

## **INTRODUCTION**

Meglumine acridone acetate; a low molecular weight immunomodulating factor or interferon inducer is the active ingredient in the pharmaceutical drug Cycloferon. It was registered in Russian Federation in 1995 and has been used as prevention and treatment for influenza and other acute respiratory infections, treatment for herpes infections, HIV infections and viral hepatitis A, B, C and D both in adults and children. Cycloferon are available as 150 mg enteric-coated tablets and 12.5% solution for injections.1

Little is known about the Cycloferon mechanism of action. However, it was assumed that Cycloferon antiviral effect was associated with its potential ability to induce type I interferon.2 Due to its antiviral effects, it was claimed that it may have potential benefit in treating COVID-19 caused by SAR-CoV-2 virus. Therefore, this rapid literature review was conducted to determine the effectiveness and safety of Cycloferon in treating COVID-19.

Currently, Cycloferon is neither registered with National Pharmaceutical Regulatory Agency nor listed in the MOH formulary.3, 4

## **EVIDENCE on EFFECTIVENESS and SAFETY**

There was no retrievable evidence from the scientific databases such as Medline, EBM Reviews, EMBASE via OVID, PubMed and from the general search engines [Google Scholar and US Food and Drug Administration (US FDA)] on effectiveness and safety of Cycloferon in treating COVID-19. There were a few non-english articles on Cycloferon in preventing and treating viral infections. However, we neither can assess/appraise nor include those articles as the articles were in Russian. No English translations were available in full text for all of those articles.

Ministry of Health of the Russian Federation in its Methodological recommendation: Prevention, diagnosis and treatment of new coronavirus infection (2019-nCoV0 version 1 (29 January 2020) document, recommends the use of interferon inducers for the management of COVID-19. However, no further information about the interferon inducers (e.g. types, dose and duration of use was provided) in the document. A few other guidelines on COVID-19;

- COVID-19 Treatment Guidelines<sup>5</sup>
- Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19<sup>6</sup>
- Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)<sup>7</sup>
- Interim Clinical Guidance for Adults with suspected of confirmed COVID-19 in Belgium<sup>8</sup>
- International Pulmonologist's Consensus on COVID-19<sup>9</sup> did not list Cycloferon or any interferon inducers as one of the treatment options for COVID-19.

Currently, there is no ongoing trial on Cycloferon for treating COVID-19 listed in the World Health Organization's International Clinical Trials Registry Platform (WHO ICTRP) and ClinicalTrial.gov.<sup>10, 11</sup>

## CONCLUSION

- Based on the review, no evidence retrieved from scientific databases on the effectiveness and safety of cycloferon for treating COVID-19.
- To date, there is no ongoing clinical trial on Cycloferon for treating COVID-19.

## REFERENCE

- 1. Polysan Ltd. Cycloferon the short summary.
- Plotnikova MA, Klotchenko SA, Kiselev AA, et al. Meglumine acridone acetate, the ionic salt of CMA and N-methylglucamine, induces apoptosis in human PBMCs via the mitochondrial pathway.Sci Rep. 2019:3;9(1):18240.
- 3. National Pharmaceutical Regulatory Agency (NPRA). Products search. Available from: <u>https://npra.gov.my/index.php/en/</u> (accessed on 27 April 2020)
- 4. Formulari Ubat Kementerian Kesihatan Malaysia. 2019. Available from: <u>https://www.pharmacy.gov.my/v2/ms/dokumen/formulari-ubat-kementerian-kesihatan-</u> <u>malaysia.html</u> (accessed on 27 April 2020)
- 5. National Institute of Health (NIH). COVID-19 Treatment Guidelines. Available from: <u>https://www.covid19treatmentguidelines.nih.gov/therapeutic-options-under-investigation/</u> (accessed on 27 April 2020)
- Infectious Diseases Society of America. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19<u>https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsacovid-19-gl-tx-and-mgmt-v1.0.4.pdf</u> (accessed on 27 April 2020)
- National Health Commission & State Administration of Traditional Chinese Medicine. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7). Available from: <u>http://www.kankyokansen.org/uploads/uploads/files/jsipc/protocol\_V7.pdf</u> (accessed online on 27 April 2020)
- Belgium Task Force on Supportive Care and Antiviral/Immunologic Treatment of Hospitalized Patients With Suspected or Confirmed COVID-19. Interim Clinical Guidance for Adults with suspected of confirmed COVID-19 in Belgium. Available from: <u>https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-</u>
  InterimQuidelines\_Treatment\_ENQ pdf (appreced on 27 April 2020).

<u>19\_InterimGuidelines\_Treatment\_ENG.pdf</u> (accessed on 27 April 2020)

- 9. International Pulmonologist's Consensus on COVID-19. COVID-19. Available from: https://scts.org/wp-content/uploads/2020/03/Pulmonologist-Consensus-COVID-19-March-2020.pdf (accessed on 27 April 2020)
- 10. ClinicalTrials.gov. National Instute of Health (NIH), US National Library of Medicine. Available <u>https://clinicaltrials.gov/ct2/results?cond=covid+&term=&cntry=&state=&city=&dist=&Search</u> =Search (accessed on 27 April 2020)

11. Clinical Trials.gov. National Instute of Health (NIH), US National Library of Medicine. COVID-19 Studies from the World Health Organization Database. Available from: https://clinicaltrials.gov/ct2/who table (accessed on 27 April 2020)

Based on available evidence up to 27 April 2020

Disclosure: The authors of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia.

Disclaimer: This rapid assessment was prepared to provide urgent evidence-based input during COVID-19 pandemic. The report is prepared based on information available at the time of research and a limited literature. It is not a definitive statement on the safety, effectiveness or cost effectiveness of the health technology covered. Additionally, other relevant scientific findings may have been reported since completion of this report.

Malaysian Health Technology Assessment Section (MaHTAS), Medical Development Division, Ministry of Health, Malaysia.



