A.30	Osimertinib – non-small cell lung cancer – EML
Draft recommendation	☐ Recommended ☒ Not recommended Justification: Not cost effective
Does the proposed medicine address a relevant public health need?	☒ Yes ☐ No ☐ Not applicable Comments: • Lung cancer is the most commonly diagnosed and the first cause of death for cancer worldwide, estimating 2 million new cases and 1.7 related deaths in 2018, according to Global Cancer Observatory 2018 • Over 80% of the lung cancers are classified as non-small cell (NSCLC), and nearly 70% are diagnosed at late stages as locally advanced or metastatic • EGFR mutation is the most frequent oncogene driver targetable aberration
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: • FLAURA trial compared osimertinib with the standard 1st generation TKI (gefitinib and erlotinib) • PFS: mPFS 18.9 versus 10.2 months; HR 0.46, 95% CI 0.37–0.57, P<0.0001). • OS: mOs 38.6 months (95% CI 34.5–41.8) in the osimertinib group and 31.8 months (95% CI 26.6–36.0) in the 1st generation TKI arm (HR 0.80, 95% CI 0.64–1.00, P=0.046), a 6.8 month gain for OS after a 35.8 and 27.0 months follow up in the osimertinib and comparator arm, respectively
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: • FLAURA trial compared osimertinib with the standard 1st generation TKI (gefitinib and erlotinib) • grade 3 or higher adverse event rates were 34% in the osimertinib group and 45% in the comparator group

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: • Use of EGFR assessment validated molecular tests • there might be a need for high skilled molecular pathology and capacity building
Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?	☒ Yes ☐ No ☐ Not applicable Comments: • the incremental cost per 1 life-year saved in USA and Brazil was respectively, $133,472 vs $95,646 for erlotinib, $136,180 vs $106,532 for gefitinib, and $129,552 vs $103,366 for afatinib. Likewise, the osimertinib ICER per QALY comparison with 1st and 2nd generation TKI in United States was $226,527 (vs erlotinib), $231 123 (vs gefitinib) $219 874 (vs afatinib), and $162 329 (vs erlotinib), $180,804 (gefitinib), and $175,432 (vs afatinib) in Brazil • “at current costs and considering the willing to-pay thresholds, we found that osimertinib is unlikely to be cost-effective for EGFR-mutated first-line therapy”.
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:
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: