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A.38 Remdesivir

MSF strongly supports the inclusion of remdesivir 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]. Regarding injectable remdesivir, there is also real life evidence for its effectiveness, for people with severe disease[4][5].

[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://jogh.org/2022/jogh-12-05031

[5] Essy Mozaffari, Aastha Chandak, Zhiji Zhang, Shuting Liang, Mark Thrun, Robert L Gottlieb, Daniel R Kuritzkes, Paul E Sax, David A Wohl, Roman Casciano, Paul Hodgkins, Richard Haubrich, Remdesivir Treatment in Hospitalized Patients With Coronavirus Disease 2019 (COVID-19): A Comparative Analysis of In-hospital All-cause Mortality in a Large Multicenter Observational Cohort, *Clinical Infectious Diseases*, Volume 75, Issue 1, 1 July 2022, Pages e450–e458, https://doi.org/10.1093/cid/ciab875

In addition, there is some evidence as well that some oral antivirals may decrease the risk of Long COVID (Post-COVID Condition)[6]. 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.

Remdesivir was developed for treatment of hepatitis C virus infection, and was also studied in Ebola and Marburg virus infections before being repurposed for SARS-CoV-2. Remdesivir is a nucleoside drug. Its mechanism of action involves chain termination, which is different to lethal mutagenesis: the drug is incorporated preferentially to the endogenous adenosine nucleoside by the SARS-CoV-2 polymerase during replication of the RNA genome.

For patients with non-severe COVID-19 at highest risk of hospitalization, the WHO "Therapeutics and COVID-19: living guideline" suggests treatment with remdesivir (conditional recommendation). People at highest risk of hospitalization include people with older age, immunosuppression and/or chronic diseases, with lack of COVID-19 vaccination as an additional risk factor to consider.
The recommended dose for remdesivir is 200 mg intravenously on day 1, followed by 100 mg intravenously on days 2 and 3. Remdesivir should be administered as soon as possible after onset of symptoms, ideally within 7 days.

For patients with severe COVID-19, the WHO "Therapeutics and COVID-19: living guideline" suggests treatment with remdesivir (conditional recommendation). The recommended dose for remdesivir is 200 mg intravenously on day 1, followed by 100 mg intravenously on days 2 to 10, although in the smaller trials, the duration is shortened to 5 days.
Administration with caution is recommended for patients with significant liver or kidney disease. 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.
Of note, for patients with critical COVID-19, the WHO "Therapeutics and COVID-19: living guideline" suggests not to use remdesivir.

The conclusions of the Guideline Development Group are that in patients with non-severe COVID-19, remdesivir probably reduces admission to hospital and may have little or no impact on mortality. The effect of remdesivir on mechanical ventilation and time to symptom resolution is very uncertain.
In patients with severe COVID-19, remdesivir possibly reduces mortality and probably reduces the need for mechanical ventilation and probably has little or no impact on time to symptom improvement.

Since 2022, remdesivir is approved by the Food and Drug Administration (FDA) for the treatment of COVID-19 in adults and pediatric patients aged ≥28 days and weighing ≥3 kg with positive results of direct SARS-CoV-2 viral testing, and who are hospitalized, or not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death[7].

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

[7] https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-approves-first-covid-19-treatment-young-children

The Guideline Development Group highlights that “obstacles to access in low- and middle-income countries (LMICs) due to cost, feasibility and availability are of concern. Challenges in shared decision-making and in communicating the harms versus benefits of remdesivir may also be increased in LMICs. The recommendations should provide a stimulus to engage all possible mechanisms to improve global access to the intervention”.

Currently, remdesivir is provided commercially by the patent holder. One generic is WHO prequalified and one is in the prequalification pipeline. The ATC-Accelerator Transition Plan is in place to promote generic product availability, although remdesivir is not part of the Medicines Patent Pool agreement.

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

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