A.14 Glucagon-like peptide-1 receptor agonists – obesity – EML

Reviewer summary	☒ Supportive of the proposal ☐ Not supportive of the proposal Justification (based on considerations of the dimensions described below): I consider this medication should be included for obese patients with increased CV risk including T2DM since clear benefits (such as CV events) have been shown.
Does the EML and/or EMLc currently recommend alternative medicines for the proposed indication that can be considered therapeutic alternatives? (**https://list.essentialmeds.org/**)	☐ Yes ☒ No ☐ Not applicable
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;) GLP-1RAs have shown to be beneficial for weight loss in adults with obesity with moderate to high certainty evidence. They also lead to improvement in waist circumference, fat mass, quality of life (minimal). No significant change was seen in all-cause mortality. Only Semaglutide showed an impact on the incidence of MI. No changes were seen in the incidence of non-fatal stroke. It is important to highlight that the SELECT trial showed that semaglutide 2.4 mg weekly significantly reduced major cardiovascular events (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke) by 20% compared to placebo in overweight or obese individuals with pre-existent CV disease without diabetes.	☒ Yes ☐ No ☐ Not applicable
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;) Short term side effects are well characterized. They are mostly predictable (GI symptoms, gallbladder issues), and appear manageable relative to the substantial benefits. Unfortunately, there is limited information regarding side effects when this medication is used for extended periods of time, which is likely the case.	☐ Yes ☒ No ☐ Not applicable
Overall, does the proposed medicine have a favourable and meaningful balance of benefits to harms? Considering the available evidence they do have a favourable profile. This is more significant for patients with CV disease. Based on the available evidence Semaglutide seems to be particularly beneficial	☒ Yes ☐ No ☐ Not applicable

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) Monitoring and adjustment: • Monitor for gastrointestinal side effects (nausea, vomiting) especially during dose escalation • Renal function should be monitored periodically. • Dose escalation is required Training and healthcare system needs: • Subcutaneous injection training is necessary. • Cold chain storage is required before first. • Patients and providers should be trained to counsel patients about recognizing symptoms of pancreatitis and when to seek medical advice.	☒ Yes ☐ No ☐ Not applicable
Are there any issues regarding price, cost-effectiveness and budget implications in different settings? These drugs are expensive (particularly semaglutide and tirzepatide), with monthly costs estimated around $400 to $450 USD. Prices can vary across countries but are generally high globally, limiting affordability, especially in LMICs. In high-income countries, some analyses suggest that semaglutide may be cost-effective when accounting for long-term benefits like reduced cardiovascular events and improved quality of life. However, cost-effectiveness is less certain in LMICs, where healthcare budgets are more constrained, and affordability challenges are much greater.	☒ Yes ☐ No ☐ Not applicable
Is the medicine available and accessible across countries? (e.g. shortages, generics and biosimilars, pooled procurement programmes, access programmes) GLP-1s are available in many countries but not yet widely accessible. While they are available in HICs there are significant limitations in LMICs due to several factors such as: delays in regulatory approval, limited availability in public health systems and affordability barriers. Supply shortages and limited distribution have already been observed in some regions.	☐ Yes ☐ No ☐ Not applicable
Does the medicine have wide regulatory approval? GLP-1s (particularly semaglutide) have wide regulatory approval in high-income regions.	☒ Yes, for the proposed indication. ☐ Yes, but only for other indications (off-label for proposed indication) ☐ No ☐ Not applicable