A.6	Baricitinib – COVID-19 – EML and EMLc
Draft recommendation	☒ Recommended ☐ Not recommended Justification: WHO COVID-19 Living Guidelines strongly recommend the use of Baricitinib for patients with severe or critical COVID-19. The WHO meta-analysis demonstrated an OR for mortality of 0.83, with a reduction in mortality of 20 fewer deaths/1000 patients. An independent Cochrane confirmed the reduction in mortality and noted a good safety profile. Although more common secondary infections are a concern with long term treatment, this has not been demonstrated in the short treatment courses used in COVID-19. The drug has not been widely studied in populations with high rates of HIV, TB and other chronic infections. Only limited data is available in children but the drug is recommended for all ages including children. The list price is over $1000.
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable Comments: COVID-19
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes ☐ No ☐ Not applicable Comments: The WHO GDG meta-analysis for this JAK inhibitor included 4 trials with 10,815 adult patients with COVID-19. The OR for mortality was 0.83 (95%CI 0.74-0.93), representing 20 fewer deaths/1000 patients. There was evidence of a probable reduction in duration of mechanical ventilation (around 3 days) and hospital length of stay (around 1 day). The reduction in mortality was confirmed by a Cochrane review in 2022.
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (this may be evidence included in the application, and/or additional evidence identified during the review process)	☒ Yes ☐ No ☐ Not applicable Comments: A Cochrane review noted that there was little difference in the rate of AEs of any grade compared to placebo. During the short treatment course, there was no evidence of any increase in the rate of secondary infections (a concern in patients given long term therapy for other indications, usually auto-immune disease). There is limited data in children, but a dosing regimen is available, and the drug is recommended in severe paediatric COVID-19 disease.

Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments: It is noted that most of the patients recruited into trials were not from LMIC settings where there are higher rates of HIV, TB and other infections.
Are there any special requirements for the safe, effective and appropriate use of the medicines? (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☐ Yes ☒ No ☐ Not applicable Comments: The drug ideally is given early in clinical disease with COVID-19 confirmed with an appropriate rapid diagnostic test.
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☒ Yes ☐ No ☐ Not applicable Comments: The application gives the list price as $1,109.
Are there any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments: The drug is not currently procured through the ACT Accelerator programme
Is the proposed medicine recommended for use in a current WHO guideline? (refer to: https://www.who.int/publications/who-guidelines)	☒ Yes ☐ No ☐ Not applicable Comments: WHO COVID-19 Living Guideline.