus should have close monitoring of drug levels when on Ivermectin given that interactions exist which can affect these levels. In studies showing tolerance and lack of adverse effects in human subjects who received escalating high doses of Ivermectin, toxicity was found to be unlikely, although a reduced efficacy due to decreased levels may be a concern. Finally, Ivermectin has been used safely in pregnant women, children, and infants.

Studies Demonstrating Anti-Inflammatory Properties of Ivermectin in COVID-19

The beneficial impacts reported from treatment studies on hospitalised and ICU patient populations suggest that potent anti-inflammatory properties of Ivermectin could play a major role given that little viral replication occurs in the later phases of COVID-19, nor can the virus be cultured, and only in a minority of autopsies can viral cytopathic changes be found. Thus, it appears that the increasingly, well-described in-vitro properties of Ivermectin as an inhibitor of inflammation are far more clinically potent and significant than previously recognised. The growing list of studies demonstrating the anti-inflammatory properties of Ivermectin includes its ability to; inhibit cytokine production after lipopolysaccharide exposure, downregulate transcription of NF-kB, and limit the production of both nitric oxide and prostaglandin E2.

Summary of studies demonstrating the clinical evidence in prophylaxis and treatment

A categorical summary of the statistically significant results found from controlled trials included are as follows:

Controlled trials in the prophylaxis of COVID-19 (n=6)

- 4 RCT's with large statistically significant reductions in transmission rates, N=851 patients
- 3 OCT's with large statistically significant reductions in transmission rates, N=1,688 patients

Controlled trials in the early, outpatient treatment of COVID-19 (n=5)

- 2 RCT's with large, statistically significant reductions in rates of deterioration or hospitalisation, N=1,085
- 1 RCT with a near statistically significant decrease in time to recovery, p=.07, N=130
- 1 RCT with a statistically significant decrease in viral load, days of anosmia and cough

Controlled trials in late phase treatment of the hospitalised patient (n=12)

- 2 RCT's with large, statistically significant reductions in mortality (N=580)
- 1 RCT with a near statistically significant reduction in mortality, p=0.052
- 3 OCT's with large, statistically significant reductions in mortality (N=1,688)

IVERMECTIN USE AND/OR APPROVAL FOR COVID-19 GLOBALLY

Regulatory approval has been provided in Belize and Macedonia. Bulgaria and India are anticipated to follow shortly along with several other LMICs. Widespread use of Ivermectin, often uncontrolled, has occurred in a number of regions and specifically in Latin America, Bangladesh, and Uttar Pardesh

Ivermectin has also been used in a controlled environment, such as in the Front Line COVID-19 Critical Care Alliance ("FLCCC") MATH+ study, with excellent results.

THE DoH AND SAHPRA STATEMENTS ON THE USE OF IVERMECTIN FOR COVID19 TREATMENT

On the 21st and 22nd of December, both the DoH and SAHPRA put out public statements warning against the use of Ivermectin in COVID-19 treatment. The drug is currently not registered for human use in South Africa, and although evidence is building on the potential efficacy of the drug, there have been no large randomised controlled trials for its use in COVID-19 treatment providing a definitively positive outcome. However, it is receiving increased attention in various parts of the world, with smaller countries such as Belize and Macedonia regulating for its use.

We contend that South Africa, as a Country, should explore the promise that Ivermectin use presents for us as a nation, using an objective, unbiased and scientific approach.

Ivermectin is a drug that is out of patent and therefore lacks any incentive for a pharmaceutical company to invest in large clinical trials. This creates a unique opportunity for the South African Government. Through its various institutions to pioneer its own local research into what is potentially game-changing addition to our limited arsenal of medicines to treat COVID-19.

Despite a proliferation of publications on the use of Ivermectin globally, most of these studies, have been hastened to publication, particularly positive ones, under the global urgency to assuage the virus's effects. In many of these studies, the numbers are small and the researchers, in doing their best to help in the pandemic and with limited resources, have resulted in the trials being underpowered. Despite some underpowered studies having shown no statistical significance because the sample sizes have been small, a number of these show a positive trend. For this reason, expert meta-analysis is required to ensure sufficient statistical power to find and validate the true efficacy of Ivermectin in COVID-19 prevention and treatment. The current meta-analyses of existing data give enough reason not to dismiss Ivermectin as a potential drug for use in COVID-19 yet.

Ivermectin has not been registered for use in COVID-19 treatment, neither have Hydroxycholoroquine, Remdesivir, Doxycycline, Melatonin, and many others used regularly as a standard of care. Remdesivir in particular is a costly drug. The combination of these drugs adds much to the cost of treatment, both from the pill burden, intravenous administration of remdesivir, and nursing role.In addition melatonin needs to be used for 14 days. The biggest interest in COVID-19 therapy has, understandably been the development of a vaccine. Vaccines are being rolled out now, almost a full year since the identification of COVID-19

in China. The vaccine rollout will not happen in time in South Africa to save those susceptible to succumbing to COVID-19 in the next few months. Even when the vaccine becomes available, the limited supply will mean that an estimated 90% of our population will be without vaccine protection and this will delay prospects of herd immunity being a reality in the foreseeable future. In reality, what South Africa has in its arsenal to protect the population at present is non-pharmaceutical interventions (NPIs) (which has limited success in a population prone to flouting the rules) and the option of exploring novel treatment options.

In a time of pandemic, where the promise of vaccine is remote, clinicians and the population at large, in desperation will resort to using any treatment or a combination of treatments with some promise. This, unfortunately, is what is happening on the ground with some of our clinicians already using Ivermectin, reportedly with success, for COVID-19. Both veterinary and illegally imported human use products are being used, based on anecdotal evidence and the proliferation of small unconnected studies coming from across the globe. Although this is seen by some as anarchical, the motives are noble and based on the need to treat patients effectively.

Whilst it is was true that weeks back the evidence of efficacy and safety of the drug in COVID-19 treatment was tentative and that individual studies did "not demonstrate any clear evidence of efficacy or safety", comprehensive meta-analyses of studies have arguably provided a proof of concept. These have been dismissed by the NDoH, prematurely we believe, as having "insufficient data available for review and evidence synthesis". They have ignored a large number of trials with over 7000 patients in total. Dr Andrew Hill's summary of a meta-analysis on the available data found that there was an 83% reduction in mortality, reduced hospital stay, a faster viral clearance, and a 43% higher rate of clinical recovery. Also, most of the 27 studies available at present show Ivermectin is beneficial in treatment.

SAHPRAs statement that "The use of such a drug could potentially lead to harmful effects or even death" appears to be unfounded. In our literature search, we have found mention of some mild side effects and rare adverse reactions, but Ivermectin has proven to be one of the safest drugs in the world.

We would like to urge the NDoH to develop a living, ongoing systematic review of all potential drugs, in particular Ivermectin, so that South Africans do not miss out on the opportunity to access a drug that could mitigate the effects of the Cov-2-virus in the immediate term, before the vaccine rollout has been

completed. It is important to state, that the signatories to this submission advocate for the introduction and use of a vaccine when one is available, but hold the view that Ivermectin is an important stop-gap in the interim.

IVERMECTIN IN SOUTH AFRICA

The desperate situation that South Africa finds itself in with a second, unrelenting wave coupled with the fact that the full benefit of a vaccine is still distant, has spurred local clinicians to explore the potential of Ivermectin. The challenge that local clinicians face is that Ivermectin is not registered for human use in South Africa.

However, it appears that there has been some use, particularly of the veterinary preparations, in humans which is continuing to feed the anecdotal evidence for the efficacy of the drug. This anecdotal evidence, along with the publications being released, and the need for as many useful drugs to be included in our armamentarium for fighting this pandemic, especially when facing a second and more severe second wave, demands that we look at this drug through the lens of legal, ethical and scientific pragmatism and are not simply dismissive of it.

We are aware of two avenues that can be implemented in order to investigate the use of Ivermectin for COVID-19. The first is to grant Ivermectin Section 21 approval for use in COVID-19, noting that it is approved for human use elsewhere, albeit for other indications. For example, according to the United States Federal Drug Administration:

> Ivermectin tablets are approved for use in humans for the treatment of some parasitic worms (intestinal strongyloidiasis and onchocerciasis) and Ivermectin topical formulations are approved for human use by prescription only for the treatment of external parasites such as headlice and for skin conditions such as rosacea.

Writing in the World Health Bulletin, Speare and Durheim (2004) highlight the relevance and use of Ivermectin globally for controlling strongyloidiasis and scabies (by breaking the infection cycle through its therapeutic effect) and filariasis, through its effect on transmission.

