Expert peer review on application for deletion of dithranol

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes √ No (if no, please provide reference and information), please see the attachment part 1-2.
   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
      Both the application and our results showed that there was no direct comparison between dithranol and drugs listed in EML for psoriasis.
      Our results show that topical steroids were superior in limited variant of alopecia areata than dithranol based on a comparative assessment (see the attachment part 2 efficacy).
   c. Please provide any additional relevant information with reference
      Please see the attachment part 1-2.

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes √ No (if no, please provide reference and information), please see the attachment part 1-2.
   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
      Both the application and our results found that dithranol performed the worst (comparing with fluticasone, tacalcitol and calcitriol) with 72% patients having adverse events in a systematic review of adverse events.
      From a systematic review, we found that the number needed to treat for dithranol to produce lesional or perilesional irritation was 4 (NNH=4, 95% confidence interval 3 to 5), while calcipotriol caused significantly more skin irritation than potent topical corticosteroids (NNH = 10, 95% confidence interval 6 to 34) (see the attachment part 2 safety).
   c. Please provide any additional relevant information with reference
      Please see the attachment part 1-2.

3. Assessment of cost and availability
   a. Have all relevant data provided
      Yes √ No (if no, please provide reference and information), please see the attachment part 2.
   b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
      Both the application and our results did not found direct data on cost and cost effectiveness comparing dithranol and what listed in EML.
      Our result found that short-contact dithranol was a more cost-effective strategy in comparison with calcipotriol from the perspective of the UK National Health Service as payer based on a cost-effectiveness analysis in 2000.
   c. Please provide any additional relevant information with reference
      Please see the attachment part 1.

d. Is the product available in several low and middle income countries?
   Yes, dithranol was listed in Chinese National Formulary in 2010 and local health insurance directory of Sichuan Province in 2010.
4. Assessment of public health need

a. Please provide the public health need for this product (1-2 sentences)

The overall situation of psoriasis in China as following (come from China health statistics yearbook, 2011):

<table>
<thead>
<tr>
<th>Number of discharged patients</th>
<th>Disease constitution (%)</th>
<th>Cure (%)</th>
<th>Improvement (%)</th>
<th>Failure (%)</th>
<th>Mortality (%)</th>
<th>Average hospitalization days</th>
<th>Average cost ($)</th>
<th>Age distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>10371</td>
<td></td>
<td>23.5</td>
<td>75.2</td>
<td>1.2</td>
<td>0.1</td>
<td>17.5</td>
<td>1045.46</td>
<td>Under 5y</td>
</tr>
</tbody>
</table>

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable

Yes, three guidelines (SIGN 2010, British Association of Dermatologists & Primary Care Dermatology Society 2010 and the New Zealand Dermatological Society 2012) recommended dithranol to be used for psoriasis, but not as the first-line medicine.

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

If yes, please provide details in 1-2 sentences

Yes, it needed a medical facility such as a day care centre or short term application in the patient’s own home after careful patient instruction.

6. Is the proposed product registered by a stringent regulatory authority?

Yes √ No

7. Any other comments

No.

8. What is your recommendation to the committee (please provide the rationale)

1. We recommend deleting dithranol in 18th Model List of Essential Medicines due to its less effectiveness and more adverse reactions than other medicines according to the evidence of our research.

2. We also suggest Expert Committee to consider including calcipotriol after evaluating its cost-effectiveness for keeping the number of medicines affecting skin differentiation and proliferation.
## Attachment

### Evaluation

<table>
<thead>
<tr>
<th>Application</th>
<th>Total</th>
<th>Addition</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/S</td>
<td>N/P</td>
<td>N/S</td>
</tr>
</tbody>
</table>

### Part 1. Number of literatures included

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Guidelines</th>
<th>SR</th>
<th>N/S</th>
<th>N/P</th>
<th>N/S</th>
<th>N/P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>21,488</td>
<td>3</td>
<td>30,175</td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>Guidelines</td>
<td>2</td>
<td>26,792</td>
<td>4</td>
<td>35,519</td>
<td></td>
</tr>
</tbody>
</table>

### Part 2. Interventions and results

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Investigator assessment of overall global improvement (IAGI)</th>
<th>Total severity scores (TSS)</th>
<th>Psoriasis area and severity index (PASI)</th>
<th>Patient assessment of overall global improvement (PAGI)</th>
<th>Combined endpoint (IAGI / TSS / PASI / PAGI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-1.14 [-2.22, -0.06], 1, NA (Vs placebo)</td>
<td>-1.06 [-1.66, -0.46], 3, 37.4% (Vs placebo)</td>
<td>0.41 [-0.47, 1.29], 4, 95.7% (Vs vitamin D analogues)</td>
<td>-0.47 [-0.65, -0.28], 1, NA (Vs vitamin D analogues)</td>
<td>-1.05 [-1.65, -0.46], 3, 36.8% (Vs placebo) 0.04 [-0.53, 0.61], 7, 95.2% (Vs vitamin D analogues)</td>
</tr>
</tbody>
</table>

### Safety

<table>
<thead>
<tr>
<th>Irritation</th>
<th>Chromatosis</th>
<th>Erythema</th>
<th>Itch</th>
</tr>
</thead>
<tbody>
<tr>
<td>√</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

### Availability

- Approved by TGA, Australia and MHRA, UK
- Not listed in FDA approved medicines and the International Drug Price Indicator Guide

### Economy

- $1.2-3.2/treatment duration in China in 2012*
- £7.7-20.5/treatment duration in England in 2000*

### Part 3. Quality of Evidence (No.)

- (The Level of evidence is from Oxford Center for Evidence-based Medicine Levels of Evidence)
- 1a(2)

### Part 4. Recommendation (strength)

- We agree to delete dithranol from EML (A)