Reviewer No.1 checklist for application of:

Lamivudine + zidovudine + nevirapine fixed-dose combination

In the WHO Essential Medicines List for Children

(1) Have all important studies that you are aware of been included?

Yes ☐ **No** ✓

Search site: Pubmed: Not enough data available in children on this FDC.

(2) Is there adequate evidence of efficacy for the proposed use?

Yes ☐ **No** ✓

- Current dosage recommendations for nevirapine (300mg/m^2) [BMJ 2006;332:1183-1187], while the manufacturer recommends 160-200mg/ m^2

- 9-11.9 kg have same dose recommendations; the lower weight being at the top range of dosing & upper weight being at the bottom range of dosing which would influence efficacy.

(3) Is there evidence of efficacy in diverse settings and/or populations?

Yes ✓ No ☐

A combination of 2NRTIs + 1NNRTIs is one of the recommended HAART treatment.

(4) Are there adverse effects of concern?

Yes ✓ No ☐

- Severe rash associated with nevirapine which may necessitate discontinuation of treatment. This side effect may occur within 6wks of initiation of therapy. However, this FDC initiation is recommended by the manufacturer after 2 wks.

- Increasing the nevirapine dose by steps reduces the incidence of rash, which may make this FDC inappropriate.

(5) Are there special requirements or training needed for safe/effective use?

Yes ☐ **No** ✓

(6) Is this product needed to meet the majority health needs of the population?

Yes ✓ No ☐

(7) Is the proposed dosage form registered by a stringent regulatory authority?

Yes ☐ **No** ✓

(8) What action do you propose for the Committee to take?

Not suitable for approval.

(9) Additional comment, if any.

FDCs are a necessity to reduce drug burden in children, however, FDCs in the form of a tablet are too restrictive combination for the paediatric population especially with drugs such as antiretrovirals where appropriate dosing is critical to ensure efficacy in reducing viral load. FDCs in the form of syrups would be more appropriate to give better flexibility in dosing.