There is currently some approved use of Ivermectin on Section 21 in private hospitals in South Africa. It is our understanding that SAHPRA collates data on certain aspects of section 21 use and that the outcome of such analysis should

be made available or published as an interim report. We request that the State sector also has access to Ivermectin through a section 21 approval, based on the positive meta-analysis and global use/registration of Ivermectin.

Secondly, a Phase 2/3 double-blinded clinical trial, which would produce definitive data either supporting or not supporting the clinical efficacy of this drug for COVID-19 is required. This will provide a good scientific evidence base that will either put to rest the claims of Ivermectin being useful in the treatment of COVID-19, or vice versa. For this to occur as quickly as possible, given our current high transmission rate, we need guidance from the MAC, SAMRC, NICD and SAHPRA on how to expedite approval for such research and to obtain the requisite funding thereof. It would be a source of great national pride if South Africa were to spearhead a cost-effective treatment breakthrough for COVID-19.

CONCLUSION

Both the Section 21 approval and the clinical trial approval and implementation will ensure that any local use of Ivermectin occurs in a controlled manner, in accordance with protocols or the best empirical evidence and where adverse events can be properly monitored and recorded. The failure to adopt this approach will have the consequence that practitioners, in desperation and under intense pressure from patients and families, will resort to experimentation. The IIG is concerned that if some avenue is not opened for the controlled use of Ivermectin, that there may be dire consequences for patients, practitioners and the Country as a whole. More worrying still, is the possible loss of opportunity to save lives.

Our request is to explore Ivermectin for prophylaxis and treatment of COVID-19. We also recommend that, as with vaccines, particular priority groups be identified for trials. For example, health care workers who are at immediate risk, and the central priority in responding to COVID-19 remains to minimise the extent of hospitalisations following infection. To this end, vaccinations have been prioritised for health care and other frontline workers, followed by persons older than 65 and persons of younger ages who have comorbidities. A similar strategy should be explored in trials, and for potential rapid implementation should trials elsewhere demonstrate efficacy for either prophylactic or treatment purposes. It would also be relevant to explore supply lines, logistics

and costs for procuring Ivermectin dosages suitable for human use. We note that Ivermectin is available as a generic at a low cost.

Its scientific properties and low cost could potentially benefit millions in our Country and other parts of the world as an addition to the vaccine. The most urgent consideration should be to allow it's use on a section 21 basis with the evidence being presented in the meta-analysis from Dr Andrew Hill from Liverpool university. His work is being funded by Unitaid, part of the WHO'S ACT accelerator initiative to provide and improve access to treatment for Covid 19.

We urge the Department of Health and the relevant regulatory institutions, such as SAHPRA to pay urgent attention to this request. Whilst we note the recent rapid review from the Department, we hold the view that this, was inadequate as the meta-analysis has not been looked at objectively or comprehensively as a number of clinical trials were overlooked. We request that the NDoH review their decision and monitor the evidence closely, allowing clinical trials, Section 21 use and potentially emergency use of Ivermectin.

The IIG urges the Minister through the MAC and the regulatory bodies listed above to accelerate research of Ivermectin and fully explore its potential in the COVID-19 response in a responsible way. The IIG would like to remind the Minister of Health, the MAC and all other leadership bodies, that it has a public duty to protect the health of the citizens of this county and that it may not be remiss in doing so. It MUST act in the public interest, and the IIG is of the belief that it has a duty to properly and expediently explore the potential of medicines such as Ivermectin.

We eagerly await an urgent and favourable response that will potentially benefit millions in our Country and beyond our borders and will be happy to engage further in this regard.

SIGNATORIES.

Prof Colleen Aldous

Prof Yunus Moosa

Ravin Singh

Warren Parker

Dr Yakub M Essack

Dr Shoyab Wadee

Dr Riyas Fadal

Dr Yasmin Goga

Dr Humza Bawa

Dr Zainab Goondiwala

Solly Suleman

SUMMARY OF POLICIES AND RECOMMENDATIONS
IVERMECTIN for COVID-19

Country	Body	Findings/Conclusions
Global	Hill et al., University of Liverpool – review funded by WHO ACT Accelerator, UNITAID (27 Dec)	• More clinical trials needed • Efficacy improved by dosing over several days / data needed on dose • Results from three more key randomised trials expected in January
Australia	NSW, Agency for Clinical Innovation (23 Dec)	• Insufficient evidence to include ivermectin in the 17 December 2020 release of the BMJ living systematic review on drug treatments, but 3 trials will be included in next • More recent systematic review found a statistically significant effect on mortality and symptoms, the quality of evidence was very low. Emerging evidence from randomised controlled trials is mixed. • Interest in the Americas, India, and Bangladesh noted
South Africa	NDOH	• The overall quality of the randomized trials involving ivermectin in COVID-19 patients is extremely low. • From the available randomised control trial evidence, ivermectin is not superior to placebo in terms of viral load reduction or clinical progression. • There is no evidence from randomised control trials for any reduction in mortality. Eligible patients with COVID-19 in South Africa should be considered for enrolment in relevant therapeutic trials.
USA	Food and Drug Administration (FDA)	• Not approved for COVID-19 prevention or treatment • No emergency use authorisation
Anecdotal reports		
Latin America	https://www.isglobal.org/en/healthisglobal/-/custom-blog-portlet/ivermectin-and-covid-19-how-a-flawed-database-shaped-the-covid-19-response-of-several-latin-american-countries/2877257/0; https://www.nature.com/articles/d41586-020-02958-2	• Peru: Ministerial level communication recommending the use of ivermectin for COVID-19, albeit recognizing the lack of evidence and requesting informed consent. • Bolivia: followed closely and even went a step further into distributing 350,000 ivermectin doses in the city of Trinidad • Paraguay: Restricted sales after surge in demand. • Brazil: Municipality of Natal, in Rio Grande Do Norte, promoted it as a preventative — to be taken by health-care professionals and people at increased risk of severe illness from the virus, because of “its safe pharmacological profile, clinical experience using it against other diseases, cost and dosage convenience”. • Colombia: Does not approve the use of Ivermectin for COVID-19. https://www.minsalud.gov.co/English/Paginas/National-Government-Does-Not-Recommend-Ivermectin-As-a-Treatment-for-Covid-19.aspx
South Asia	https://covidindia.org/treatment/ https://www.goa.gov.in/wp-content/uploads/2020/10/Home-Isolation-Monitoring-Kits-For-COVID-19-Launched.pdf	• India: Uttar Pradesh. The UP government has decided to replace Hydroxychloroquine with Ivermectin for the prevention and treatment of COVID-19 after the promising results seen in Agra, where it was used on an experimental basis • India: Goa. Home isolation kits include Ivermectin.

Appendix 1
SUMMARY OF RESEARCH
IVERMECTIN for COVID-19

Title	Methodology	Sample	Findings/Conclusions
Ivermectin is effective for COVID-19: meta-analysis of 28 studies Version 7: 26 December 2020 https://ivmmeta.com/	Meta-analysis	28 studies	• Ivermectin is an effective treatment for COVID-19. The probability that an ineffective treatment generated results as positive as the 28 studies to date is estimated to be 1 in 268 million (p = 0.0000000037). As expected for an effective treatment, early treatment is more successful, with an estimated reduction of 87% in the effect measured using a random effects meta-analysis, RR 0.13 [0.04-0.40].
A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness (24 November 2020)	Randomized, double-blind, placebo-controlled trial	72 patients 18-65 years old	• Although the study sample was too small (n=72) to make any solid conclusions, the results provide evidence of the potential benefit of the early intervention with the drug ivermectin for the treatment of adult patients diagnosed with mild SARS-CoV-2. First, early intervention promoted faster viral clearance during disease onset which might have prevented significant • immune-system involvement and speed recovery. Secondly, early intervention reduced the viral load faster, thus may help block disease transmission in the general population.
Antiviral Activity of Ivermectin Against SARS-CoV-2: An Old-Fashioned Dog with a New Trick—A Literature Review (17 August 2020)	Literature review	Relevant articles on PubMed and Google Scholar until 10 May 2020: "coronavirus", OR "SARS-CoV", OR "MERS-CoV", OR "SARS-CoV-2" AND "ivermectin" in the title or abstract.	• Ivermectin is an antiparasitic drug with potential use as a broad-spectrum antimicrobial agent for the treatment of viral infections. Initial evidence indicated that ivermectin, an importin α/β-mediated nuclear import inhibitor, inhibited SARS-CoV-2 in vitro. In a small clinical study, the administration of ivermectin (150μg/kg) in hospitalized patients with COVID-19 was associated with a lower mortality rate and a shorter hospital stay. Several randomized controlled trials are ongoing to investigate the efficacy of ivermectin against COVID-19. In addition to ivermectin, several drugs either currently classified as an antiviral or alternative class of drug, have been the subject of clinical trials as a part of the drug repurposing effort in the fight against COVID-19. The results of these clinical trials are required to confirm the efficacy of these drugs for the treatment of patients with COVID-19.
Controlled randomized clinical trial on using Ivermectin with Doxycycline for treating COVID-19 patients in Baghdad, Iraq (27 October 2020)	Randomised controlled trial	140 Covid-19 patients at different stages of the diseases	• The findings of the current trial showed that Ivermectin-Doxycycline reduced the mean time to recovery from 17.9 to 10.61 days in the recruited COVID-19 patients. Alike, for mild moderate patients, Ivermectin-Doxycycline reduced mean time to recovery from 13.66 to just 6.34 days with reduction in time up to 7.32 days. Nevertheless, Ivermectin-Doxycycline reduced the mean time to recovery in severe patients only 4 days, from 24 to 20 days. Based on these findings, Ivermectin and Doxycycline protocol proves to be effective in speeding up recovery in both mild moderate outpatients and severe inpatients.
Efficacy and Safety of Ivermectin for Treatment and prophylaxis of COVID-19 Pandemic (16 November 2020)	Multicentre randomised controlled clinical trial	600 subjects: 400 patients and 200 health care and household contacts that were divided into 6 groups	• Addition of Ivermectin to standard care is very effective drug for treatment of COVID-19 patients with significant reduction in mortality compared to Hydroxychloroquine plus standard treatment only. Early use of Ivermectin is very useful for controlling COVID 19 infections and improving cytokines storm.

