

C.3	Chlorpromazine, fluphenazine decanoate/enantate and haloperidol – review of square box alternatives – EML
Draft recommendation	<p><input checked="" type="checkbox"/> Recommended</p> <p><input type="checkbox"/> Not recommended</p> <p>Justification:</p> <p>Pharmacological options to treat psychotic disorders in the current WHO Model List of Essential Medicines (EML) (section 24.1) include haloperidol, chlorpromazine, risperidone, fluphenazine enantate/decanoate, paliperidone/risperidone injection (prolonged-release).</p> <p>Considering the evidence on FGA showing better efficacy in comparison with placebo for acute and maintenance treatment for psychotic disorders, and moderate-to-high certainty of evidence according to the GRADE/CINEMA approach for acute or maintenance treatment or both. When compared head-to-head, no statistical differences emerged with FGAs already included in the WHO EML. However, the profiles adverse effects among FGAs are quite different. For example, compared with haloperidol, chlorpromazine showed a higher risk of weight gain and anticholinergic side effects, but its risk of extrapyramidal symptoms was lower.</p> <p>So, in the current version of the WHO EML, both oral haloperidol and chlorpromazine are marked with a square box indicating any FGA as a therapeutic alternative each other.</p> <p>More importantly, with exception of risperidone (only SGA the list), all antipsychotic list above marked with square box symbol indicating that any FGA can be considered as a therapeutic alternative to risperidone, which is also redundant. The evidence showed that some individuals may benefit more from the FGA treatment.</p> <p>Applicants requested:</p> <p>(1) Among oral FGAs, maintaining only haloperidol, marked with a “restricted” square box indicating chlorpromazine therapeutic alternative;²</p> <p>(2) Among long-acting FGAs, maintaining fluphenazine enantate/decanoate, marked with a “restricted” square box indicating haloperidol decanoate and zuclopenthixol decanoate as therapeutic alternatives.</p> <p>Of relevance, the Guidelines Development Group of WHO Mental Health Gap Action Programme (mhGAP) revision is considering recommending these medications as representative of FGAs for the treatment of schizophrenia and related psychoses in the forthcoming update of the mhGAP Guideline.</p> <p>Another issued should be also discussed that a proposal for putting the addition of a selected square box symbol to risperidone to the WHO EML core list and including aripiprazole, olanzapine, paliperidone, and quetiapine as therapeutic alternatives (see c8_risperidone.pdf).</p>
Does the proposed medicine address a relevant public health need?	<p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input checked="" type="checkbox"/> Not applicable</p> <p>Comments:</p>

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<p>Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication?</p> <p>(this may be evidence included in the application, and/or additional evidence identified during the review process)</p>	<p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input checked="" type="checkbox"/> Not applicable</p> <p>Comments:</p>
<p>Does adequate evidence exist for the safety/harms associated with the proposed medicine?</p> <p>(this may be evidence included in the application, and/or additional evidence identified during the review process)</p>	<p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input checked="" type="checkbox"/> Not applicable</p> <p>Comments:</p>
<p>Are there any adverse effects of concern, or that may require special monitoring?</p>	<p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input checked="" type="checkbox"/> Not applicable</p> <p>Comments:</p>
<p>Are there any special requirements for the safe, effective and appropriate use of the medicines?</p> <p>(e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)</p>	<p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input checked="" type="checkbox"/> Not applicable</p> <p>Comments:</p>
<p>Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?</p>	<p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input checked="" type="checkbox"/> Not applicable</p> <p>Comments:</p>
<p>Are there any issues regarding the registration of the medicine by national regulatory authorities?</p> <p>(e.g. accelerated approval, lack of regulatory approval, off-label indication)</p>	<p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input checked="" type="checkbox"/> Not applicable</p> <p>Comments:</p>

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<p>Is the proposed medicine recommended for use in a current WHO guideline?</p> <p>(refer to: https://www.who.int/publications/who-guidelines)</p>	<p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input checked="" type="checkbox"/> Not applicable</p> <p>Comments:</p>
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