21st Expert Committee on Selection and Use of Essential Medicines

Peer Review Report

[emtricitabine/rilpivirine/tenofovir alafenamide; FTC/RPV/TAF]

(1) Does the application adequately address the issue of the public health need for the medicine?

Yes ☐ No ☐

Please provide brief details:
Main rationale for this application is to replace efavirenz with rilpivirine to reduce adverse neuropsychiatric adverse effects. Replace TDF with TAF for reduction in adverse renal and bone effects.

(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: medline search conducted, but not clear if all trials included in application

(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:
Different trials have tested the RPV component and TAF component, so no direct evidence. RPV: noninferiority adult trials showed RPV and efavirenz reduced viral load 83 and 80% respectively at week 96. Similar results for adolescents and switching studies. TAF: main evidence is from 2 RCTs that were pooled for regulatory approval. Test non-inferiority against combination with TAF vs. TDF. At 48 weeks, viral suppression achieved in 92% and 90% patients, respectively. Open label study in treatment naïve adolescents; viral suppression in all subjects. No GRADE tables or assessment of risk of bias in trials; For RPV: pooled trials published. Individual trials published and pooled data (Nelson). Pooled TAF studies published.

(b) Is there evidence of efficacy in diverse settings and/or populations? Please provide brief details: Yes
(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: based on only patients who have participated in the trials (about 1500). For RPV vs EFV regimens, some significant lower adverse neurological and psychiatric events for RPV. Elvitegravir / TAF regimens have less impact on renal function (not tested in combo with RPV). Data on bone health weak for TAF. Very small differences in bone mineral density; no data on fractures.

(5) Please comment on the overall benefit to risk ratio of the medicine (e.g., favourable, uncertain etc). slightly favourable compared to EFV / TDF regimens.

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: registered in US and EU

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

Yes ☐  No ☐

Please provide brief details: recommended in US and EU guidelines (as alternative rather than preferred treatment option). Consistent with WHO guideline, FTC/RPV/TAF provides an NRTI backbone of FTC and tenofovir (as TAF) as preferred first-line therapy but includes the second-generation NNRTI, RPV, in place of first-generation EFV

(9) Please comment briefly on issues regarding cost and affordability of this medicine.
Gilead has licensing, manufacturing provisions, access price for low and middle income countries $32.00 US

(10) Any additional comments?

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

emtricitabine/rilpivirine/tenofovir alafenamide; FTC/RPV/TAF for treatment naïve and virally suppressed adults and adolescents (> 12 yo) to provide an option that may have a more favourable side effect profile.

(12) References (if required)