Ivermectin as a potential COVID-19 treatment from the pharmacokinetic point of view: antiviral levels are not likely attainable with known dosing regimens (May 2020)	Literature survey		• The available pharmacokinetic data for ivermectin indicate that at the doses routinely used for the management of parasitic diseases the SARS-CoV-2 inhibitory concentrations are practically not attainable. At present • Any empiric treatment with ivermectin or its inclusion in therapeutic protocols are not scientifically justifiable. The very consideration of the drug as a broad spectrum antiviral agent is incorrect because it has failed to demonstrate antiviral effects beyond the in vitro level. Pending the paucity of reliable data from controlled studies and the aforementioned pharmacokinetic considerations, the application of ivermectin in COVID-19 patients is to be decisively discouraged.
Review of the Emerging Evidence Demonstrating the Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19 (18 December 2020)	Comprehensive review of the available efficacy data as of December 14, 2020, taken from in-vitro, animal, clinical, and real-world studies all showing the above impacts of ivermectin in COVID-19	Review includes a total of 7,300 patients from 24 controlled studies [15 RCTs (n= 3,080)]; with 12 published in peer-reviewed journals including 4,054 patients	• In summary, based on the existing and cumulative body of evidence, we recommend the use of ivermectin in both prophylaxis and treatment for COVID-19. In the presence of a global COVID-19 surge, the widespread use of this safe, inexpensive, and effective intervention would lead to a drastic reduction in transmission rates and the morbidity and mortality in mild, moderate, and even severe disease phases.
Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: A randomised multi-centre clinical trial (24 November 2020)	45-days randomized, double-blind, placebo-controlled, multicentre, phase 2 clinical trial was designed at five hospitals	180 mild to severe patients with confirmed PCR and chest image tests	• Results: Average age of the participants was 56 years (45-67) and 50% were women. The primary and secondary results showed significant changes between day zero and day five of admission (Δ 0/5) in terms of ΔALC5/0, ΔPLT5/0, ΔESR5/0, ΔCRP5/0, duration of low O2 saturation, and duration of hospitalization (CI = 95%). • Risk of mortality was also decreased significantly in the study groups. • Conclusion: Ivermectin as an adjunct reduced the rate of mortality, low O2 duration, and duration of hospitalization in adult COVID 19 patients. The improvement of other clinical parameters showed that the • ivermectin, with a wide margin of safety, had a high therapeutic effect on COVID-19.

Ivermectin as Pre-exposure Prophylaxis for COVID 19 among Healthcare Providers in a Selected Tertiary Hospital in Dhaka An Observational Study (15 December 2020)	Observational Study	118 health care workers – enrolled purposively	• Result: 73.3% (44 out of 60) subjects in control group were positive for COVID-19, whereas only 6.9% (4 out of 58) of the experimental group were diagnosed with COVID-19 (p-value < 0.05). • Conclusion: Ivermectin, an FDA-approved, safe, cheap and widely available drug, should be subjected to large-scale trials all over the world to ascertain its effectiveness as pre-exposure prophylaxis for COVID-19.
Ivermectin in COVID-19: What do we know? Letter to the editor: Diabetes & Metabolic Syndrome: Clinical Research & Reviews (14 September 2020)	Hospital-based matched case-control		• The clinical efficacy and utility of ivermectin in SARS CoV-2 infected patients are unpredictable at this stage, as we are dealing with a completely novel virus. However, repurposing existing drugs as possible COVID-19 treatment is astute usage of existing resources, and we await results of well-designed large scale randomized controlled clinical trials exploring treatment efficacy of ivermectin to treat SARS-CoV-2.
Lack of efficacy of standard doses of ivermectin in severe COVID-19 patients (11 November 2020)	Retrospective Study		• …it is unlikely that the widespread use of IVM at standard doses may have an impact in decreasing the mobility related with COVID-19. We suggest the evaluation of high-doses of IVM in randomized clinical trials to test the efficacy of IVM in COVID-19 patients, especially in early stages of the disease.
Role of ivermectin in the prevention of COVID-19 infection among healthcare workers in India: A matched case-control study (3 November 2020)	Hospital-based matched case-control	186 case-control pairs	• We conclude that two-dose ivermectin prophylaxis at a dose of 300 µg/kg body weight with a gap of 72 hours was associated with a 73% reduction of COVID-19 infection among HCWs in the following one month. This is an intervention worth replicating at other centres until a vaccine is available.
Safety of oral ivermectin during pregnancy: systematic review and meta-analysis (8 January 2020)	Systematic review and meta-analysis	147 records	• There is insufficient evidence to conclude on the safety profile of ivermectin during pregnancy. • Treatment campaigns should focus additional efforts on preventing inadvertent treatment of pregnant women.

Therapeutic potential of ivermectin as add-on treatment in COVID 19: A systematic review and meta-analysis (17 November 2020)	Systematic review and meta-analysis	629 patients from 4 studies All were RT-PCR positive. Among them, 397 patients received ivermectin along with usual therapy. Ivermectin treated group had 233 mild cases and 104 moderate to severe cases.	• The random effect model showed the overall pooled OR to be 0.53 • (95%CI: 0.29 to 0.96) for the primary outcome (all-cause mortality) which was statistically significant (P=0.04). • Similarly, the random effect model revealed that adding ivermectin led to significant clinical improvement compared to usual therapy (OR=1.98, 95% CI: 1.11 to 3.53, P=0.02). However, this should be inferred cautiously as the quality of evidence is very low. Currently, many clinical trials are on-going, and definitive evidence for repurposing this drug for COVID-19 patients will emerge only in the future.
White paper on Ivermectin as a potential therapy for COVID-19 (19 July 2020)	Outcome of a panel review by senior doctors		• After critical panel discussion, all the attending doctors came to a conclusion that Ivermectin can be a potential molecule for prophylaxis and treatment of people infected with Coronavirus, owing to its anti-viral properties coupled with effective cost, availability and good tolerability and safety.
Therapeutic potential of ivermectin for COVID-19 (26 May 2020)	Systematic, hybrid, theoretical essay.		• The search of the databases led to the retrieval of 25 articles. After the different phases of the selection process, eight articles were included in the present review for the extraction of relevant data. The results suggest that ivermectin inhibits the viral replication of SARS-CoV-2 through the action of the hypoxia- inducible factor (HIF-1α) and consequent destabilization of importin α/β1 proteins. Conclusions • Ivermectin inhibits the viral replication of SARS-CoV-2. Laboratory and clinical studies are needed to provide more evidence in terms of the best posology and possible associations with other drugs for combatting COVID-19.

Use of Ivermectin Is Associated with Lower Mortality in Hospitalized Patients with Coronavirus Disease 2019 The ICON Study (27 October 2020)	Charts of consecutive patients hospitalised at four Broward Health hospitals in Florida with confirmed COVID-19 between March 15 and May 11, 2020, treated with or without ivermectin were reviewed.	Two hundred eighty patients, 173 treated with ivermectin and 107 without ivermectin, were reviewed.	• We showed that ivermectin administration was associated significantly with lower mortality among patients with COVID-19, particularly in patients with more severe pulmonary involvement. • Interpretation of these findings are tempered by the limitations of the retrospective design and the possibility of confounding. Appropriate dosing for this indication is not known, nor are the effects of ivermectin on viral load or in patients with milder disease. • Further studies in appropriately designed randomized trials are recommended before any conclusions can be mad

IVERMECTIN: CONTRA-INDICATIONS, SIDE EFFECTS, OVERDOSAGE, AND DRUG INTERACTIONS

CONTRA-INDICATIONS[i]

Asthma

Patients with a history of severe asthma should receive ivermectin with caution. Occasionally, systemic ivermectin has been reported to worsen bronchial asthma.

