A.47	Tocilizumab – COVID-19 – EML and EMLc
Draft recommendation	☒ Recommended – square box ☐ Not recommended Justification: Tocilizumab is a monoclonal antibody that acts as an IL-6 receptor antagonist. It is approved for intravenous use in rheumatoid arthritis. The 2022 WHO Covid-19 living guideline noted that there was high level evidence of a reduction of mortality based on 27 studies including 10,930 patients. There were an estimated 16/1000 fewer deaths in the IL-6 blocker group. There was also high-level evidence for a reduction in the need for mechanical ventilation. Sub-group analysis noted no modification of effect based on whether the patient had critical or severe disease. There was greater benefit in patients receiving steroids. A Cochrane review confirmed that tocilizumab reduced all cause day 28 mortality compared to standard care or placebo. The GDG noted high uncertainty about the effect of tocilizumab on adverse events. The Cochrane review also noted similar uncertainty but concluded that there were probably fewer serious adverse events than placebo. The WHO living guideline has a strong recommendation for the use of IL-6 receptor blockers in patients with severe and critical Covid-19 disease.
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable Comments: There have been an estimated 600 million cases of Covid-19 with 6 million deaths.
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 2022 WHO Covid-19 living guideline noted that there was high level evidence of a reduction of mortality based on 27 studies including 10,930 patients. There were an estimated 16/1000 fewer deaths in the IL-6 blocker group. There was also high-level evidence for a reduction in the need for mechanical ventilation. Sub-group analysis noted no modification of effect based on whether the patient had critical or severe disease. There was greater benefit in patients receiving steroids. A Cochrane review confirmed that tocilizumab reduced all cause day 28 mortality compared to standard care or placebo.

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: The GDG noted high uncertainty about the effect of tocilizumab on adverse events. The Cochrane review also noted similar uncertainty but concluded that there were probably fewer serious adverse events than placebo.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
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: None of the trials enrolled children or pregnant women.
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☒ Yes ☐ No ☐ Not applicable Comments: The drug has been made available through the ACT-Accelerator platform. The ICER for combination therapy for tocilizumab with dexamethasone compared to dexamethasone alone was between around $16-26,000 dollars in the higher and lower mortality scenarios.
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: Tocilizumab is not part of the MPP initiative.

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: The WHO living guideline has a strong recommendation for the use of IL-6 receptor blockers in patients with severe and critical Covid-19 disease. This included tocilizumab and sarilumab.