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A.6 Baricitinib

MSF strongly supports the inclusion of baricitinib 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 as well that some oral antivirals may decrease the risk of Long COVID (Post-COVID Condition)[4].

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[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

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

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.

Type I and type II cytokine receptors are a family of receptors employed by over 50 interleukins, interferons, colony stimulating factors, and hormones. The intracellular signalling triggered by these receptors is mediated by Janus kinases (JAKs), a family of kinases including J AK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2). JAK inhibitors are a class of drugs which inhibit intracellular signalling through multifactorial effects on cytokine signalling. As a consequence, they interfere with many cellular responses, including antiviral responses[2]. Baricitinib is a non-specific J AK inhibitor, described as a J AK1/JAK2 inhibitor.

For patients with severe or critical COVID-19, the WHO "Therapeutics and COVID-19: living guideline" makes a strong recommendation for the use of baricitinib; corticosteroids and IL-6 receptor blockers (tocilizumab and sarilumab) are also recommended, and may be administered in combination with baricitinib. The recommended dose is a once-daily intake of 4 mg in adults for 14 days or until hospital discharge. 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 guideline highlights that none of the included randomized controlled trials enrolled children, and therefore the applicability of this recommendation to children remains uncertain. However, in November 2020, the United States Food and Drug Administration (FDA) issued an emergency use authorization (EUA 092) for baricitinib, in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients two years of age or older requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation[5] and this authorization was regularly reissued, most recently in March 2022[6].

The conclusion of the Guideline Development Group is that in patients with severe or critical illness, baricitinib reduces mortality and probably reduces duration of mechanical ventilation and hospital length of stay. It probably results in little or no increase in serious adverse events.

Currently, this medicine is provided commercially by its producer, which has been granted patents in over 50 countries. Baricitinib is not part of the Medicines Patent Pool initiative, and is not being currently procured through the ACT Accelerator programme.

MSF would like to highlight that in hospitalised patients, baricitinib can be a potential alternative to current WHO-recommended IL-6 receptor blockers monoclonal antibody treatments (tocilizumab and sarilumab) that remain in short supply for governments and patients in many low- and middle-income countries. Baricitinib is already approved for other indications such as rheumatoid arthritis, and generic

[5] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-drug-combination-treatment-covid-19 and https://www.fda.gov/media/143822/download

[6] Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization (EUA) of baricitinib. 2022. Available at: https://www.fda.gov/media/143823/download

versions are already available in India and Bangladesh at much lower prices than those of the patent holder. However, in many countries including in countries hit hard by the pandemic, such as Brazil, Russia, South Africa and Indonesia, generic baricitinib remains unavailable due to patent restrictions[7].

MSF urges the 24th Expert Committee on the Selection and Use of Essential Medicines to include baricitinib in both the WHO Model List of Essential Medicines and the WHO Model List of Essential Medicines for Children.

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[7] https://msfaccess.org/latin-america-how-patents-and-licensing-hinder-access-covid-19-treatments