Hepatic disease

Although not extensively studied, due to its extensive hepatic metabolism, ivermectin should be administered with caution in patients with significant hepatic disease.

Human immunodeficiency virus (HIV) infection, immunosuppression

In patients with immunosuppression (including those with human immunodeficiency virus (HIV) infection) treated for intestinal strongyloidiasis, repeated ivermectin courses may be necessary. Adequate and well-controlled clinical studies have not been conducted in such patients to determine the optimal dosing regimen. Several treatments (i.e., at 2-week intervals) may be required and a cure may not be achievable. Control of extra-intestinal strongyloidiasis in these patients is difficult, however, suppressive therapy (i.e., once per month) may be helpful.

Pregnancy

Data with oral ivermectin use during pregnancy are insufficient to inform a drug-associated risk. Systemic exposure from topical use of ivermectin is much lower than from oral use. Four published epidemiology studies evaluated the outcomes of a total of 744 women exposed to oral ivermectin in various stages of pregnancy. In the largest study, 397 women in the second trimester of pregnancy were treated open-label with single doses of ivermectin or ivermectin plus albendazole; there was no observed difference in pregnancy outcomes between treated and untreated populations. However, these studies cannot definitely establish or exclude the absence of drug-associated risk during pregnancy, because either the timing of the administration during gestation was not accurately ascertained or the administration only occurred during the second trimester. In animal embryofoetal development studies of oral ivermectin given during organogenesis, adverse developmental outcomes, including cleft palate, exencephaly, wavy ribs, and clubbed forepaws, occurred at or near doses that were maternally toxic. Pre-implantation loss and abortion were also noted.

Breast-feeding
After oral administration, ivermectin is excreted in human breast milk in low concentrations. Excretion in human breast milk after topical administration has not been evaluated. According to the manufacturer, treatment with oral ivermectin in mothers who are breast-feeding should only be undertaken when the risk of delayed treatment to the mother outweighs the possible risk to the new-born. Previous American Academy of Pediatrics (AAP) recommendations considered oral ivermectin to be usually compatible with breast-feeding. The amount of ivermectin present in human milk after topical application has not been studied; however, systemic exposure from topical ivermectin use is much lower than from oral use. According to the manufacturer, discontinue nursing or discontinue the topical cream, taking into account the importance of the drug to the mother. Women who are breast-feeding while using topical ivermectin should avoid accidental transfer of ivermectin to the breast area where it might be directly ingested while nursing.

Children, infants
The topical administration of ivermectin to infants and children should be under the direct supervision of an adult to prevent ingestion of the lotion.

Loa loa coinfection
Rarely, patients with onchocerciasis and Loa loa coinfection may develop a serious or even fatal encephalopathy either spontaneously or after treatment with an effective microfilaricide. This syndrome has been seen very rarely after the use of ivermectin. In individuals who warrant treatment with ivermectin for any reason and have had significant exposure to Loa loa-endemic areas of West and Central Africa, pre-treatment assessment for loiasis and careful posttreatment follow-up is recommended.

Onchodermatitis
Patients with hyperreactive onchodermatitis (i.e., sowda) may be more likely than others to experience severe oedema and worsening of onchodermatitis after ivermectin use.

SIDE EFFECTS/ADVERSE REACTIONS	OVERDOSAGE
In four clinical studies involving a total of 109 patients given either one or two doses of 170 to 200 mcg/kg of STROMECTOL, the following adverse reactions were reported as possibly or definitely related to STROMECTOL: **Body as a Whole:** asthenia/fatigue (0.9%), abdominal pain (0.9%) **Gastrointestinal:** anorexia (0.9%), constipation (0.9%), diarrhoea (1.8%), nausea (1.8%), vomiting (0.9%) **Nervous System/Psychiatric:** dizziness (2.8%), somnolence (0.9%), vertigo (0.9%), tremor (0.9%) **Skin:** pruritus (2.8%), rash (0.9%), and urticaria (0.9%)[ii] Adverse effects seen in filarial infections include fever, myalgia, malaise, light-headedness, and occasionally postural hypotension. In onchocerciasis, skin oedema, pruritis and mild eye irritation may be seen.[iii] Adverse effects are more common (up to 1/3 of patients) in patients with onchocerciasis due to allergic or inflammatory responses to the death of the parasite (Mazzotti reaction). These reactions generally occur within 3 days and tend to lessen with repeated courses **Common:** diarrhoea, nausea, dizziness and somnolence. Mazzotti reaction (arthralgia, lymphadenopathy, itch, oedema, rash, fever,tachycardia, hypotension, and temporary worsening of ocular symptoms **Rare:** fatigue, abdominal pain, constipation, vomiting, tremor, headache, toxic epidermal necrolysis, eosinophilia, increased haemoglobin, reduction in leucocytes[iv] Transient and mild adverse reactions have been reported in 24% of filarial disease patients, with signs and symptoms including anorexia, asthenia, headache, arthralgia, myalgia, fever, and eosinophilia. Mazzotti reactions and sudden death from the release of degradation products of microfilaria were observed in patients with filarial diseases. Macular and papular rashes and pruritus (33%) between 2 and 4 days after oral ivermectin in patients with scabies has been noted. (This adverse reaction is the result of the release of toxic products from dying or dead mites.) Hematomas and an increase in prothrombin time in a few patients have been observed. Occasionally, nausea and a decrease in blood pressure, as well as flat T waves or prolonged PR times on ECG, have been described.[v]	In accidental intoxication with, or significant exposure to, unknown quantities of veterinary formulations of ivermectin in humans, either by ingestion, inhalation, injection, or exposure to body surfaces, the following adverse effects have been reported most frequently: rash, oedema, headache, dizziness, asthenia, nausea, vomiting, and diarrhoea. Other adverse effects that have been reported include: seizure, ataxia, dyspnoea, abdominal pain, paraesthesia, urticaria, and contact dermatitis.[vi] Cases of accidental overdose with ivermectin have been reported, but none have resulted in fatalities. In cases of accidental intoxication with unknown doses of products destined for veterinary use (oral use, as an injection, cutaneous use), the symptoms described were rash, contact dermatitis, oedema, headache, vertigo, asthenia, nausea, vomiting, diarrhoea and abdominal pain. Other effects have also been observed, including seizures, ataxia, dyspnoea, paraesthesia and urticaria.[vii]

DRUG INTERACTION[viii]

Aprepitant, Fosaprepitant: (Moderate) Use caution if ivermectin and aprepitant, fosaprepitant are used concurrently and monitor for an increase in ivermectin-related adverse effects for several days after administration of a multi-day aprepitant regimen. Ivermectin is a CYP3A4 substrate. Aprepitant, when administered as a 3-day oral regimen (125 mg/80 mg/80 mg), is a moderate CYP3A4 inhibitor and inducer and may increase plasma concentrations of ivermectin. For example, a 5-day oral aprepitant regimen increased the AUC of another CYP3A4 substrate, midazolam (single dose), by 2.3-fold on day 1 and by 3.3-fold on day 5. After a 3-day oral aprepitant regimen, the AUC of midazolam (given on days 1, 4, 8, and 15) increased by 25% on day 4, and then decreased by 19% and 4% on days 8 and 15, respectively. As a single 125 mg or 40 mg oral dose, the inhibitory effect of aprepitant on CYP3A4 is weak, with the AUC of midazolam increased by 1.5-fold and 1.2-fold, respectively. After administration, fosaprepitant is rapidly converted to aprepitant and shares many of the same drug interactions. However, as a single 150 mg intravenous dose, fosaprepitant only weakly inhibits CYP3A4 for a duration of 2 days; there is no evidence of CYP3A4 induction. Fosaprepitant 150 mg IV as a single dose increased the AUC of midazolam (given on days 1 and 4) by approximately 1.8-fold on day 1; there was no effect on day 4. Less than a 2-fold increase in the midazolam AUC is not considered clinically important.

