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

   Please provide brief details: Not for the general epileptic population. This drug may be more suitable than other antiepileptics for special populations (HIV/AIDS, pregnant women) and for patients who don’t respond to or cannot tolerate first line therapy. but not clear what proportion do not respond or tolerate.

(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: Yes, GRADE tables presented. Evidence for use as add-on therapy based on good to high quality evidence (see starting p. 18 of application). Lamotrigine does not have significant advantage as monotherapy compared to first line treatments for primary, important outcome – time to first seizure (see pg 19-21).

   (b) Is there evidence of efficacy in diverse settings and/or populations? Please provide brief details: yes; some trials from developing countries focus on parasite-induced epilepsy

(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: A Cochrane review suggests “fair” tolerability. Cochrane review suggests lower risk of malformed children compared to other antiepileptics used by pregnant women. NICE review (low to moderate GRADE evidence) suggests better tolerability; Cochrane review fewer withdrawals compared to other antiepileptics (p. 25)

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

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:

(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: No WHO guidelines cited. Other guidelines (eg, NICE) recommend lamotrigine for focal and generalized epilepsy, usually as adjunct therapy.

(9) Please comment briefly on issues regarding cost and affordability of this medicine.
Price can be variable, but comparable to carbamazepine. UK Cost-effectiveness analysis suggest lamotrigine is cost-effective.

(10) Any additional comments?
Head to head comparisons of antiepileptics are rare. Application provides rationale for focusing the application on lamotrigine
(11) Please frame the decisions and recommendations that the Expert Committee could make.
Add lamotrigine to anticonvulsants / antiepileptic section of EML and EMLc; for use in special populations or those who are unresponsive or cannot tolerate first line antiepileptics.

(12) References (if required)