

<b>A.24</b>  (item number)	<b>Paliperidone and risperidone LAI - schizophrenia</b> (application title)	
Does the application adequately address the issue of the public health need for the medicine?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable  Comments: It is a chronic severe disease affecting a significant number of people globally and causing a large burden due to disability which increases over time. As it is a life long condition which requires long term treatment, adherence to medication is an important issue.	
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.	The EML currently list 5 drugs under the indication of schizophrenia and psychotic disorders (only 1 is long acting). That only long-acting drug currently facing an issue on its availability due to discontinuation of its production.  The proposed drugs are the 2 <sup>nd</sup> generation of the long-acting anti-psychotic medication intended to provide a wider treatment option to the specific health problem and improve treatment adherence.	
Have all important studies and all relevant evidence been included in the application?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable  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?	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable  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).  The evidence on the effectiveness included 4 systematic reviews and the applicants also conducted a network meta-analysis to present head to head comparison on the effect of different medications to two clinical outcomes (relapse and acceptability) which show sound benefits for both medications with moderate to high certainty of evidence.	

	<p>Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)?</p> <p>Risperidone LA has been marketed in 37 countries which include several LMICs</p> <p>Paliperidone palmitate LA has been marketed in 37 countries which include several LMICs.</p> <p>None of these medications has been approved for use in children and adolescents.</p> <p>No data regarding its use in pregnancy and lactation.</p>
<p>Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p> <p>Tolerability is comparable with other anti-psychotic medications; other side effects include weight gain and hyperprolactinaemia. No increase risk of death or suicide.</p>
<p>Are there any adverse effects of concern, or that may require special monitoring?</p>	<p><input type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p>
<p>Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)</p>	<p>Favourable benefit</p>

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<p>Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)</p>	<p>The overall quality of evidence is moderate to high</p>
<p>Are there any special requirements for the safe, effective and appropriate use of the medicine(s)? (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)</p>	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable</p> <p>Comments: Risperidone LA needs to be stored in refrigerator.</p>
<p>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)</p>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not applicable</p> <p>Comments: Risperidone LA has been marketed in 37 countries which include several LMICs Paliperidone palmitate LA has been marketed in 37 countries which include several LMICs.</p>
<p>Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: <a href="https://www.who.int/publications/who-guidelines">https://www.who.int/publications/who-guidelines</a>)</p>	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable</p> <p>Comments: WHO Mental Health Gap Action Programme (mhGAP), Version 2.0 (2016)</p>

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Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	The availability is yet to be improved globally as it is now currently marketed in only 36-37 countries (according to its manufacturer). However, I happen to know that paliperidone palmitate long-acting also available in one Asian LMIC list of essential medicine (2019), which is not listed in the list of 36-27 countries in the application. The applicants did not included a cost-effectiveness analysis, and the cost of both medications are highly varied and relatively higher compare to the short acting which might affect affordability. Yet, in the low resources setting less frequent visit to health center might be preferrable also in the emergency situation like pandemic.
Any additional comments	There is also a request by the manufacturer to include the 3 month long-acting paliperidone palmitate, which they suggested that it has similar efficacy with greater conveniency for patients.
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.	Similar risk and benefit were shown between the two proposed medications with other anti-psychotic medications. However, the use of long-acting medication improve adherence to treatment due to its conveniency for this chronic long-life condition. Hence we recommend the inclusion of paliperidone palmitate LA and risperidone LA in the eml.
References (if required)	