Boceprevir: (Moderate) Close clinical monitoring is advised when administering ivermectin with boceprevir due to an increased potential for ivermectin-related adverse events. If ivermectin dose adjustments are made, re-adjust the dose upon completion of boceprevir treatment. Although this interaction has not been studied, predictions about the interaction can be made based on the metabolic pathway of ivermectin. Ivermectin is partially metabolized by the hepatic isoenzyme CYP3A4; boceprevir inhibits this isoenzyme. Coadministration may result in elevated ivermectin plasma concentrations.

Idelalisib: (Major) Avoid concomitant use of idelalisib, a strong CYP3A inhibitor, with ivermectin, a CYP3A substrate, as ivermectin toxicities may be significantly increased. The AUC of a sensitive CYP3A substrate was increased 5.4-fold when co-administered with idelalisib.

Mirabegron: (Moderate) Mirabegron is a moderate CYP2D6 inhibitor. Exposure of drugs metabolized by CYP2D6 such as ivermectin may be increased when co-administered with mirabegron. Ivermectin has been shown to be a CYP2D6 substrate in vitro. Appropriate monitoring and dose adjustment may be necessary.

Mitotane: (Moderate) Use caution if mitotane and ivermectin are used concomitantly and monitor for decreased efficacy of ivermectin and a possible change in dosage requirements. Mitotane is a strong CYP3A4 inducer and ivermectin is a CYP3A4 substrate. Coadministration may

result in decreased plasma concentrations of ivermectin; however, ivermectin is administered as a single dose, and significant clinical interactions are not expected.

Posaconazole: (Moderate) Posaconazole and ivermectin should be co-administered with caution due to an increased potential for ivermectin-related adverse events. Posaconazole is a potent inhibitor of CYP3A4, an isoenzyme partially responsible for the metabolism of ivermectin. These drugs used in combination may result in elevated ivermectin plasma concentrations, causing an increased risk for ivermectin-related adverse events.

Telaprevir: (Moderate) Close clinical monitoring is advised when administering ivermectin with telaprevir due to an increased potential for ivermectin-related adverse events. If ivermectin dose adjustments are made, re-adjust the dose upon completion of telaprevir treatment. Although this interaction has not been studied, predictions about the interaction can be made based on the metabolic pathway of ivermectin. Ivermectin is partially metabolized by the hepatic isoenzyme CYP3A4; telaprevir inhibits this isoenzyme. Coadministration may result in elevated ivermectin plasma concentrations.

Warfarin: (Moderate) Concurrent administration of warfarin and oral ivermectin has been associated with post marketing reports of elevated INR. In 1 case report, a patient who was previously stable on warfarin developed supratherapeutic INR concentrations (greater than 20) and subsequent hematoma after receiving two 3 mg oral ivermectin doses. Although data are limited, ivermectin has been shown to antagonize vitamin K-dependent clotting factors II, VII, IX, and X.

Drug	Interaction[ix]
(R)-warfarin	Ivermectin may decrease the anticoagulant activities of (R)-warfarin.
(S)-Warfarin	Ivermectin may decrease the anticoagulant activities of (S)-Warfarin.
4-hydroxycoumarin	Ivermectin may decrease the anticoagulant activities of 4-hydroxycoumarin.
9-aminocamptothecin	The metabolism of 9-aminocamptothecin can be increased when combined with Ivermectin.
Abametapir	The serum concentration of Ivermectin can be increased when it is combined with Abametapir.
Abemaciclib	The metabolism of Ivermectin can be increased when combined with Abemaciclib.
Acalabrutinib	The metabolism of Acalabrutinib can be increased when combined with Ivermectin.
Acenocoumarol	Ivermectin may decrease the anticoagulant activities of Acenocoumarol.
Acipimox	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Acipimox.
Afatinib	Afatinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Albendazole	The metabolism of Albendazole can be increased when combined with Ivermectin.
Alectinib	The metabolism of Ivermectin can be increased when combined with Alectinib.
Alendronic acid	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Alendronic acid.
Allylestrenol	The metabolism of Allylestrenol can be increased when combined with Ivermectin.
Alpelisib	The metabolism of Alpelisib can be increased when combined with Ivermectin.
Aluminium clofibrate	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Aluminium clofibrate.
Ambrisentan	The excretion of Ambrisentan can be decreased when combined with Ivermectin.
Aminophylline	The metabolism of Aminophylline can be increased when combined with Ivermectin.
Amiodarone	The metabolism of Amiodarone can be increased when combined with Ivermectin.
Amlodipine	The metabolism of Ivermectin can be increased when combined with Amlodipine.
Amphotericin B	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Amphotericin B.
Apalutamide	Apalutamide may increase the excretion rate of Ivermectin which could result in a lower serum level and potentially a reduction in efficacy.
Astemizole	The metabolism of Astemizole can be increased when combined with Ivermectin.
Asunaprevir	The excretion of Asunaprevir can be decreased when combined with Ivermectin.
Atazanavir	The metabolism of Atazanavir can be increased when combined with Ivermectin.
Atorvastatin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Atorvastatin.
Atrasentan	The excretion of Atrasentan can be decreased when combined with Ivermectin.

Avatrombopag	Avatrombopag may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Axitinib	The metabolism of Axitinib can be increased when combined with Ivermectin.
Azithromycin	The serum concentration of Ivermectin can be increased when it is combined with Azithromycin.
Baclofen	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Baclofen is combined with Ivermectin.
Baricitinib	The metabolism of Ivermectin can be increased when combined with Baricitinib.
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Ivermectin.
Beclomethasone dipropionate	Beclomethasone dipropionate may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Belantamab mafodotin	The excretion of Belantamab mafodotin can be decreased when combined with Ivermectin.
Bempedoic acid	The excretion of Bempedoic acid can be decreased when combined with Ivermectin.
Benzylpenicillin	The excretion of Benzylpenicillin can be decreased when combined with Ivermectin.
Betamethasone	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Betamethasone is combined with Ivermectin.
Bezafibrate	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Bezafibrate.
Bicalutamide	The metabolism of Bicalutamide can be increased when combined with Ivermectin.
Bortezomib	The metabolism of Bortezomib can be increased when combined with Ivermectin.
Bosentan	The excretion of Bosentan can be decreased when combined with Ivermectin.
Bosutinib	The metabolism of Bosutinib can be increased when combined with Ivermectin.
Brentuximab vedotin	The metabolism of Brentuximab vedotin can be increased when combined with Ivermectin.
Brigatinib	The metabolism of Ivermectin can be increased when combined with Brigatinib.
Bumetanide	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Bumetanide.
Buprenorphine	Buprenorphine may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Busulfan	The metabolism of Busulfan can be increased when combined with Ivermectin.
Cabazitaxel	The metabolism of Ivermectin can be increased when combined with Cabazitaxel.
Cabergoline	The metabolism of Cabergoline can be increased when combined with Ivermectin.
Caffeine	Caffeine may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Cannabidiol	Cannabidiol may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Capmatinib	The serum concentration of Ivermectin can be increased when it is combined with Capmatinib.
Captopril	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Captopril.
Carbamazepine	The metabolism of Carbamazepine can be increased when combined with Ivermectin.
Carbimazole	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Carbimazole is combined with Ivermectin.

Caspofungin	The excretion of Caspofungin can be decreased when combined with Ivermectin.
Cenobamate	The serum concentration of Ivermectin can be decreased when it is combined with Cenobamate.
Cephalexin	The metabolism of Cephalexin can be increased when combined with Ivermectin.
Ceritinib	The metabolism of Ceritinib can be increased when combined with Ivermectin.
Cerivastatin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Cerivastatin.
Chlormadinone	The metabolism of Chlormadinone can be increased when combined with Ivermectin.
Chloroquine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Chloroquine.
Chlorpromazine	The metabolism of Chlorpromazine can be increased when combined with Ivermectin.
Cholecystokinin	The excretion of Cholecystokinin can be decreased when combined with Ivermectin.
Cholesterol	Cholesterol may increase the excretion rate of Ivermectin which could result in a lower serum level and potentially a reduction in efficacy.
Cholic Acid	The excretion of Cholic Acid can be decreased when combined with Ivermectin.
Cimetidine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Cimetidine is combined with Ivermectin.
Ciprofibrate	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ciprofibrate.
Ciprofloxacin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ciprofloxacin is combined with Ivermectin.
Cisapride	The metabolism of Cisapride can be increased when combined with Ivermectin.
Cladribine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Cladribine is combined with Ivermectin.
Clofazimine	Clofazimine may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Clofibrate	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Clofibrate.
Clofibride	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Clofibride.
Clomipramine	The metabolism of Clomipramine can be increased when combined with Ivermectin.
Clonidine	The metabolism of Clonidine can be increased when combined with Ivermectin.
Cloprostenol	The metabolism of Cloprostenol can be increased when combined with Ivermectin.
Clorindione	Ivermectin may decrease the anticoagulant activities of Clorindione.
Cobicistat	Cobicistat may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Cobimetinib	The metabolism of Cobimetinib can be increased when combined with Ivermectin.
Colchicine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Colchicine.
Conivaptan	The metabolism of Conivaptan can be increased when combined with Ivermectin.
Conjugated estrogens	The excretion of Conjugated estrogens can be decreased when combined with Ivermectin.
Copanlisib	The metabolism of Copanlisib can be increased when combined with Ivermectin.
Coumarin	Ivermectin may decrease the anticoagulant activities of Coumarin.
Crizotinib	The metabolism of Crizotinib can be increased when combined with Ivermectin.

