International Office

140 Route de Ferney, Case Postale 1224

CH-1211 Geneva 1, SWITZERLAND

Phone: +41 (0)22 849 84 00

Fax: +41 (0)22 849 84 88

www.msf.org

A.47 Tocilizumab

MSF strongly supports the inclusion of tocilizumab with a square box symbol, as representative of therapeutic class in both the WHO Model List of Essential Medicines (EML) and the WHO Model List of Essential Medicines for Children (EMLc).

Currently, there is no medicine included in the EML for the treatment of patients with COVID-19.

Globally, as of 21 March 2023, there have been 761 071 826 confirmed cases of COVID-19, including 6 879 677 deaths, reported to WHO and a total of 13 260 401 200 vaccine doses have been administered[1].

The 2023 WHO "Therapeutics and COVID-19: living guideline" states that vaccination is having a substantial impact on hospitalizations and death in a number of high-income countries, but limitations in global access to COVID-19 vaccines mean that many populations remain vulnerable. Even in vaccinated individuals, uncertainties remain about the duration of protection and effectiveness of current vaccines – and the efficacy of existing treatments for COVID-19 – against emerging SARS-CoV-2 variants and subvariants and resistance to monotherapies. Therefore, there remains a need for more effective treatments for COVID-19[2] and further evidence on oral antiviral combination therapy in the context of resistance.

Real life evidence from big cohort studies that oral antivirals (notably Nirmatrelvir/ritonavir, also some evidence for molnupiravir) have a positive impact in preventing hospitalizations and/or deaths even among those who have received COVID-19 vaccine, if high risk[3]. In addition, there is some evidence

[1] WHO Coronavirus (COVID-19) Dashboard - https://covid19.who.int/

[2] Therapeutics and COVID-19: living guideline, 13 January 2023. Geneva: World Health Organization; 2023 (WHO /2019-nCoV/therapeutics/2023.1).

[3]https://www.cdc.gov/mmwr/volumes/71/wr/mm7148e2.htm
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(23)00011-7/fulltext
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01586-0/fulltext
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(23)00118-4/fulltext

as well that some oral antivirals may decrease the risk of Long COVID (Post-COVID Condition)[4]. Furthermore, the longer-term harms (including genotoxicity, emergence of resistance, emergence of new variants) of many oral antiviral therapeutics remain unknown in the absence of clinical evidence.

Interleukine 6 (IL-6) is a pleiotropic cytokine that plays a central role in immune regulation and inflammation, including in case of infections. Elevated IL-6 concentrations are associated with severe outcomes in COVID-19, including respiratory failure and death. Patients severely or critically ill with COVID-19 often suffer from an overreaction of the immune system; IL-6 receptor blockers act to suppress this overreaction. Tocilizumab and sarilumab are monoclonal antibodies, IL-6 receptor blockers, already approved for use in the treatment of rheumatoid arthritis.

For patients with severe or critical COVID-19, the WHO "Therapeutics and COVID-19: living guideline" makes a strong recommendation for treatment with IL-6 receptor blockers (tocilizumab or sarilumab); systemic corticosteroids are also recommended in association with IL-6 receptor blockers. The recommended dose of tocilizumab is a single intravenous dose of 8 mg/kg, up to a maximum of 800 mg, and a 400 mg dose for sarilumab. A second dose may be administered 12 to 48 hours after the first dose. Baricitinib, also recommended for the treatment of patients with severe and critical COVID-19 can be associated to tocilizumab or sarilumab. The guideline highlights that none of the included randomized controlled trials enrolled children, and therefore the applicability of this recommendation to children remains uncertain. Clinical trials did not enroll pregnant or breastfeeding women; the benefit/risk ratio is unknown and the decision should be taken jointly by the patient and her health care provider.

The conclusions of the Guideline Development Group are that IL-6 receptor blockers reduce mortality and need for mechanical ventilation and probably may also reduce duration of mechanical ventilation and hospitalization.

Currently, tocilizumab is provided commercially by the patent holder, which has committed up to 250,000 doses through the ACT-Accelerator Transition Plan. Three generics have been already WHO prequalified. Sarilumab is currently under patent. Tocilizumab and sarilumab are not part of the Medicines Patent Pool initiative.

MSF would like to highlight that even though tocilizumab has been on the market since 2009 for treatment of rheumatologic diseases, access has remained a challenge. As most of the existing monoclonal antibodies, tocilizumab has been priced extremely high, and are hence virtually impossible to access in low- and middle-income countries. The main patent on tocilizumab expired in 2017, yet several secondary patents remain on the medicine in a number of low- and middle-income countries that may cause uncertainties[5].

[4] https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2802878

[5] https://msfaccess.org/tocilizumab-second-drug-ever-recommended-who-covid-19-will-remain-unaffordable-and-inaccessible

MSF urges the 24th Expert Committee on the Selection and Use of Essential Medicines to include tocilizumab with a square box symbol, as representative of therapeutic class in both the WHO Model List of Essential Medicines and the WHO Model List of Essential Medicines for Children.

Dr. Daniela Belen Garone

Infectious Diseases specialist and DTM&H
International Medical Coordinator

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