| D.1 | **Antiretrovirals – EXCLUSION OF ARV'S**<br>Lamivudine (3TC) Tablet: 150 mg. EMLc Only<br>Abacavir (ABC) Tablet (dispersible, scored): 60 mg (as sulfate). EMLc only<br>Efavirenz (EFV or EFZ) Tablet: 200 mg (scored<br>Ritonavir (RTV) Oral liquid: 400 mg/5 ml. Oral powder: 100 mg in sachet<br>Atazanavir Solid oral dosage form: 300 and 100 mg; (as sulfate)<br>Lopinavir + ritonavir (LPV/r) Oral liquid: 400 mg + 100 mg/5 mL<br>Raltegravir (RAL) Chewable tablet: 100 mg, [400mg for EMLc only ]<br>Lamivudine + nevirapine + zidovudine Tablet: 200 mg + 300 mg + 150 mg<br>Lamivudine + nevirapine + zidovudine Tablet: 30 mg + 50 mg + 60 mg.EMLc only<br>(application title) |
|---|---|
| Does the application adequately address the issue of the public health need for the medicine? | ☒ Yes<br>☐ No<br>☐ Not applicable<br><br>Comments: demonstrates dire public health need spanning worldwide based on current WHO update |
| Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market. | These drugs listed for deletion were included on WHO recommendations guidelines and EML earlier than 2019 for treatment of HIV, however, with recent updates and data provided , new drugs such as dolutegravir and lower doses of existing drug EFV has replaced the need for many of these combinations an drugs by reducing viral load and resistance strains and tolerability . With recent updates and improved availability of new drugs through global collaboration it is recommended the WHO guidelines and EML are in sync. Many come as single or fixed dose combinations. |
| Have all important studies and all relevant evidence been included in the application? | ☒ Yes<br>☐ No<br>☐ Not applicable<br>If no, please provide brief comments on any relevant studies or evidence that have not been included: |

| | |
|---|---|
| Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication? | ☐ Yes<br>☐ No<br>☒ Not applicable<br>The submission is based on new updated WHO guideline which has all the studies<br>10 mg addition of Dolutegravir is for children and is is in generic format to improve access.<br><br>Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s).<br>This is based on a trial of 75 children Dolutegravir achieving 69% undetectable viral load at 48 weeks , others drugs are considered suboptimal.<br><br>Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? |
| Does the application provide adequate evidence of the safety and adverse effects associated with the medicine? | ☐ Yes<br>☐ No<br>☒ Not applicable<br>Comments: based on WHO guidelines , these arguments have been made . |
| Are there any adverse effects of concern, or that may require special monitoring? | ☐ Yes<br>☐ No<br>☒ Not applicable<br>Comments: |
| Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.) | These drugs are assessed to be less effective and have worse AE than the new recommendations and there of low benefit and high risk or are redundant. |
| Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.) | HIV has attracted a lot of research funding with many these studies performed in LMIC and LIC with high burden. This is highly commendable and a strive towards equity of care based on evidence from high level trials. T |
| Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?**<br>(e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc) | ☐ Yes<br>☐ No<br>☒ Not applicable<br>Comments: |

| | |
|---|---|
| Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication) | ☐ Yes<br>☐ No<br>☐ Not applicable<br>Comments: |
| Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines) | ☐ Yes<br>☒ No<br>☐ Not applicable<br>Comments: These medicines have been deleted from the WHO guideline for HIV based on new information of less efficacy and tolerability . |
| Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings. | With many collaborative efforts new drugs in the WHO guideline are currently widely available and therefore these drugs must be deleted as EML. |
| Any additional comments | |
| Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal. | 1.Lamivudine (3TC) Tablet: 150 mg. EMLc Only<br>To be deleted as oral solutions preferred in children and is being phased out for this indication.<br>2.Abacavir (ABC) Tablet (dispersible, scored): 60 mg (as sulfate). EMLc only<br>Still recommended for children in combination as first or second line but at doses >150mg . IN TB RTV 25 and DTG superior , super boosting LPRi recommended<br>Testing for HLA-B*5701 not available to most.<br>Delete<br>2. Efavirenz (EFV or EFZ) Tablet: 200 mg (scored<br>Recommended in 2nd line setting in children as weight and metabolizer dependent and could be as low as 100 mg or 200 mg .400mg dose is an alternative 1st line in adults ,<br>Removed for children . as 200mg tablet<br>Not recommended in adults<br>delete<br>3. Ritonavir (RTV) Oral liquid: 400 mg/5 ml. Oral powder: 100 mg in sachet<br>Replaced by combination granules and pellets with increased dose flexibility .<br>25 mg preferred to improve flexibility.<br>delete<br>4. Atazanavir Solid oral dosage form: 300 and 100 mg; (as sulfate)<br>Requires a booster not deemed currently appropriate , not prefared |

| | |
|---|---|
| | Delete<br>5. Lopinavir + ritonavir (LPV/r) Oral liquid: 400 mg + 100 mg/5 mL<br>Replaced by granules and pellets which can be dispensed for younger childrern<br>delete<br>6. Raltegravir (RAL) Chewable tablet: 100 mg, [400mg for EMLc only ]<br>100mg tablet replaced by 100mg granules and 25 mg tablets in adults<br>An alternative 1st line and 2nd line in special circumstances like if LPV/r not available ,<br>Delete<br>7. Lamivudine + nevirapine + zidovudine Tablet: 200 mg + 300 mg + 150 mg<br>Less optimal choice with DTG availability , not recommended<br>Delete<br>8. Lamivudine + nevirapine + zidovudine Tablet: 30 mg + 50 mg + 60 mg.EMLc only<br>Less optimal choice , not recommended<br>Delete |
| References<br>(if required) | 1. WHO. The selection and use of essential medicines. Report of the WHO Expert<br>Committee, 2019 (including the 21st WHO Model List of Essential Medicines and the 7th WHO<br>Model List of Essential Medicines for Children). Geneva: World Health Organization. (WHO<br>Technical Report Series, No. 1021); 2019.<br>2. Update of recommendations on first- and second-line antiretroviral regimens. Geneva,<br>Switzerland: World Health Organization; 2019 (WHO/CDS/HIV/19.15).<br>Licence: CC BY-NC-SA 3.0 IGO. Available from<br>https://apps.who.int/iris/handle/10665/325892.<br>3. THE 2021 OPTIMAL FORMULARY AND<br>LIMITED-USE LIST FOR ANTIRETROVIRAL<br>DRUGS FOR CHILDREN |