Cyclophosphamide	The metabolism of Cyclophosphamide can be increased when combined with Ivermectin.
Cyclosporine	The metabolism of Ivermectin can be increased when combined with Cyclosporine.
Cyproterone acetate	The metabolism of Cyproterone acetate can be increased when combined with Ivermectin.
Cytarabine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Cytarabine.
Dabrafenib	The metabolism of Ivermectin can be increased when combined with Dabrafenib.
Daclatasvir	Daclatasvir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Dacomitinib	The metabolism of Ivermectin can be increased when combined with Dacomitinib.
Daidzin	Daidzin may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Daptomycin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Daptomycin is combined with Ivermectin.
Darolutamide	The serum concentration of Ivermectin can be increased when it is combined with Darolutamide.
Dasabuvir	Dasabuvir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Dasatinib	The metabolism of Dasatinib can be increased when combined with Ivermectin.
Demegestone	The metabolism of Demegestone can be increased when combined with Ivermectin.
Desogestrel	The metabolism of Desogestrel can be increased when combined with Ivermectin.
Dexamethasone	Dexamethasone may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Dicoumarol	Ivermectin may decrease the anticoagulant activities of Dicoumarol.
Dienogest	The metabolism of Dienogest can be increased when combined with Ivermectin.
Diethylstilbestrol	Diethylstilbestrol may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Digitoxin	The metabolism of Digitoxin can be increased when combined with Ivermectin.
Digoxin	The excretion of Digoxin can be decreased when combined with Ivermectin.
Dihydroergocornine	The metabolism of Dihydroergocornine can be increased when combined with Ivermectin.
Dihydroergocristine	The metabolism of Dihydroergocristine can be increased when combined with Ivermectin.
Dihydroergocryptine	The metabolism of Dihydroergocryptine can be increased when combined with Ivermectin.
Dihydroergotamine	The metabolism of Dihydroergotamine can be increased when combined with Ivermectin.
Dinoprostone	The excretion of Dinoprostone can be decreased when combined with Ivermectin.
Diphenadione	Ivermectin may decrease the anticoagulant activities of Diphenadione.
Docetaxel	The metabolism of Docetaxel can be increased when combined with Ivermectin.
Dofetilide	The metabolism of Dofetilide can be increased when combined with Ivermectin.
Dovitinib	Dovitinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Doxazosin	The metabolism of Doxazosin can be increased when combined with Ivermectin.
Doxorubicin	The metabolism of Doxorubicin can be increased when combined with Ivermectin.
Dronabinol	Dronabinol may decrease the excretion rate of Ivermectin which could result in a higher serum level.

Dronedarone	The metabolism of Dronedarone can be increased when combined with Ivermectin.
Drospirenone	The metabolism of Drospirenone can be increased when combined with Ivermectin.
Duloxetine	The metabolism of Duloxetine can be increased when combined with Ivermectin.
Duvelisib	The metabolism of Duvelisib can be increased when combined with Ivermectin.
Ebastine	The metabolism of Ebastine can be increased when combined with Ivermectin.
Elacridar	Elacridar may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Elagolix	The excretion of Elagolix can be decreased when combined with Ivermectin.
Elexacaftor	The metabolism of Elexacaftor can be increased when combined with Ivermectin.
Eltrombopag	Eltrombopag may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Eluxadoline	The serum concentration of Eluxadoline can be increased when it is combined with Ivermectin.
Emetine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Emetine.
Enalapril	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Enalapril is combined with Ivermectin.
Enasidenib	The metabolism of Ivermectin can be increased when combined with Enasidenib.
Entrectinib	The metabolism of Entrectinib can be increased when combined with Ivermectin.
Eprosartan	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Eprosartan.
Erdafitinib	The metabolism of Erdafitinib can be increased when combined with Ivermectin.
Ergotamine	The metabolism of Ergotamine can be increased when combined with Ivermectin.
Erlotinib	The metabolism of Ivermectin can be increased when combined with Erlotinib.
Erythromycin	The excretion of Erythromycin can be decreased when combined with Ivermectin.
Estradiol	Estradiol may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Estradiol acetate	Estradiol acetate may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Estradiol benzoate	Estradiol benzoate may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Estradiol cypionate	Estradiol cypionate may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Estradiol dienanthate	Estradiol dienanthate may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Estradiol valerate	Estradiol valerate may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Estrone	Estrone may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Estrone sulfate	The metabolism of Estrone sulfate can be increased when combined with Ivermectin.
Ethanol	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ethanol.
Ethinylestradiol	The metabolism of Ethinylestradiol can be increased when combined with Ivermectin.
Ethyl biscoumacetate	Ivermectin may decrease the anticoagulant activities of Ethyl biscoumacetate.
Ethynodiol diacetate	The metabolism of Ethynodiol diacetate can be increased when combined with Ivermectin.
Etofibrate	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Etofibrate.

Etonogestrel	The metabolism of Etonogestrel can be increased when combined with Ivermectin.
Etoposide	The metabolism of Etoposide can be increased when combined with Ivermectin.
Etynodiol	The metabolism of Etynodiol can be increased when combined with Ivermectin.
Everolimus	The metabolism of Everolimus can be increased when combined with Ivermectin.
Ezetimibe	The excretion of Ezetimibe can be decreased when combined with Ivermectin.
Famciclovir	The metabolism of Famciclovir can be increased when combined with Ivermectin.
Fedratinib	Fedratinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Fenofibrate	The metabolism of Fenofibrate can be increased when combined with Ivermectin.
Fenofibric acid	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Fenofibric acid.
Fexofenadine	The excretion of Fexofenadine can be decreased when combined with Ivermectin.
Fimasartan	The excretion of Fimasartan can be decreased when combined with Ivermectin.
Fluindione	Ivermectin may decrease the anticoagulant activities of Fluindione.
Fluvastatin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Fluvastatin.
Fosaprepitant	The metabolism of Fosaprepitant can be increased when combined with Ivermectin.
Fosphenytoin	The metabolism of Fosphenytoin can be increased when combined with Ivermectin.
Fostamatinib	Fostamatinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Fostemsavir	Fostemsavir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Fusidic acid	Fusidic acid may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Gadoxetic acid	The excretion of Gadoxetic acid can be decreased when combined with Ivermectin.
Ganciclovir	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ganciclovir.
Gefitinib	Gefitinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Gemfibrozil	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Gemfibrozil.
Genistein	Genistein may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Gestodene	The metabolism of Gestodene can be increased when combined with Ivermectin.
Gestrinone	The metabolism of Gestrinone can be increased when combined with Ivermectin.
Gilteritinib	Gilteritinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Gimatecan	The excretion of Gimatecan can be decreased when combined with Ivermectin.
Glasdegib	Glasdegib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Glecaprevir	Glecaprevir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Gossypol	The metabolism of Gossypol can be increased when combined with Ivermectin.
Grazoprevir	The excretion of Grazoprevir can be decreased when combined with Ivermectin.
Haloperidol	The serum concentration of Haloperidol can be increased when it is combined with Ivermectin.

Hesperetin	Hesperetin may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Hydroxyprogesterone caproate	The metabolism of Hydroxyprogesterone caproate can be increased when combined with Ivermectin.
Ibandronate	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ibandronate.
Idelalisib	The metabolism of Idelalisib can be increased when combined with Ivermectin.
Ifosfamide	The metabolism of Ifosfamide can be increased when combined with Ivermectin.
Iloprost	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Iloprost.
Imatinib	Imatinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Indinavir	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Indinavir is combined with Ivermectin.
Infliximab	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Infliximab is combined with Ivermectin.
Ipecac	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ipecac.
Irinotecan	The metabolism of Irinotecan can be increased when combined with Ivermectin.
Isavuconazole	Isavuconazole may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Isoniazid	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Isoniazid.
Isosorbide	The metabolism of Isosorbide can be increased when combined with Ivermectin.
Isotretinoin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Isotretinoin.
Istradefylline	Istradefylline may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Ivosidenib	The metabolism of Ivosidenib can be increased when combined with Ivermectin
Ixabepilone	The metabolism of Ixabepilone can be increased when combined with Ivermectin.
Ixazomib	The metabolism of Ixazomib can be increased when combined with Ivermectin.
Lacosamide	The metabolism of Lacosamide can be increased when combined with Ivermectin.
Lactulose	The therapeutic efficacy of Lactulose can be decreased when used in combination with Ivermectin.
Lamivudine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Lamivudine.
Lansoprazole	Lansoprazole may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Lasmiditan	The serum concentration of Ivermectin can be increased when it is combined with Lasmiditan.
Lefamulin	The metabolism of Lefamulin can be increased when combined with Ivermectin.
Leflunomide	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Leflunomide.
Lercanidipine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Lercanidipine is combined with Ivermectin.
Letermovir	Letermovir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Letrozole	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Letrozole.
Leuprolide	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Leuprolide is combined with Ivermectin.

