(1) Does the application adequately address the issue of the public health need for the medicine?
Yes ☑ No ☐

Please provide brief details:
EGFR mutations in NSCLC occur in 15% of the US population. The mutation is more common in non-smokers and females. In Asia EGFR mutation in NSCLC occurs in 22-62% of the patients.

(2) Have all important studies/evidence of which you are aware been included in the application?
Yes ☑ No ☐

Please provide brief comments on any relevant studies that have not been included:

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?
Yes ☑ No ☐

(a) Briefly summarise the reported benefits (e.g. clinical versus surrogate) and comment, where possible, on the actual magnitude of benefit associated with use of the medicine:

EGFR-TKIs are universally recommended as first line therapy in EGFR mutated advanced lung cancers.

**ERLOTINIB versus chemotherapy gemcitabine/cisplatin or carboplatin**
OPTIMAL TRIAL; 154 patients
PFS: 13.1 versus 4.6 months, HR 0.16 (95% CI 0.10-0.26).
ENSURE TRIAL: n=275. Trial conducted in Asia. PFS 11 months versus 5.5 months. 85.6% patients randomised to chemotherapy received EGFR-TKIs post chemotherapy.
EURTAC trial; 174 patients: PFS 9.7 versus 5.2 months. HR 0.34 (95%CI 0.22-0.54)

**GEFITINIB versus paclitaxel/carboplatin**
IPASS: n=1217 Asian
PFS significantly better. 12-month progression free rate 25 versus 7%.
WEST JAPANESE ONCOLOGY GROUP 172 trial & North-East Japan Study Group 002: Magnitude of benefit similar to IPASS.

AFATINIB versus cisplatin/pemetrexed LUX 3: At a median follow up of 16 months: PFS 11.1 versus 6.9 months.
LUX 6: Afatinib versus gemcitabine/cisplatin n=364.
PFS 11 versus 5.6 months.
In the combined analysis of LUX 3 & 6: Statistically significant OS benefit observed in patients with exon 19 deletion.
EGFR-TKIS have higher, efficacy, improved PFS and better QoL across all subgroups of EGFR mutated NSCLC. In addition, less access of health-related resources is utilised.
Benefit of overall survival not shown as cross-over to TKIs upon progression on chemotherapy was allowed in all trials.

(b) Is there evidence of efficacy in diverse settings and/or populations? Please provide brief details:

Yes. Phase III trials of EGFR-TKIs have been conducted all over the world. Asian populations have a higher level of EGFR mutated lung cancers and with more advanced disease.

(4) Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?

Yes ☒ No ☐

Please provide brief details:

(5) Please comment on the overall benefit to risk ratio of the medicine (e.g., favourable, uncertain etc).

ESMO MCBS: 4. Level of Evidence 1
NCCN: Category 1A.

ADDITIONAL CONSIDERATIONS:

(6) Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?

Yes ☒ No ☐

Please provide brief details:

EGFR mutation analysis by PCR. This test is performed in most LMICs.
(7) Are there any issues regarding the registration of the medicine by regulatory authorities? (e.g., recent registration, new indications, off-label use)

Yes ☐ No ☑

Please provide brief details:

(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?

Yes ☑ No ☐

Please provide brief details:

Approved USA, Europe, Japan, in nearly all Asian countries

(9) Please comment briefly on issues regarding cost and affordability of this medicine.

Comparison of cost-effectiveness between EGFR-TKIs and chemotherapy in advanced NSCLC showed the drugs to be highly cost effective in LMICs.

EGFR-TKIs are cost effective especially in the generic forms. Require less access to hospital care and specialised services. Due to tolerable side effects over 90% patients can continue to lead a productive working life.

(10) Any additional comments?

(11) Please frame the decisions and recommendations that the Expert Committee could make.

APPROVED

(12) References (if required)

Comparison of cost-effectiveness between EGFR-TKIs therapy and chemotherapy for advanced NSCLC. Zhang et al. Value in Health. PCN 21. 19(2016); A807-A918