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

Yes ☒ No ☐

Please provide brief details: Sort of. It seems to say that this is an important treatment in invasive fungal infections.

(2) Have all important studies that you are aware of been included in the application?

Yes ☐ No ☒

Please provide brief comments on any relevant studies that have not been included:
The importance of this is that all cause mortality is higher in itraconazole and the azole drugs.


Little difference

da Mota Menezes V, Soares BGO, Fontes CJF. Drugs for treating paracoccidioidomycosis. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD004967. DOI: 10.1002/14651858.CD004967.pub2 (up to date 2011)
Insufficient data

No difference found

No impact on mortality, but is on incidence.

Clinical Evidence assessment, October 2013, shows no advantage over fluconazole for vulvo-vaginitis

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?

Yes ☐ No ☒
Briefly summarise the reported outcomes (e.g. clinical, surrogate, other) and comment, where possible, on the magnitude of clinical benefit associated with use of the medicine:

There is no summary of the evidence on effects across the various conditions. For preventing fungal infection in immunocompromised individuals, the authors cite a meta-analysis supported by the manufacturer, which focuses on fungal associated mortality. In fact, total mortality does not show a difference.

(4) Is there evidence of efficacy in diverse settings and/or populations?
   Yes ☐ No ☒

Please provide brief details:

(5) 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:

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: there may be, because of it’s poor bioavailability the instructions in relation to food are complicated.

(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: I don’t think so.

(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?
   Yes ☐ No ☒
Please provide brief details:

(9) Please comment briefly on issues regarding cost and affordability of this medicine.
Not that I am aware of.

(10) Any additional comments?

(11) Please summarise the action you propose the Expert Committee takes.

I find the submission rather weak particularly in terms of what adding it does in terms of the existing fluconazole. The bioavailability is poor, it's protein bound so doesn't penetrate the CSF, and the submission is clearly biased. This causes me some problems in stating it should be approved.


<table>
<thead>
<tr>
<th>GRADE Evaluation of interventions for Candidiasis (vulvovaginal).</th>
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<tbody>
<tr>
<td>Click here to find out how we arrive at our judgements about the quality of the evidence.</td>
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<tr>
<th>Important outcomes</th>
<th>Clinical cure rates</th>
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<tr>
<td>Studies (Participants)</td>
<td>Outcome</td>
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<tr>
<td>6 (1003)[13]</td>
<td>Clinical cure rates</td>
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What are the effects of drug treatments for acute vulvovaginal candidiasis in non-pregnant symptomatic women?