Levacetylmethadol	The metabolism of Levacetylmethadol can be increased when combined with Ivermectin.
Levamisole	The bioavailability of Ivermectin can be increased when combined with Levamisole.
Levonorgestrel	The metabolism of Levonorgestrel can be increased when combined with Ivermectin.
Levosalbutamol	The excretion of Levosalbutamol can be decreased when combined with Ivermectin.
Linagliptin	The metabolism of Linagliptin can be increased when combined with Ivermectin.
Liothyronine	The excretion of Liothyronine can be decreased when combined with Ivermectin.
Liotrix	The excretion of Liotrix can be decreased when combined with Ivermectin.
Lomitapide	The metabolism of Lomitapide can be increased when combined with Ivermectin.
Lonidamine	The metabolism of Lonidamine can be increased when combined with Ivermectin.
Lorazepam	The metabolism of Lorazepam can be increased when combined with Ivermectin.
Lovastatin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Lovastatin.
Lynestrenol	The metabolism of Lynestrenol can be increased when combined with Ivermectin.
Mebeverine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Mebeverine.
Medical Cannabis	Medical Cannabis may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Medroxyprogesterone acetate	The metabolism of Medroxyprogesterone acetate can be increased when combined with Ivermectin.
Mefloquine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Mefloquine is combined with Ivermectin.
Megestrol acetate	The metabolism of Megestrol acetate can be increased when combined with Ivermectin.
Meperidine	The metabolism of Meperidine can be increased when combined with Ivermectin.
Mestranol	The metabolism of Mestranol can be increased when combined with Ivermectin.
Methotrexate	The metabolism of Methotrexate can be increased when combined with Ivermectin.
Methyldopa	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Methyldopa.
Methylprednisone	The metabolism of Methylprednisone can be increased when combined with Ivermectin.
Methysergide	The metabolism of Methysergide can be increased when combined with Ivermectin.
Metoclopramide	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Metoclopramide.
Metoprolol	The metabolism of Metoprolol can be increased when combined with Ivermectin.
Metreleptin	The metabolism of Ivermectin can be increased when combined with Metreleptin.
Mevastatin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Mevastatin.
Midostaurin	The metabolism of Midostaurin can be increased when combined with Ivermectin.
Mifepristone	The metabolism of Mifepristone can be increased when combined with Ivermectin.
Minocycline	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Minocycline.

Montelukast	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Montelukast is combined with Ivermectin.
Mycophenolate mofetil	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Mycophenolate mofetil.
Nabiximols	Nabiximols may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Nafarelin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Nafarelin.
Naltrexone	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Naltrexone.
Naringenin	Naringenin may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Nelfinavir	Nelfinavir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Neratinib	The metabolism of Neratinib can be increased when combined with Ivermectin.
Netupitant	The metabolism of Netupitant can be increased when combined with Ivermectin.
Niacin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Niacin.
Nilotinib	The metabolism of Ivermectin can be increased when combined with Nilotinib.
Nintedanib	The metabolism of Nintedanib can be increased when combined with Ivermectin.
Nizatidine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Nizatidine is combined with Ivermectin.
Nomegestrol	The metabolism of Nomegestrol can be increased when combined with Ivermectin.
Nomegestrol acetate	The metabolism of Nomegestrol acetate can be increased when combined with Ivermectin.
Norelgestromin	The metabolism of Norelgestromin can be increased when combined with Ivermectin.
Norethindrone enanthate	The metabolism of Norethindrone enanthate can be increased when combined with Ivermectin.
Norethisterone	The metabolism of Norethisterone can be increased when combined with Ivermectin.
Norethynodrel	The metabolism of Norethynodrel can be increased when combined with Ivermectin.
Norfloxacin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Norfloxacin.
Norgestimate	The metabolism of Norgestimate can be increased when combined with Ivermectin.
Norgestrel	The metabolism of Norgestrel can be increased when combined with Ivermectin.
Norgestrienone	The metabolism of Norgestrienone can be increased when combined with Ivermectin.
Nortriptyline	The metabolism of Nortriptyline can be increased when combined with Ivermectin.
Novobiocin	Novobiocin may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Octylphenoxy polyethoxyethanol	The metabolism of Octylphenoxy polyethoxyethanol can be increased when combined with Ivermectin.
Ofloxacin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ofloxacin.
Olaparib	The metabolism of Ivermectin can be increased when combined with Olaparib.
Omeprazole	Omeprazole may decrease the excretion rate of Ivermectin which could result in a higher serum level.

Ormeloxifene	The metabolism of Ormeloxifene can be increased when combined with Ivermectin.
Osimertinib	The metabolism of Osimertinib can be increased when combined with Ivermectin.
Ouabain	The excretion of Ouabain can be decreased when combined with Ivermectin.
p-Coumaric acid	The metabolism of p-Coumaric acid can be increased when combined with Ivermectin.
Paclitaxel	The metabolism of Paclitaxel can be increased when combined with Ivermectin.
Palbociclib	The metabolism of Ivermectin can be increased when combined with Palbociclib.
Pamidronic acid	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Pamidronic acid is combined with Ivermectin.
Panobinostat	The metabolism of Panobinostat can be increased when combined with Ivermectin.
Pantoprazole	Pantoprazole may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Paritaprevir	Paritaprevir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Pazopanib	The metabolism of Pazopanib can be increased when combined with Ivermectin.
Penicillamine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Penicillamine.
Pexidartinib	The metabolism of Pexidartinib can be increased when combined with Ivermectin.
Phenindione	Ivermectin may decrease the anticoagulant activities of Phenindione.
Phenprocoumon	Ivermectin may decrease the anticoagulant activities of Phenprocoumon.
Phentermine	The metabolism of Phentermine can be increased when combined with Ivermectin.
Phenytoin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Phenytoin is combined with Ivermectin.
Pibrentasvir	Pibrentasvir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Picosulfuric acid	The therapeutic efficacy of Picosulfuric acid can be decreased when used in combination with Ivermectin.
Pimozide	The metabolism of Pimozide can be increased when combined with Ivermectin.
Pitavastatin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Pitavastatin.
Pitolisant	The serum concentration of Ivermectin can be decreased when it is combined with Pitolisant.
Pomalidomide	The metabolism of Pomalidomide can be increased when combined with Ivermectin.
Ponatinib	The metabolism of Ivermectin can be increased when combined with Ponatinib.
Pralsetinib	Pralsetinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Pranlukast	The metabolism of Pranlukast can be increased when combined with Ivermectin.
Pravastatin	Pravastatin may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Procainamide	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Procainamide.
Procarbazine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Procarbazine.
Prochlorperazine	The metabolism of Prochlorperazine can be increased when combined with Ivermectin.
Progesterone	Progesterone may decrease the excretion rate of Ivermectin which could result in a higher serum level.

Propofol	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Propofol.
Propylthiouracil	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Propylthiouracil is combined with Ivermectin.
Prucalopride	The metabolism of Prucalopride can be increased when combined with Ivermectin.
Quercetin	Quercetin may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Quingestanol	The metabolism of Quingestanol can be increased when combined with Ivermectin.
Quinidine	The metabolism of Quinidine can be increased when combined with Ivermectin.
Rabeprazole	Rabeprazole may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Raloxifene	The excretion of Raloxifene can be decreased when combined with Ivermectin.
Raltegravir	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Raltegravir.
Ranitidine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ranitidine.
Regorafenib	The metabolism of Ivermectin can be increased when combined with Regorafenib.
Remdesivir	The excretion of Remdesivir can be decreased when combined with Ivermectin.
Repaglinide	The excretion of Repaglinide can be decreased when combined with Ivermectin.
Revefenacin	Ivermectin may decrease the excretion rate of Revefenacin which could result in a higher serum level.
Ribociclib	The metabolism of Ribociclib can be increased when combined with Ivermectin.
Rifampicin	The excretion of Rifampicin can be decreased when combined with Ivermectin.
Rilpivirine	Rilpivirine may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Ripretinib	Ripretinib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Risedronic acid	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Risedronic acid.
Ritonavir	The serum concentration of Ivermectin can be increased when it is combined with Ritonavir.
Roflumilast	The metabolism of Roflumilast can be increased when combined with Ivermectin.
Rolapitant	Rolapitant may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Romidepsin	The metabolism of Romidepsin can be increased when combined with Ivermectin.
Ronifibrate	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ronifibrate.
Rosuvastatin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Rosuvastatin.
Rucaparib	Rucaparib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Rufinamide	The metabolism of Rufinamide can be increased when combined with Ivermectin.
Ruxolitinib	The metabolism of Ruxolitinib can be increased when combined with Ivermectin.
Safinamide	Safinamide may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Salmeterol	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Salmeterol.

Saquinavir	Saquinavir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Satralizumab	The serum concentration of Ivermectin can be decreased when it is combined with Satralizumab.
Selexipag	The excretion of Selexipag can be decreased when combined with Ivermectin.
Sildenafil	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Sildenafil is combined with Ivermectin.
Simeprevir	Simeprevir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Simfibrate	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Simfibrate.
Simvastatin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Simvastatin.
Sincalide	The excretion of Sincalide can be decreased when combined with Ivermectin.
Siponimod	The metabolism of Siponimod can be increased when combined with Ivermectin.
Sirolimus	The metabolism of Sirolimus can be increased when combined with Ivermectin.
Somatotropin	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Somatotropin is combined with Ivermectin.
Sonidegib	The metabolism of Sonidegib can be increased when combined with Ivermectin.
Sorafenib	The metabolism of Ivermectin can be increased when combined with Sorafenib.
St. John's Wort	The metabolism of St. John's Wort can be increased when combined with Ivermectin.
Stavudine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Stavudine.
Sulfamethoxazole	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Sulfamethoxazole.
Sulfasalazine	Sulfasalazine may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Sumatriptan	The excretion of Sumatriptan can be decreased when combined with Ivermectin.
Sunitinib	The metabolism of Ivermectin can be increased when combined with Sunitinib.
Suvorexant	The metabolism of Suvorexant can be increased when combined with Ivermectin.
Tacrine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Tacrine is combined with Ivermectin.
Tacrolimus	The metabolism of Tacrolimus can be increased when combined with Ivermectin.
Tafamidis	The serum concentration of Ivermectin can be increased when it is combined with Tafamidis.
Tamoxifen	The metabolism of Tamoxifen can be increased when combined with Ivermectin.
Tasimelteon	The metabolism of Tasimelteon can be increased when combined with Ivermectin.
Taurocholic acid	Taurocholic acid may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Tazemetostat	The metabolism of Tazemetostat can be increased when combined with Ivermectin.
Technetium Tc-99m mebrofenin	The excretion of Technetium Tc-99m mebrofenin can be decreased when combined with Ivermectin.
Telmisartan	Telmisartan may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Temocapril	The excretion of Temocapril can be decreased when combined with Ivermectin.

Temsirolimus	The metabolism of Temsirolimus can be increased when combined with Ivermectin.
Teniposide	The metabolism of Teniposide can be increased when combined with Ivermectin.
Tenofovir	The metabolism of Tenofovir can be increased when combined with Ivermectin.
Tenofovir alafenamide	The metabolism of Tenofovir alafenamide can be increased when combined with Ivermectin.
Terbinafine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Terbinafine.
Terfenadine	The metabolism of Terfenadine can be increased when combined with Ivermectin.
Teriflunomide	Teriflunomide may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Testosterone	The excretion of Testosterone can be decreased when combined with Ivermectin.
Testosterone enanthate	The metabolism of Testosterone enanthate can be increased when combined with Ivermectin.
Theophylline	The metabolism of Theophylline can be increased when combined with Ivermectin.
Thiotepa	The metabolism of Thiotepa can be increased when combined with Ivermectin.
Tianeptine	The metabolism of Tianeptine can be increased when combined with Ivermectin.
Ticlopidine	The metabolism of Ticlopidine can be increased when combined with Ivermectin.
Tioclomarol	Ivermectin may decrease the anticoagulant activities of Tioclomarol.
Tolvaptan	The metabolism of Tolvaptan can be increased when combined with Ivermectin.
Topiroxostat	Topiroxostat may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Torasemide	The excretion of Torasemide can be decreased when combined with Ivermectin.
Trabectedin	The metabolism of Trabectedin can be increased when combined with Ivermectin.
Trastuzumab emtansine	The metabolism of Trastuzumab emtansine can be increased when combined with Ivermectin.
Trestolone	The metabolism of Trestolone can be increased when combined with Ivermectin.
Triamcinolone	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Triamcinolone.
Triazolam	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Triazolam.
Trimethoprim	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Trimethoprim is combined with Ivermectin.
Triptolide	The metabolism of Triptolide can be increased when combined with Ivermectin.
Tucatinib	The metabolism of Tucatinib can be decreased when combined with Ivermectin.
Typhoid vaccine	The therapeutic efficacy of Typhoid vaccine can be decreased when used in combination with Ivermectin.
Ubidecarenone	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Ivermectin is combined with Ubidecarenone.
Ulipristal	The metabolism of Ulipristal can be increased when combined with Ivermectin.

Valsartan	The excretion of Valsartan can be decreased when combined with Ivermectin.
Vandetanib	The metabolism of Ivermectin can be increased when combined with Vandetanib.
Velpatasvir	Velpatasvir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Vemurafenib	The metabolism of Ivermectin can be increased when combined with Vemurafenib.
Venetoclax	The metabolism of Ivermectin can be increased when combined with Venetoclax.
Venlafaxine	Venlafaxine may increase the excretion rate of Ivermectin which could result in a lower serum level and potentially a reduction in efficacy.
Vibrio cholerae CVD 103-HgR strain live antigen	The therapeutic efficacy of Vibrio cholerae CVD 103-HgR strain live antigen can be decreased when used in combination with Ivermectin.
Vinblastine	The metabolism of Vinblastine can be increased when combined with Ivermectin.
Vincristine	The metabolism of Ivermectin can be increased when combined with Vincristine.
Vindesine	The metabolism of Vindesine can be increased when combined with Ivermectin.
Vinflunine	The metabolism of Vinflunine can be increased when combined with Ivermectin.
Vinorelbine	The metabolism of Vinorelbine can be increased when combined with Ivermectin.
Vismodegib	Vismodegib may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Vitamin D	The metabolism of Vitamin D can be increased when combined with Ivermectin.
Vorapaxar	The metabolism of Vorapaxar can be increased when combined with Ivermectin.
Voxilaprevir	Voxilaprevir may decrease the excretion rate of Ivermectin which could result in a higher serum level.
Warfarin	Ivermectin may decrease the anticoagulant activities of Warfarin.
Zafirlukast	The metabolism of Ivermectin can be increased when combined with Zafirlukast.
Zanubrutinib	The metabolism of Zanubrutinib can be increased when combined with Ivermectin.
Zidovudine	The risk or severity of myopathy, rhabdomyolysis, and myoglobinuria can be increased when Zidovudine is combined with Ivermectin.
Ziprasidone	The metabolism of Ziprasidone can be increased when combined with Ivermectin.
Zolpidem	The metabolism of Zolpidem can be increased when combined with Ivermectin.
Zuclopenthixol	The metabolism of Zuclopenthixol can be increased when combined with Ivermectin.

[i] https://www.pdr.net/drug-summary/Stromectol-ivermectin-391

[ii] https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/050742s022lbl.pdf

[iii] http://www.antimicrobe.org/new/drugpopup/Ivermectin.pdf

[iv] Ivermectin Monograph – Paediatrics Perth's Children's Hospital Available here: https://www.pch.health.wa.gov.au/-/media/Files/Hospitals/PCH/General-documents/Health-professionals/ChAMP-Monographs/Ivermectin.pdf

[v] Chhaiya, Sunita & Mehta, Dimple & Kataria, Bhaven. (2012). Ivermectin: pharmacology and therapeutic applications. International Journal of Basic & Clinical Pharmacology. 1. 132. 10.5455/2319-2003.ijbcp002712. Available here: https://www.researchgate.net/publication/271362867_Ivermectin_pharmacology_and_therapeutic_applications/citation/download

[vi] https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/050742s022lbl.pdf

[vii] https://mri.cts-mrp.eu/Human/Downloads/NL_H_3952_001_FinalSPC.pdf

[viii] https://www.pdr.net/drug-summary/Stromectol-ivermectin-391

[ix] https://go.drugbank.com/drugs/DB00602